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Contents

Case Report

Journal of Emergency Medicine Case Reports

Stewart-Treves Syndrome: An Interesting Case of Angiosarcoma after Radical Mastectomy

Cosmin Florescu[1], MD, MA, MPH and Christine Ahn[2], MD
[1]Department of Emergency Medicine, Eisenhower Medical Center, Rancho Mirage, California, USA
[2]Department of Emergency Medicine, Stony Brook University Hospital, Stony Brook, New York, USA

Abstract

Introduction: This article discusses Stewart Treves Syndrome, a rare form of angiosarcoma that occurs with chronic lymphedema after radical mastectomy with lymph node dissection. STS presents with purplish cutaneous nodules or reddish blue macules that enlarge. The mortality rate is high and survival is low.

Case Report: A 68 year old female with history of breast cancer status post radical mastectomy with lymph node dissection, radiation and chemotherapy six years prior was evaluated in the Emergency Department for bleeding from her left upper arm lesion. The patient required resuscitation and was subsequently admitted to the ICU. The following day, she suffered a stroke and, after discussion with her family, she was placed on comfort care measures. She died three days after admission.

Conclusion: Emergency physicians should be aware of this rare, but highly lethal, malignant syndrome. A patient with history of breast cancer and radiation therapy who presents with an enlarging red-purple plaque should be admitted or referred to oncology or plastic surgery for immediate biopsy and discussion with family and palliative care specialists regarding goals of care.

Key words: Stewart Treves Syndrome, angiosarcoma, lymphagiosarcoma, chronic lymphedema

Introduction

This article discusses Stewart Treves Syndrome (STS), a rare disease that presents with purplish cutaneous nodules or reddish blue macules that enlarge. The mortality rate is high and survival is low. Background research does not reveal any articles within the Emergency Medicine literature regarding STS. The purpose of this case report is to introduce for emergency medicine physicians the highly lethal form of angiosarcoma that can arise in patients after radical mastectomy with lymph node dissection or those with chronic lymphedema.

Case Report

A 68 year old female with history of hypertension, hyperlipidemia, left MCA aneurysm diagnosed one month before, obesity, left breast cancer status post modified axillary lymph node dissection, radiation and chemotherapy six years prior who presented to the Emergency Department for evaluation of bleeding from her left upper extremity lesion. She reported burning pain and bleeding from the left arm lesion, fatigue, lightheadedness, and shortness of breath. Two months prior to presentation, the patient injured her arm while cleaning a litter box and noticed a small bruise that had enlarged since then. Nine days prior, she was evaluated by plastic surgery and had biopsy of the lesion, which showed atypical vascular neoplasm consistent with angiosarcoma.

In ED triage, patient was hypotensive to 86/57 and sent to the Critical Care area for evaluation. The remaining vital signs were Tmax 36.8, HR 102, RR 16, and O2 saturation 96% on room air. On physical exam, the patient had a 12cm x 8cm x 4cm red violaceous lesion on the left upper arm. She was resting comfortably in bed in no acute distress.

Initial ED labs were significant for lactic acid 2.5, BNP 11201, ESR 43, CRP 5.9, potassium 3.4, glucose 262, Mg 1.5, Ca 8.1, troponin 0.38, and anion gap 20. Hemoglobin decreased from 12.9 two months prior to 8.9. Chest x-ray showed pulmonary vascular congestion and left pleural effusion. CT pulmonary angiogram was negative for pulmonary embolism with extensively calcified, but normal caliber, aorta. CT chest showed a 2.3cm x 1.7cm x 2.7cm enhancing fluid collection within the left anterior chest wall and diffuse skin thickening of the left breast.

Despite 2 liters of IV fluids, the patient was persistently hypotensive with SBP in the 70s. The ED team placed a midline catheter and arterial line, and the patient was subsequently started on norepinephrine and vasopressin with im-

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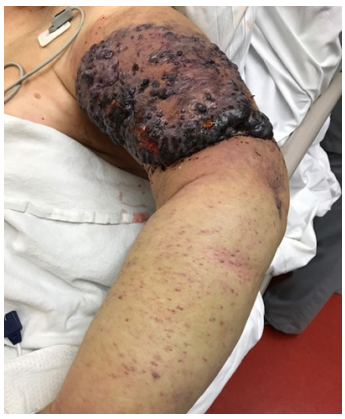

Figure 1a: Patient's lesion: note new petechiae on forearm

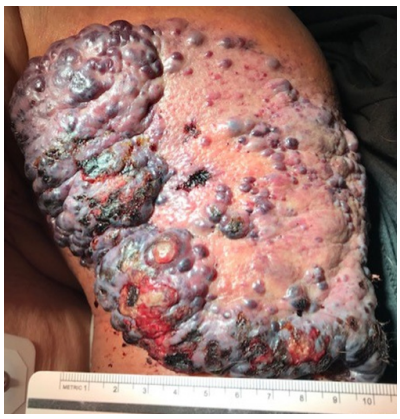

Figure 1b: Patient's lesion: width of 12cm: note draining and bleeding areas

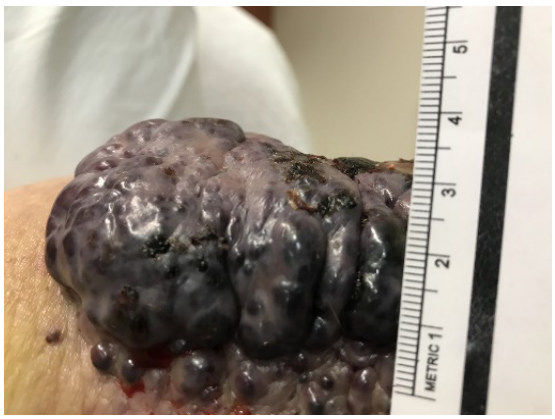

Figure 1c: Patient's lesion: height of 4cm: note dark purple blue characteristics

provement in SBP and MAP. Additionally, over the course of three hours, the patient's left forearm started developing petechiae and she became febrile. Antibiotic coverage with cefepime and vancomycin was started due to concern for septic shock. Plastic surgery and ICU were consulted and the patient was admitted to the ICU for further management.

After admission to the ICU, our patient's troponins started to increase, so cardiology was consulted. Transthoracic echocardiogram showed EF 22% (previous TTE six years prior to presentation showed EF 64%). The following day, the patient suffered an acute stroke, confirmed on CT and MRI, and the patient required intubation. Neurosurgery evaluated the patient and reviewed imaging, which showed the left MCA aneurysm had enlarged over the past month. However, due to patient's clinical condition, worsening multi-organ system failure, and poor prognosis in the setting of STS, the patient's family elected to pursue palliative comfort measures. The patient died three days after presenting to the ED and admission to the ICU.

Discussion

Stewart-Treves Syndrome is lymphangiosarcoma seen in patients after breast cancer treatment with radiation and lymph-node dissection. The eponymous syndrome was first described by Drs. Stewart and Treves in 1948 in a case series of six patients[1,2]. There are approximately 400 cases reported worldwide in the literature[3]. Lymphangiosarcoma is one of the rarest and most aggressive forms of soft tissue neoplasms[4]. It is therefore important for physicians to consider this syndrome in patients with a history of breast cancer with radiation and lymph-node dissection who present with limb edema.

The incidence of STS in patients who survive more than 5 years after radical mastectomy with axillary node dissection is between 0.07% to 0.45%[2]. The mean time of onset is approximately 10-11 years after radical mastectomy. The mean age of presentation is 60 years and the highest incidence occurs in patients between 50 and 70 years old[5]. After diagnosis, survival is low, typically 8-15 months[5].

The pathophysiology of STS is complex, and research has elucidated some of the process by which a patient can develop angiosarcoma after lymphedema. Sarcomas of the soft tissue account for less than 1% of all cancers, and angiosarcoma is a subset that is particularly aggressive[2] with a high rate of local recurrence and potential for metastasis[6]. Angiosarcoma includes malignant sarcomas originating from either lymphatic (lymphangiosarcoma) or capillary endothelium (hemangiosarcoma), although the clinical differences have not been formalized due to the rarity of both tumors. The cutaneous sub-type accounts for 50-60% of cases[2]. The etiologies of cutaneous angiosarcoma are idiopathic, post radiation treatment, and chronic lymphedema after mastectomy (also known as STS)[7]. The exact mechanism by which Stewart-Treves syndrome arises is currently unclear, although research has suggested systemic carcinogenic factors and neoplastic transportation that arises in edematous tissue as collateral circulation develops after radiation therapy[2].

There are multiple risk factors for the development of STS. The most important cause of STS is congenital or acquired chronic lymphedema[8]. While the majority of angiosarcomas are idiopathic, notable risk factors include exposure to ionizing radiation and chronic lymphedema[2]. In approximately 90% of cases, the angiosarcoma is associated with lymphedema after mastectomy[2]. Additional risk factors include chronic infections, chronic venous stasis, morbid obesity, malignant obstruction, surgical procedures that disrupt lymphatic flow, and hereditary lymphatic malformations such as Noonan syndrome and Milroy disease[2].

There are no pathognomonic physical exam findings for STS. There are some common characteristics that emergency medicine physicians should consider. Cutaneous angio-

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sarcoma appears as a "spreading bruise" with subsequent edema, ulceration, and hemorrhage[2]. The lesions of angiosarcoma can be purplish cutaneous nodules or reddish blue macules that enlarge and coalesce[8,6]. Lesions are typically 3-6cm, although if left untreated, they can grow to 20cm or larger and begin to drain[2]. The most common site of metastasis is the lung, and patients may present with pleural effusion, pneumothorax, or pleural disease, although the cancer can also spread to the liver, bone, soft tissue, and lymph nodes[2].

The differential diagnosis includes hemangioma, hemangioblastoma, squamous cell carcinoma, Kaposi sarcoma, anaplastic melanoma, cutaneous telangiectatic metastatic breast disease[2], and venous ulcer of the extremity[7]. Kaposi sarcoma is difficult to distinguish from STS[8]. Kaposi sarcoma is positive for human herpesvirus 8 (HHV-8) and does not have lymphedema as much as Stewart Treves syndrome does[8].

Since STS is so rare, there is no standard treatment[8]. Emergency medicine management of STS has not been described in the literature. As is the case with an undifferentiated patient with a skin lesion, the emergency physician should obtain vital signs and begin resuscitation efforts as needed. A set of labs should include a CBC, BMP, LFTs, inflammatory markers such as lactic acid, ESR, and CRP. An HIV test is warranted if status is unknown. Imaging should be obtained in consultation with specialists, typically hematology-oncology and/or plastic surgery. Evaluation with CT or MRI helps to evaluate the tissue, including lymph node involvement[2]. The mortality rate for STS is high, and as such, most patients will require close observation in a telemetry unit or an intensive care unit. Our patient required hemodynamic support with vasopressors. Placing a central line or midline, if available, and arterial line are prudent measures in a hypotensive patient suspected of STS. The health care team should engage the patient and family early to discuss goals of care if the diagnosis of STS is already known. It is important to consult specialists early, as evaluation requires immediate biopsy. Inpatient management includes surgery, radiation therapy, and chemotherapy[2-4].

