E-ISSN
e-ISSN 2149-9934
Volume: 15 **Issue:** 1 March 2024

Journal of Emergency Medicine Case Reports

EPAT
1999
Emergency Physicians Association of Turkey

Owner and
Responsible Manager
Başar Cander
Bezmialem Vakif University,
Department of Emergency Medicine
İstanbul, Turkey

Editors in Chief
Doç. Dr. Muhammed EKMEKYAPAR

Editorial Board
Doç. Dr. Levent ŞAHİN
Dr. Öğr. Üyesi Muhammed Semih GEDİK
Dr. Öğr. Üyesi Ayça ÇALBAY

Printing and Graphics Department

PUNTO
AJANS

Seyrantepe Mah. İbrahim Karaoğlanoğlu Cd. İspar İş Merkezi,
D: No: 105 D:124, 34418 Kâğıthane/İstanbul
Telefon: 0553 199 95 59
info@puntodizgi.com
www.puntoajans.com

Contents

Case Report

Journal of Emergency Medicine Case Reports

Recluse Spider Bite (Loxosceles sp.): A Case Report from Jordan

Hazem Abdulra'of Al-Talafha[1], Ishraq Saleh Abu-Darweesh[2], Zuhair Sami Amr[3]

[1]Department of Biological Sciences, AL Al-Bayt University, Al-Mafraq, Jordan.

[2]Jordanian Royal Medical Services, Department of Radiology, Al-Mafraq, Jordan.

[3]Department of Biotechnology and Genetic Engineering, Jordan University of Science and Technology, Irbid, Jordan

Abstract

Loxosceles is a genus of spiders belongs to the family Sicariidae, known as recluse spiders. These spiders are considered venomous and are distinguished by three pairs of eyes, arranged in triangular pattern. In Jordan, only *Loxosceles rufescens* was recorded. A 75-year-old female with history of hypertension was bitten by a recluse spider. The case developed cellulitis and secondary infection at the site of the bite. The patient showed no response to the treatment with antibiotics either at home or in the emergency department. She was admitted as an inpatient and given Tinam (Cephalosporin / 4th generation). The patient left the hospital after improvement of the symptoms on day 14. Bite of *Loxosceles* spider cause serious poisoning and lead to severe skin infection that needs hospitalization.

Keywords: Loxosceles, bite, poisoning, Jordan, recluse spider

Introduction

Loxosceles spiders are of medical importance. Their bites cause symptoms range from local lesions to serious dermonecrotic ones that may reach up to 30 cm in diameter (1). In addition, the venom can cause renal failure and hematological abnormalities in severe cases. Few patients brought the spider that caused the injury to the hospital for identification, making the diagnosis of the spider bites difficult and frequently presumptive (2). In this report, the patient developed sever dermonecrotic wound and systemic symptoms likely secondary to Loxosceles spider bite. This report is the first documented case of spider bites in Jordan.

Case Report

A 75-year-old woman with no medical history, except hypertension, was presented to Al-Mafraq Government Hospital in August suffering froma painful wound on her left lower limb. The patient reported that a brown spider has bitten her extremity while she was sitting at home. Initial symptoms (included acute ankle pain, mild swelling, redness, and itching) took less than 60 minutes to appear.

The patient received anti-inflammatory drugs, but without response and the symptoms persisted. After 12 hours, ecchymosis was noted which forced the patient to refer to the emergency department at the hospital. The patient received anti-inflammatory drugs consist of I.V hydrocortisone and oral antibiotic and was discharged to the house with close observation. The symptoms persisted and became intense, forcing the patient to require hospitalization again. Routine blood analysis was performed with increase in WBC and ESR (Table 1). Medication was administered and the patient was discharged. Over the next 3 days, the case was deteriorated, and blisters appeared (Figure 1). The patient again seek medical attention.

Table 1: Results of the Blood Tests upon Second Visit

Parameter	Patient value	Reference value
WBC count	19X 10^3	4.50-11.00 X 10^3/µL
Hemoglobin	10	12.0-15.7 g/dL
Platelet count	200 X 10^3	140-440 X 10^3/µL
Creatinine	1.7	0.50-1.50 mg/dL
Erythrocyte Sedimentation Rate (ESR)	150	0 to 29 mm/hr
C-reactive protein	+ve	0.8-1.0 mg/dL

The patient started on a broad-spectrum antibiotics (flagyl and vancomycin). CT scan of the injured leg excluded necrotizing fasciitis and osteomyelitis, the result

Corresponding Author: Hazem Abdulra'of Al-Talafha
e-mail: hazt@aabu.edu.jo
Received: 01.06.2023 • **Accepted:** 27.06.2023
DOI: 10.33706/jemcr.1293334

Cite this article as: Al-Talafha H, Abu-Darweesh IS, Amr ZS. Recluse Spider Bite (Loxosceles sp.): A case report from Jordan. Journal of Emergency Medicine Case Reports. 2024;15(1): 1-3

DOI: 10.33706/jemcr.1293334
Journal of emergency medicine case reports. 2024;15(1): 1-3

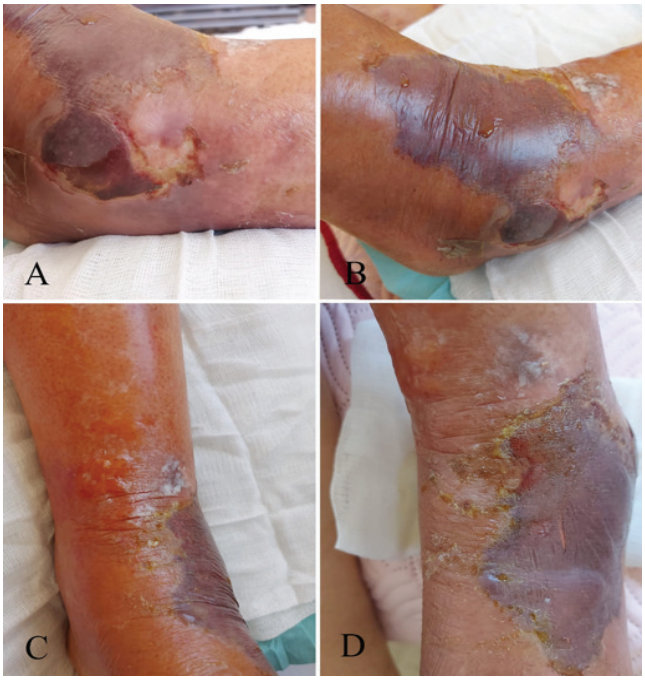

Figure 1. A. Erythema of skin with area of ulceration covered partially by dark necrotic crusty tissue (eschar formation). **B.** Erythema with sub-epidermal bullous formation which is oozing serous fluid with adjacent ulcer covered partially by dark necrotic tissue (eschar formation). **C & D.** Erythema with associated bullous formation with early necrotic changes at the edges. Crust formations at viable skin

showed normal foot and ankle. Moreover, blood culture and methicillin-resistant *Staphylococcus aureus* (MRSA) screen were ordered with negative result. After one week, skin necrosis developed with blisters with formation of green pus. Previous antibiotics were discontinued and Tinam 4th generation (Cephalosporin) was administered. The case started to improve, however with persistent swelling, redness, discharge, and pain. Tinam was continued for another week and notable progress was observed. After 14 days, the patient was discharged with advice to seek for local wound care and using the prescribed antibiotics.

Discussion

Loxosceles is a genus of recluse spiders known as fiddle-backs or violin spiders. This genus includes about 133 species, the most common ones are *L. laeta L. reclusa,* and *L. rufescens* (3). The species *laeta* is known as the Chilean recluse spider and it is native to South America, however it has been introduced into several new areas (4). *Loxosceles* reclus *a* commonly known as the brown recluse spider have a global distribution (3). The third species, rufescens is known to occure in the Mediterranean region, but now recorded outside its native range and considered one of the most invasive spiders' species in the world. In Jordan, only *L. rufescens* was recorded (5).

The spiders of Jordan were studied with 57 species recorded (5, 6). In the current case, we could not confirm the species of the spider.The patient did not bring the specimen to the hospital, and just mentioned that the spider was brown. So, the bite presumptively identified as a bite of *Loxosceles* spider.

Loxosceles spider bite presents four clinical categories (7); (i) Unremarkable (restricted localized damage and the lesion spontaneously heals), (ii) Mild (redness, itching, and small lesion spontaneously heals) (iii) Dermonecrotic (necrotic skin lesion), (iv) Systemic or viscerocutaneous (impacting the circulatory system, extremely uncommon, and perhaps lethal). The current case can be considered Dermonecrotic as it includes sever cellulitis and tissue necrosis.

The necrotic wound-caused by the spider's bite-arises because of the venom components. The venom of *Loxosceles* spiders contains several enzymes and biologically active compounds including phospholipases D, the major dermonecrotic factor (8).This Loxesceles venom enzyme modifies the membrane raft's structure, which activates a protease on the membrane. This will cause cell necrosis and proteolytic cleavage of cell surface proteins.

Presented is a case of a severe necrotic ulcer secondarily caused by a spider bite. *Loxosceles* bite frequently offers a diagnostic problem, unless the patient have the spider for accurate identification. In the current case, the patient saw a spider around the biting time. In a study included 111 cases of brown recluse spider bites, only 22 patients have seen a spider delivering a bite but without capturing the arachnid, moreover 78 patients were diagnosed completely on clinical manifestations (9).

Diagnosis solely depends on the clinical presentations (signs, symptoms) and the history of bite including observing or capturing the spider. Currently, there is no diagnostic test available commercially, but some laboratorial tests are in progress (10).

Symptoms of the recluse spider bite (loxoscelism) range from painless signs at the bite site, skin necrosis, and, less frequently, systemic effects.The pain begins within the first few hours and gets worse with erythema and pruritus (11). In our patient, the pain begun within the first hour. Moreover, a dusky, erythematous, ring-shaped area around the bite occurs 24 hours after the bite, and within 48–72 hours, it develops into an ischemic ulcer (11). Our case showed ischemic and necrotic ulcer after 48 hours (Figure 1).There have been instances where these ischemic ulcers have grown to a diameter of 30 cm, necessitating surgical debridement and, on rare occasions, skin grafts (9).

Moreover, the list of possible diagnoses for necrotic skin lesions is extensive and includes cellulitis, contact dermatitis, anthrax, tularemia, Lyme disease, herpes simplex infection, sporotrichosis, toxic epidermal necrolysis, pyogenic gangrenosum, pyoderma gangrenosum, ecthyma gangrenosum, vasculitis, vascular insufficiency, Martorell ulcers, diabetes, medication reactions, thermalburns, and Chagas disease (11, 12). The current case, however, had lived in the area for a long time and had not recently left the

country. She did not use any medications, have any recent contacts with illness, or have a history of immunological, endocrine, or rheumatologic disease. The patient had no history of methicillin-resistant *Staphylococcus aureus*, and laboratory test was negative. He had already finished two antibiotic treatments and showed no evidence of a persistent infection. There were no burns or injuries to the affected area. The lesions appeared during the summer, a time of increased *Loxesceles* activity. The likelihood of a mistake in this case is decreased by the clinical appearance and lack of other etiologies.

The severity of the spider bites symptoms depends on the quantity of venom injected, the victims' age, and how susceptible person is to the poison (highly allergic person). Steroids, dapsone, antibiotics, hyperbaric oxygen therapy, conservative wound management, and scar repair are used to treat *loxosceles* spider bites (12). However, neither one of these treatments has been shown to be effective in helping infected persons recover. Most cutaneous wounds heal successfully with standard wound care.

The current report is the first study documenting spider bites in Jordan. More attention should be paid to loxoscelism in Jordan. Recently, several *loxosceles* bites were recorded with increasing frequency in the neighboring countries like Iraq, Saudi Arabia, and Turkey (13-15).

Conclusion

In conclusion, diagnosis of *loxosceles* poisoning is not an easy task. The bite history should be considered if the patient reports the spider bite. In the current report, we presented a case of a 75-year-old female who developed sever dermonecrotic wound secondary to a recluse spider bite. The current case highlighted the difficulties of differentiation between loxoscelism and other necrotic soft tissue infections. Physicians should receive training to identify the bite of *loxosceles* based on epidemiological and clinical data available.

Acknowledgment
We would like to thank our patient for trusting us enough to share her case and health concerns.

Conflict of Interest
All authors declare that they have no conflicts of interest

References

1. Everson GW. Spider, Brown Recluse. In Wexler P, Bruce D, Anderson C, Peyster A.Editor. Encyclopedia of Toxicology.2nd ed.Amsterdam: Elsevier; 2005. p. 73-4.
2. Abdelazeem B, Eurick-Bering K, Ayad S, Malik B, Kalynych Z. A case report of brown recluse spider bite. Cureus 2021; 13:e16663.
3. Taucare-ríos A, Nentwig W, Bizama G, Bustamante RO. Matching global and regional distribution models of the recluse spider *Loxosceles rufescens*: to what extent do these reflect niche conservatism? Med Vet Entomol 2018; 32(4): 490-96.
4. Gertsch WJ, Ennik F. The spider genus Loxosceles in North America, Central America, and the West Indies (Araneae, Loxoscelidae). Bull Am Mus Nat Hist 1983; 175: 264-360.
5. Amr ZS. Arthropods of medical importance in Jordan. Jordan Med J 1988; 22: 125-37.
6. Shakhatreh M, Zuhair A, Abu Baker M. Spiders of Jordan: A preliminary study. Turkish Jbiosci collect 2020; 15(1): 1-11.
7. Vetter RS. Spiders of the genus *Loxosceles* (Araneae, Sicariidae): a review of biological, medical, and psychological aspects regarding envenomation.J Arachnol 2008;36(1):150-63.
8. Lajoie DM, Zobel-Thropp PA, Kumirov VK, Bandarian V, Binford GJ, Cordes MHJ. Phospholipase D toxins of brown spider venom convert lysophosphatidylcholine and sphingomyelin to cyclic phosphates.PLoS ONE 2013; 8(8): e72372.
9. Norden PS, Phillips TJ. Brown recluse spider bite: a rare cause of necrotic wounds. Wounds 2005;17(11): 304-12.
10. Stoecker WV, Green JA, Gomez HF. Diagnosis of loxoscelism in a child confirmed with an enzyme-linked immunosorbent assay and noninvasive tissue sampling. J Am Acad Dermatol 2006; 55(5): 888-90.
11. Baden LR. Cutaneous loxocelism. N Engl J Med 2013;369: 5.
12. Rees R, Campbell D, Rieger E, King LE. The diagnosis and treatment of brown recluse spider bites. Ann Emerg Med1987; 16: 945-49.
13. Yigit N, Bayram A, Ulasoglu D, Danisman T, CorakOcal I, Sancak Z. *Loxosceles* spider bite in Turkey *(Loxosceles rufescens*, Sicariidae, Araneae). J Venom Anim Toxins Incl Trop Dis 2008;14: 178-87.
14. Bucur IJ, Obasi OE.Spider bite envenomation in Al Baha region, Saudi Arabia. Ann Saudi Med1999; 19(1): 15-9.
15. Sharquie KE, Jabbar RI. Spider bites might present as cellulitis like in early cases and pyoderma gangrenosum like in late cases. J Turk Acad Dermatol 2020; 14(3): 70-5.

Case Report

Journal of Emergency Medicine Case Reports

Superior Vena Cava Thrombosis in a Young Hemodialysis Patient After 1 year of Central Venous Catheter Removal: A Case Report

Osman Beyduz[1], Abdul Samet Sahin[2], Ragip Kadi[3], Muhammet Fatih Beser[4]

[1]Republic of Turkey Ministry of Health Bitlis State Hospital, Bitlis, Türkiye.

[2]Republic of Turkey Ministry of Health Çarşamba State Hospital, Department of Emergency Medicine, Samsun, Türkiye.

[3]Republic of Turkey Ministry of Health Çarşamba State Hospital, Department of Internal Medicine, Samsun, Türkiye.

[4]Karadeniz Technical University, Farabi Hospital, Department of Emergency Medicine, Trabzon, Türkiye.

Abstract

Superior vena cava (SVC) syndrome is a rare but serious condition resulting from obstruction of the superior vena cava or its tributaries. Although often associated with malignancy, it can also occur due to central venous catheterization. Acute SVC syndrome following catheter removal is uncommon. We present a 35-year-old hemodialysis patient with a history of central venous catheterization for hemodialysis one year prior. During a routine hemodialysis session, the patient developed symptoms of shortness of breath, neck swelling, and cyanosis of the lips. Physical examination revealed neck edema and prominent superficial vascular bifurcations. Without imaging studies, it was confused with cellulitis, but CT angiography later confirmed SVC thrombosis. The patient was started on anticoagulation and transferred to a tertiary hospital for further management. Emergency physicians should be aware of SVC syndrome, especially in hemodialysis patients with a history of central venous catheterization. Although it is often associated with malignancy, this case highlights the importance of considering SVC thrombosis even after catheter removal. Prompt diagnosis and appropriate management are essential to prevent life-threatening complications. Therefore, recognition and inclusion of SVC syndrome in the differential diagnosis is essential for timely intervention and improved patient outcomes..

Keywords: Thrombosis, central venous catheterization, SVC syndrome

Introduction

Superior Vena Cava (SVC) syndrome is a condition resulting from obstruction of the superior vena cava or brachiocephalic veins. While malignancy is the primary cause, other causes include mediastinitis, granulomatous disease, iatrogenic causes associated with radiation therapy or cardiac pacemakers. It is also a rare but serious complication of central venous catheterization. It can cause a variety of symptoms and can lead to life-threatening complications such as organ damage (1). This case report discusses a 35-year-old patient who presented with a history of jugular hemodialysis catheterization one year prior and was currently undergoing hemodialysis with a left arm arteriovenous fistula.

Case Report

A 35-year-old male patient with a known history of chronic kidney disease secondary to vesicoureteral reflux was referred to the emergency department by an internal medicine specialist. The patient was referred to our department after reporting symptoms of shortness of breath, throat swelling, and lip cyanosis that had persisted for two days during a routine hemodialysis session. The patient was undergoing hemodialysis three days per week through an arteriovenous fistula in his left arm. In addition, there was a history of jugular vein catheter placement one year ago for temporary vascular access during hemodialysis.