Prognosis of STS is grim, with poor long-term survival. The median survival is 7-19 months[2] and mean survival is 19-31 months[8]. The 3 year survival rate is 55% and by 5-years, survival decreases to 8.5-13.6%[2,3]. Between 20-45% of patients have metastatic disease when they present to a health care provider[2]. Survival outcomes are significantly worse with high grade tumors and tumor size greater than 5cm[9]. Adverse predictors of survival include metastasis at presentation, visceral/deep soft tissue location, tumor size greater than 5cm, tumor necrosis, and absence of surgical excision[10]. Good prognostic factors include age less than 50, localized tumor stage, and tumor located on the trunk rather than the extremities[2].

Conclusion

Emergency physicians should be aware of Stewart Treves Syndrome, a rare, but highly lethal, syndrome. A patient with a history of breast cancer and radiation therapy who presents with an enlarging red-purple plaque should be admitted or referred for rapid follow up with surgical oncology or plastic surgery for immediate biopsy and early discussion with the patient regarding goals of care.

Conflict of Interest

The authors declared no conflict of interest.

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Author Contributions

Concept – CF, CA; Design – CF, CA; Supervision – CF, CA; Resource – CF, CA; Materials – CF, CA; Data Collection and/or Processing – CF, CA; Analysis and/or Interpretation – CF, CA; Literature Search – CF, CA; Writing – CF, CA; Critical Reviews – CF, CA

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Case Report

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Be Aware of Critical Drugs in Emergency Departments: An Extreme İatrogenic İnsulin Overdose via Subcutaneous and İntramuscular Routes

Figen ÇOŞKUN[1], Sevilay VURAL[2], Oğuz EROĞLU[3], Ertan CÖMERTPAY[3], Şenay Arıkan DURMAZ[4]
[1]Dokuz Eylül University, Faculty of Medicine, Department of Emergency Medicine
[2]Yozgat Bozok University, Faculty of Medicine, Department of Emergency Medicine
[3]Kırıkkale University, Faculty of Medicine, Department of Emergency Medicine
[4]Kırıkkale University, Faculty of Medicine, Department of Endocrinolgy

Abstract

Introduction: Insulin is a highly used parenteral medication in emergency departments. Although most severe insulin overdoses occur as suicide attempts, medication errors can be the reason. We aimed to highlight the potential medication errors in emergency departments due to the poor control of critical drugs like insulin and the similarities between the brand names of drugs, as we experienced during this case.

Case Report: We present a 75-year-old diabetic woman with an extreme insulin overdose. A total of 3000 UI of insulin was administered by subcutaneous and intramuscular routes. She developed typical and atypical episodes of hypoglycemia requiring intravenous dextrose, a high-calorie diet, and glucagon administration. Almost all of the classic side effects of glucagon occurred during her intensive care unit follow-up. She recovered without any sequela or recurrence of hypoglycemia at the end of 5 days of admission.

Conclusion: Insulin overdose can be a life-threatening condition by causing hypoglycemia. Albeit rare, insulin overdose can occur as a medication error in hospitals. To prevent such incidents for emergency departments, the medication errors should be objectively laid out, and proactive strategies should be integrated without adversely affecting acute care.

Keywords: insulin, overdose, misadministration, critical drugs, emergency department, medication error

Introduction

The term "medication error" can be described as any preventable event that may cause or lead to inappropriate medication use or patient harm based on The National Coordinating Council for Medication Error Reporting and Prevention. Healthcare professionals, patients, and consumers are potential culprits for this error. Medication errors can occur at any step of the medication-use process, including dosing, dispensing, administrating, and preparation for health care professionals[1]. The most common medication errors are associated with inappropriate usage and dosage of drugs and inappropriate indication selection[2]. Being medical hotpoints where various critical drugs are used frequently in the hustle and bustle, emergency departments (EDs) are very susceptible to these incidents[3]. Safe medication applications can only be achieved in the presence of well-planned management and attentive staff.

The investigations on medication errors have discovered some critical topics like awareness of confused drugs and control of high-risk drugs. The confused drugs, including look-alike, sound-alike (LASA) name pairs, are a critical group for medication errors[4]. LASA covers medications with visual similarities in physical appearance, packaging, and/or name (in the form of spelling and/or phonetics). One of the best examples is the drugs named Losec® (omeprazole) and Lasix® (furosemide), widely used in many countries. Potentially severe results are not surprising when these two are mixed[5]. Another aspect of medication errors is associated with high-risk drugs. The list of high-alert medications in acute care settings of The Institute for Safe Medication Practices (ISMP) covers the drugs bearing a heightened risk of causing significant patient harm. ISMP underlines the importance of and warns about all forms of insulin in their 2018 list.

A problem can only be solved after it is defined and understood comprehensively. It is only possible with the systematic reporting of medication errors in healthcare settings with a nonpunitive approach. The concept of "medication error" has been covered in the literature with an increasing trend since the 1970s[6]. Since then, some strategies were suggested to prevent iatrogenic medication errors, includ-

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ing medication error analysis, computerized provider-order entry systems, automated dispensing cabinets, bar-coding systems, medication reconciliation, standardizing medication-use processes, education, and emergency-medicine clinical pharmacists[7].

Herein, we present a massive iatrogenic insulin overdose case. We believe that this case we witnessed is a vivid example of medication errors and shows the medication error susceptibility of emergency departments.

Case Report

A 75-year-old diabetic woman was admitted to the ED because of a dog bite on the dorsal side of her right wrist. Post-exposure prophylaxis (PEP) regimen for Rabies (administration of immune globulin (Ig), given only once, and a series of five dose rabies vaccinations) was planned. A junior resident took out the Ig vials from the vaccine refrigerator. The half dose of PEP Ig (calculated totally as 3000 UI; 40 IU/kg, body weight: 75 kg) was injected into and around the wound. The remaining dose was administered intramuscularly into the deltoid muscle. The administrations were done by an intern. It was noticed immediately after the standard control procedure of matching vial labels to the patient's file that regular insulin (Humulin R®) was used accidentally instead of Rabies Ig.

The close monitoring of the patient was started instantly. Her GCS was 15, with finger-stick glucose of 116 mg/dl. A central venous catheter was placed, and 10% dextrose infusion with a rate of 250 cc/h and 20 mEq/L/h KCl were initiated. Baseline blood samples and electrocardiogram were in the normal range. The patient was admitted to the intensive care unit (ICU). The first measured blood glucose and potassium levels were 207 mg/dl and 4.2 mEq/L, respectively. The blood insulin level was measured 1000 uU/ml at 2nd hour after the insulin injection. An individualized oral diet program (1600 kcal/day) containing high levels of glucose, potassium, magnesium, and phosphate was initiated and given hourly manner. Due to a sudden drop of her blood glucose to 79 mg/dl approximately at the 4th hour, glucagon 1 mg was applied subcutaneously, and 30% dextrose infusion was given. During the 7th minute of glucagon injection, the patient had nausea and vomiting episodes. No significant heart rate or blood pressure changes were noted. The glucose level increased within 15 minutes. An additional 1 mg iv glucagon administration with 30% dextrose was required due to the second drop of glucose (70 mg/dl) at the 7th hour after the first glucagon injection. No additional side effects were noted during glucose monitoring (**Table 1**). No additional medical treatment like steroids was needed. A stable blood glucose level was achieved following the end of the first 24 hours.

The patient was fully conscious and able to take oral diet during the whole ICU follow-up. The patient was discharged to home after 5 days of hospitalization (2 days in ICU and 3 days in the ward) with full recovery.

Discussion

Accidental and suicidal intakes are the most common causes of fatal insulin overdoses[8]. Insulin is a high-risk drug with its narrow therapeutic index for accidental or intentional overdoses. Johansen and colleagues found that 95% of insulin overdose cases were intentional among 45 case reports and the median total insulin dose was 900 IU (range 26–4800 IU)[9]. Another interesting point of insulin overdose is that it is commonly used by medical staff for suicidal attempts[10]. Our literature search shows several examples of massive insulin overdose. However, our case is one of the highest doses by receiving 3000 IU.

Humulin R® U-100 is human insulin that acts within a short duration. It is expected to affect approximately in 30-

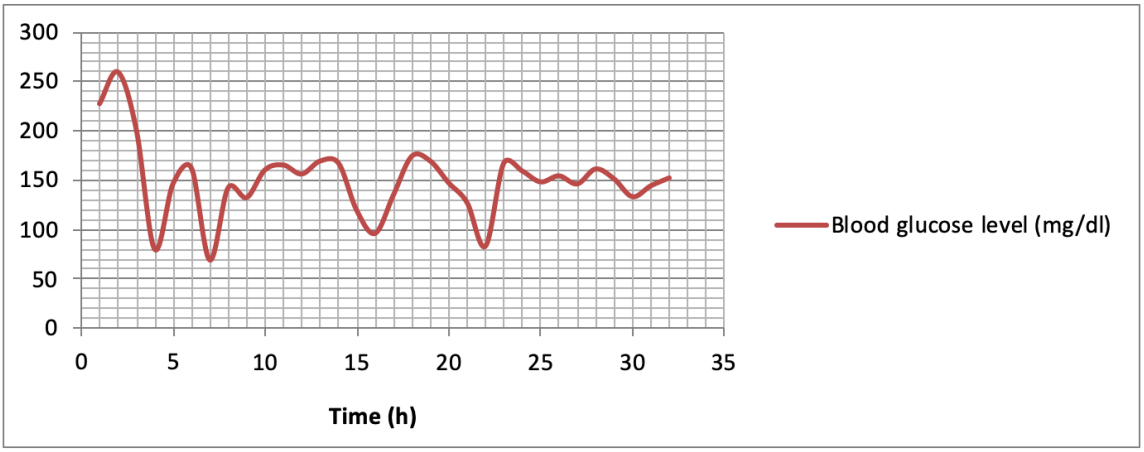

Table 1. The blood glucose levels of the patient by time.

60 minutes following subcutaneous administration. The peak effect starts approximately at 2.5 hours and terminates in 5-8 hours after the incident. However, the half-life of insulin is elongated after massive overdosing, necessitating more prolonged close monitoring of glucose levels[11]. Our patient stayed in ICU for two days in total. While blood glucose levels were irregular on the first day, a stable interval was achieved on the 2nd day. She could only be transferred to the ward on the 3rd day. In our case, dextrose had been started immediately after the misadministration of insulin was noticed. However, mild hypoglycemia (Glucose: 79 mg/dl) was observed with the expected insulin peak time at the 4th hour. Another hypoglycemic episode (Glucose: 70mg/dl) was observed approximately 7 hours after the injection. This unexpected hypoglycemic peak could be attributed to intramuscular administration of 1500 IU insulin. In a report describing the case of an 80-year-old non-diabetic male patient who used 10,000 IU Humulin R® and 6000 IU of Humulin N® subcutaneously for a suicide attempt, intravenous dextrose infusion was needed for 13 days in order to stabilize blood glucose between 100-180 mg/dl. Hyponatremia, hypokalemia, hypophosphatemia, and elevated liver enzymes were also detected during the follow-up[8]. The regarding electrolyte disorders or other possible complications were not seen in our patient. We believe that it might result from variables such as a relatively lower dose of insulin, immediate recognition and management of the medical error, and use of intravenous dextrose infusion and potassium replacement.

Although healthcare providers aim for patients' good under the motto of "*primum non nocere*," they can be the origin of harm. Our main intention was to apply Rabies Ig (Equirab®) prophylaxis to our patient who was bitten by a stray dog. However, regular insulin (Humulin R®), stored in the same fridge in a similar bottle, was applied. Although these drugs seem to have no name similarity, at first sight, Human-Immunoglobulin and Humulin R may cause confusion. The "R" could also be perceived as Rabies. Larger font sizes for brand names and smaller font sizes for nonproprietary names and doses in labels may result in such mistakes (**Figure 1**).

Another possible cause of the error would be the similarity of the containers of the drugs. Containers of both drugs were in the form of flacon bottles. The spelling and the physical form similarities suggest a LASA-like situation in this incident like Losec-Lasix[5]. However, we assumed that the medication error in our case was not limited to LASA for two reasons: First, both drugs were stored in the same refrigerator section. Second, the area where drugs were stored was accessible for all healthcare providers. The management of critical drugs, authority protocols for the accessibility of such drugs, and emergency staff training could prevent these medication errors in future applications. Real-time and post-application controls, recording and reviewing, and implementing technology strategies are as critical as pre-application controls, as Monroe and colleagues suggested[12].

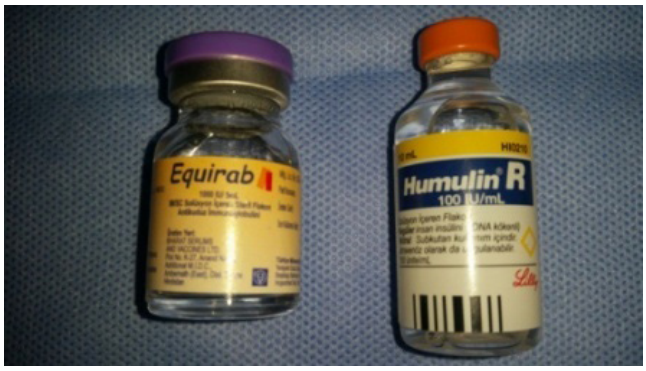

Figure 1. The vials of Rabies Ig (Equirab®) and Regular insulin (Humulin R®).

Medicine should not consider medication errors as random accidental misfortune. They should be treated as a disease, its pathophysiology should be revealed, controlling risk factors should be provided, and preventive medicine approaches should be developed[1]. Voluntary reporting of medication errors should be promoted so that problems could be identified[3]. The voluntary reporting system cannot be expected to be successful if the evaluation system focuses on punishment and affects providers' lives irreparably. The aim should not be to blame the person but to obtain data and develop systemic adjustment strategies [6]. It should also be kept in mind that some medication errors may not be easily noticed. Checklists during the application and verification procedures held by more than one person after the application are useful approaches, as our case exemplifies.

The significant risk factors include special populations exposed to medical harm and the high-risk areas for patient care. The vulnerability of the population to harm and the nature of the provided health care may cause the distributional variation in medication errors. The well-known vulnerable groups include geriatric, pediatric, pregnant groups, and patients with communication problems. Goal-oriented software and warning systems are among the options for drug applications to these particular groups. They are also crucial in terms of drug interactions. The high-risk zones are ICU, oncology units, units with thrombolytic therapy (coronary or stroke units), pre-hospital settings, and emergency departments. Computerized provider-order entry systems, automated dispensing cabinets, bar-coding systems, medication reconciliation, standardizing medication-use processes, education, and emergency-medicine clinical pharmacists are suitable for the aforementioned selected zones [1, 7, 12]. The integration of these systematic changes is likely to be considered unnecessary, tiring, time-consuming, or even prolonging the treatment process for providers and patients. Therefore, it is essential that existing and future systems focus not solely on safety but also to be more user-friendly, practical, and faster.

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Conclusion

The potential medication errors due to the poor control of critical drugs and the similarities between the brand names of drugs used in EDs should be prevented by well-designed medication-use process strategies.

Conflict of interest statement

None of the authors have any conflict to disclose.

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Statement on informed consent

Verbal consent to use this case for publication was obtained from the patient during a routine clinical care encounter, documented in the medical records. This case report was deemed as being appropriate by the IRB for publication purposes as no patient-specific identifiable health information was disclosed.

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Case Report

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Paracetamol Overdose May Cause Transudative Pleural Effusion in Adults

Ilker Akbas[1], Abdullah Osman Kocak[2], Sıbel Guclu Utlu[3],Sinem Doğruyol[4], Zeynep Çakır[2]
[1]Bingöl State Hospital, Bingol, Turkey
[2]Department of Emergency Medicine, Faculty of Medicine, University of Ataturk, Erzurum, Turkey
[3]Department of Emergency Medicine Erzurum Regional Training and Research Hospital, Erzurum, Turkey
[4]Department of Emergency Medicine, Manisa Merkez Efendi State Hospitai, Manisa Turkey

Abstract

Paracetamol is the most widely used and prescribed drug word-wide. It is the most common cause of the poisoning and of the fatality due to the toxic administration throughout the world. A 34-year-old female patient applied to our ED with the complaint of swallowing 33 g of paracetamol. After routine toxicity treatment, on the third day of the hospitalization, dyspnea and pain on the right hemithorax and right flank occurred. Chest X-ray showed blunted right sinus. CT revealed bilateral pleural effusion. With thoracentesis, clear, colorless and odor-free fluid of about 500cc was drained. Laboratory examination of the fluid confirmed it as transudate. We believed pleural effusion is related to high-dose paracetamol intake and it occurred due to decrease in pleural permeability and the consequent decrease of the fluid absorption. In conclusion, high-dose intake of paracetamol might cause transudative pleural effusion as a complication.

Keywords: paracetamol, acetaminophen, over dose, pleural effusion

Introduction

Since its first clinical introduction about 50's in the United States, acetaminophen (paracetamol, N-acetyl-p-aminophenol, APAP) is one of the most widely used drugs in the world as a result of its strong antipyretic, analgesic, low peripheral anti-inflammatory and antiplatelet activity[1, 2]. It is a medication of many of over-the-counter and prescription medications used worldwide. It is highly effective and safe in the recommended doses[2]. Although it is a remarkably safe drug, it is also the most common cause of the poisoning and of the fatality due to the toxic administration throughout the world and in Turkey[3]. Liver and kidney damage after its toxic administration are well-known, but the direct damage in other organs was rarely reported[1, 2, 4].

Our objective with this case report is to present an adult patient, who had pleural effusion after high-dose administration of acetaminophen.

Case Report

A 34-year-old female patient applied to our emergency department (ED) with the complaint of swallowing 66 tablets, each containing 500 mg paracetamol (total 33 g). The patient took the drugs in a suicidal attempt 3 hours before her application. The initial vital signs were within normal range (blood pressure: 111/70 mmHg, pulse: 55 beats/minute, respiratory rate: 8/minute, fever: 36.7°C, oxygen saturation at the fingertip: 98%). Physical examination was normal. After the insertion of the nasogastric tube, gastric lavage was performed and few drug particles were aspirated. Activated charcoal (50 gr) was administered through the nasogastric tube. Afterwards, N-acetylcysteine therapy (a total of 200 mg/kg) was initiated in accordance with the 21-hour IV administration protocol. There were no pathological findings in the whole blood count, liver functions and bleeding time tests. The patient was hospitalized in the intensive care unit (ICU) of our ED.

On the third day of the hospitalization, dyspnea and pain on the right hemi-thorax and right flank occurred. There was a decrease in the respiratory sounds at the right lung base. The abdominal examination was normal. The vital signs and the laboratory analysis were within the normal range. Liver function tests values were in normal ranges. Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) values of admission, 24th hour, 48th hour and 96th hour were respectively 21,10; 14, 9; 17,12 and 17,10. The posteroanterior chest X-ray showed blunted right sinus, which was not observed in the first radiological examination (Figure 1a, b). To rule out pulmonary embolism, contrast-enhanced CT angiography was conducted which revealed bilateral pleural effusion that was more prominent on the right side and had a thickness of 4 cm at the thickest part (Figure 2). Additionally, minimal free fluid was observed in the cross-sectional

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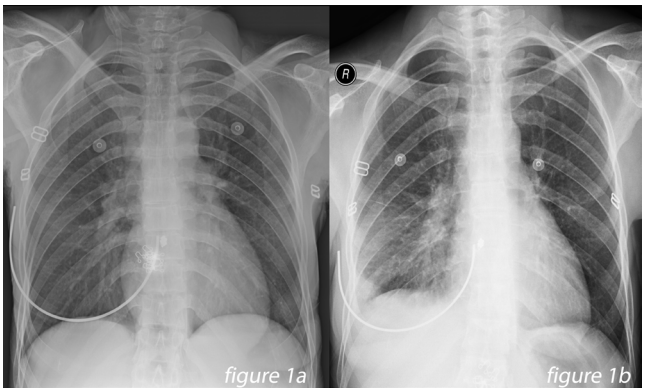

Figure 1a: The posteroanterior initial chest X-ray with normal findings; b, the chest roentgenogram after 3 days of the same patient showing blunted right sinus.

abdominal images. She had no abdominal pain, fever and leukocytosis. There wasn't any pathological finding in the echocardiography performed by cardiologists.

She was hospitalized in the pulmonology department on the third day of observation in ICU of our ED. With thoracentesis, clear, colorless and odor-free fluid of about 500 cc with the characteristics of transudate was drained. Laboratory analysis of the pleural fluid were as follows: pH: 7.48, glucose: 147 mg/dl, albumin: 1,1g/dl, total protein: 2 g/dl, LDH: 83 U/L, white blood cells: 300, neutrophils: 200, hemoglobin: 0,1 g/dl, cholesterol: 20 mg/dl. In the simultaneous blood analysis, LDH was 83 U/L, total protein was 5.4 g/dl and cholesterol was 82 mg/dl. There was no microbial growth in the blood, sputum, urine and pleural fluid cultures. ARB staining did not reveal tuberculosis bacilli. Mycobacterium by PCR analysis was negative. Procalcitonin level was measured as 0.2 ng/ml. No pathological change in the liver function tests and in other laboratory analysis was encountered during this period. The patient left the hospital of her own accord, while her monitoring was on-going in the pulmonology department.