On physical examination, the patient was alert, oriented, and coherent. Vital signs were stable but, the respiratory and circulatory examinations were anormal. Neck examination revealed no palpable crepitation, tenderness, lymphadenopathy, erythema, or elevated temperature. However, skin examination revealed edema of the eyelids, bruising and swelling of the lips, and diffuse subcutaneous edema of the neck. Prominent superficial vascular branching was also observed on the upper and lower half of the trunk and neck. On previous physical examination, prominent superficial veins measuring approximately 1 cm were noted between the umbilicus and the chest (Figure 1).

Corresponding Author: Abdul Samet Şahin
e-mail: abdulsahin61@gmail.com
Received: 14.11.2023 • **Accepted:** 08.12.2023
DOI: 10.33706/jemcr.1389895

Cite this article as: Beydüz O, Sahin AS, Kadı R, Beser MF. Superior Vena Cava Thrombosis in a Young Hemodialysis Patient After 1 year of Central Venous Catheter Removal: A Case Report. Journal of Emergency Medicine Case Reports. 2024;15(1): 4-6

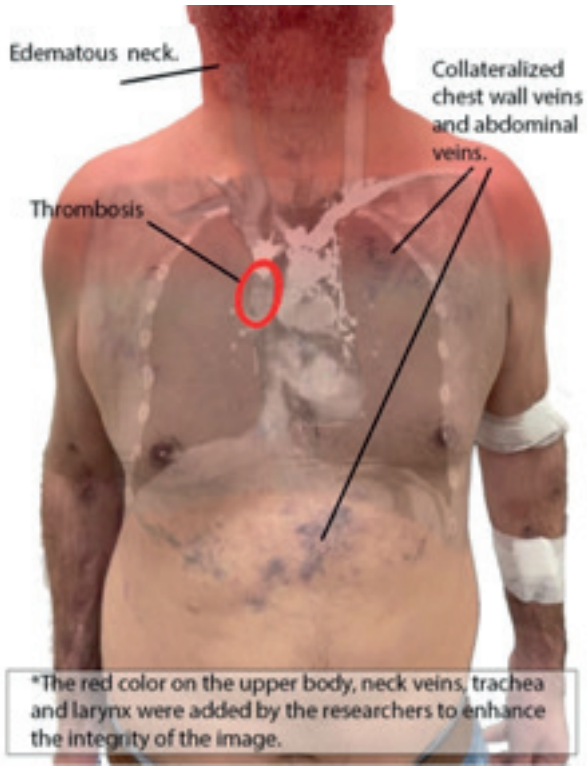

Figure 1. Prominent superficial veins measuring approximately 1 cm between the umbilicus and the chest

Laboratory results showed a significantly elevated C-reactive protein (CRP) level of 29 mg/L. The patient's complete blood count (CBC), biochemistry, and blood gas results were all within normal limits, with a white blood cell (WBC) count of 5 x 10^9/L, procalcitonin (PROC) of 0.8 ng/mL, creatinine (Cr) of 10mg/dL, sodium (Na) of 135 mmol/L, venous pH of 7.31, pCO2 of 53 mmHg, HCO3 of 27 mmol/L, and INR of 1.08.

Doppler ultrasound of the carotid and vertebral arteries was performed to evaluate the patient's symptoms, and a preliminary diagnosis of superior vena cava syndrome wasn't made. However, no pathology was found. He was referred to a tertiary hospital for further investigation. The patient was diagnosed with cellulitis, started on treatment and then discharged. However, the patient's symptoms persisted, and a CT angiography was performed at our hospital on the second visit to the emergency department. Subsequent carotid CT angiography revealed a thrombus in the middle and distal part of the superior vena cava, obstructing blood flow in the lumen along a 5 cm segment (Figure 2). The patient was diagnosed with superior vena cava thrombosis and started on a therapeutic dose of enoxaparin. The patient was transferred to a tertiary hospital for further management.

Discussion

SVC syndrome is a rare but potentially life-threatening condition caused by obstruction of the superior vena cava or its tributaries. The most common cause of SVC syndrome

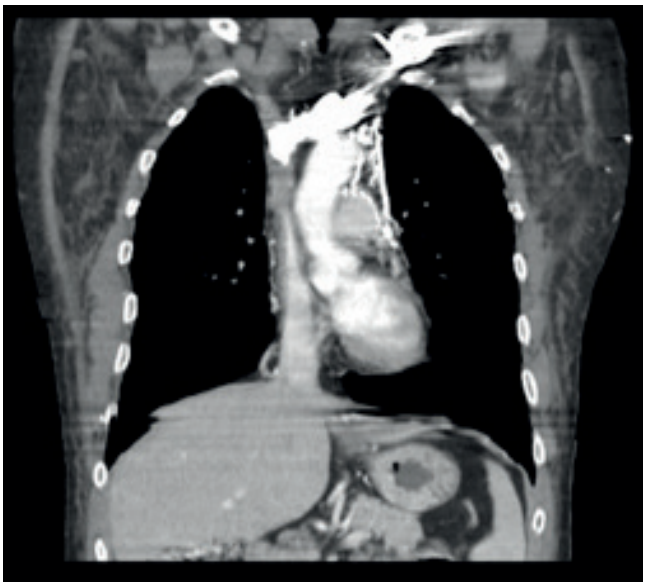

Figure 2. Carotid CT angiography a thrombus in the middle and distal part of the superior vena cava, obstructing blood flow in the lumen along a 5 cm segment

is the presence of malignancy, accounting for up to 70% of cases (2). Other causes include benign mediastinal tumors, thrombosis, and infection. In the present case, the patient had a history of jugular hemodialysis catheterization, which is a known risk factor for the development of SVC syndrome.

A history of central venous catheter use in hemodialysis patients is also a cause of SVC syndrome; however, most cases occur in patients who develop acutely after catheter insertion or chronically after long-term use. In this case, acute SVC syndrome occurred in a patient undergoing hemodialysis through an arteriovenous fistula after removal of his hemodialysis catheter one year ago.

Previous studies have shown a high incidence of superior vena cava stenosis in dialysis patients with hemodialysis catheters, but a lower incidence of SVC syndrome (3,4). However, the occurrence of SVC syndromeafter removal of a hemodialysis catheter, as observed in our case, is rarely reported in the literature (5).

Several risk factors contribute to catheter-associated thrombosis in hemodialysis patients. These factors include catheter size-to-vein ratio, procedural trauma, catheter positioning (especially distal to the superior vena cava), vein diameter, and medical history including malignancy, previous thromboembolic events, and coagulopathy. The mechanism underlying hemodialysis catheter-associated thrombosis has not been elucidated, but factors such as repeated vascular interventions, platelet dysfunction, endothelial factors, inflammation, and coagulation abnormalities have been suggested (6).

Superior vena cava syndrome can present with a wide range of clinical manifestations. It can range from asymptomatic cases to severe conditions such as life-threatening upper airway obstruction and increased

10.33706/jemcr.1389895
Journal of emergency medicine case reports. 2024;15(1): 4-6

intracranial pressure. Symptoms correlate with the severity and extent of venous obstruction and inversely with the development of venous collateral vessels. Manifestations can vary from localized facial edema to erythema, edema, cyanotic changes, telangiectatic veins and collaterals in the head, neck, and upper trunk. Symptoms such as shortness of breath, cough, blurred vision, orthopnea, hoarseness, nausea, headache, chest pain, dizziness, or fainting may also occur, and may worsen in the supine position. In severe cases, more serious symptoms such as stridor and confusion may develop. Symptoms such as headache, dizziness, visual disturbances, impaired consciousness, and seizures may also occur due to cerebral edema. Cases with laryngeal edema may present with symptoms such as hoarseness and stridor.

In addition to clinical findings, imaging modalities can be used to diagnose superior vena cava syndrome. Imaging techniques are particularly important for determining the location and extent of the lesion, planning treatment, and monitoring the patient. Chest radiography is a preliminary imaging modality that can be used in the initial step of diagnosing SVC syndrome. However, other imaging modalities may be required to differentiate it from conditions such as congestive heart failure or Cushing's syndrome. Computed tomography, magnetic resonance imaging, conventional venography, angiography, ultrasonography, and echocardiography are among the other imaging modalities that may be used in the diagnosis of SVC syndrome (7). Magnetic resonance angiography and computed tomography angiography have high sensitivity (96%) and specificity (92%) in monitoring collaterals and diagnosing SVC syndrome. Therefore, it is recommended that these methods be used in the diagnosis of SVC syndrome (8).

In the management of superior vena cava syndrome, it is important to identify the underlying cause and develop a targeted treatment plan accordingly. Several treatment modalities are available to restore normal venous flow. Surgical interventions such as autologous saphenous vein bypass surgery, excisional procedures, or endovascular treatments may be used. In addition, non-invasive treatments such as radiation therapy, pharmacologic thrombolysis may be used. In catheter related SVC syndrome, the first step is to remove the catheter. Systemic anticoagulation should then be initiated to prevent further blood clotting. In refractory or recurrent cases, invasive treatment modalities such as pharmacologic thrombolysis or mechanical thrombectomy may be considered.

Conclusion

In conclusion, the management of SVC syndrome is based on the identification of the underlying cause and the development of an appropriate treatment plan. Therefore, it is crucial to evaluate patients diagnosed with SVC syndrome with a multidisciplinary team and establish a comprehensive treatment approach (9). This case report describes a patient with a history of central venous hemodialysis catheter removal one year ago who developed superior vena cava syndrome. While malignancy is a common cause of SVC syndrome, hemodialysis patients with a history of central venous catheter use are also at risk. However, most cases of SVC syndrome occur acutely after catheter placement or chronically after prolonged use. In the case presented, the patient developed acute SVC syndrome despite having had the hemodialysis catheter removed one year earlier and receiving hemodialysis through an arteriovenous fistula. Symptoms of SVC syndrome can range from asymptomatic to life-threatening upper airway obstruction and increased intracranial pressure. SVC syndrome may be confused with cellulitis in hemodialysis patients with a history of central venous catheterization and should be considered in the differential diagnosis.

References

1. Küçükarslan N, Yilmaz M, Us M, Arslan Y, Güler A, Yilmaz A (2007). Diyalizkateterininnedenolduğu vena kava süperiorsendromu: Olgusunumu. UlusalTravmaveAcilCerrahiDergisi, 13(1), 63 - 66.
2. Azizi, A. H., Shafi, I., Shah, N., Rosenfield, K., Schainfeld, R., Sista, A., & Bashir, R. (2020). Superior Vena Cava Syndrome. JACC. Cardiovascular interventions, 13(24), 2896–2910. https://doi.org/10.1016/j.jcin.2020.08.038
3. Labriola, L., Seront, B., Crott, R., Borceux, P., Hammer, F., &Jadoul, M. (2018). Superior vena cava stenosis in haemodialysis patients with a tunnelled cuffed catheter: prevalence and risk factors. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association, 33(12), 2227–2233. https://doi.org/10.1093/ndt/gfy150
4. Arasu, M., Thangaswamy, C. R., Chakravarthy, D., &Elakkumanan, L. B. (2021). Catheter-related superior vena cava thrombosis-how do we face it?. Annals of cardiac anaesthesia, 24(4), 512–514. https://doi.org/10.4103/aca.ACA_119_20
5. Janssen M, Logtenberg S. (2022). Vena Cava Superior Syndrome Six Years after Central Venous Catheter Removal in a Patient on Hemodialysis. Case Rep Nephrol Dial, 12(2):132-137. doi:10.1159/000525795
6. Thapa, S., Terry, P. B., &Kamdar, B. B. (2016). Hemodialysis catheter-associated superior vena cava syndrome and pulmonary embolism: a case report and review of the literature. BMC research notes, 9, 233. https://doi.org/10.1186/s13104-016-2043-1
7. Shaikh, I., Berg, K., &Kman, N. (2013). Thrombogenic catheter-associated superior vena cava syndrome. Case reports in emergency medicine, 2013, 793054. https://doi.org/10.1155/2013/793054
8. Adışen E, Özer İ, Gürer MA. (2016). Vena Kava SüperiorSendromu. Dermatoz, 7(2):0-0. doi: 10.15624.dermatoz16072o5
9. Cui, J., Kawai, T., & Irani, Z. (2015). Catheter-directed Thrombolysis in Acute Superior Vena Cava Syndrome Caused by Central Venous Catheters. Seminars in dialysis, 28(5), 548–551. https://doi.org/10.1111/sdi.12362

Case Report

Journal of Emergency Medicine Case Reports

Death Due to Furosemide Anaphylaxis and The Importance of Serum Tryptase Level in Diagnosing Anaphylaxis: A Case Report

Soner Dagli[1], Mustafa Talip Sener[2], Ahmet Nezih Kok[3], Ahmet Sahpaz[4]

[1]Department of Forensic Medicine, Faculty of Medicine, Ataturk University, Erzurum, Türkiye.
[2]Denizli Branch of Council of Forensic Medicine, Denizli, Türkiye.
[3]Department of Forensic Medicine, Faculty of Medicine, Ataturk University, Erzurum, Türkiye.
[4]Department of Histopathology, Antalya Branch of Council of ForensicMedicine, Antalya, Türkiye

Abstract

Anaphylaxis is a severe systemic hypersensitivity reaction with a sudden onset and may result in death. In this study, we report the case of a 71-year-old female patient who died within seconds after the administration of intravenous furosemide in emergency service; shehad high serum tryptase levels at postmortem examination and nonspecific findings at autopsy, and death due to anaphylaxis was reported. With this study, we wanted to point to the rare and potentially fatal drug anaphylaxis, such as furosemide anaphylaxis. Also, our results indicate the importance of serum tryptase levels in the diagnosis of death due to anaphylaxis.

Keywords: Furosemide, anaphylaxis, postmortem diagnosis, serum tryptase levels

Introduction

Anaphylaxis is an immunoglobulin E (IgE)-mediated hypersensitivity reaction that can cause cardiovascular collapse within minutes (1). Triggers for anaphylaxis include drugs, foods, insect stings, and animal bites (2). Furosemide-induced anaphylaxis has not been extensively reported in the studies performed thus far. Our literature review yielded 4 case reports of furosemide anaphylaxis. Death was reported in 2 of the 4 case reports (3–5).

In this study, we report the case of a 71-year-old female patient who died within seconds after the administration of intravenous furosemide, and her cause of death was determined by autopsy as anaphylaxis. We have discussed the importance of serum tryptase levels in the diagnosis of death due to furosemide anaphylaxis and anaphylaxis in light of the findings reported in the literature thus far.

The ethical permission was granted by the education and scientific research commission of the Council of Forensic Medicine (No:2021/839, 21/06/2021).

Case Report

We report the case of a 71-year-old woman who was receiving medical treatment for approximately 8 years for chronic obstructive pulmonary disease and essential hypertension. She was taking furosemide tablets and ampoules intermittently in the previous year. In medical records, furosemide was prescribed five months before her death, a box of 12 tablets, and about seven months ago, a box of 5 ampoules. She used furosemide at the time it was prescribed. In the medical history of the case, she was treated in the hospital with the complaint of rash after the use of analgesic drugs. However, there is no history of allergy-related to previous use of furosemide. On the day of the incident, she was admitted to the emergency department with a complaint of shortness of breath. Physical examination of the patient showed body temperature, 36.5 °C; arterial blood pressure, 190/110 mmHg; pulse, 113/min, respiratory rate; 22/min, oxygen saturation (SpO_2), 98 (in room air); decreased inspiration; increased expiration; and hyperemia in the tonsils. The results of biochemical tests like urea (44.00 mg/dl - on the day of incident) and creatinine (1.25 mg/dl - on the day of incident) and complete blood count were within normal limits. Antihypertensive treatment included 2 ampoules of furosemide (Lasix®) administered as an intravenous push, but the condition of the patient started deteriorating drug administration, and cardiopulmonary arrest developed within seconds. Considering that an allergic reaction had developed, an antiallergic treatment was administered for anaphylaxis. However, the case did not respond to the medical intervention, and she died. Because of the sudden death, the case was considered to be a forensic case, and a declaration was submitted to the prosecutor's office.

Corresponding Author: Mustafa Talip Sener
e-mail: mustafatalipsener@gmail.com
Received: 07.08.2023 • **Revision:** 16.10.2023 • **Accepted:** 19.12.2023
DOI: 10.33706/jemcr.1338799

Cite this article as: Dagli S, Sener MT, Kok AN, S Ahmet. Death Due to Furosemide Anaphylaxis and The Importance of Serum Tryptase Level in Diagnosing Anaphylaxis: A Case Report. Journal of Emergency Medicine Case Reports. 2024;15(1): 7-9

DOI: 10.33706/jemcr.1338799
Journal of emergency medicine case reports. 2024;15(1): 7-9

An autopsy was performed within 24 hours of the death of the case. External examination observed needle puncture marks on the dorsal side of both hands and the left elbow because of medical intervention as a positive finding. At autopsy, venous engorgement was observed on the brain surface and petechial hemorrhage was observed in the brain sections. The uvula had a mild edematous appearance. No macroscopic edema was observed in the epiglottis, vocal cords, larynx, and trachea. Anthracosis and petechiae were present on both lung surfaces. Right lung weight was 590 gr., left lung weight was 550 gr. Slight edema and congestion were seen in the lung sections. Heart weight was 580 gr. Moderate atherosclerotic narrowing of the coronary arteries was observed. No abnormal findings were observed in the abdominal organs.

Results of histopathological examination showed intra-alveolar fresh bleeding, edema, and ruptured capillaries in the lungs; subepithelial chronic nonspecific inflammation, edema, and extravasated erythrocytes in the uvula, epiglottis, and larynx (Figure 1, 2); areas of fibrosis secondary to cardiac ischemia and signs of hypertrophy; and a moderate atherosclerotic narrowing and locally calcified plaque was observed in the left coronary artery.

Toxicological analyses of the samples obtained from the heart and femoral blood were performed using quadrupole time-of-flight (X500R; Sciex®, Toronto, Canada) and gas chromatography-mass spectrometry (GC-MS; QP 2010; Shimadzu®, Kyoto, Japan) in toxicology laboratory of our Forensic Medicine Institute. Paracetamol (402 ng/mL) and Pheniramine (47.7 ng/mL) were detected in the samples. Furosemide was not detected in the blood using both methods of analysis. Diltiazem, Chlorpheniramine, andTrazodone were detected in the urine.

Measurement of serum tryptase levels could not be performed at our institution; therefore, the sample was sent to an accredited private laboratory in a box covered with dry ice for analysis. The results of the analysis showed a serum tryptase level of 199.00 ng/mL.

No criminal element was found in the crime scene investigation by the prosecutor's office. Based on witness statements, medical documents, the manner of death, autopsy findings, and findings of high serum tryptase level, a report was prepared to indicate that the death of the case as a result of anaphylaxis due to furosemide.

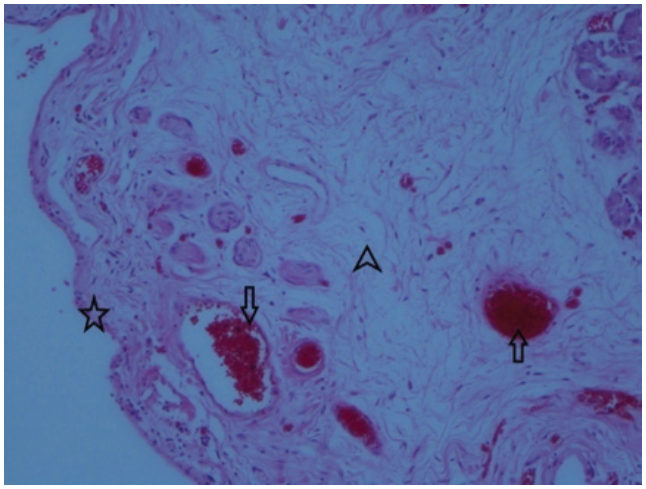

Figure 1: Larynx, shedding of the surfaceepithelium, dilated congested vascular structures in the subepithelial space, and edematous stroma (Arrow: congested vascular structures, Arrowhead: edema in the stroma, Star: surfaceepithelial area (shed) (H&E; x10)

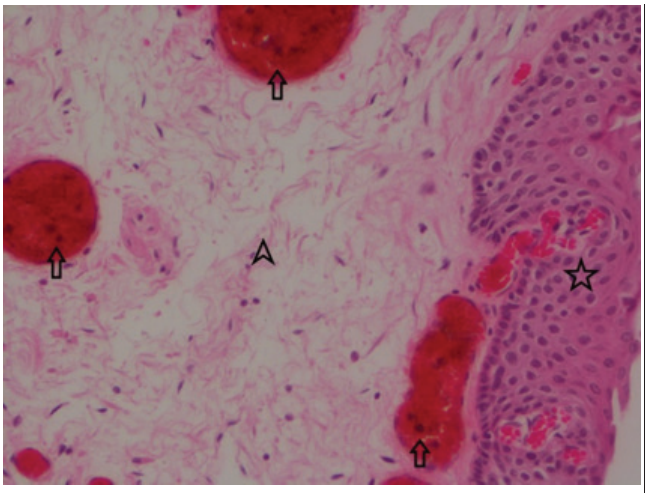

Figure 2: Uvula, congestion of the surfaceepithelium dilated congested vascular structures, and edematous stroma in the subepithelial space (Arrow: congested vascular structures, Arrowhead: edema in the stroma, Star: surfaceepithelial area)(H&Ex20)

Discussion

In this study, we presented a case of death due to furosemide anaphylaxis. According to our literature review, this is the first case report of furosemide-induced anaphylaxis in Turkey. Anaphylaxis was diagnosed by postmortem examinations like postmortem serum tryptase level. Diagnosing anaphylaxis in emergency rooms can be difficult, as some patients' conditions may be misdiagnosed as myocardial infarction and asthma-related death (6). At the same time, postmortem diagnosis of anaphylaxis is difficult for forensic experts because of nonspecific findings.

Classically, in cases of allergy/anaphylaxis, symptoms such as urticaria, itching, rash, edema, and respiratory distress develop acutely and can be seen by the clinician. In postmortem diagnosis, unfortunately, classical findings are not usually seen in these cases. For postmortem diagnosis of anaphylaxis, witness statements must be recorded, a comprehensive crime scene examination must be carried out, a detailed medical history examination for allergens, a detailed external examination, and an autopsy must be performed. In addition, additional tests to determine postmortem serum tryptase level, total IgE level, and allergen-specific IgE level should be performed (6).

Serum tryptase values are between 1–15 ng/mL in a healthy person, and the mean value is 5 ng/mL (7). In the 2010 Working Conference on Mast Cell Disorders, 80% of the members agreed that the acute serum total tryptase level should be at least 20% plus 2 ng/ml over the baseline level (peak mast cell tryptase ≥ (1.2 x baseline tryptase +2 ng/mL)) to be indicative of mast cell activation such as anaphylaxis (8, 9). Tryptase remains stable in the blood, and therefore, significant results can be obtained even if the autopsy is performed

days after death in the postmortem period (6). In corpses with postmortem serum tryptase levels<100 ng/mL, it can be concluded that death may have been due to anaphylaxis if the clinical and autopsy findings are consistent (6). The threshold level of tryptase in corpses with anaphylaxis is 53.8 ng/mL (10). Additionally, we found that the serum tryptase level in our case (199 ng/mL) was well above the threshold value reported previously. Thus, the high levels of serum tryptase in our case were significant for the diagnosis of anaphylaxis.

Old age and chronic diseases like previous cardio vascular morbidity, and chronic obstructive pulmonary disease are risk factors for fatal drug anaphylaxis (11). Previous studies indicate that although serum tryptase levels are higher than normal in corpses who die because of acute cardiovascular diseases, these levels are not above the thres hold value (12,13). Our case had a history of chronic obstructive pulmonary disease and essential hypertension. Histopathological examination at autopsy showed areas of ischemia in the heart and moderate atherosclerotic narrowing in the coronary arteries. In our case, we found the serum tryptase level to be much higher than the levels found in deaths due to cardiovascular diseases. This postmortem-detected high level of tryptase indicated that the subject did not die of cardiovascular disease (3-5).

Determining the causative agent of anaphylaxis is important for diagnosis. However, in many patients with anaphylaxis, identification of the allergen is not possible. Although skin and mucous membrane symptoms are the most common signs in the diagnosis of anaphylaxis, they may sometimes be absent. Laboratory tests such as serum/plasma tryptase, plasma histamine, and measurement of histamine and histamine metabolites (N-methyl histamine) in 24-hour urine become more important in the diagnosis of sudden shock without urticaria and angioedema-like findings (14). In our case, an allergic reaction developed immediately after the administration of furosemide. However, the factor responsible forcausing anaphylaxis could not be detected by advanced methods of toxicological analysis. This may be due to the inability of furosemide to adequately pass into the circulation due to circulatory arrest as a result of anaphylaxis.

Despite the presence of history and clinical findings suggestive of anaphylaxis, we were unable to detect the allergen responsible for causing anaphylaxis in our case. Findings of anaphylaxis may not be evident at autopsy. In such cases, besides the medical history, witness statements, crime scene information supporting anaphylaxis, and high serum tryptase levels postmortem can be very valuable in the diagnosis of anaphylaxis. Since tryptase remains stable in the blood, if the blood sample is taken and stored under appropriate conditions, significant diagnostic results can be obtained as tryptase analysis can be performed months after the autopsy. Since the serum tryptase level increases in many diseases such as coronary artery disease and mast cell disorders besides anaphylaxis, it is important to know the basal serum tryptase level in the diagnosis of anaphylaxis. Basal serum tryptase value can be obtained by analyzing the samples taken for "complete blood count and routine biochemical tests" in people who applied to the hospital before their death. Then "Peak mast cell tryptase ≥ (1.2 x baseline tryptase +2 ng/mL)" formula can be used for a more precise evaluation.

Conclusion

In conclusion, we present a rare case of death due to intravenous furosemide-induced anaphylaxis that we detected high serum tryptase levels postmortem. In deaths with suspected anaphylaxis, the allergen may not be known or detected. Signs of anaphylaxis may not be evident at autopsy. These factors complicate the postmortem diagnosis of anaphylaxis. In such cases, high serum tryptase levels postmortem can be very important in diagnosing anaphylaxis. In addition, with this study, we wanted to draw attentionto the fact that furosemide, which is frequently used in emergency departments, can cause anaphylaxis, although it is rare.

References

1. Muñoz-Cano R, Picado C, Valero A, Bartra J. Mechanisms of Anaphylaxis Beyond IgE. J Investig Allergol Clin Immunol. 2016;26:73-82.
2. Simons FER, Ebisawa M, Sanchez-Borges M, Thong BY, Worm M, Tanno LK, et al. 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. World Allergy Organ J. 2015;8:32.
3. Hansbrough JR, Wedner HJ, Chaplin DD. Anaphylaxis to intravenous furosemide. J Allergy Clin Immunol. 1987;80:538-41.
4. Domínguez-Ortega J, Martínez-Alonso JC, Domínguez-Ortega C, Fuentes MJ, Frades A, Fernández-Colino T. Anaphylaxis to oral furosemide. Allergol Immunopathol (Madr). 2003;31:345-7.
5. Machtey I. Sudden death after intramuscular frusemide. Lancet. 1968;2:1301.
6. Osborn, M, Chambers, D, Parcq, J, et al. Guidelines on autopsy practice: Autopsy for suspected acute anaphylaxis (includes anaphylactic shock and anaphylactic asthma). R. Coll. Pathol. 2018;1–12
7. Schwartz LB. Diagnostic Value of Tryptase in Anaphylaxis and Mastocytosis. C. 26, Immunology and Allergy Clinics of North America. Immunol Allergy Clin North Am; 2006;26:451-63.
8. Passia E, Jandus P. Using Baseline and Peak Serum Tryptase Levels to Diagnose Anaphylaxis: a Review. Clin Rev Allergy Immunol. 2020;58:366-76.
9. Valent P, Akin C, Arock M, Brockow K, Butterfield JH, Carter MC, et al. Definitions, criteria and global classification of mast cell disorders with special reference to mast cell activation syndromes: a consensus proposal. Int Arch Allergy Immunol. 2012;157:215-25.
10. Tse R, Wong CX, Kesha K, Garland J, Tran Y, Anne S, et al. Post-mortem tryptase cut-off level for anaphylactic death. Forensic Sci Int. 2018;284:5-8.
11. Turner PJ, Jerschow E, Umasunthar T, Lin R, Campbell DE, Boyle RJ. Fatal Anaphylaxis: Mortality Rate and Risk Factors. J Allergy Clin Immunol Pract. 2017;5:1169-78.
12. Xiao N, Li DR, Wang Q, Zhang F, Yu YG, Wang HJ. Postmortem Serum Tryptase Levels with Special Regard to Acute Cardiac Deaths. J Forensic Sci. Eylül 2017;62:1336-8.
13. Kervinen H, Kaartinen M, Mäkynen H, Palosuo T, Mänttäri M, Kovanen PT. Serum tryptase levels in acute coronary syndromes. Int J Cardiol. 2005;104:138-43.
14. Orhan F, Civelek E, Şahiner ÜM, Arga M, Can D, Çalıkaner AZ, et al. Anaphylaxis: Turkish National Guideline 2018. Asthma Allergy Immunol 2018; 16 (Suppl 1):1-62.

Case Report

Journal of Emergency Medicine Case Reports

Top of Basilar Syndrome

Bilgehan Demir[1]
[1]Department of Emergency Medicine, Malatya Turgut Ozal Unicersity Education and Research Hospital, Malatya, Türkiye

Abstract

Top of Basilar syndrome(BTS) is defined as ischemia of the areas fed by the distal basilar artery (brainstem, thalamus, cerebellum, temporal and occipital region). It shows many different symptoms. Usually visual and oculomotor disorders, changes of mind, speech disorders, seizures and hallucinations are observed. Beginning symptoms include epileptic seizures, decreased speech and inappropriate laughter, and hallucinations.This our article is that prensentation of neurological analysis in the management of cases with sudden behavioral disorders.The aim of our study is to show the presence of rare diseases among the symptoms commonly seen in the emergency department, like BTS disease. In study, A patient diagnosed with BTS with rare symptoms is presented. Clinicians should be careful about BTS.Because BTS can be encountered with sudden mood swings, personality changes and behavioral disorders and is a high rate of mortality.

Keywords: Hallucinations, distal basilar artery, oculomotor disorders

Introduction

Cerebro Vascular Disease (CVD), which develops due to bacillary artery occlusion, accounts for 4% of all CVDs. Top of Bacillary syndrome, due to distal bacillary artery occlusion, causes a clinical figure with various loss of consciousness, amnestic states, involuntary movements, and hallucinations (1). In the etiology of the disease; Congestive Heart Failure (CHF), Coronary Artery Disease (CAD), Atrial Fibrillation (AF), Diabetes Mellitus (DM), Hypertension (HT).DM alone is a risk factor with a higher mortality rate in CVD patients (2). It is usually fatal and may not be diagnosed because it does not contain specific findings. Patients are generally male and the lesion is generally located in the thalamic region.

Case Report

A 53-year-old male patient was brought to the emergency, due to sudden loss of consciousness.Etiology included only heart failure. in patient's blood tests hasn't got abnormal values, only CRP: 1.3 mg/dl and WBC: 18.34 10^3/ uLwas. On physical examination, there is no neck stiffness, breathing sounds are normal and skin color is natural. Vitals were also evaluated as normal except for high blood pressure (180/95 mmHg). In the echocardiography (ECO), ejection fraction was 60%, no valve movement limitation was detected. Imaging techniques were used because the physical examination was natural and there was no time and place orientation. Firstly, brain tomography was performed to exclude the diagnosis of brain hemorrhage (Figure 2). And then, diffusion MRI (dMRI) was performed to exclude the diagnosis of cerebrovascular disease (Figure 1). The patient's dMRI and brain tomography (CT) were normal. The patient was followed for a while in the emergency room.Toxicological markers and urine tests were studied and analyse result was normal.The patient was evaluated as normal by neurology and cardiology department consultations.The patient was followed up in the emergency room for 10 hours.There was no change in the patient's state of consciousness.Due to high blood pressure, CT and dMRI scans were repeated for subaracnoide blood (SAB) and hypertensive encephalopathy.The patient's CT scan was also normal, but it was determined that the patient had an infarction in the bacillary area on dMRI (Figure 3) The patient was consulted again to the neurology department, the patient was admitted to the intensive care unit and her treatment was started with the preliminary diagnosis of bacillary apex infarction.

Discussion

BTS is a CVD disease.The etiology includes many diseases of cardiac origin. In the literature, Ayas Z. et al. In a study he conducted, it was determined that the prevalence of underlying diseases was HT (64.5%), CAD (45.2%), DM

Corresponding Author: Bilgehan Demir
e-mail: bilgehan.demir@ozal.edu.tr
Received: 05.12.2023 • **Revision:** 12.01.2024 • **Accepted:** 16.01.2024
DOI: 10.33706/jemcr.1400820

Cite this article as: Demir B. Top of Basilar Syndrome. Journal of Emergency Medicine Case Reports. 2024;15(1): 10-11

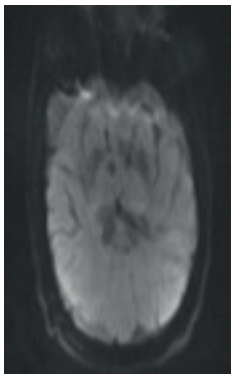

Figure 1. dMRI

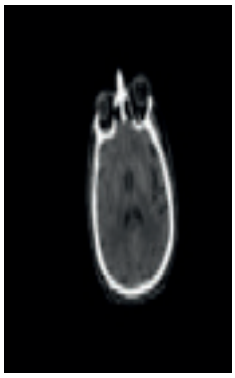

Figure 2. CT

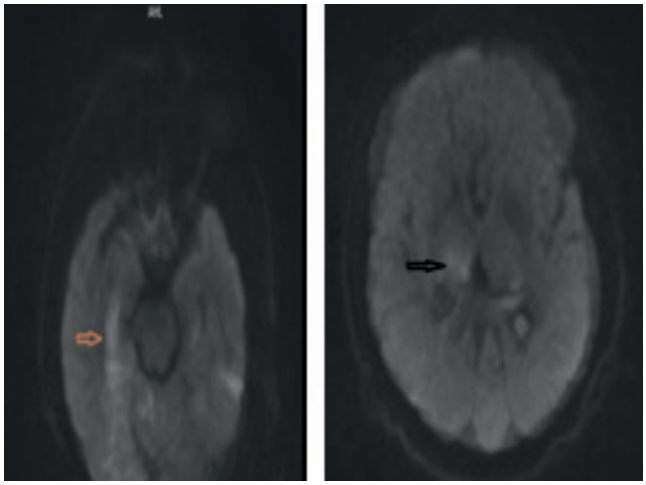

Figure 3. dMRI

(31.9%), CHF (9.7%), AF (6.5%) (3). AF is a 5-fold greater risk factor for ischemic stroke compared to the general population (4). The most common symptom seen in this study was a decrease in the level of consciousness (48.4%). Our patient had a decrease in the level of consciousness. In another study, Kıroğlu et al. reported that the most common symptoms of BTS were motor deficits (53.3%). Loss of consciousness (46.6%), visual/oculomotor symptoms (43.3%), cerebellar dysfunction (40.0%), behavioral disorder (26.6%) and speech disorder (16.6%) were detected (5).There was no sign of motor deficits in our the patient. Since BTS disease is fatal, deaths generally occur in middle ages, and our patient is over middle age, it was thought that BTS increases the death rate depending on age, but according to a study; it was observed that there was no significant difference between age, gender, presenting symptoms, premorbid diseases, infratentorial, supratentorial infarct volume and mortality (3).