Discussion

The pleural fluid is a parietal supernatant from the capillaries, which penetrates through mesothelial barriers into the pleural cavity[5] . Pleural effusion is defined as an abnormal fluid accumulation as a result of the penetration of excessive fluid in the pleural cavity or of the decrease of the absorption of the fluid or of both[6]. Increase of the interstitial fluid in the lung as a result of the increase in the pulmonary capillary pressure or permeability, decrease of the intrapleural pressure, decrease of the pleural oncotic pressure, increase of the pleural membrane permeability and obstruction of the lymphatic flow, defects of diaphragm, rupture of the ductus thoracicus are the potential causes of the pleural fluid

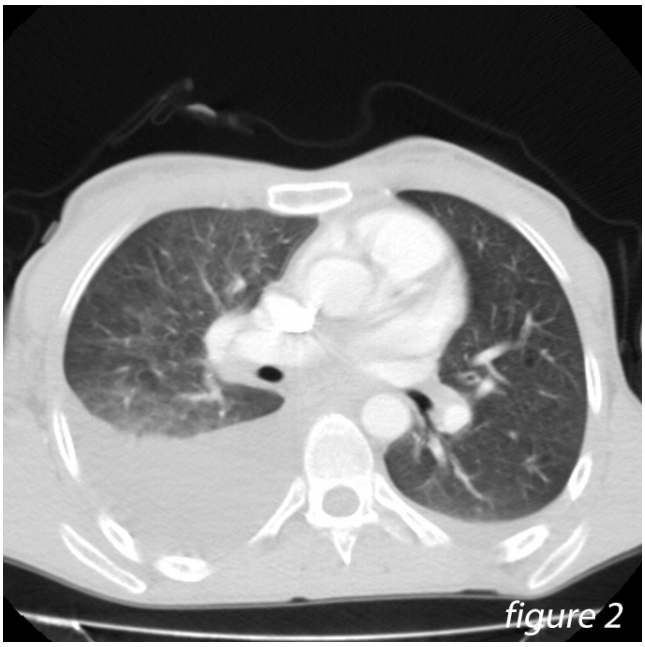

Figure 2: contrasted thorax computerized tomoghraphy image of the patient on the third day demonstrating bilateral pleural effusion that was more prominent on the right side and had a thickness of 4 cm at the thickest part.

accumulation. Although pleural effusion can develop as a complication of various diseases; heart failure, pneumonia, tuberculosis and pulmonary embolism are the most common underlying factors in adults[6].

Pleural effusion due to drug intake is rare. Even though hypersensitivity reactions, oxidative stress on the mesothelial cells, dose-dependent direct toxic exposure, fluid retention and chemical inflammation are blamed as the cause of the drug-induced pleural fluid accumulation, the clinical mechanism is not fully elucidated[7, 8]. There are more than thirty drugs which are known to cause drug-induced pleural damage[8]. Drug-induced pleural effusion may appear just after the first dose of the drug or after its usage for many years[7, 8]. However, there is no such general knowledge about the relationship between APAP and pleural effusion. In a clinical study on IV paracetamol, it was reported that pleural effusion might occur as a rare adverse effect in the pediatric patient population. There was no reports on the risk in adults[9, 10].

Under physiological conditions, the approximate amount of the pleural fluid is between 0.26-1ml/kg for each hemithorax and this amount is determined by the dynamic balance between its production and resorption[5]. The drainage of the fluid from the pleural cavity occurs through a few different mechanisms. The channels and pumps in the mesothelial cells in the pleural surface, lymphatic stomata located in the parietal pleura, passive diffusion caused by the Starling forces and the removal of the large molecules with transcytosis enables the excretion of the pleural fluid. The balanced microvascular filtration rate or pleural fluid

flow rate is equal to the excretion rate from the lymphatic stomata[5, 11]. Pharmacological substances may influence the amount of the pleural fluid[5]. It was shown that paracetamol and the NSAIDs blockaged the Na^+ channels and the Na^+/K^+ pumps in the normally functioning parietal pleura. As a result of this blockage, the permeability of the pleural membrane decreases. Thus, the absorption of the fluid from the pleural membrane is also decreased[12, 13]. In an in vivo study conducted on rats, paracetamol and NSAIDs were shown to delay pleural fluid absorption in rats with postoperative hydrothorax[13]. In our case report, we think that high-dose paracetamol reduces pleural fluid absorption and disrupts the balance in terms of fluid accumulation, similar to the literatüre. This disruption in normal functioning resulted in pleural effusion in our patient.

In the literature, there was only one case report with similar features to our patient, and this report was about a 6-month-old girl[14]. However, as far as we know, we have not encountered a case report about an adult patient. In addition, in a report published by the U.S Food and Drug Administration (FDA) on the use of APAP intravenously, it was stated that APAP may cause pleural effusion in pediatric patients, although the incidence is below 1%[15]. In a clinical review published by the FDA in 2009 showed treatment-emergent adverse events (an event that emerges during treatment, having been absent pretreatment, or worsens relative to the pretreatment state-TEAE) after IV paracetamol injection. In this publication, it was stated that pleural effusion as an adverse event constitutes 7.8% of all TEAEs in adolescents and 2.1% in neonates[16].

In the evaluation of the patients with pleural effusion, the first step is to determine whether the fluid is transudate or exudate[6]. In the clinics, with the help of the Light criteria, exudative fluids can be easily distinguished from the transudates[6]. The pleural effusion of our patient had the characteristics of a transudate both macroscopically and regarding the Light criteria. Moreover, there were no cardiovascular, pulmonary, renal or hepatic findings, which might explain the transudative character of the pleural effusion. We believe that the cause of the pleural effusion in our patient was the variability of the pleural permeability and the consequent decrease of the fluid absorption caused by the high-dose intake of paracetamol.

Conclusion

Pleural effusion is common in adult patients and its causes are difficult to diagnose. We think that this is the main reason why there is no similar case reports in the literature. The clues in the diagnosis process of our patient were; the absence of a chronic disease in the history, the occurrence of the event during the follow-up of the patient immediately after drug intake, the transudative character of the fluid and the exclusion of other conditions that may cause pleural effusion.In conclusion, it should be kept in mind that high-dose intake of paracetamol might cause transudative pleural effusion as a rare complication.

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The written consent form is taken from the patient.

"The case report has written in an anonymous characteristic, thus secret and detailed data about the patient has removed. Editor and reviewers can know and see these detailed data. These data are backed up by editor and by reviewers."

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Case Report

Journal of Emergency Medicine Case Reports

Late Acute Spontaneous Giant Epidural Hematoma After Ventriculoperitoneal Shunt Surgery: A Case Report

Engin YÜCEL[1], Nilüfer TAŞ[2]

[1]Alanya Eğitim Araştırma Hastanesi

[2]Sağlık Bilimleri Üniversitesi, İstanbul Gaziosmanpaşa Taksim Sağlık Uygulama Ve Araştırma Merkezi

Abstract

Paracetamol is the most widely used and prescribed drug word-wide. It is the most common cause of the poisoning and of the fatality due to the toxic administration throughout the world. A 34-year-old female patient applied to our ED with the complaint of swallowing 33 g of paracetamol. After routine toxicity treatment, on the third day of the hospitalization, dyspnea and pain on the right hemithorax and right flank occurred. Chest X-ray showed blunted right sinus. CT revealed bilateral pleural effusion. With thoracentesis, clear, colorless and odor-free fluid of about 500cc was drained. Laboratory examination of the fluid confirmed it as transudate. We believed pleural effusion is related to high-dose paracetamol intake and it occurred due to decrease in pleural permeability and the consequent decrease of the fluid absorption. In conclusion, high-dose intake of paracetamol might cause transudative pleural effusion as a complication.

Keywords: paracetamol, acetaminophen, over dose, pleural effusion

Introduction

Subdural hematoma, which is currently one of the common complications following ventriculoperitoneal (VP) shunt, was discussed in detail for the first time by Dandy[1]. It is generally observed in the first days following shunt placement or in the late period, but non-traumatic epidural hematoma always occurs in a few hours following shunt placement [2]. Especially, the mechanism of epidural hemorrhage that develops in the burr hole site in pediatric patients and in a few hours following shunt placement is also known clearly. The mechanism of ossified epidural hematoma, which generally causes patients to present with chronic headache in the late period following VP shunt placement, has been partially explained. In fact, the time of onset of calcification of epidural hemorrhage has been found to be 10 days-50 years in cases of traumatic hemorrhage [3,4]. Sengupta et al. stated that 2 factors were required for development of epidural hemorrhage. The first factor was reported to be origin of hemorrhage, and the second factor was reported to be separation of duramater from the osseous tissue [5]. The development of epidural hemorrhage in the burr hole site can be explained by vascular injury in the dura or inadequate bleeding control in the bone. However, the development of hemorrhage away from the burr hole site, especially in the frontal region, has been associated by Luys with the result that the dura mater is attached to the bone more loosely in the anterior part of the cranium compared to the posterior part [6]. Hemorrhages developing in different regions following changes in intracranial pressure have also been explained with this mechanism. Although this mechanism has been considered and cited many times in those periods, current modern medicine discredits this mechanism.