Our patient is male and a lesion was seen at the thalamic level, which supports the study conducted by Martin et al.In BTS, extensive lesions involving the thalamus, cerebellum and midbrain are observed. The disease is observed more frequently in men than in women (6). The disease begins with confusion and hallucinations and progresses to death. The lack of clinical change in our patient despite treatment prevented the decision to discharge him. Discharge decisions should not be made by doctors without a clear assessment of the patient's well-being. Because under situations that we consider normal, fatally important diseases can occur, such as BTS. Make a treatment for BTS, which the old study said was 86% fatal, may be life-saving.

Conclusion

Clinicians should be vigilant in terms of BTS for this disease, which often results in death and whose initial symptoms are common in emergency situations and do not suggest serious disease. Identifying even one patient is vitally important.

References

1. Caplan LR. 'Top of the basilar' syndrome. Neurology 1980;30(1):72-79
2. Shou J, Zhou L, Zhu S, Zhang X. Diabetes is an Independent Risk Factor for Stroke Recurrence in Stroke Patients: A Meta-analysis. J Stroke Cerebrovasc Dis. 2015;24:1961-1968.
3. Ayas Z., Kotan D., Asil K.,The Effect of Clinical and Radiological Features on Prognosis in the Top of The Basilar Syndrome. Sakarya Med J 2021, 11(3):639-646) DOI: 10.31832/smj.937034
4. Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. Am J Cardiol 1998; 82:2N–9N.
5. Kıroğlu Y, Onur S, Herek D, Agladıoglu K, Teke E, Cıtıslı V. Neuroimaging evaluation of non-aneurismatic 'Top of the Basilar' Syndrome. J Neurol Sci Turkish. 2016;33(2):286-295.
6. Usón-Martín M, Gracia-Nava M. Top of the basilar artery syndrome: clinico-radiological aspects of 25 patients. Rev Neurol 1999;28(7): 698-701.

Case Report

Journal of Emergency Medicine Case Reports

Increasing Cases of Retroperitoneal Fibrosis After Covid-19: Case Report, Did She Die Retroperitoneal Fibrosis or Cancer?

Gulnihal Deniz[1], Murteza Cakir[2], Serpil Bilgin Akyagci[3]

[1]Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Erzurum Technical University, Erzurum, Türkiye.

[2]Department of Neurosurgery, Faculty of Medicine, Ataturk University, Erzurum, Türkiye.

[3]Department of General Surgery, VM Medical Park Bursa Hospital, Mudanya University, Bursa, Türkiye.

Abstract

This case report details the unfortunate journey of a 59-year-old breast cancer survivor who developed secondary Retroperitoneal Fibrosis (RPF) in 2022. Despite diligent treatment efforts, her condition took a devastating turn when, in June 2023, she was diagnosed not only with persistent RPF but also with advanced liver, omental, and duodenal cancer. Tragically, her condition deteriorated rapidly, leading to her passing on day 41 following her presentation. This case underscores the challenges of diagnosing and treating RPF. It highlights the importance of considering cancer development in advanced RPF cases that do not respond to treatment, often leaving limited options for effective intervention.

Keywords: Retroperitoneal fibrosis, liver cancer, metastasis, steroid, azathioprine.

Introduction

Retroperitoneal-fibrosis (RPF) is a rare fibroinflammatory disease that usually occurs in the retroperitoneal space surrounding the ureters and vascular structures such as the abdominal aorta, inferior vena cava, iliac artery, and ureters, often causing ureteral obstruction and renal failure. The annual incidence of RPF is 0.1/100.000, and the prevalence is 1.4/100.000 (1). Men are affected by the disease more than women. The male-to-female ratio is between 2/1 and 3/1. The mean age at diagnosis is 50-60 years. RPF is etiologically divided into idiopathic and secondary causes. Idiopathic RPF accounts for approximately 2/3 of all patients. Secondary RPF can be caused by drugs, malignancy, surgery, infection, and radiation. Malignancies are essential among secondary causes, accounting for 8-10% of all RPF cases. Malignancy-related RPF can be caused by desmoplastic tissue resulting from the impact of metastatic cells in the retroperitoneum or by the presence of a primary mass such as Hodking, Non-Hodking Lymphoma, and sarcomas. Although metastases from all malignancies can occur in the retroperitoneum, the most common ones are from the breast, stomach, colon, prostate, lung, and kidney. Surgical and medical treatment is used. The majority of the etiology needs to be clarified; symptoms and signs are non-specific, they are confused with many other conditions in differential diagnosis, and there is no generalizable treatment regimen (2).

Case Report

A 59-year-old female smoker was diagnosed with a 28*18 mm solid lesion or mass in the upper outer quadrant of the left breast on ultrasonography and magnetic resonance imaging performed in 2015. She was diagnosed with invasive carcinoma in TRU-CUT biopsy results evaluated at a university hospital. She underwent left breast-conserving surgery + chemotherapy + radiotherapy + anastrozole treatment for five years, and regular follow-up visits were performed.The female case, who was vaccinated with three doses of sinovac, had covid-19 twice in January and December 2021.

In September 2022, the patient was admitted to our center with complaints of leg swelling and inability to urinate and underwent a non-contrast MRI due to mildly elevated urea and creatinine values.. He was diagnosed with bilateral renal RPF and hydronephrosis. Laboratory tests revealed Fasting Blood Glucose (FBSG): 90 mg/dL, Urea: 41 mg/dL, Sodium: 143 mmol/L, Potassium: 4.8 mmol/L, Gamma Glutamyltransferase (GGT): 46 U/L, Calcium: 9.3 mg/dL, ALT (SGPT): 16 U/L, AST (SGOT): 14 U/L, Creatinine

Corresponding Author: Murteza Cakir
e-mail: murtezacakir28@gmail.com
Received: 14.01.2024 • **Accepted:** 16.01.2024
DOI: 10.33706/jemcr.1419408

Cite this article as: Deniz G, Cakir M, Bilgin Akyagcı S. Increasing Cases of Retroperitoneal Fibrosis After Covid-19: Case Report, Did She Die Retroperitoneal Fibrosis or Cancer? Journal of Emergency Medicine Case Reports. 2024;15(1): 12-15

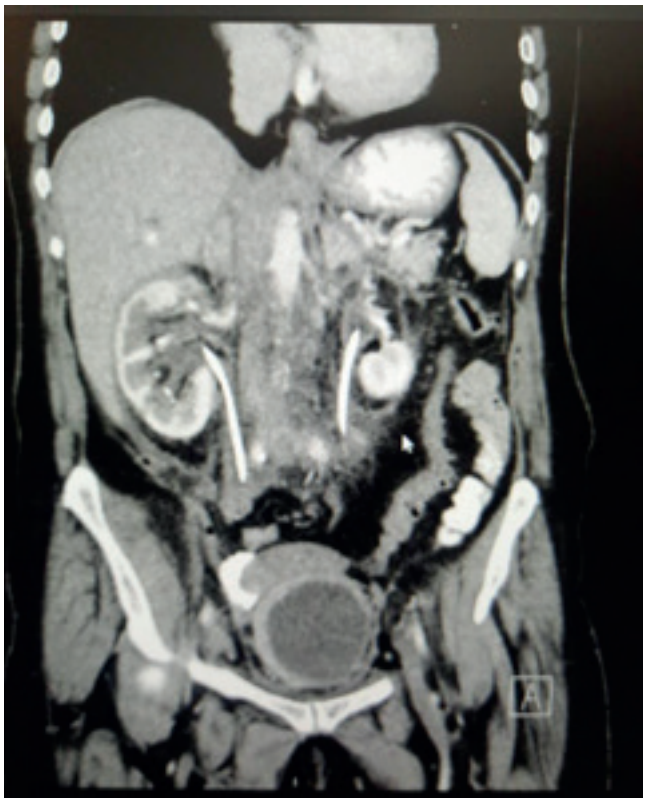

Figure 1. At the level of both retroperitoneal areas, diffuse thickening and heterogeneity extending along the paraaortic, paracaval, and aortocaval areas surrounding both kidneys.

(Serum): 1.96 mg/dL, CRP (quantitative): 13.3 mg/L. A bilateral double-J catheter (3 months use) was placed in both kidneys three days after the diagnosis. The biopsy obtained from RPF was also negative for urothelial carcinoma. The patient was referred to the Rheumatology Outpatient Clinic for RPF treatment at the same center, and therapy with Prednol 48mg was started. She received lymphedema treatment from the Physical Therapy Department at the same center for swelling and leg edema.

Afterward, he was followed up regularly for two months and continued to use Prednol. However, the patient continued complaining of edema and leg pain despite having bilateral double-J catheters. Upper abdominal computed tomography revealed diffuse heterogeneous density changes in the retroperitoneal area extending from the paraaortic neighborhood inferiorly towards the iliac artery neighborhood. Laboratory tests at the same center revealed creatinine values of 1.78 mg/dL, CRP 23.6 mg/L, GGT 77.00. In November 2022, the patient's bilateral double-J catheter was removed and replaced with a bilateral double-J (6 CH tumor stent) catheter for one year. Imuran 50 mg 1*1 was started in addition to Prednol for RPF. She received lymphedema treatment from the physical therapy department for both legs. The patient continued regular rheumatology, nephrology, gastroenterology, and urology visits.

In June 2023, the patient was admitted to our center complaining of vomiting, abdominal pain, abdominal distension, constipation, and flank pain. Contrast-enhanced MRI and ultrasound revealed a 24x18 mm hypoechoic solid mass lesion (metastasis) at the left lobe lateral segment level in the liver. At the level of both retroperitoneal areas, diffuse thickening and heterogeneity were observed extending along the paraaortic, paracaval, and aortocaval areas surrounding both kidneys (Figure 1). The findings were due to retroperitoneal diffuse fibrosis. Hospitalization was recommended, and the patient was followed up. Contrast-enhanced MR examination of the abdomen revealed a subcapsular mass in the left lobe of the liver, and a US-guided percutaneous biopsy was performed. Pathology revealed a diagnosis of poorly differentiated carcinoma in the liver on true-cut biopsy. Laboratory tests revealed AST 109.8, ALT 181.1, GGT 487, and hemoglobin 9.6. Surgery revealed a two cm metastatic mass in segment 4 of the left lobe of the liver. It was excised with the help of ligasure. Bleeding was controlled with a liver suture, and a surgicelle was placed. There was diffuse fibrosis in the abdomen due to retroperitoneal fibrosis (also evident in the duodenum). The boundaries of the tumoral mass could not be palpated clearly because it was diffuse, and fibrosis surrounded all vital vessels. Duodenal obstruction was present due to retroperitoneal fibrosis.Biopsies were taken from the liver, omentum, and duodenum during surgery. Gastroenterostomy and metastasectomy were performed. During surgery, metastasectomy was performed on a 2 cm. diameter mass in liver segment 4. There were multiple millimetric metastatic masses in the mesosoma and omentum of the small intestine. Biopsies were also taken from these. The duodenum tumor was considered unresectable due to the extent of metastasis. Gastroenterostomy was performed due to the absence of duodenal passage. The patient was placed on NG. She was fed with TPN. Medical treatment was applied (Table 1). On post-op day 2, NG was removed, and water was given. However, when vomiting recurred, NG was inserted and fed with TPN. The patient's general condition was good on post-op day 5. When no fluid came from the clamped NG, it was removed, oral nutrition was started and he was discharged on post-op day 10. However, two days later, she presented to our center again with vomiting, pain, and constipation.Pathology results revealed adenocarcinoma of the liver, duodenum, and omentum. On post-op day 13, GGT 279, CRP 313, Bilirubin 12, Na 126, and hemoglobin 8.3 were evaluated in laboratory tests. Hyponatremia and hyperbilirubinemia were detected. Medical treatment was initiated (Table 1). Antibiotherapy, fluid replacement therapy, and TPN continued. Percutaneous Transhepatic Cholangiography, Percutaneous Biliary Drainage, and Percutaneous Choledochal Dilation were performed post-op day 16. Durogesic treatment was started. Due to low hemoglobin, two units of ES were given. A biliary stent and drain for ascites were placed by interventional radiology on post-op day 20. The patient continued to vomit 5-6

DOI: 10.33706/jemcr.1419408
Journal of emergency medicine case reports. 2024;15(1): 12-15

Table 1: Drugs administered to the patient for 41 days

Medicine Name	Amount
PANTONIX IV MG 1 FLK	21 Pieces
ANTI-NAUSEA IM/IV 10MG/2ML INJECT. COZ. ICRN. AMP	37 Pieces
PARACEROL 10MG/ML 100 ML FLK	34 Pieces
DORIFEN 400 MG 4 ML	12 pieces
KEMOSET 8 MG 4 ML AMPOULE	15 pieces
HYPERTONIC SODIUM CHLORIDE 3%150 ML OSEL	144 Pieces
POLYNUTHREE EN-550 1000 ML	18 Pieces
ISOTONIC SODIUM CHLORIDE 0.9%500 ML NEOFLEX	9 pieces
SAFRAX Capsules 250 mg pack of 100 capsules	48 Pieces
ISOTONIC SODIUM CHLORIDE 0.9%500 ML	15 pieces
METICURE LIYO 20 MG AMP	7 pieces
CİPRASEL I.V 400- 200 ML	12 pieces
MANNITOL 20%100 ML OSEL	4 pieces
MIDAJECT 15 MG/3 ML IM/IV/RECTAL SOLUTION CONTAINING 5 AMPOULES	2 pieces
FENTAVER IM/IV Ampoule0,5 mg/10 ml 1x10 ml ampoule	2 pieces
MOLIT 1 ML 6 AMPOULES	2 pieces
PRILOC 2% INJECTABLE VIAL	4 pieces
KONAKION MM.10 MG.5 AMPOULES	2 pieces
DUROGESIC 25 MCG/HOUR TRANSDERMAL PATCH	2 pieces
ALDACTONE-A 25 MG TABLET	35 Pieces
NUTRICLIN N7-1000E 1500 ML	3 pieces
GENTHAVER 160 MG.1 AMPOULE	1 Piece
ISOTONIC SODIUM CHLORIDE 0.9%100 ML TURK-TIPSAN	1 Piece
IRRIGATION ISOTONIC SODIUM CHLORIDE 0.9%1000 ML TURKTIPSAN	1 Piece

times a day. Medical treatment continued. The patient was mobilized and could walk 500 m. per day until post-op day 30. It gradually decreased in the last week, and on the 37th day, he was mobilized at the bedside, cared for, walked four to five steps towards the bed, and lost consciousness when he moved to the bed. Post-op 38 days, he was in the 1st-level intensive care unit. There was no septic shock or sepsis status, or need for ventilation. On day 39, the patient was transferred to our intensive care unit due to respiratory failure. In the 2nd level intensive care unit, septic shock occurred. However, there was no sepsis and no need for ventilation. On day 41, the patient died due to terminal malignancy and concomitant RPF.

Discussion

RPF is a rare disease characterized by inflammation and fibrosis in the retroperitoneal region, starting at the level of the renal vessels and involving the ureters, periaortic, and parailiac. Although the histological event in the tissue is benign, it is a malignant disease when the clinical course is considered. The main difficulty in diagnosing the disease is that patients do not consult a physician before renal function deteriorates and specific symptoms occur, or a non-specific symptom such as abdominal pain is the most common. Peripheral edema associated with deep vein thrombosis may occur due to vena cava compression. Gastrointestinal complications include constipation and abdominal angina due to vascular compression (3). In this case, RPF started with abdominal pain and bilateral leg edema. Evaluation of renal and urinary tract involvement is essential in patients affected by RPF. At diagnosis, 8-30% of patients lose renal function due to persistent hydroureteronephrosis, which is usually asymptomatic and leads to a delay in diagnosis (4). A 59-year-old woman was admitted to a university hospital with renal dysfunction, but the diagnosis was delayed by three months. The patient was admitted to our center and diagnosed with RPF and hydronephrosis in bilateral kidneys after an MRI.

The role of smoking in the progression of RPF is also essential (5). Goldoni et al. (6) reported that exposure to cigarette smoke is a significant risk factor for RPF. Raglianti et al. (7) argued that smoking increases the progression of RPF disease. In this case, a 59-year-old female patient was found to be an active smoker for 40 years.

In the literature, most patients were given corticosteroids for the medical treatment of RPF. In addition, methotrexate, azathioprine, mycophenolate mofetil, and tamoxifen were use(8). In this case, a steroid was used in the initial diagnosis. As the patient's complaints did not change, azathioprine (3 months in total) was used in addition to steroids (6 months in whole) after the second double j catheter was inserted. Medical treatment was discontinued due to deterioration in the general condition and persistence of complaints.

In studies, high rates of developing cancer within one year have been recorded in RPF patients. Cancer cases are mostly in the stomach, lung, colon, and renal pelvis(9). Studies have shown that cancers that develop after RPF cases progress and spread more rapidly. Malignant RPF has a poor prognosis with a median survival of up to 3-6 months(10). In the study by Chen et al. (4) 56 of the 80 patients followed unfortunately died due to the progression of primary malignancy (4). Lee et al. (2) found that patients diagnosed with RPF were associated with subsequent cancer. In our case, a metastatic lesion in the liver was detected

approximately nine months after the diagnosis of RPF, and primary duodenal malignancy was seen within 15 days. RPF and cancer spread very rapidly.

Conclusion

Early diagnosis is essential in RPF. The physician should be determined to use advanced diagnostic tests before renal dysfunction occurs and specific symptoms develop. The possibility of cancer development in RPF patients should be emphasized. Since malignancy is frequently associated with RPF, malignancy should be meticulously investigated with contrast-enhanced studies if necessary, especially if the symptoms progress rapidly. However, cancers detected after the diagnosis of RPF are typically advanced. Unfortunately, the options for effective treatment are limited.

Acknowledgments: We would like to thank the deceased A. S. and her precious family for their contributions to science.