Case

A 7-year old female patient had been operated for meningomyelocele after birth. One month later, VP shunt had been placed. The patient who had paraparesis, had undergone shunt revision for the third time at the age of 3 years. She presented to the emergency department with nausea, vomiting, blurred consciousness and loss of strength (2/5) in the left upper extremity 4 years after the revision. She had a Glasgow Coma Scale (GCS) score of 10. The patient did not have a history of trauma, and physical examination did not reveal any finding of trauma. The patient had 2 siblings, and these 2 siblings had no history of morbidity. All hematological parameters were found to be normal. Brain computed tomography (BCT) revealed a giant epidural hematoma

Corresponding Author: Engin YÜCEL **e-mail:** drengin2005@yahoo.com

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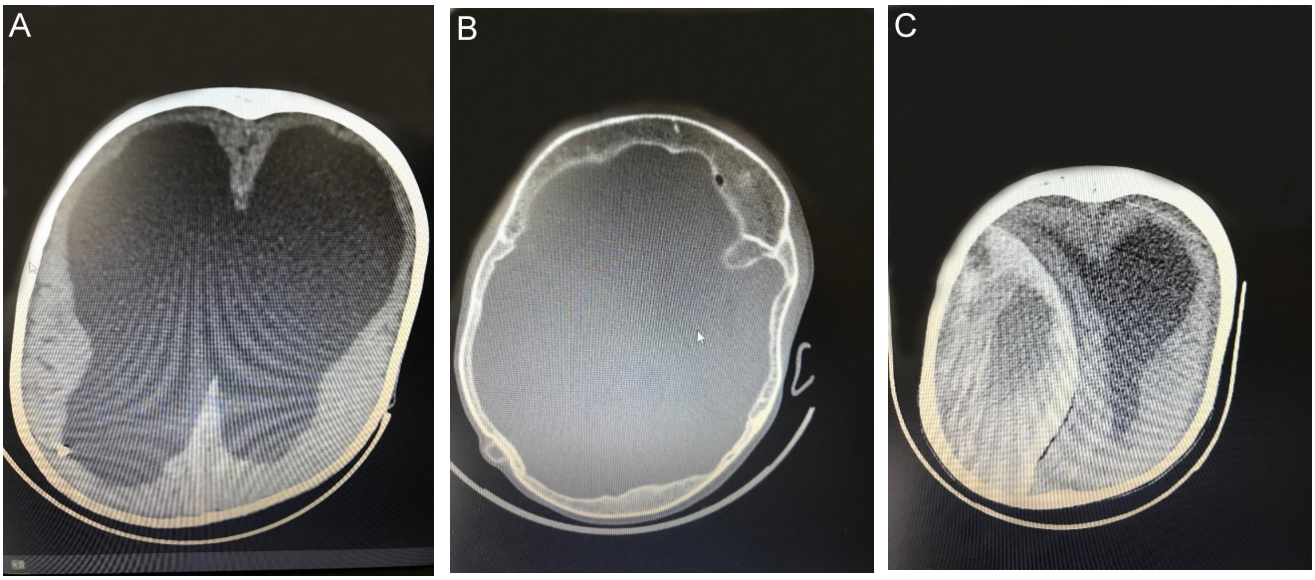

Figure 1: Preoperative BCT figures: A. Axial BCT demonstrating 4 years ago. **B.** Axial BCT demonstrating right-sided epidural hematoma Axial BCT demonstrating bone Picture. **C.**

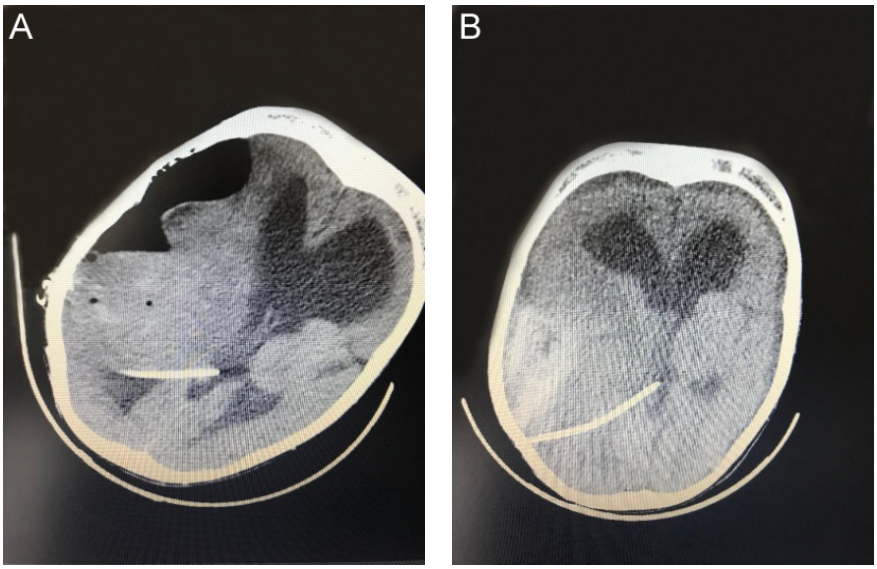

Figure 2: Postoperative BCT figures.
A. Immediately after surgery.
B. 1 week after surgery

in the right hemisphere (Figure 1). The patient underwent emergency surgery (Figure 3). Most of the hematoma was drained and no fracture was observed in the bone (Figure 2). However, she intraoperatively developed respiratory arrest. The dura was suspended, and the bone was replaced rapidly, and the operation was terminated. The patient remained connected to mechanical ventilator for 2 days, and she was extubated on the 3rd day. The GCS score of the patient who gained consciousness was 15. The paresis in the left upper extremity persisted when the patient was discharged.

Discussion

We reviewed the entire literature to explain the mechanism of epidural hemorrhage, which is among the hemorrhages that develop following VP shunt procedure. Maurice et al. Presented 104 pediatric patients with traumatic epidural hemorrhage in detail. They injected warm gel into the epidural space of operated patients and observed that there was tight connection only between the dura and bone in the coronal suture region [7]. This study supports Luys's (in 1901) argument that the dura-bone connection in the frontal region is loose. Moderate-high pressure shunts, anti-siphon devices and adjustable pressure or flow control devices have generally been recommended to prevent this complication. However, non-traumatic hemorrhage developed in a moderate-pressure, flow control shunt used in a case presented by Seyithanoglu et al. [8]. A high pressure and flow control shunt was used in the case we presented. In the literature, we could not find any non-traumatic spontaneous epidural hemorrhage developing in the long period to such an extent as in the case we presented.

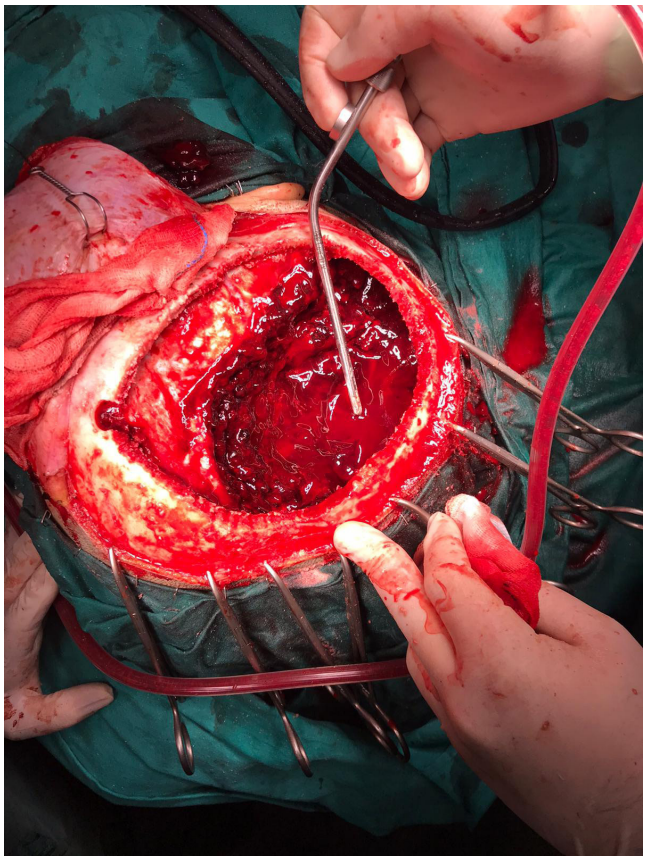

Figure 3: Peroperative view

Conclusion

We recommend that bleeding and cerebrospinal fluid (CSF) leak control should be performed accurately, patients should be brought to the sitting position slowly and in a controlled manner, BCT should be obtained in the postoperative period and anti-siphon device should be used when placing VP shunt. In addition, we argue that use of moderate-high pressure shunt is not definitely effective in preventing development of epidural hemorrhage.

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Case Report

Journal of Emergency Medicine Case Reports

Mediterranean Black Widow Spider (Latrodectus Tredecimguttatus) Poisoning in a Metropolitan City in Turkey

Fikret Bildik[1], Burhan Çomruk[1], Başak Yüksek[1], Mehmet Ali Aslaner[1], Tuncay Türkeş[2]
[1]Department of Emergency, Gazi University School of Medicine, Ankara, Turkey
[2]Department of Biology, Ömer Halisdemir University, Niğde, Turkey

Abstract

Introduction: Black widow spider bites cause severe poisoning (latrodectism) with symptoms such as muscle spasm, rigidity, pain, vomiting, hypertension, and tachycardia. Although Latrodectus mactans (L. mactans) is the most well-known species to cause latrodectism, it has not been reported in Turkey. We report a poisoning case caused by Latrodectus tredecimguttatus (L. tredecimguttatus) spider a species known to be in Turkey for the first time in the literature.

Case: A 35-year-old male patient presented with complaints of pain in the lower extremities and excessive sweating due to a spider bite. Discomfort, agitation, a sweaty appearance, tachycardia, and hypertensive attack were observed in the patient. Because black widow antivenom is not available in Turkey and because of the continuation of symptoms despite treatment for 12 hours in the emergency department, the patient was transferred to the intensive care unit, where he was given IV sedoanalgesia. Nicardipine infusion was administered to treat hypertension attack. The patient's symptoms improved on the fifth day. The dead spider that was brought in was identified by an expert biologist as L. tredecimguttatus.

Conclusion: It should be considered that latrodectism due to L. tredecimguttatus spider bite may be resistant to emergent treatment and hospitalization may be required.

Keywords: black widow; Latrodectus tredecimguttatus; poisoning

Introduction

Latrodectism is a syndrome characterized by vomiting, tachycardia, and hypertension in addition to severe spasm, rigidity, and pain in the muscles, and it is caused by alpha-latrotoxin, which is found in the venom of black widow spiders (*Latrodectus* spp.) [1, 2]. Although *L. mactans* is the most well-known species to cause latrodectism, it has not been reported in Turkey [3]. In addition, other *Latrodectus* species distinction has not been made in previously published poisoning cases [4, 5]. This paper presents a poisoning case caused by the Mediterranean black widow *L. tredecimguttatus* spider that occurred in a metropolitan city, the capital of Turkey.

Case

A 35-year-old male shepherd who was otherwise healthy woke up in a field in Ankara, the capital of Turkey, with left chest pain and saw a black insect and killed it. Shortly after, he went to the hospital with severe pain at the bite site and in all of his joints, and the following medications were administered: methyl prednisolone, pheniramine maleate, a nonsteroidal anti-inflammatory drug (NSAID), ketamine, and tetanus vaccine. However, as the patient's complaints persisted, he was referred to our tertiary care hospital.

The patient was observed to be sweaty, restless, and agitated on admission, and he had severe pain, especially in the lower extremities and at the bite site. His vital signs were BP: 153/122 mmHg, P: 120/min, F: 36.7 °C, RR: 20/min, and SaO_2: 96%. A hyperemic area of approximately 2×2 cm was found on the left anterior aspect of the patient's chest (Fig 1). The results of other physical examinations were considered normal. The results of his blood tests were Hb: 11.7 g/dl, Wbc: 17.460/mm^3, and platelets: 446.000/mm^3. The results of venous blood gas analysis, liver function tests, kidney function tests, coagulation tests, troponin measurement, and complete urine analysis were all within normal limits. His total creatine phosphokinase (CK) was measured as 282 U/L, and his ECG revealed sinus tachycardia.

During the patient's 12 hour stay in the emergency department, H1 and H2 receptor antagonists (pheniramine

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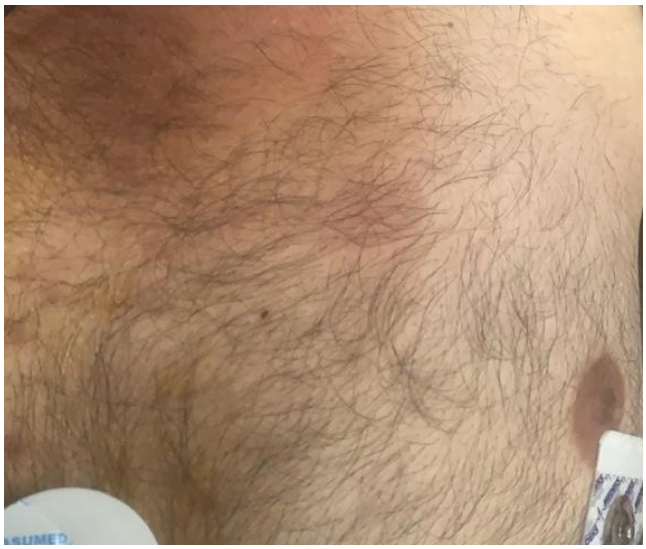

maleate, 45.5 mg, and ranitidine 50, mg, intravenous (IV)), methyl prednisolone (40 mg, IV), diclofenac Na (75 mg, intramuscular (IM)), tenoxicam (20 mg, IV), fentanyl (100 µg, IV), paracetamol (1 g, IV), thiocolchicoside (4 mg, IM), and diazepam (10 mg, IV) were administered, but the pain, sweating, and restlessness could not be controlled. Fortunately, the patient brought in the dead spider that bit him, and because the clinical findings were compatible with poisoning, it was thought that his condition may be black widow poisoning, which is very rare in Turkey and the region. However, the spider's species distinction was not clearly made at that time. Because black widow antivenom is not available in Turkey and because his symptoms continued, the patient was transferred to the intensive care unit.

On the second day, CK increased to 2749 U/L, AST to 75 U/L, and ALT to 52 U/L. Sedoanalgesia (fentanyl, midazolam, dexmedetomidine) and non-steroidal anti-Inflammatory drugs were administered to the patient for pain control for 5 days. IV metoprolol and a glyceryl trinitrate infusion were administered for blood pressure control, and when no response was obtained, a nicardipine infusion was started. The patient was discharged from the hospital on the eighth day. During this time, the dead spider that the patient brought with him was examined by a biologist, who is an expert on spiders, and it was determined to be *L. tredecimguttatus* (Fig 2).

Discussion

The *Latrodectus* spiders are called Black Widows because of their powerful venom, and they are found in different parts of the world. The best known and most dangerous is *L. mactans*, which is found in North America [3]. *L. tredecimguttatus* lives in regions extending from Central Europe to Central Asia, the Caucasus, North Africa, and Saudi Arabia [6]. It lives in the Marmara, Mediterranean, and Central, Eastern, and Southeastern Anatolia regions in Turkey [7]. Although it is common in all Mediterranean regions, the incidence of *L. tredecimguttatus* poisoning is very low [6]. It primarily lives in steppes and grasslands and can be a major problem in areas where grain is harvested by hand. These spiders bite if disturbed, and the female, which is 7–15 mm in size, is responsible for poisoning. Some have red spots on the dorsal surface of the abdomen, and some may be completely black[6].

The venom released in bites by *Latrodectus* spiders contains the neurotoxin α-latrotoxin (α-LTX), which has neurological and autonomic effects in humans. This venom stimulates the release of neurotransmitters, such as acetylcholine, catecholamines, and glutamate, in humans [1, 2]. Muscle spasms and head, back, lower extremity, and abdominal pain develop because of the increase in acetylcholine. Pain is an almost universal feature of latrodectism. In more than half of cases, pain increases within the first hour and often spreads to the extremities or may result in abdominal pain mimicking acute abdomen. Pain is typically severe and difficult to treat, lasting from hours to days [2, 6, 8].

Systemic effects are present in 20–30% of cases and severe sweating in approximately 70%. Other symptoms such as restlessness, nausea and vomiting, high fever, increased secretions, tremor, increased reflexes, paresthesia, priapism, and ptosis may also develop in patients [6, 8-10]. Hypertension develops in less than 10% of cases [6]. In Turkey, a few cases of acute myocardial injury and severe hypertension resistant to antihypertensive therapy have been reported [9, 11, 12]. In a study published by Isbister and Fan in 2011, local pain was reported in 90% of 56 *L. tredecimguttatus* bite cases and sweating in 55%, while hypertension, agitation, and pain spreading to the extremities were not observed [2]. In the *L. tredecimguttatus* bite case presented here, the patient experienced pain that spread to the extremities, agitation, severe sweating, and treatment-resistant hypertension.

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The diagnosis of latrodectism is based on a history of a spider bite and consistent clinical findings in patients. There is no analytical method for detecting the neurotoxin α-latrotoxin in blood, urine, or the bite site [2]. Tests that can aid in monitoring and treatment include complete blood cell count, electrolytes, CK, and urinalysis. Leukocytosis, albuminuria, and increased CK are common laboratory findings [8, 10]. Obtaining an ECG and cardiac enzymes are recommended, especially in *L. tredecimguttatus* bites [2]. In our case, there were no ECG findings except tachycardia. Troponin at follow-up remained within normal limits.

Between 1982 and 1990, 163 cases of black widow spider envenomation in the USA were reviewed and categorized according to severity as grade 1, 2, or 3 [13]. Patients (grade 1) who were asymptomatic, except for local pain at the bite site, accounted for 9% of all cases. Patients (grade 2) with muscle pain in the bitten extremity, muscle pain spreading to the abdomen if bitten on a lower extremity, muscle pain spreading to the chest if bitten on an upper extremity, local sweating at the bite site or extremity, and stable vital signs constituted 37% of all patients. Widespread muscle pain in the back, abdomen, and chest; sweating outside the bitten area; and abnormal vital signs such as hypertension, tachycardia, nausea, vomiting, and headache were present in 54% of all patients (grade 3). The most common laboratory findings were increases in white blood cell count, CK levels, and lactic dehydrogenase levels [13]. Our case was determined to be grade 3 in severity, and leukocytosis and an increase in CK levels were observed.

The goal for the treatment of latrodectism is pain control. However, pain control can be difficult, often requiring large doses of pain medication and/or hospitalization. Although there is no evidence that analgesics are effective, muscle relaxants and non-opioid and opioid analgesics are well tolerated and considered suitable for the symptomatic relief of pain [2]. The dose administered is similar to that for other acute painful disorders and should initially consist of a combination of non-opioid and opioid oral analgesia. Persistent pain should then be treated with parenteral opioids, such as intravenous morphine. In patients with latrodectism, benzodiazepines can be used to treat restlessness, muscle spasm, and increased adrenergic activity, such as hypertension, tachycardia, and sweating [2, 8]. Although some previous studies have indicated that the IV use of 10% Ca gluconate will produce immediate and long-term relief of muscle pain by lowering the depolarization threshold at the neuromuscular junction, there is little information on the effects of calcium and magnesium, and therefore, they are currently not recommended [1, 2, 8]. In our case, pain and sweating that were resistant to various analgesic and sedative drugs were observed for about 5 days.

Developed hypertension will usually respond to treatment with antivenom, but patients with underlying medical problems and severe hypertension may require additional antihypertensive therapy. Hospitalization may be required in cases where antivenom is not available or in hypertensive situations that are not suitable for antivenom and/or do not respond to treatment [13]. One case study reported that peripheral vasodilators and beta-blockers were not effective in the treatment of a pediatric patient with severe hypertension, but blood pressure returned to normal after the venom wore off [9]. In our case, who had no previously known hypertension diagnosis, there was no response to IV nitroglycerin and a beta blocker, IV nicardipine treatment was administered, and blood pressure was brought under control after a few days.

To date, a number of antivenoms have been developed against specific *Latrodectus* spp. in various parts of the world, including Australia and America. Among these, *L. mactans* antivenom (Antivenom *L. mactans*, Merck Sharp & Dohme®) and Latrodectus spp. antivenom (Aracmyn Plus, Instituto Bioclon®) are not available in Europe. Although the use of antivenom is controversial, one +study has claimed that it provides rapid pain relief and reduces hospitalization or re-admissions to the emergency department [14]. However, these previous studies were on *L. mactans* species. Although no scientific report has described the use of *L. mactans* antivenom to treat *L. tredecimguttatus* poisoning, this antivenom was reported to be effective in one case in Italy [15]. However, it should be taken into account that antivenoms have serious side effects. In our case, antivenom was not used because it was not available in Turkey.

Conclusion

It should be kept in mind that a patient who comes to the emergency department in Mediterranean region with complaints of muscle, joint, and abdominal pain resistant to treatment as well as hypertension, tachycardia, and sweating as a result of an insect bite may have latrodectism syndrome caused by the bite of the Mediterranean black widow spider *(L. tredecimguttatus)*, and hospitalization may be required.

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Case Report

Journal of Emergency Medicine Case Reports

Lemierre's Syndrome: A Case Report

İsmail Ataş[1], Özlem Bilir[1], Alpaslan Ünlü[1]

[1]Recep Tayyip Erdoğan University Medical Faculty Training and Research Hospital, Emergency Department, Rize, Turkey

Abstract

Lemierre's syndrome is a syndrome with high mortality, causing internal jugular vein (IJV) thrombophlebitis, septic lung and other organ embolism, which often develops as a complication of oropharyngeal infections. Mortality can be reduced with early diagnosis and appropriate antibiotic treatment. It is a rare syndrome and the case we have presented here differs from the cases with lemierre syndrome previously reported because of the involvement of superior vena cava (SVC) and subclavian vein.

Keywords: Lemirerre's syndrome, Thrombophlebitis, retropharyngeal abscess, vena cava superior syndrome

Introduction

Lemirerre's syndrome is a mortal condition that often progresses with septic thrombophlebitis of the IJV caused by Fusobacterium necrophorum. Thrombophlebitis can cause metastatic septic emboli and bacteremia by hematogenous spread. Although the primary site of the infection is palatine tonsillar and peritonsillar tissue, it has been determined that mastoiditis, odontogenic infections, parotitis, sinusitis or the skin and subcutaneous tissue of the head and neck region may also be sources[1]. Mortality and morbidity can be prevented with early diagnosis and appropriate antibiotherapy.

Case

A 35-year-old male patient, who had no known additional disease, came to the emergency department with the complaint of pain and swelling in the throat that started a week ago. He was diagnosed with upper respiratory tract infection and was discharged with oral symptomatic treatment. After 3 days, he came back to the emergency department with the complaint of increased swelling in the head and neck and not decreasing his symptoms.