References

1. ŞEKERCİ ÇA. Experience with treatment of retroperitoneal fibrosis: Collaboration of urology and nephrology departments for 26 years in Marmara University. 2017.
2. Lee SJ, Eun JS, Kim MJ, Song YW, Kang YM. Association of retroperitoneal fibrosis with malignancy and its outcomes. Arthritis Research & Therapy. 2021;23:1-9.
3. Runowska M, Majewski D, Puszczewicz M. Retroperitoneal fibrosis–the state-of-the-art. Reumatologia/Rheumatology. 2016;54(5):256-63.
4. Chen T, Tian L, Fan D, Wu F, Lu J, Ding S. Retroperitoneal fibrosis secondary to non-urology carcinomas: a clinical and outcome analysis of 97 cases. Clinical and Translational Oncology. 2019;21:373-9.
5. Cansu DÜ. Retroperitoneal fibrozis: Ayırıcı tanı ve tedavi. Journal of Turkish Society for Rheumatology. 2022;14.
6. Goldoni M, Bonini S, Urban ML, Palmisano A, De Palma G, Galletti E, et al. Asbestos and smoking as risk factors for idiopathic retroperitoneal fibrosis: a case–control study. Annals of internal medicine. 2014;161(3):181-8.
7. Raglianti V, Rossi GM, Vaglio A. Idiopathic retroperitoneal fibrosis: an update for nephrologists. Nephrology Dialysis Transplantation. 2021;36(10):1773-81.
8. Giannese D, Moriconi D, Cupisti A, Zucchi A, Pastore AL, Simonato A, et al. Idiopathic Retroperitoneal Fibrosis: What Is the Optimal Clinical Approach for Long-Term Preservation of Renal Function? Urologia Internationalis. 2023;107(2):134-47.
9. Karbasi A, Karbasi-Afshar R, Ahmadi J, Saburi A. Retroperitoneal fibrosis as a result of signet ring cell gastric cancer: a case-based review. Journal of gastrointestinal cancer. 2013;44:94-7.
10. Urban M, Palmisano A, Nicastro M, Corradi D, Buzio C, Vaglio A. Idiopathic and secondary forms of retroperitoneal fibrosis: a diagnostic approach. La Revue de medecine interne. 2015;36(1):15-21.

Case Report

Journal of Emergency Medicine Case Reports

Two Cases of Digoxin Intoxication: Insights into ECG Findings and Visual Disturbances

Zulfi Engindeniz[1], Busra Nallar[1], Muhammed Dayi[1]

[1]Department of Emergency Medicine, University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital, Bursa, Türkiye

Abstract

Digoxin, a widely prescribed cardiac glycoside, is known for its therapeutic benefits in managing various cardiac conditions. However, its narrow therapeutic index poses a significant risk of toxicity. We present two cases of digoxin intoxication with pathognomic electrocardiographic (ECG) findings and visual disturbances. The detailed analysis of ECG abnormalities and visual disturbances associated with digoxin toxicity will aid in prompt diagnosis and appropriate management, ultimately improving patient outcomes.

Keywords: Digoxin intoxication, electrocardiography, color vision disturbance

Introduction

Digoxin is a medication derived from the foxglove plant (Digitalis purpurea). It belongs to a class of drugs known as cardiac glycosides. Digoxin exerts its effects primarily on cardiac tissue by inhibiting the sodium-potassium ATPase pump. By inhibiting this pump, digoxin leads to an increase in intracellular calcium levels. This, in turn, enhances cardiac contractility (positive inotrope) and improves electrical conduction through the heart (negative chronotropic and decreased atrioventricular conduction). Digoxin is commonly used in the management of heart failure (HF), rate control ofatrial fibrillation (AF), and atrial flutter (1-5).

The pharmacokinetics of digoxin can be influenced by various factors, which can impact the risk of toxicity. Some of these factors include renal function, drug interactions, electrolyte imbalances, age, and body weight (3).

While digoxin offers therapeutic benefits, it also carries a significant risk of toxicity. This risk arises from the narrow therapeutic index of digoxin. Digoxin toxicity can lead to severe and even life-threatening complications, including cardiac arrhythmias, central nervous system disturbances, and visual disturbances (1-7). Therefore, recognizing the early signs and symptoms of digoxin toxicity is crucial for patient safety and optimal therapeutic outcomes.

Case Reports

Case-1

A69-year-old female patient was admitted to the emergency department with nausea and vomiting. Medical history revealed she had coronary artery disease, low cardiac output, atrial fibrillation, and hypertension. She was on rivaroxaban, metoprolol, digoxin, valsartan, spironolactone, and furosemide.Her vital signs were: blood pressure: 116/77 mmHg, pulse rate: 47 bpm (irregular), body temperature: 36.6 0C, and oxygen saturation 97% at room air. Her physical and neurological examinations were normal other than rare fine rales on lung osculation and minimal pretibial edema. Her ECGis shown in figure 1.

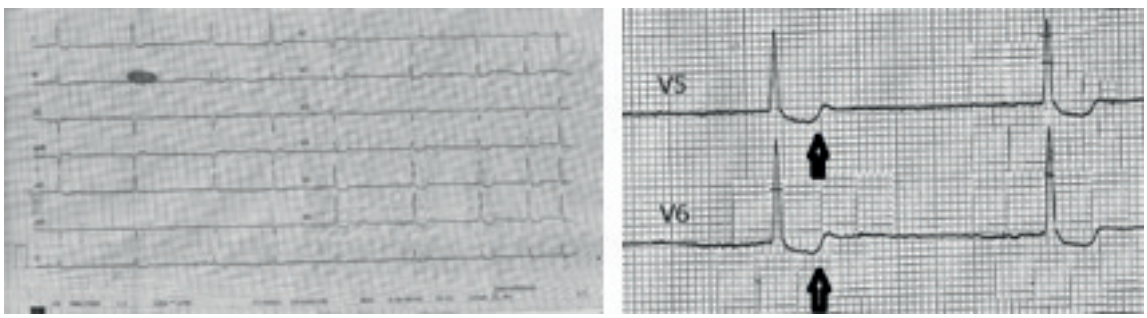

Figure 1. 12 lead ECG of the first case; atrial fibrillation with ST-segment depressions at I, AVL, V4,5,6. At a closer look (small figure), scooping of ST segments (Dali's mustache sign) is evident (arrows).

Corresponding Author: Zulfi Engindeniz
e-mail: zengindeniz@gmail.com
Received: 29.09.2023 • **Revision:** 12.12.2023 • **Accepted:** 29.01.2024
DOI: 10.33706/jemcr.1368189

Cite this article as: Engindeniz Z, Nallar B, Dayı M. Two Cases of Digoxin Intoxication: Insights into ECG Findings and Visual Disturbances. Journal of Emergency Medicine Case Reports. 2024;15(1): 16-18

Upon examining the ECG in light of the patient's history and findings, digoxin level was ordered in suspicion of digoxin intoxication. Herdigoxin level was 3.31ng/ml (reference range: 0 – 2 ng/ml) and other laboratory tests (renal and hepatic function tests, Na, K, Ca, and troponin) were normal. She was admitted to the coronary care unitand digoxin was stopped. Medications other than digoxin were continued. She was monitored for possible life–threatening arrhythmias and none were observed. Nausea and vomiting were controlled with metoclopramide and ondansetron on different occasions. After the second day of hospitalization, nausea and vomiting were stopped. Digoxin levels were followed daily. By the end of the seventh day, her digoxin level was 0.81ng/ml, she was asymptomatic and discharged from the hospital.

Case-2

An 83-year-old female patient was admitted to the emergency department with nausea and vomiting, palpitations, and blurred vision. She had coronary artery disease, heart failure, diabetes mellitus, hypertension, and atrial fibrillation. She was on diltiazem, digoxin, and furosemide. Her vital signs were: blood pressure: 113/92 mmHg, pulse rate: 44 bpm (irregular), body temperature: 36oC, and oxygen saturation 98% at room air. Her physical and neurological examinations were normal. During the visual examination, she stated that she had green-red flying visions for a few days. ECGwas atrial fibrillation with a slow ventricular response (Figure 2). Her digoxin level was 4.14ng/ml. At the emergency department follow- up she had an episode of hypotension and severe bradycardia (mean heart rate was 32 and blood pressure was 80/60mmHg) which responded well to 1 mg of intravenous atropine and hydration. She was admitted to the coronary care unit and followed – up closely. After admission, she received controlled intravenous hydration, and metoclopramide for nausea and her medications other than digoxin were continued. No life-threatening arrhythmias were observed during the follow-up. Digoxin levels decreased gradually together with the symptoms and she was discharged after 8 days of admission.

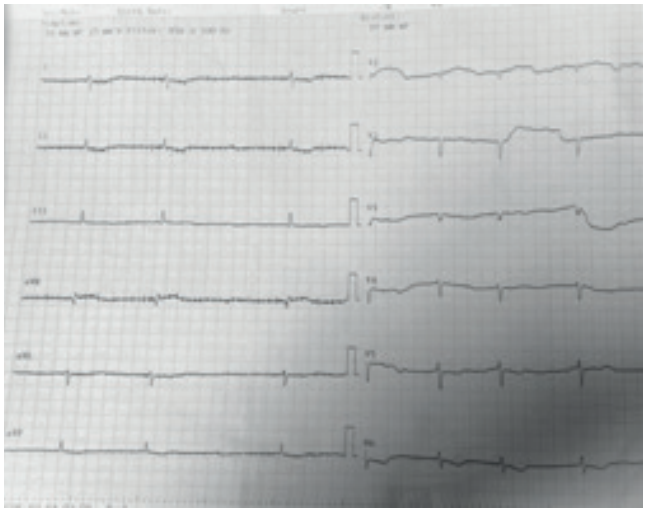

Figure 2. ECG of the second case: Atrial fibrillation with slow ventricular response and non-specific ST segment and T wave changes.

Discussion

Although common indications of digoxin are narrowed mainly to HF and AF it is still widely prescribed. As HF and AF's incidence increases with age, digoxin is prescribed mainly to a digoxin intoxication susceptible population. Furthermore, the number of accompanying diseases and polypharmacy increases in this group of patients which also increases the risk of digoxin toxicity (4). We have presented 2 cases of digoxin intoxication with pathognomonic findings of Dali's mustache sign on ECG and colored floaters symptoms.

ECG is a rapid, powerful, non–invasive, and cheap test that helps physicians determine not only cardiac conditions but also conditions that affect myocardial electrical activity. Including electrolyte abnormalities and intoxications such as digoxin toxicity (7). In the therapeutic range, digoxin has a positive inotropic effect by inhibiting Na/K ATPase and increasing the myocardial concentration of calcium. Digoxin also affects the vagal system and decreases heart rate. In toxic doses, various ECG abnormalities including first-degree AV block, extrasystoles, supraventricular tachycardias, and other arrhythmias may be observed. As well as arrhythmias, characteristic scooping of the ST segment resembling famous painter Salvador Dali's mustache may be observed (Figure 1). Getting familiar with this pattern may help prompt recognition of digoxin intoxication (3,7).

The second case we presented was admitted to the emergency department with non-specific nausea and vomiting. After a thorough medical history and examination, a history of visual green-red colored floaters suggesting digoxin intoxication was acquired, and a laboratory test for digoxin level was ordered. Various visual disturbances related to digoxin use have been reported in the literature including snowy vision, flashing and flickering lights, flowerlike figures, green and yellow vision, and colored floaters. Many mechanisms including the central nervous system, optic nerve, andretinal photoreceptor toxicity of digoxin, were suggested as the cause of the optical effects of digoxin (6). Independent of the mechanism, visual disturbances attributed to digoxin tend to increase with age and multidrug use (6). A history of visual disturbances combined with digoxin use should prompt suspicion of digoxin toxicity.

Management of digoxin intoxication, whether chronic or acute, primarily targets the stabilization of the patient by controlling arrhythmias, CNS manifestations, and gastrointestinal symptoms, correcting electrolyte imbalances, and improving renal function. Digoxin-binding antibodies were reported to reduce the mortality of digoxin intoxication from 20 – 30% to 5-8%. However, there are no clinical studies demonstrating a net clinical benefit.

DOI: 10.33706/jemcr.1368189
Journal of emergency medicine case reports. 2024;15(1): 16-18

Current indications for digoxin–binding antibody use are; life-threatening arrhythmias, cardiac arrest, hyperkalemia with serum potassium level of more than 5 mmol/L, end-organ dysfunction, or a digoxin level of more than 10ng/ml (acute intoxication), or 6 ng/ml (chronic intoxication) (2-4,7). Our cases were chronic intoxications and digoxin–binding antibodies were not indicated. They were managed symptomatically and responded well to cessation of digoxin.

Conclusion

Digoxin intoxication is a life-threatening condition that may easily be overlooked. Getting familiar with Dali's mustache ECG sign and colored floater symptoms may prompt a rapid diagnosis.

References

1. Ahmed A, Rich MW ., Love TE, et al. Digoxin and reduction in mortality and hospitalization in heart failure: a comprehensive post hoc analysis of the DIG trial. European Heart Journal. 2006;27(2):178-186.
2. Clifford LM, Meere W. Chronic Digoxin Toxicity: An Evaluation of Digoxin-Specific Antibodies and Other Management Options. Cureus. 2023;15(5):e38692.
3. Patocka J, Nepovimova E, Wu W, Kuca K. Digoxin: Pharmacology and toxicology-A review. Environmental toxicology and pharmacology. 2020;79:103400.
4. Peters AE, Chiswell K, Hofmann P, Ambrosy A, Fudim M. Characteristics and Outcomes of Suspected Digoxin Toxicity and Immune Fab Treatment Over the Past Two Decades-2000-2020. The American journal of cardiology. 2022;183:129-136.
5. Vamos M, Erath JW, Benz AP, Lopes RD, Hohnloser SH. Meta-Analysis of Effects of Digoxin on Survival in Patients with Atrial Fibrillation or Heart Failure: An Update. The American journal of cardiology. 2019;123(1):69-74.
6. Shi L, Sun LD, Odel JG. Colored floaters as a manifestation of digoxin toxicity. American journal of ophthalmology case reports. 2018;10:233-235.
7. Yates C, Manini AF. Utility of the electrocardiogram in drug overdose and poisoning: theoretical considerations and clinical implications. Current cardiology reviews. 2012;8(2):137-151.

Case Report

Journal of Emergency Medicine Case Reports

Isolated Cricoid Cartilage Fracture After Blunt Thoracocervical Trauma: A Case Report

Ahmet Aksoy[1], Kursat Guresci[2]

[1]Department of Otorhinolaryngology, Faculty of Medicine, Sivas Cumhuriyet University, Sivas, Türkiye.

[2]Department of Radiology, Niğde Omer Halisdemir Educational and Training State Hospital, Niğde, Türkiye.

Abstract

Although cricoid cartilage fracture is rare because of the firm and stable structure of the cricoid cartilage, it can cause fatal complications. Prompt diagnosis and rapid airway safety are incredibly vital. A 24-year-old male patient was admitted to the emergency department due to blunt trauma to the thoracocervical region. The computed tomography taken after the first interventions detected a displaced fracture of the cricoid cartilage. In light of the patient's clinical findings, the patient was treated conservatively and non-surgically with close follow-up of the airway safety.

Keywords: Cricoid fracture, subcutaneous emphysema, larynx trauma, thoracocervical blunt trauma, conservative treatment

Introduction

Laryngeal traumas are rare but potentially fatal, and ensuring emergency airway safety is essential (1). The frequency of laryngeal trauma exhibits variations contingent upon the demographic under examination. Among adults, the estimated population incidence of external laryngeal trauma is 1 in 137,000, with blunt trauma prevailing over penetrating trauma, particularly in developing nations (2). The occurrence of laryngeal trauma is estimated to fall within the range of 1 in 5,000 to 1 in 137,000 emergency room admissions in the United States. The principal etiology of airway trauma often stems from the application of blunt force to the anterior neck. Simultaneously, instances of penetrating injuries to the neck contribute to laryngeal trauma, underscoring the critical necessity for prompt airway management. This urgency is underscored by the typically more extensive tissue damage associated with penetrating injuries as compared to blunt force impacts (3). Fractures of the cricoid cartilage carry noteworthy clinical ramifications, manifesting as dyspnea, neck pain, and hoarseness. They merit consideration in cases where patients present with unexplained dyspnea, irrespective of the persistence or intermittence of symptoms (4). Blunt trauma directed to the anterior neck has the potential to induce fractures in the cricoid cartilage, culminating in compromised integrity of vital structures and subsequent constriction of the airway (5).The cricoid cartilage is a significant anatomical landmark, pivotal in preserving airway patency and producing sound (6).A thorough comprehension of the developmental embryology, anatomy, and injury patterns related to cricoid cartilage fractures is crucial for precise diagnosis and proper management (7). In cricoid fractures, tracheotomy is the preferred method primarily to protect the airway. Still, after the airway stabilization, there are various methods, from the conservative close follow-up to follow-up with tracheostomy or surgical restoration (8-10). In this case, the patient with an isolated cricoid fracture was treated conservatively without sequelae.