Vitals were normal on physical examination. Oropharynx hyperemic, tonsillar hypertrophic, distended neck veins, pletorrhea, upper extremity/face/neck swelling were present. Other system examinations were normal. Leukocyte was 8200 / µL, and neutrophil was 72.3%. C-reactive protein (CRP) (2.61 mg / dL) increased. Since the patient's symptoms were compatible with vena cava superior syndrome (VCSS), first thorax computed tomography (CT) with contrast was performed to detect thrombus in the SVC. Thorax CT showed a thrombus that extended to the subclavian vein and filled the lumen in the SVC.

Abdominal ultrasonography and cranial magnetic resonance imaging were performed because the possible neoplasm that caused thrombosis at a young age needed to be excluded. But no additional pathology was found. The patient was consulted to the department of cardiovascular surgery and hematology. Low molecular weight heparin subcutaneous treatment was recommended and tests were taken by hematology considering the causes that may cause hereditary thrombosis. These tests include; complete blood count (CBC) and morphology (for myeloproliferative diseases), prothrombin time (for low protein C and S), partial thromboplastin time (for antiphospholipid syndrome), thrombin time (for dysfibrinogenemia), antinuclear antibody test, coagulation tests for lupus anticoagulant, Enzyme-Linked ImmunoSorbent Assay (ELISA) for anticardiolipin antibodies, factor V leiden or activated protein C resistance, fasting total plasma homocysteine level, protein C and protein S levels, antithrombin III level, plasma factor VIII levels, Prothrombin 20210 mutation by Polymerase Chain Reaction (PCR) method.

Corresponding Author: İsmail Ataş **e-mail:** drismailatas@gmail.com

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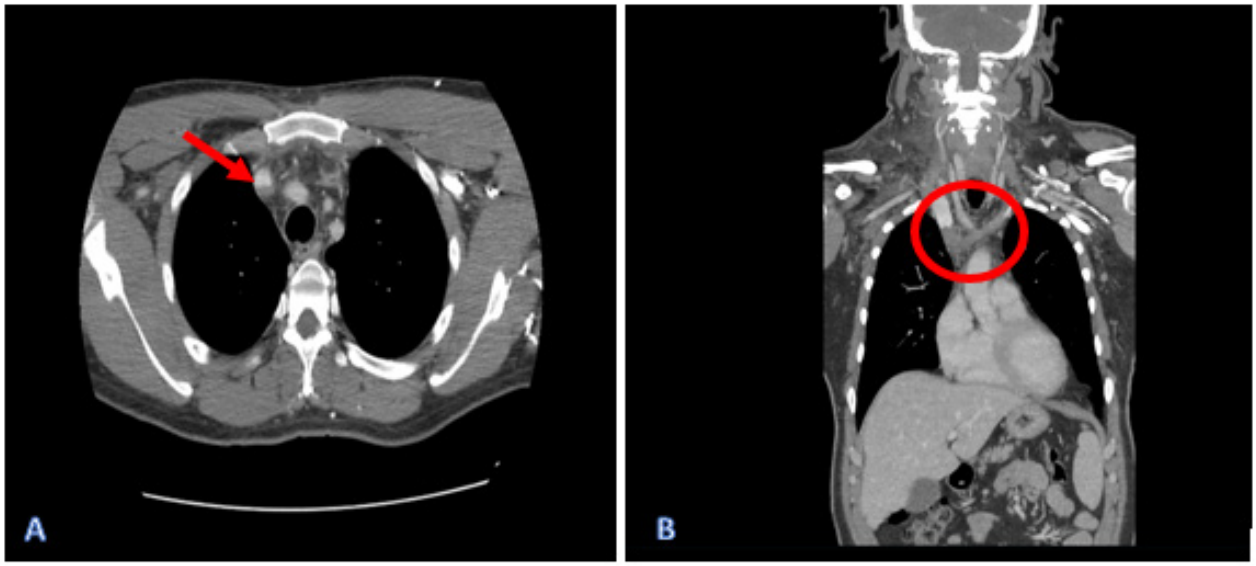
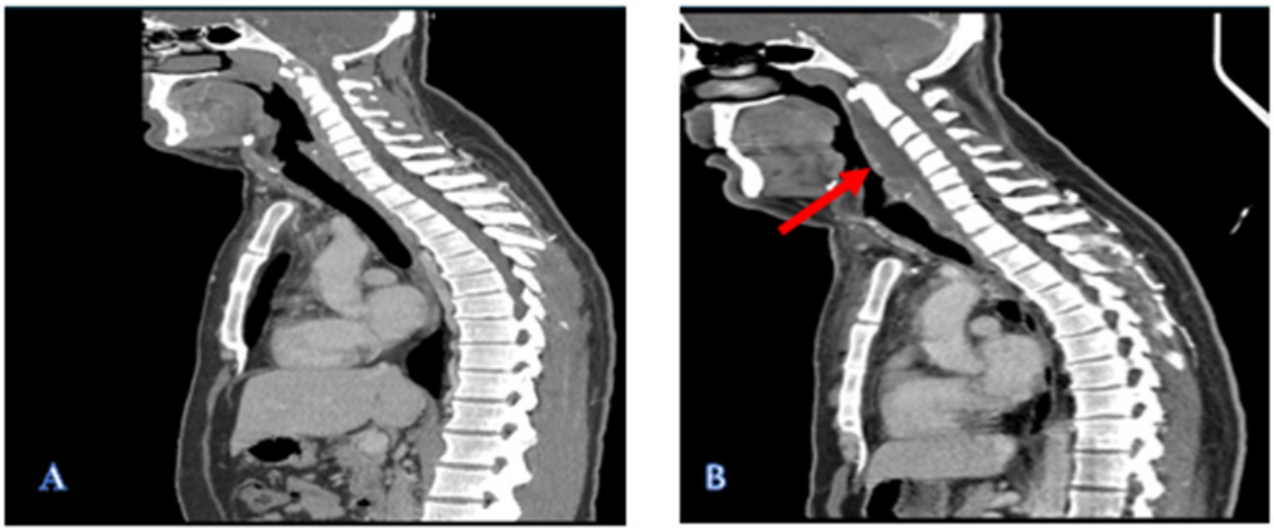


Figur 1. A: Thrombus in the subclavian vein as shown in the Computed Tomography of the Thorax. B: Thrombus that extended to the subclavian vein and filled the lumen in the superior vena cava vein as shown in the Computed Tomography of the Thorax

Throat and neck swelling increased and his symptoms progressed for three days despite treatment. Considering that interventional thrombectomy could be performed, thorax CT with contrast was taken again three days later in order to determine the size of the thrombus in the veins. Retropharyngeal abscess was detected on thorax CT with contrast. The patient was consulted to the department of Otorhinolaryngology. He was hospitalized in the service with a pre-diagnosis of Lemierre's Syndrome and intravenous antibiotherapy was started. Surgical abscess drainage was added to intravenous antibiotherapy because of abscess development. Both thrombosis and retropharyngeal abscess regressed with antibiotic and surgical abscess drainage therapy for 2 weeks.

Discussion

Lemierre's Syndrome is a mortal condition caused by Fusobacterium necrophorum, often in healthy individuals aged 16-25. Many organisms including Bacteroides, Eikenella, Porhyromonas, Prevotella, Proteus, Streptococus, Peptostreptococcus and Staphylococcus aureus have been reported in the etiology of Lemierre's syndrome. The clinical findings of the patients develop depending on the primary site of the infection Although sore throat is the first common finding, fever, neck swelling, dyspnea and hemoptysis due to pulmonary involvement, muscle and joint pains can also be seen in the classic clinical findings[2]. In this case, swelling



Figur 2. A: No pathology in the pharynx in the Computed Tomography of the Thorax B: After 3 days, retropharyngeal abscess as shown in the Computed Tomography of the Thorax

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that spread from the head-neck region to the shoulders after admission with a simple upper respiratory tract infection was the main symptom.

Infection passes from most commonly in the primary area of the palatine tonsils and pharynx and the middle ear, paranasal sinuses or parotid gland to the lateral pharyngeal region where the internal jugular vein is located, and causes septic thrombophlebitis. Septic thrombophlebitis causes septic embolization in the distal regions[3]. In terms of septic embolization that may occur in this case, the patient was evaluated as multisystemic and no pathological condition was found.

The disease should be considered in line with the present symptoms and the diagnosis should be confirmed with examinations. Therefore, CT with contrast of the neck region is the preferred imaging method for showing thrombus. Here, too, the thrombus was visualized with CT. In addition, as an alternative to CT, the existing thrombus can be imaged by using Doppler ultrasonography at the bedside. Although this method is less invasive, it is less sensitive to detect thrombus in deeper regions under the clavicle and manbidula[4].

Complications can lead to death if the diagnosis is not made quickly and antibiotherapy is not initiated[5]. The first step should be the initiation of intravenous antibiotherapy for all factors in the etiology[6, 7]. As penicillin-resistant strains have been reported, empiric therapy should consist of clindamycin or metronidazole or the use of a combination of betalactams with beta-lactamase inhibitors[8]. Although there is no consensus on the duration of treatment in the literature, 4-6 weeks is the general approach[9, 10]. If abscess development occurs during the course of the disease, surgical evacuation must be provided. In this case, surgical abscess drainage was added to intravenous antibiotherapy because of abscess development. There is controversy about the place of anticoagulation therapy for developing thrombus[11, 12].

Conclusion

In conclusion, Lemierre's syndrome is classically defined as a rare disease with a mortal course and manifested by fever, swollen neck and sore throat in young people. Initial clinical findings may be mild and atypical. We think that for early and accurate diagnosis, the disease should be kept in mind and skeptical.

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Contributors: All authors have substantial contributions to the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; and final approval of the version to be published.

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Case Report

Journal of Emergency Medicine Case Reports

Idiopathic Isolated Hypoglossal Nerve Palsy: Case Report

Selim Tetik[1], Oya Güven[2], Mehmet Çoban[3]

[1]Kırklareli Training and Research Hospital, Department of Emergency Medicine, Kırklareli Turkey

[2]Kırklareli University School of Medicine, Kırklareli Training and Research Hospital Department of Emergency Medicine, Kırklareli Turkey

[3]Medikent Hospital Otorhinolaryngology Department, Kırklareli Turkey

Abstract

Introduction: Nerve Hypoglossal, which innervates the tongue muscles; provides language movements, speech and chewing functions. This nerve palsy may develop during tumor, trauma, or infection but idiopathic nerve palsy is rare. In this article; We tried to examine the diagnosis and treatment process of twelfth nerve palsy cases whose cause could not be determined.

Case Report: 16 years old female patient; She applied to our emergency service with the complaint of her tongue turning left in the mouth. In the tests carried out, no reason was found to cause this. The patient was diagnosed with twelfth nerve palsy and treatment was initiated by neurology. The patient recovered after 10 days of treatment.