Case Report

A 24-year-old male patient was admitted to the emergency department due to a blunt blow to the thoracic and cervical region due to the work vehicle hitting his back and then falling on a hard floor. The patient's vital signs were typical, with complaints of sore throat, bloody cough, and pressure on the throat at the initial evaluation. Ecchymous, bruise areas on the neck on inspection; tenderness in the neck and crepitations indicating subcutaneous emphysema were detected on palpation. In the patient's thorax, computed tomography (CT), mild hemothorax, atelectasis, mild contusion areas in the parenchyma, and free air densities in the mediastinum are more prominent on the left, were observed in both hemithorax. In neck CT, fracture in the posterior part of the cricoid cartilage (Figure 1a), submucosal hematoma in the right vocal cord (Figure 1b) and right aryepiglottic fold (Figure 2a), diffuse air densities in the cervical region, under the skin, between the neck

Corresponding Author: Ahmet Aksoy
e-mail: ahmetaksoy@cumhuriyet.edu.tr
Received: 18.06.2023 • **Revision:** 28.12.2023 • **Accepted:** 30.01.2024
DOI: 10.33706/jemcr.1316442

Cite this article as: Aksoy A, Guresci K. Isolated Cricoid Cartilage Fracture After Blunt Thoracocervical Trauma: A Case Report. Journal of Emergency Medicine Case Reports. 2024;15(1): 19-22

DOI: 10.33706/jemcr.1316442
Journal of emergency medicine case reports. 2024;15(1): 19-22

fascia, in the supraclavicular and axillary region (Figure 2a-2b) was observed. In this case, unlike similar cases, the initial safety of the airway was primarily provided by orotracheal intubation instead of tracheotomy. Extubation was performed because the patient's saturation was good. In the fiberoptic laryngoscopic examination at the diagnosis stage, post-cricoid hyperemia with hematoma in the mucosa of the right arytenoid-aryepiglottic structures, hyperemia, and increased vascularity in the bilateral vocal cord and left arytenoid mucosa was present in both inspiration (a) and phonation (b). Bilateral vocal cords were mobile, but there was limited patency due to oedema of the rima glottis (Figure 3a-3b). in the fiberoptic laryngoscopic examination during the first week of the follow-up, the right arytenoid mucosa was mildly edematous in both inspiration (a) and phonation (b). At the same time,oedema, hematoma, and vascularity increased in the postcricoid region, and vocal cords were completely regressed (Figure 4a-4b). The fiberoptic laryngoscopic examination during the first month of the follow-up showed mild edema in the right arytenoid in both inspirations (a) and phonation (b). In contrast,edema, hematoma, and vascularity increased in the postcricoid region, and vocal cords were wholly regressed. When the rima glottis opening was optimal, polypoid tissue was in the subglottic area at the level of the posterior commissure (Figure 5a-5b).

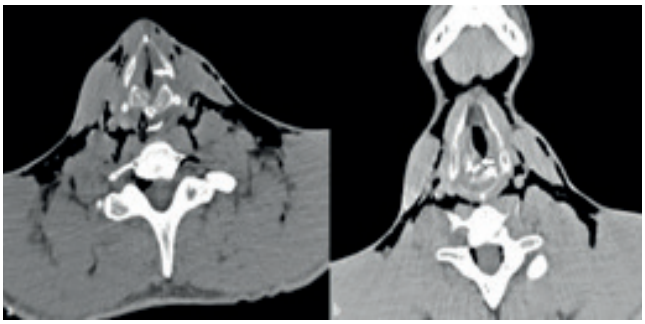

Figure 1. On CT images of the neck, the cricoid cartilage is fractured posteriorly (black arrow) and anteriorly displaced in the axial section bone window. At this level, the air passage (white arrow) is significantly narrowed (a). In the image in the axial section soft tissue window, thickening compatible with submucosal hematoma is observed in the right vocal cord (white arrow) (b).

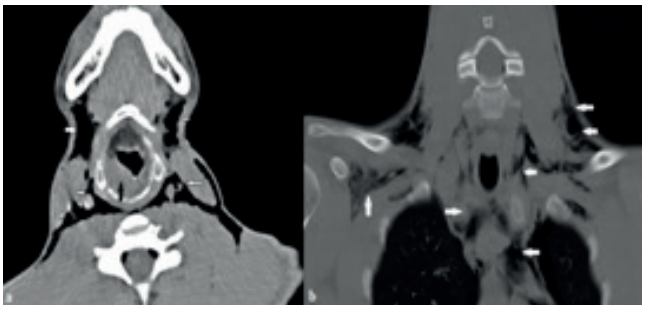

Figure 2. In the image viewed in the axial section bone window, thickening compatible with submucosal hematoma in the right aryepiglottic fold (black arrow) and air densities (white arrows) under the skin and between the neck fascia in the cervical region are observed. (a). Air densities (white arrows) are kept in the supraclavicular, axillary area, paratracheal, paratracheal levels, and mediastinum in the image in the coronal section bone window (b).

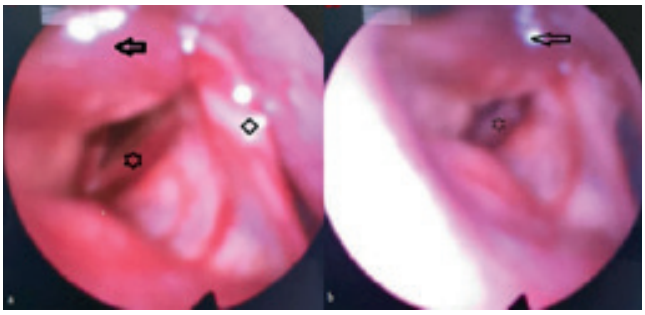

Figure 3. In the fiberoptic laryngoscopic examination at the diagnosis stage, post cricoid hyperemia with hematoma in the mucosa of the suitable arytenoid-aryepiglottic structures, hyperemia and increased vascularity in the bilateral vocal cord and left arytenoid mucosa were present in both inspiration (A) and phonation (B), Bilateral The vocal cords were mobile, but there was limited opening due to oedema of the rima glottis. (Arrow; Right arytenoid mucosa, Square; Left arytenoid, Star; Left vocal cord).

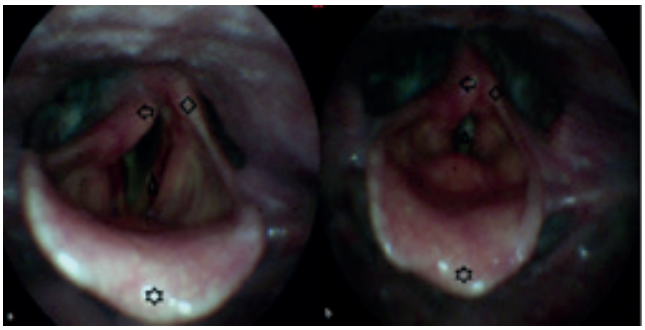

Figure 4. In the fiberoptic laryngoscopic examination at the first week of the follow-up, the right arytenoid mucosa was mildly edematous in both inspiration (A) and phonation (B), while edema, hematoma, and vascularity increased in the postcricoid region and vocal cords wholly regressed. (Arrow; Right arytenoid, Square; Left Arytenoid, Triangle; Left vocal cord, Star; Epiglottis).

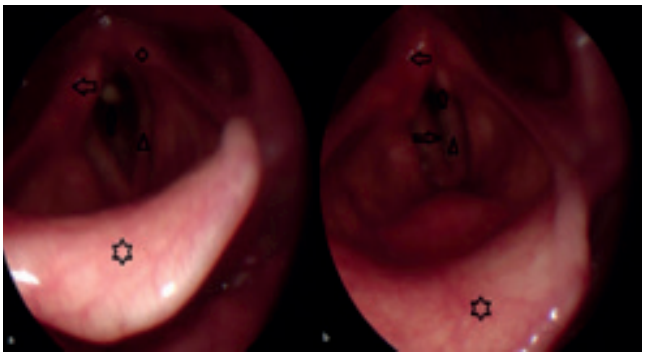

Figure 5. In the fiberoptic laryngoscopic examination at the first month of the follow-up, there is very mild edema in the right arytenoid in both the inspiration (A) and phonation (B), while edema, hematoma, and vascularity increase in the postcricoid region and cord vocals have completely regressed. When the rima glottis patency wasoptimal, polypoid tissue was in the subglottic area at the posterior commissure level. (Right Arrow; Right arytenoid, Upward-pointing arrow (A); Polypoid tissue, Left-facing arrow (B); Minimal opening in primal glottis closure, Upward-pointing arrow (B); Laceration in the mucosa of the left arytenoid medial wall, Square; Left Arytenoid, Triangle; Left vocal cord, Star; Epiglottis).

Discussion

The ring-shaped cricoid cartilage, located under the vocal cords, is the most muscular laryngeal structure and is essential in protecting the larynx from trauma. Fractures are rare since other external arrangements protect the cricoid cartilage (8,10). The diagnosis of cricoid cartilage fractures is made in the presence of clinical, radiological and endoscopic findings. Cricoid cartilage fracture and displacement can be detected on CT images. Subcutaneous emphysema and cervical, supraclavicular, axillary, mediastinal, and abdominal free air can also be observed on CT. Mucosal structures can be evaluated endoscopically. Findings in endoscopy can be obtained with a direct or indirect laryngoscope, flexible nasopharyngoscope, bronchoscope, and esophagoscope (11). The most crucial factor in diagnosis is the suspicion of the clinician or radiologist (10,11). In acute cricoid fracture, symptoms include dyspnea, hoarseness, vocal cord paralysis, airway obstruction, coarse voice, tenderness in the neck, pain, ecchymosis, subcutaneous emphysema, and hemoptysis may be present (8). Fuhrman et al., the most common finding in laryngeal traumas has been reported as neck tenderness, subcutaneous emphysema, and lack of tolerance to the supine position. In the presence of such symptoms, emergent tracheostomy should be considered before the laryngeal examination. Although iatrogenic complications of orotracheal intubation are more common than emergent tracheostomy in patients with laryngeal trauma, orotracheal intubation may also be preferred because emergent tracheotomy can cause surgically time-consuming and massive bleeding (11). In various case reports, there are cases in which airway safety was provided by emergent tracheotomy, tracheostomy, or cricotracheostomy after the first diagnosis. Still, there are cases where initial airway safety was achieved with orotracheal intubation (8-10). In this study, orotracheal intubation was preferred first to ensure airway safety. Afterwards, bronchoscopic and laryngoscopic evaluations were made. Although cricoid cartilage fractures are fatal complications due to acute obstruction of the upper respiratory tract, good algorithms for cricoid cartilage fractures are not available in the literature. Treatment management is based on a limited number of case reports or the recommendations of experts (4). The most important thing in managing cricoid fractures is to closely monitor the safety of the airway and the state of voice functions (4,10,11).Various treatment methods are tried to treat a cricoid fracture, from conservative treatment to surgical restoration. This patient was extubated and treated conservatively with close follow-up. In the two-case presentation of Je Hyeok et al., since the patients did not have symptoms such as hoarseness or dyspnea, airway safety was treated with direct fiberoptic laryngoscopy with close monitoring and short intervals without complications (11). Falcon et al. In the case report, although the patients had symptoms such as hoarseness and hemoptysis, airway safety was followed closely as extubated, and isolated displaced cricoid cartilage fracture was treated conservatively (12).

In cricoid injuries, the severity of the damage is essential in terms of treatment management and prognosis (8,11). How to ensure emergent airway safety in treating laryngeal traumas, classification of fractures, and surgical indications are still controversial (12). The literature shows that early surgical treatment is the method of choice, especially in cases of massive edema, mucosal tears, exposed cartilage, cord paralysis, or multiple displaced fractures (8,11,12). In our case, a displaced isolated cricoid fracture was observed, and since the patient did not have dyspnea or significant hoarseness, the airway was followed closely and extubated.

Although there is no generally accepted scheme in the conservative treatment approach, various patients were treated with intravenous steroids, non-steroidal anti-inflammatory, anti-reflux therapy, cold steam application, and absolute sound therapy (10-12).

Conclusion

In conclusion, fracture and the severity of the injury should be respiratory tract safety monitored closely in patients with cricoids determined clinically, radiologically, and endoscopically in this process. It should be remembered that treatment options range from conservative treatment to surgical restoration.

References

1. Buch K, Takumi K, Curtin HD, Sakai O. CT-based assessment of laryngeal fracture patterns and associated soft tissue abnormality. European Radiology. 2021 Jul;31(7):5212-21.
2. Masoud N, Shahidi N, Mohammadi F. Epidemiology, clinical presentations and radiologic findings of blunt laryngeal trauma. Medical Journal of Tabriz University of Medical Sciences and Health Services.2020; 42(4) 476-82. doi: 10.34172/MJ.2020.070
3. Preston T, Fedok FG. Blunt and penetrating trauma to the larynx and upper airway. Operative Techniques in Otolaryngology-Head and Neck Surgery .2007;18.(2)140-3.
4. Matsuo Y, Yamada T, Hiraoka E. Unique presentation of cricoid cartilage fracture causing intermittent dyspnea without preceding trauma. Nagoya J Med Sci. 2019 Nov;81(4):687-691. doi: 10.18999/nagjms.81.4.687.
5. Mehrabi S, Hosseinpour R, Yavari Barhaghtalab MJ. Isolated comminuted fracture of the cricoid cartilage and narrowing of the airway after a traumatic blunt injury of the neck: a case report. Int J Emerg Med. 2022 Oct 5;15(1):55. doi: 10.1186/s12245-022-00459-9.
6. Rutty GN. "The Cricoid Cartilage." Essentials of Autopsy Practice: Reviews, Updates and Advances Springer Cham. 2019: 89-110. doi.org/10.1007/978-3-030-24330-2

DOI: 10.33706/jemcr.1316442
Journal of emergency medicine case reports. 2024;15(1): 19-22

7. Mathews S, Jain S. Anatomy, Head and Neck, Cricoid Cartilage. 2023 Aug 7. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 30969643.

8. Kragha KO. Acute traumatic injury of the larynx. Case Rep Otolaryngol. 2015:393978. doi: 10.1155/2015/393978.

9. Chitose SI, Sato K, Nakazono H, Fukahori M, Umeno H, Nakashima T. Surgical management for isolated cricoid fracture causing arytenoid immobility. Auris Nasus Larynx. 2014 Apr 1;41(2):225-8.

10. Cınar F, Evren C, Ugur MB, Corakcı S, Erdem CZ. Conservative approach to isolated cricoid cartilage fracture. Turkish Journal of Trauma & Emergency Surgery. 2012;18(6):539-41.

11. Oh JH, Min HS, Park TU, Lee SJ, Kim SE. Isolated cricoid fracture associated with blunt neck trauma. Emergency Medicine Journal. 2007 Jul 1;24(7):505-6.

12. Falcone TE, Schwartz MA, Lee AS, Anderson TD. Conservative Treatment of Isolated Cricoid Cartilage Fractures From Blunt Trauma. JAMA Otolaryngology–Head & Neck Surgery. 2017 Jun 1;143(6):633-4.

Case Report

Journal of Emergency Medicine Case Reports

An Uncommon Presentation of Septum Pellucidum Anatomical Variations: A Case Report of Generalized Tonic-Clonic Seizure in a Healthy Adult

Nurullah Parca[1], Ismail Atas[2], Ali Celik[1], Ozlem Bilir[1]
[1]Recep Tayyip Erdoğan University Training and Research Hospital, Department of Emergency Medicine, Rize, Türkiye.
[2]Rize State Hospital, Department of Emergency Medicine, Rize, Türkiye.

Abstract

The septum pellucidum (SP) is a thin, transparent, dual-membrane structure located between the lateral ventricles of the brain. Incidentally identified through imaging modalities, this variation, while rare, may manifest with symptoms such as neuropsychiatric disorders, headache, dizziness, seizures, nausea, and vomiting. In this report, we present the case of a healthy middle-aged man with cavum vergae (CV) and cavum septum pellucidum (CSP), who sought medical attention in the emergency department (ED) due to a generalized tonic-clonic seizure (GTCS). A 40-year-old male without any known medical history presented to our emergency department with a GTCS. Considering this as the first seizure, blood and imaging tests were conducted, all of which showed no abnormalities. Non-contrast computed tomography revealed sequel cystic encephalomalacic areas in the left occipital and right frontal cerebral hemispheres, consistent with a parapharyngeal epidermoid cyst, and the presence of cavum septum pellucidum et vergae. Emergency consultation from the neurological clinic was sought, and an electroencephalogram showed no seizure activity. He was subsequently discharged with a recommendation for follow-up at the neurology outpatient clinic. This case prompts critical considerations in the emergency medicine realm regarding the potential relationship between anatomical variations in the septum pellucidum and emergent seizure activity.

Keywords: Septum pellucidum, seizure, cavum vargae, emergency

Introduction

The septum pellucidum (SP) is a thin, transparent, dual-membrane structure located between the lateral ventricles of the brain. Typically, this bilayered membrane structure tightly closes, separating the two ventricles, either during the late fetal period or shortly after birth (1). Cavum septum pellucidum (CSP) and cavum vergae (CV) indicate persistent variations in the adult brain when SP's membranous layers fail to close properly, with CV denoting the extension of CSP (2). Although this anatomical variation is observed in 85% of term newborns, it usually resolves in the first 3-6 months postnatally. However, approximately 12% of children aged 6 to 16 may retain this variation (2-5).

Incidentally identified through imaging modalities, this variation, while rare, may manifest with symptoms such as neuropsychiatric disorders, headache, dizziness, seizures, nausea, and vomiting (2-4). If the cavity in this anatomical variation is larger than normal, it is defined as a cyst (2). Depending on the CSP and CV size, the severity of clinical symptoms that can be seen in this variant may increase (6). In this report, we present the case of a healthy middle-aged man with CV and CSP, who sought medical attention in the emergency department (ED) due to a generalized tonic-clonic seizure (GTCS).

Case Report

A 40-year-old male without any known medical history presented to our emergency department with a GTCS. According to information obtained from the patient's relatives, he experienced a complete loss of consciousness during the seizure, with approximately half an hour required for normal consciousness to return. The patient did not report any symptoms preceding the episode. Upon arrival, the patient was conscious, oriented, and cooperative, with vital signs within normal ranges. Detailed neurological and systemic examinations revealed no abnormalities. Considering this as the first seizure, blood and imaging tests were conducted. The patient underwent blood tests including complete blood count, biochemical panel, cardiac enzymes, and blood gas analysis. Considering the patient's clinical condition and history, toxicological causes contributing to the seizure etiology were not considered. Therefore, toxicology laboratory tests were

Corresponding Author: Nurullah Parca
e-mail: nrllhprca@gmail.com
Received: 17.01.2024 • **Revision:** 06.02.2024 • **Accepted:** 11.02.2024
DOI: 10.33706/jemcr.1421495

Cite this article as: Parca N, Atas I, Celik A, Bilir O. An Uncommon Presentation of Septum Pellucidum Anatomical Variations: A Case Report of Generalized Tonic-Clonic Seizure in a Healthy Adult. Journal of Emergency Medicine Case Reports. 2024;15(1): 23-25

DOI: 10.33706/jemcr.1392555
Journal of emergency medicine case reports. 2024;15(1): 23-25

not conducted in our emergency department, and referral to a specialized center was not deemed necessary due to the absence of clinical suspicion. The initial finger stick blood glucose measure ment upon the patient's presentation to the emergency department was 115 mg/dL. Serum electrolytes were within normal limits, and the lactate level measured in the blood gas analysis was 2.8 mmol/L. Non-contrast computed tomography revealed sequel cystic encephalomalacic areas in the left occipital and right frontal cerebral hemispheres, consistent with a parapharyngeal epidermoid cyst, and the presence of cavum septum pellucidum et vergae (Figure 1). No specific treatment was given to the patient, who did not have an active epileptic seizure when he was admitted to the emergency department. Emergency consultation from the neurological clinic was sought, and an electroencephalogram showed no seizure activity. The patient was monitored for seizures in the emergency department and remained free of active complaints or recurring seizures throughout the observation period. He was subsequently discharged with a recommendation for follow-up at the neurology outpatient clinic.

Discussion

In the etiology of epileptic seizures; There are acute hemorrhagic and ischemic stroke, metabolic diseases, electrolyte disorders, substanceabuse, head trauma, medications, infective processes and other causes. Additionally, in a study, it was thought that air temperature, relative humidity, wind speed and moon cycle may also cause epileptic seizures (7). In our patient, septumpellicidum anatomical variation was considered as a rare etiological cause.

This case underscores the uncommon occurrence of GTCS in an otherwise healthy middle-aged patient with persistent septum pellucidum anatomical variations—specifically CSP and CV. While CSP and CV are typically considered benign, their association with emergent neurological symptoms raises important considerations in emergency medicine.

Typically observed in 85% of term newborns, anatomical variations in the septum pellucidum often resolve spontaneously early in postnatal life (2). However, our case diverges from this pattern, presenting a healthy adult with GTCS, prompting an in-depth emergency investigation. Non-contrast computed tomography revealed sequel cystic encephalomalacic areas and a parapharyngeal epidermoid cyst. While evidence linking CSP and CV to seizure disorders is limited, these imaging findings suggest potential structural abnormalities contributing to the observed clinical manifestation, especially in the context of an emergency department presentation.

In the blood gas analysis performed in our patient, pH: 7.35, pCO2: 41 mmHg, pO2: 14 mm Hg and lactate: 2.8 mmol/L. A study found a negative and significant correlation between pH and pO2, pCO2, lactate (8). We could not find such a finding in our case. For this purpose, case series that are multicenter and have a large sample size can be studied.

The absence of abnormal findings in blood tests and electroencephalogram complicates interpretation. Despite identifying structural anomalies through imaging, the lack of abnormal electrical activity challenges the direct link between anatomical variations and seizures. This discrepancy highlights the intricacies of understanding structural brain changes and their impact on emergent clinical scenarios.

Surgical procedures may be considered in the event of disruption of cerebrospinal fluid flow, direct compression on adjacent brain structures, or the occurrence of focal neurological deficits, contingent upon the magnitude of this variation's size (3).

Conclusion

In conclusion, this case prompts critical considerations in the emergency medicine realm regarding the potential relationship between anatomical variations in the septum pellucidum and emergent seizure activity. Further research and collaborative efforts across emergency and neurology

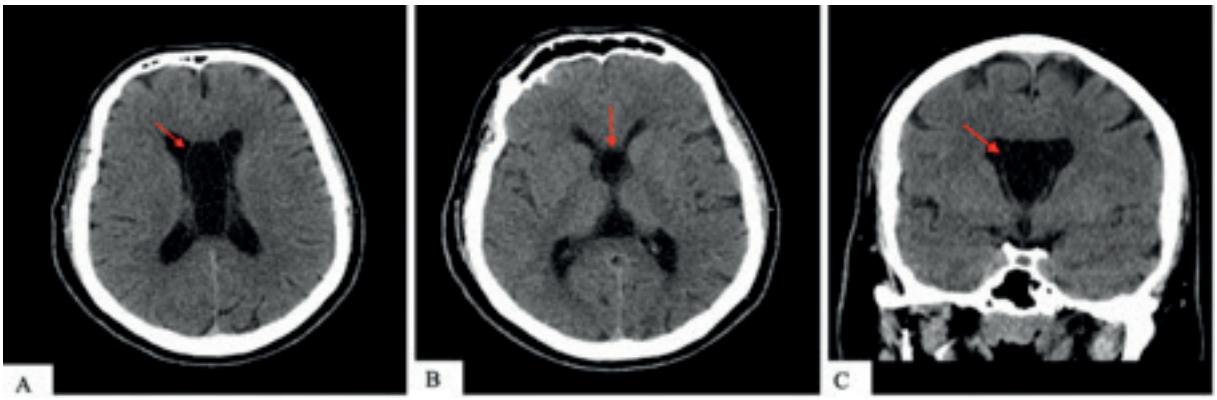

Figure 1. A-B axial section view of cavum septum pellucidum et vergae on non-contrast cranial tomography, C. Coronal section view of cavum vergae on non-contrast cranial tomography.

disciplines are crucial for unraveling this potential causal relationship, especially when routine diagnostic tests yield inconclusive results in the acute setting.

References

1. Rajasekharan C, Karthik V, Harikrishnan M, Lekshmi S. Cavum vergae and psychiatric illness: substantive or serendipity? BMJ Case Rep. 2018 Jun 28;2018:bcr2018225511. doi: 10.1136/bcr-2018-225511. PMID: 29954773; PMCID: PMC6040555.
2. Ferreira DBCO, Medeiros JW, Cwajg E, Ferreira-Pinto PHC, de Carvalho LU, Nigri F. Cavum septum pellucidum and vergae cyst: A symptomatic case with intracranial hypertension and multiple nerve involvement. Surg Neurol Int. 2022 Dec 2;13:564. doi: 10.25259/SNI_822_2022. PMID: 36600739; PMCID: PMC9805640.
3. Das JM, Dossani RH. StatPearls. Treasure Island, FL: StatPearls Publishing; 2022. Cavum septum pellucidum. Available from: https://www.pubmed.ncbi.nlm.nih.gov/30725733 [Last accessed on 2022 Apr 13]
4. Kryukov EV, Stanishevsky AV, Gavrilov GV, Gizatullin SK. Cysts of septum pellucidum, cavum vergae and cavum veliinterpositi. Meta-analysis of 368 cases. ZhVoprNeirokhirIm N NBurdenko. 2020;84:111–8.
5. Oktem H, Dilli A, Kurkcuoglu A, Pelin C. Prevalence of septum pellucidum variations: A retrospective study. Open Access Libr J. 2018;5:e5017.
6. Martins LP, Leitão AM, de Lucena JD, Gondim FA. Cavum septum pellucidum, da embriologia à clínica: Uma revisão da literatura. J Sağlık Biol Bilim. 2018;7:89–96.
7. Sahin L, Gur A. Association of the Meteorological Parameters and Epileptic Seizures. Int J Crit Care Emerg Med 2023, 9:151.
8. Ekmekyapar T. The effects of systemic inflammatory indices, lactate, and blood gas parameters on drug-resistant and drug-nonresistant epilepsy. Journal of Experimental and Clinical Medicine. 2023:40(3); 640-645.

Case Report

Journal of Emergency Medicine Case Reports

Forensic Emergencies in The Context Of Genital Injuries: A Case Report

Zafer Liman[1], Ugur Kayhan[2]

[1]Department of Forensic Medicine, Karabük University, Karabük, Türkiye.

[2]Department of Forensic Medicine, Afyonkarahisar Health Sciences University, Afyonkarahisar, Türkiye.

Abstract

A review of gynecological emergency cases shows that traumatic injuries observed in consensual sexual relations, sexual abuse victims or following an abortion, secondary infections, internal organ injuries, and massive bleeding are gynecological forensic cases that may require an emergency approach. In this case; it is aimed to discuss the case of a child who was diagnosed as sexual abuse and reported as a forensic case. In the evaluation of the case of a 15-year-old girl who applied to the emergency service with a history of the foot of a stool entering her vaginal area, it was seen that she had a complaint of active vaginal bleeding but was referred to Child Monitoring Center (CİM) without taking a detailed anamnesis or performing any tests. During the forensic interviews at CİM, on account of the fact that the patient complained of dizziness, an emergency forensic vaginal examination and operation was performed. Active vaginal bleeding, 3 cm transverse laceration, and uterine artery injury were found in the area between the upper cervix and lower uterine segment. Our study aims to contribute to raising awareness about the importance of medical evaluation and healthy anamnesis in the emergency department regarding these issues.

Keywords: Forensic medicine, emergency medical services, child abuse, accidental falls, medical history taking

Introduction

Emergency services include all health services that take measures to prevent the deterioration of the current health status of a person whose health has been jeopardized for any reason and also dispatching the patient to an appropriate unit in the same hospital or to a different health institution if necessary (1). In emergency cases, emergency medical intervention, consultation, or a referral chain should be established immediately after the preliminary diagnosis or definitive diagnosis is made, if necessary.

Gynecologic emergencies are among the groups that constitute a majority of the workload of an emergency department. A review of gynecological emergency cases shows that traumatic injuries observed in consensual sexual relations, sexual abuse victims or following an abortion, as well as secondary infections, internal organ injuries, and massive bleeding are gynecological forensic cases that may require an emergency approach (2).

The process is carried out by the Child Monitoring Center (CMC) in sexual abuse cases where the victims are under the age of 18 after a judicial notification is made by the emergency service (3). However, prior to the forensic process, determining whether the case needs urgent medical attention and implementation or not is considered one of the main professional responsibilities of a physician. The process may be prolonged for minors referred to the CMC as it also includes forensic medical stages. In child abuse cases admitted to the emergency department, it should first be determined whether emergency intervention is required, and later on, the victim should be included in the forensic medical process after the primary treatment is completed.

Case Report

Our case is a 15-year-old girl who lives with her family. The day before the incident, she watched a video of sexual intercourse between a man and a woman with adult content on social media applications. On the day of the incident, she stated that while she was taking a bath she inserted the foot of the shower stool into her vagina for masturbation out of curiosity. And added that she felt on the stool because the floor was slippery. She also said that 13-15 cm of the foot of the stool entered her vagina after which she started to bleed. The patient was admitted to the emergency department with her mother, the preliminary examination revealed active bleeding in the vaginal area and her Hgb was: 12 mg/dL, Hct: 34.4. The case was reported as a forensic case without any further consultation or examination and transferred to the CMC after informing the hospital police. At the CMC, the victim had to wait for the public prosecutor to arrive after which her statement was taken with a forensic interviewer. During the interview, the forensic medicine specialist was informed that the patient was complaining of dizziness and

Corresponding Author: Zafer Liman
e-mail: zaferliman@yahoo.com
Received: 17.11.2023 • **Revision:** 16.01.2024 • **Accepted:** 15.02.2024
DOI: 10.33706/jemcr.1392555

Cite this article as: Liman Z, Kayhan U. Forensic Emergencies In The Context Of Genital Injuries: A Case Report. Journal of Emergency Medicine Case Reports. 2024;15(1): 26-28

in the following examination active vaginal bleeding, low blood pressure, and increased pulse were detected. Then the patient was evaluated together with a pediatric surgeon and gynecologist and consulted for preoperative emergency examination. In the subsequent follow-up, the Hgb value first decreased to 10.3 mg/dL and then to 8 mg/dL. In the preoperative examination, the hymen was elastic and intact. During the operation, a 3 cm transverse laceration and uterine artery injury were found in the area between the upper cervix and lower uterine segment and sutured. A postoperative genital examination revealed a delaceration and abrasion of the hymen in the 6 o'clock direction due to the iatrogenic use of an excavator. In addition, 2 units of erythrocyte suspension treatment were administered during the operation. The patient was hospitalized and discharged the following day.

There is a detailed statement that written patient consent/ next of kin. And also the study was approved by Karabük University Non-Interventional Clinical Research Ethics Committee's decision dated 07/11/2023 and numbered 2023/1482.

Discussion

The most important duty and responsibility of a physician is to provide the necessary medical response to every patient admitted to the emergency department, regardless of whether the case is forensic or not (4). In forensic cases evaluated in the emergency department, physicians are expected to prioritize the necessary diagnosis, treatment, effective medical response, and referral procedures by acting according to medical protocols.

Some of the emergency cases are etiologically forensic cases. Emergency departments are frequently the first place where forensic cases as well as emergency cases are admitted. The rate of competency felt by both physicians and other healthcare personnel regarding forensic cases is quite low and avoidance of taking responsibility is frequently observed (5)working at 112 emergency stations in the province of Artvin, to encounter with regarding forensic cases and determine their practices aimed at recognizing, protecting, and reporting the evidences that may affect the forensic process.\nMaterials and methods\nThis descriptive study was conducted with nurses and emergency medicine technicians working at 112 emergency stations in Artvin between January 2013 and February 2014.\nResults\nOf 141 health personnel that constituted sample of the study, 48.9% were nurses, 9.9% emergency medicine technicians, and 41.1% ambulance and emergency care technicians. The rate of feeling sufficient in coping with forensic cases and incidents was 20.6%. There was a lower rate of receiving education about the approach towards forensic cases (15.6%.

Although forensic emergency cases do not constitute a significant portion of the emergency department workload, the uneasiness felt by physicians during the forensic notification phase and their insufficient level of knowledge can sometimes make the process difficult in forensic cases. An examination of the literature reveals that most of the studies conducted for emergency workers are about recognizing and reporting forensic cases. However, in cases that involve serious injuries, the medical needs of the person should be countered before the forensic process. In this regard, while priority is given to medical response by healthcare personnel in cases such as traffic accidents, sharp object injuries, and gunshot wounds, this issue can sometimes be overlooked in forensic cases of sexual nature. In a forensic case, especially in cases of sexual abuse, inadequate response or hesitation to intervene in a patient, "perhaps out of fear of punishment if evidence is lost" can jeopardize the patient and healthcare professionals.

Since suspected sexual assault cases require more expertise than other forensic cases and are often avoided by healthcare personnel, referrals without adequate evaluation can lead to significant deficiencies. In the literature, it is stated that incomplete, superficial, and inaccurate medical history taking in cases of suspected sexual assault can incur significant damage to the forensic process (6). In genital injuries which have been caused without sexual assault, the patient may give an inadequate history as a result of embarrassment and shyness, and therefore the physician needs to take this into consideration and approach the patient with empathy and take a full history.

Genital injuries are rarely encountered in emergency room admissions. Some of these injuries are associated with sexual activity. However, when taking an initial history in such cases, detailed questions should be asked to obtain information about sexual activity, and sexual toys or other foreign objects should not be forgotten (7). Injuries incurred in the context of sexual acts are frequently encountered in males and in the rectal-anal region (8). However, the first question to be excluded in detecting an anal or intravaginal foreign body due to sexual curiosity or accident is the exposure to sexual abuse.

Our patient presented with a history of accidental vaginal injury during masturbation. It has been reported in the literature that even minor trauma can cause significant blood loss since the genital area is anatomically one of the areas with a high blood supply (9). Taking an inadequate anamnesis with the thought that the patient could be a victim of sexual assault, refraining from requesting examinations and consultations, and referring the patient to the CMC is considered to be a medically incomplete evaluation. In emergency treatment, the physician is expected to fulfill his/her medical duty systematically in a short time and save lives, as well as refrain from compromising his/her legal responsibilities and comply fully with the rules of law. Although the case is a forensic case and should be referred to the CMC, the priority is to control the bleeding.

DOI: 10.33706/jemcr.1421495
Journal of emergency medicine case reports. 2024;15(1): 26-28

Another point that needs to be clarified within the scope of our study is that a genital examination is not carried out only in a forensic context. Genital examinations can be performed in pregnancy follow-up and gynecological ailments after consent is obtained by the responsible physicians. It should be kept in mind that genital injuries can also occur due to any trauma (such as traffic accidents, or falls) (9). Whether these injuries are forensic or not can be determined primarily on the basis of a genital examination and detailed anamnesis, which should be performed for medical reasons. Nowadays, the fact that judicial processes are rather formidable for physicians causes genital examinations that should be performed for medical purposes to be ignored.

Adolescence is a period when the awareness of sexual identity characteristics becomes evident in children and self-care for sexual interaction increases. Curiosity about sex starts in children aged 14-15 years initiating a tendency to establish sensual contact with the opposite sex. Sex education contributes significantly to the development of sexual behavior, the establishment of a healthy sexual life, and the acquisition of a social-sexual role (10). In our case the victim could not tell her mother about the incident because she was afraid. Considering such situations, the importance of providing proper sexuality education, especially during adolescence when sexual identity becomes clear, is also seen in our case example.

Conclusion

The emergency department is considered one of the areas in hospitals with the highest workload and stress. This stress can cause disruptions from time to time. However, the duty and accepted responsibility of medical professionals requires that the emergency physician delivers the most effective treatment to emergency cases. As well as judicial notification process in severe traumatic forensic cases starts after the treatment is organized, for forensic outpatient cases with serious injuries the initial action also must be planning the treatment and synchronously reporting the situation to the judicial authorities due to the risk of evidence loss. As in our case, internal organ or large vessel injuries that may occur in forensic sexual cases without any signs of severe trauma with an external examination can have severe consequences, and therefore the primary bleeding agent should be identified and treated. Our study aims to contribute to this awareness.

Another result of our study is about sex education. Sexuality is a biological condition and as a result of the lack of education that should be provided by competent people on the subject, especially adolescents can make erroneous decisions and mistakes with what they learn from social media and peers. In this respect; the case, which came with a serious injury, may serve as an example of the necessity of sex education in society.

References

1. Koç S, Celasun B, Yorulmaz C, Tuğcu H, Baykal B, Ceylan S. Acil servis hizmetine katılan hekimlerin, acil olgularda hekim sorumluluğu ve adli tıp sorunları konusundaki bilgi ve düşünceleri. Gülhane Tıp Dergisi. 2003;45(2):175-179. AccessedSeptember 27, 2023.
2. Özorhan EY. OBSTETRİK ACİLLERDE ADLİ VAKALAR. Kocatepe Tıp Dergisi. Published online July 3, 2017:119-129. doi:10.18229/kocatepetip.344755
3. İkiişik H, Ari A, Kirlangiç M, et al. Bir Üniversite Hastanesi Sağlık Çalışanlarının Çocuk İstismarına Yaklaşımları Ve Çocuk İzlem Merkezleri Hakkındaki Farkındalıklarının Değerlendirilmesi. Akd Med J. 2022;8(3):263-269. doi:10.53394/akd.1059052
4. Amiri H, Vahdati SS, Ghodrat N, Sohrabi A, Marzabadi LR, Garadaghı A. EmergencyMedicinePhysicians can Manageall Emergent Procedures in the Emergency Department. Turk J EmergMed. 2009;9(3):101-104. AccessedSeptember 30, 2023
5. Asci O, Hazar G, Sercan I. Theapproach of prehospital healthcare personnel working at emergency stations towards forensic cases. Turkish Journal of Emergency Medicine. 2015;15(3):131-135. doi:10.1016/j.tjem.2015.11.007
6. Tozzo P, Ponzano E, Spigarolo G, Nespeca P, Caenazzo L. Collecting sexual assault history and forensic evidence from adult women in the emergency department: a retrospective study. BMC Health Serv Res. 2018;18(1):383. doi:10.1186/s12913-018-3205-8
7. Senthilkumaran S, Jena NN, Jayaraman S, Benita F, Thirumalaikolundusubramanian P. Post coital hemoperitoneum: Thepain of love. Turkish Journal of Emergency Medicine. 2018;18(2):80-81. doi:10.1016/j.tjem.2018.03.002
8. Schellenberg M, Brown CVR, Trust MD, et al. Rectal Injury After Foreign Body Insertion: Secondary Analysis Fromthe AAST Contemporary Management of Rectal Injuries Study Group. Journal of Surgical Research. 2020;247:541-546. doi:10.1016/j.jss.2019.09.048
9. Muram D, Levitt CJ, Frasier LD, Simmons KJ, Merritt DF. Genital Injuries. Journal of Pediatricand Adolescent Gynecology. 2003;16(3):149-155. doi:10.1016/S1083-3188(03)00042-1
10. Yakut Hİ, Özgü BS. ADOLESANLARDA CİNSEL EĞİTİM. JGON. 2013;10(39):1633-1635. Accessed October 2, 2023. https://dergipark.org.tr/en/pub/jgon/issue/51912/676208

Case Report

Journal of Emergency Medicine Case Reports

Cornelia De Lange Syndrome with Left Heart Hypoplasia: A Case Study

Elif Sena Ozcan[1], Sevim Yener[2], Gulam Hekimoglu[3], Nurullah Yucel[4], Zekeriya Ilce[5]

[1]Department of Anatomy, School of Medicine, University of Altınbas, Istanbul, Türkiye.

[2]Pediatric Urology Clinic, Umraniye Training and Research Hospital, University of Health Sciences, Istanbul, Türkiye.

[3]Department of Histology and Embryology, Hamidiye International School of Medicine, University of Health Sciences, Istanbul, Türkiye.

[4]Department of Anatomy, Hamidiye International School of Medicine, University of Health Sciences, Istanbul, Türkiye.

[5]Pediatric Surgery Clinic, Umraniye Training and Research Hospital, University of Health Sciences, Istanbul, Türkiye.

Abstract

Cornelia de Lange syndrome (CdLS) is characterized by slow growth that can lead to short stature. Despite mutations in the NIPBL, RAD21, or SMC3 genes, CdLS is thought to be inherited in an autosomal dominant manner. Findings include intellectual disability bone abnormalities in the upper extremities and distinct facial features. It has similar characteristics to autism spectrum disorder, which is a developmental condition that affects communication and social interaction. The physical and clinical findings of a one-and-a-half-year-old girl patient diagnosed with CdLS were reported. In addition to NIPBL gene mutation, atrioventricular septal defect (AVSD), an overriding aorta, and a hypoplastic left heart (HLH) were observed in our case. This study revealed the patient's physical and clinical findings consistent with the diagnosis of CdLS. Additionally emphasized HLH. The importance of performing corrective surgery immediately following the evaluation of congenital heart diseases in CdLS patients can be emphasized..

Keywords: Cornelia de Lange syndrome, congenital heart diseases, overriding aorta, HLH

Introduction

Cornelia de Lange syndrome is characterized by slow growth that can lead to short stature before or after birth. Findings include moderate to severe intellectual disability, and bone abnormalities in the upper extremities. Different facial features such as arched eyebrows (synophrys) meeting in the middle, long eyelashes, low-set ears, small and widely spaced teeth, and a small and upturned nose are also observed. It has similar characteristics to autism spectrum disorder, which is a developmental condition that affects communication and social interaction (1).

In addition, excessive body hair (hypertrichosis), an unusually small head (microcephaly), hearing loss, and digestive problems may occur. Some cases of this condition are born with an opening in the roof of the mouth, called a cleft palate. Seizures, heart defects, and eye problems have also been reported in cases of this disorder (1).

Cornelia de Lange syndrome occurs as a result of mutations in the NIPBL, RAD21, or SMC3 genes, however, it is thought to be inherited in an autosomal dominant manner. Autosomal dominant inheritance means that the presence of one changed chromosome in the cells is sufficient for the disease to occur (2).

This study aimed to reveal the physical and clinical findings of the patient diagnosed with Cornelia de Lange syndrome.

Case Report

A female baby was born by cesarean section (C/S) on March 9, 2022, weighing 2130 g, 43 cm tall, with a head circumference of 28 cm, and an APGAR score of 7/8. She was born at 37 weeks 4 days and has 0 Rh+ blood group. The other family members were all healthy. There was no consanguineous marriage. The double Screening Test result showed cystic hygroma. Herfree fetal DNA result was low risk. She was placed under a radiant warmer as soon as she was born, and she had a peak heart rate (HRV) of more than 100/min, free-flow oxygen was started because her breathing was irregular. Her general condition was stable during follow-up. Corrective surgery for a hypoplastic left heart (HLH) was performed. She was fed with formula. There was motor retardation.

The patient was diagnosed with Cornelia Delange syndrome. Her general condition was good, consciousness

Corresponding Author: Gulam Hekimoglu
e-mail: gulam.hekimoglu@sbu.edu.tr
Received: 23.11.2023 • **Revision:** 16.01.2024 • **Accepted:** 15.02.2024
DOI: 10.33706/jemcr.1395190

Cite this article as: Ozcan ES, Yener S, Hekimoglu G, Yucel N, Ilce Z. Cornelia De Lange Syndrome with left heart hypoplasia: a case study. Journal of Emergency Medicine Case Reports. 2024;15(1): 29-31

DOI: 10.33706/jemcr.1395190
Journal of emergency medicine case reports. 2024;15(1): 29-31

was clear, color was natural, and turgor and tone were normal. There was no problem with vision. Heterozygous variants of unknown clinical significance have been detected in the NIPBL gene. Dysmorphia was present and there was no weight gain. It was followed by nephrology. A consultation was requested from pediatric gastroenterology to regulate weight-gaining nutrition.

Antenatal intrauterine development delay and oligohydramnios were present. It was observed that the baby had a single umbilical artery. Atrioventricular Septal Defect (AVSD) and Overriding Aorta were present. The left side of the heart was hypoplastic compared to the right. Ventricular Septal Defect (VSD), and large mitral atresia or hypoplasia in the ultrasonographic (USG) imaging in the patient diagnosed with Unstable AVSD. Double Outlet Right Ventricle was determined because both large vessels originate from the right ventricle (Figure 1A).

No epileptogenic potential was detected as a result of sleep electroencephalography (EEG), where age-appropriate maturation was observed. The general condition of the patient was moderate, consciousness was clear and active. A short forehead and low-set ears were observed. Doublehemi thoraxes were ventilated equally. Coarse rales and tachypnea were observed in the respiratory system. In the cardiovascular system, S1, and S2 were normal, and the heart was rhythmic. No additional sound was heard, there was a murmur. The control of femoral artery pulses (AFN) was positive. The abdomen was comfortable in the gastrointestinal system. There was no rebound defense, hepatosplenomegaly, or dysmorphic findings. The liver and spleen were nonpalpable. Bowel sounds were normoactive. There was no mass. Extremities were natural. There was a sacral dimple. The fingers were short and had simian lines. There was a location anomaly in the lower extremities. In the neurological examination, newborn reflexes were taken, and the tone was normal (Figure 1B).

Atrioventricular (AV) valve insufficiency (mild-moderate), Patent Ductus Arteriosus (PDA) and Patent Foramen Ovale (PFO) were present. Pulmonary artery band (PAB) application was performed at 2-3 weeks of clinical follow-up. Infarction has been started and GLENN surgery would be planned.

In neck USG examination, thyroid gland sizes were within normal limits. Thyroid gland parenchyma was homogeneous. No nodule was detected. Lymphadenopathy (LAP) was not detected in the bilateral neck lymphatic chain. The size and echo of bilateral submandibular and parotid glands were normal.

The evaluation was suboptimal since the entire abdominal USG was performed with a bedside mobile Ultrasound (US) device in the intensive care unit. The size of the liver was within normal limits. Liver contours were smooth and marginal angles were sharp. Parenchymal echo was homogeneous. No solid or cystic mass lesion was observed in the liver. The gallbladder

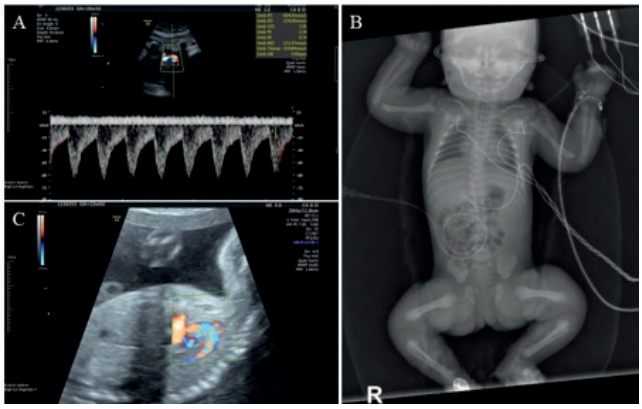

Figure 1. Echocardiography, X-ray, and prenatal ultrasonography of the patient were taken before and after birth. A) Atrioventricular Septal Defect (AVSD) was detected in Echocardiography. B) Abnormal extremities were shown in vertebra, lower and upper extremity radiography. C)Uterus didelphys anomaly was observed in USG.

was contracted. No dilatation was observed in the intrahepatic bile ducts. Both kidneys' size and localization were normal. Kidney contours were smooth and cortex thickness was natural. A corticomedullary distinction could be made clearly in both kidneys. No visible calculus or a dilated renal pelvis and calyces were observed in both kidneys. Grade 1 pelviectasis was observed in the left kidney. Pancreas and midline structures could not be evaluated due to intense gas superposition. Spleen size was within normal limits. Its echo structure was homogeneous. The bladderlumen was homogeneous, and no pathological state was observed. Uterus didelphys anomaly was observed. The right ovary could not be evaluated due to gas, and the left ovary appearednatural. Parenchymal organ evaluation could not be performed due to extensive dressing materials in the abdomen. Pelvic minimal free fluid was detected in the abdomen. Gallbladder sludge was observed. Fluid reaching a depth of 2cm was observed in all quadrants of the abdomen (Figure 1C).

The patient's Papanicolaou smear (PAP) result was HPV subtype 90, 92. The cornea and lens were transparent. Papilla, macula, and vascular structures were natural.

During the checks, the general condition was found to be good. The Glasgow Coma Scale (GCS) score was determined as 15. The skin, oropharynx, tonsils, and bilateral tympanic membrane are natural. Direct-indirect light reflex was positive. There was no sign of meningeal irritation.

Discussion

Our case reported a novel cardiac finding (AVSD, Overriding Aorta, and HLH) associated with CdLS. According to several studies, the most common defects were pulmonary stenosis and ventricular and atrial wall defects, followed by aortic coarctation, bicuspid aortic valve, hypertrophic cardiomyopathy, and others (3,4). The presence of heart disease is associated with a higher need for neonatal hospitalization and a mortality rate that triples that of non-

cardiac patients, with 19.2% of cases requiring cardiac surgical correction (3).

We found in our case, the heterozygous variants of unknown clinical significance in the NIPBL gene. Gillis et al. reported NIPBL mutations in a large well-characterized cohort of individuals with sporadic or familial CdLS (2). Another study supported the idea that the NIPBL gene was mutated in individuals with CdLS (5). Avagliano et al. revealed that many genes were associated with chromatinopathies classified as "Cornelia de Lange Syndrome-like". It is known that the phenotype of these patients becomes less recognizable, overlapping with features characteristic of other syndromes caused by genetic variants affecting different regulators of chromatin structure and function. Therefore, the diagnosis of Cornelia de Lange syndrome can be difficult due to the occasional discrepancy between the unexpected molecular diagnosis and clinical evaluation (6).

In the present study, we found no mental retardation in our case. However, Berney et al. used a mailed questionnaire to examine 49 people with Cornelia de Lange syndrome to determine behavioral phenotype. Ages range from early childhood to adulthood, with the degree of mental retardation ranging from borderline (10%), mild (8%), moderate (18%), severe (20%), and very profound (43%). A wide range of symptoms occurred frequently, particularly hyperactivity (40%), self-harm (44%), daily aggression (49%), and sleep disturbance (55%). These were closely related to the presence of autistic-like syndrome and the degree of mental retardation. The frequency and severity of the disorder, which continues after childhood, were important when planning the amount and duration of support needed by parents (7).

Moreover, we detected no motor retardation in the present case. This was not in accordance with a case study that was reported recently. Deardorff et al. reported a wide range of findings, from mild to severe CdLS. Severe CdLS was characterized by distinctive facial features, growth restriction, hypertrichosis, and upper limb reduction defects ranging from thin phalanx abnormalities to oligodactyly. Craniofacial features include synopsis, highly arched and/or thick eyebrows, long eyelashes, short nasal bridge with forward-facing nostrils, small, widely spaced teeth, and microcephaly. Individuals with a milder phenotype have less severe growth, cognitive, and limb involvement but often have facial features consistent with CdLS. Other common findings include hearing loss, myopia, and cryptorchidism or hypoplastic genital organs (8).

In addition, no digestive system abnormalities were found in our patient. It was supported by Husain et al. that a variety of gastrointestinal anomalies have been described, including malrotation, colonic duplication, and non-fixation of the colon (9). In the Husain et al. study, two patients with CdLS were admitted to the hospital due to acute distal intestinal obstruction. In both cases, cecal volvulus was observed with necrosis in the terminal ileum, cecum, and ascending colon secondary to non-fixation of the colon during emergency laparotomy (9). However, in our case, cystic hygroma, oligohydramnios, uterus didelphys anomaly, and a single umbilical artery were detected.

Conclusion

The findings of this study provide valuable insights into the physical and clinical manifestations that align with the diagnosis of CdLS. Furthermore, a noteworthy emphasis is placed on the recognition of HLH in the context of CdLS. These findings underscore the significance of promptly conducting corrective surgical interventions upon the identification of congenital heart diseases during the assessment of CdLS patients. Meanwhile, parents of children with CdLS should be counseled about the possibility of intestinal obstruction resulting from cecal volvulus. This awareness may lead to earlier identification and treatment of this potentially fatal gastrointestinal tract anomaly. The implications of these revelations suggest that early surgical intervention can play a crucial role in optimizing patient outcomes and managing associated health complications. This underscores the importance of a comprehensive and timely approach to the medical care of individuals with CdLS.

References

1. DeScipio C, Kaur M, Yaeger D, Innis JW, Spinner NB, Jackson LG, et al. Chromosome rearrangements in Cornelia de Lange syndrome (CdLS): report of a der (3) t (3; 12) (p25. 3; p13. 3) in two half sibs with features of CdLS and review of reported CdLS cases with chromosome rearrangements. Am J Med Genet Part A2005; 137(3): 276-82.
2. Gillis LA, McCallum J, Kaur M, DeScipio C, Yaeger D, Mariani A, et al. NIPBL mutational analysis in 120 individuals with Cornelia de Lange syndrome and evaluation of genotype–phenotype correlations. Am J Hum Genet 2004; 75: 610–23.
3. Ayerza Casas A, PuisacUriol B, Teresa Rodrigo ME, Hernández Marcos M, Ramos Fuentes FJ, Pie Juste J. Cornelia de Lange syndrome: Congenital heart disease in 149 patients. Med Clin (Barc). 2017;149(7):300-2.
4. Chatfield KC, Schrier SA, Li J, Clark D, Kaur M, Kline AD, et al. Congenital heart disease in Cornelia de Lange syndrome: phenotype and genotype analysis. Am J Med Genet A. 2012;158a(10):2499-505.
5. Tonkin ET, Wang TJ, Lisgo S, Bamshad MJ, Strachan T. NIPBL, encoding a homolog of fungal Scc2-type sister chromatid cohesion proteins and fly Nipped-B, is mutated in Cornelia de Lange syndrome. Nat Genet2004; 36(6): 636-41.
6. Avagliano L, Parenti I, Grazioli P, Di Fede E, Parodi C, Mariani M, et al. Chromatinopathies: A focus on Cornelia de Lange syndrome. Clin Genet 2020; 97(1): 3-11.
7. Berney TP, Ireland M, Burn J. Behavioural phenotype of Cornelia de Lange syndrome. Arch DisChild 1999; 81(4): 333-6.
8. Deardorff MA, Noon SE, Krantz ID. Cornelia de Lange syndrome.2020.
9. Husain K, Fitzgerald P, Lau G. Cecal volvulus in the Cornelia de Lange syndrome. J Pediatr Surg1994; 29(9): 1245-7.