Conclusion: Twelfth nerve palsy is usually seen with other nerve palsy, isolated twelfth nerve palsy is rare. In this article; We tried to emphasize that this isolated situation may be a harbinger of neurological diseases.

Key Words: Hypoglossal nerve palsy, Tongue diseases, Neurological diseases

Introduction

The hypoglossal nerve (XII. Nerve, N.Hypoglossus) originates from the bulbus and contains only motor fibers. After these fibers leave the brainstem, they pass through the canalis hypoglossia in the occipital bone to the parapharyngeal space and the occipital artery level. Finally, it comes to the suprahyoid region. It passes behind the mylohyoid and hyoglossus muscles and reaches the intrinsic muscles of the tongue. It also innervates the styloglossus, hyoglossus and genioglossus muscles[1,2]. Any lesion, trauma or infection can cause hypoglossal nerve palsy, both during the bulbus and the nerve trace.

N. Hypoglossus, which innervates the tongue muscles; Provides language movements, speech and chewing functions. It gives segments in the medullary (nuclear), cisternal (extramedullary intracranial), skull base (hypoglossal canal), oropharyngeal, nasopharyngeal (close to the 9th and 10th nerves and the internal carotid artery) and sublingual space along the nerve trace. Therefore, it can be damaged due to many etiological reasons, which vary according to its segments throughout its course[3]. Lesions of N. hypoglossus are usually seen with other cranial nerves in close neighborhood. In Collet-Sicard syndrome IX., X., XI. and XII. in cranial nerves; Villaret's syndrome IX., X., XI. and XII. cranial nerves, plexus sympathicus and sometimes VII. in the cranial nerve; In Jackson syndrome X., XI. and XII. in cranial nerves; In Tapia's syndrome, the X. and XII. In addition to cranial nerves, sometimes XI. lesions are seen in the cranial nerve.

A tongue examination is performed to detect N.hypoglossus lesions. During the examination; The shape of the tongue at rest, its protrusion forward in the midline, other movements and muscle volume are examined. Sensory pathology is not observed in N. hypoglossus lesions. The most basic way to distinguish N. hypoglossus lesions is to move the tongue forward by asking to examine the function of the M. genioglossus. In the unilateral loss of function of M. genioglossus, the tongue deviates to the side of the loss of function while advancing forward[4].

Case Report

A 16-year-old female patient admitted to our emergency room with the complaint of her tongue turning left (not ro-

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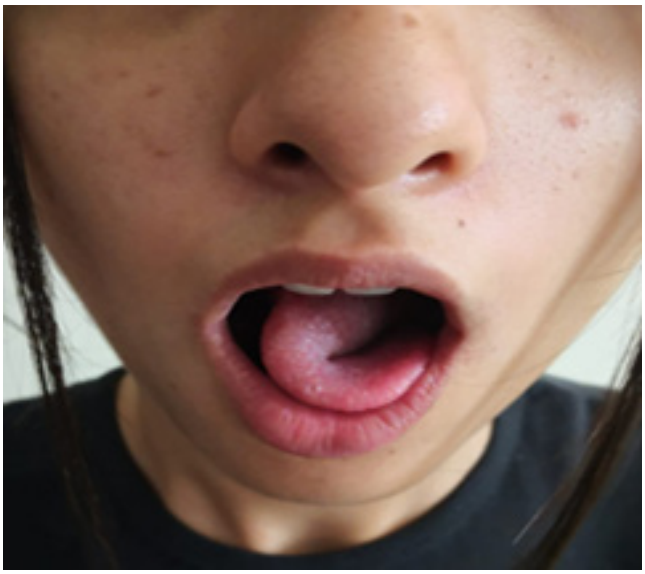

Figure-1: Tongue was observed turn to left-handed inside the mouth

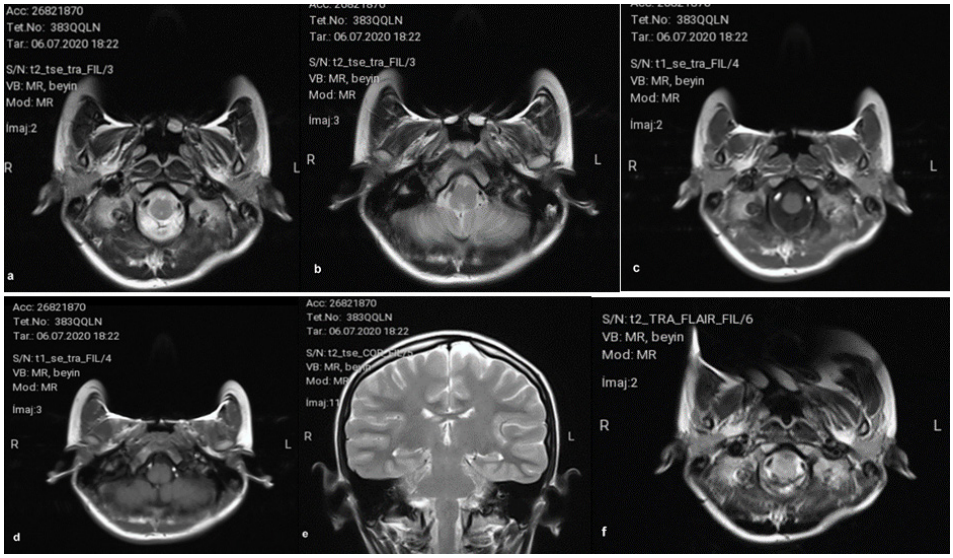

Figure-2(a-b-c-d-e-f): Brain MRI showing the normal course of the hypoglossus nerve

tating) in her mouth for 3 days. The general condition was good, orientated, cooperative. There was no risk of pregnancy or a history of smoking and alcohol abuse. Vital signs; blood pressure: 120/60 mm / Hg, pulse: 92 / min, fever: 36.7 degrees measured. On physical examination, when the tongue was released inside the mouth and at rest, it was seen turned to the left; when moving left-right and outside the mouth, normal movements were observed. There was no fasciculation (Figure-1). There was a lisping, especially when she says the letters c, ç, l, n, r in Turkish. Anterior rhinoscopy examination was normal. There was no mass under the tongue and under the mandible in palpation. Other cranial nerve examinations were normal. Motor, sensory and cerebellar system examinations were normal and deep tendon reflexes were normoactive. There was no prominent feature in her background and family history. Blood count, biochemistry panel (including C-Reactive Protein, sedimentation, vitamin D, magnesium, calcium) results were measured within normal limits. Viral serology tests were normal. Brain Magnetic Resonance I maging (MRI) was performed to rule out stroke, demyelinating diseases, space-occupying lesions and infectious causes (such as abscess). It was normal (Figure-2 (a-b-c-d-e-f)). Antipsychotic (haloperidol), dopaminergic (amantadine sulphate), anticholinergic (biperidene hydrochloride), vitamin B12, vitamin D were prescribed by the neurologist. On the 3rd day of treatment, her complaints subsided. On the 10th day, she recovered completely.

The case report has written in an anonymous characteristic, thus secret and detailed data about the patient has removed. Editor and reviewers can know and see these detailed data. These data are backed up by editor and by reviewers.

Discussion

Literature research has shown that; in case of isolated Hypoglossal nerve paralysis, Intracranial or extracranial space occupying lesion, head and neck injury (including injuries during intubation and cuff compression), vascular abnormality, infection, autoimmune disease or neuropathy are seen. Reports of idiopathic cases are rare.

When imaging is performed, one of the space-occupying lesions can be detected, except that there are normal imaging findings.

In diagnosis; blood count, sedimentation, C-Reactive Protein, antiviral tests (Ebstein-Barr Virus, Herpes Simplex Virus, Cytomegalo Virus), cancer screening tests can be performed. Brain Computed Tomography (CT), brain MRI should be seen to rule out neurological diseases.

Isolated hypoglossal nerve palsy is rare in the literature. In the article of Combarros et al., Which is the most comprehensive study ever, there are 9 patients. No factors were detected in 4 of these patients. 3 patients had malignancy and 2 patients had arterio-venous malformation. It was emphasized that the number of idiopathic forms is significant and it can also be a sign of malignancy[5]. In our case, it is compatible with the literature as no factor can be detected. In a retrospective study by Keane et al., 12 nerve palsy was also detected in 100 people who were seen with other cranial nerve lesions. 49 of them were from tumor origin and prognosis was poor in these patients with tongue involvement[6].

Cranial nerve palsy finding in young patients may be a sign for secondary parkinsonism[7]. The response of our patient to dopaminergic and anticholinergic treatment supports this pre-diagnosis. Although there is no convincing suggestion in the literature about the treatment of this type of cranial nerve paralysis, it has been reported that high dose steroid administration with vitamin complexes (especially vitamin B) accelerates recovery[8].

Detailed anamnesis, process of the neurological state, knowing the anatomy and physiology of the hypoglossal nerve; It is important when choosing tests for diagnosis. MRI may be a good option to confirm or rule out multiple diagnoses. Even today, most of these patients are misdiagnosed. Because hypoglossal paralysis accompanies other symptoms in general.

Conclusion

Isolated hypoglossal nerve palsy is rare and should not be considered as a disease alone, it should be used to rule out other diagnoses and followed considering that it is a symptom of another disease. We could not detect any other disease in our patient to explain this situation. However, if we consider that we received a response to treatment, the patient should be followed up for long-term demyelinating diseases.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Case Report

Journal of Emergency Medicine Case Reports

A Rare Thyroid Gland Emergency: Thyroid Abscess

Hakan ARTAŞ[1], Yeşim EROĞLU[1]
[1]Fırat University, School of Medicine, Department of Radiology, Elazig, Turkey

Abstract

Introduction: Thyroid abscess is a serious head and neck infection that may easily be overlooked. İt is a rare disease with serious complications when the diagnosis is delayed. In this paper, we present a case of thyroid abscess who presented with fever, fatigue, neck pain and swelling, and rapidly deteriorated general condition.

Case Report: A 28-year-old female patient had painful swelling and redness on the left side of the neck. She had fever, fatigue, and dysphagia. Laboratory tests revealed leukocytosis, elevated CRP, and sedimentation rate. The patient who was detected to have thyroid abscess on ultra-sonography and computed tomography was discharged with recovery through surgery and appropriate antibio-therapy.

Conclusion: Thyroid gland abscess is a rare, serious clinical condition with high morbidity and mortality. Thyroid abscess should be kept in mind while performing radiological evaluation in cases presenting with swelling and redness in the neck. In these cases, quite good clinical outcomes may be achieved with early diagnosis and appropriate treatment.

Key words: Thyroid, abscess, emergency

Introduction

Thyroid abscess is a rare infection of the head and neck region that can cause serious complications[1]. It frequently develops following acute suppurative thyroiditis that does not respond to treatment. The most common causative agent is Staphylococcus aureus[2]. Since the clinical findings of thyroid abscess are nonspecific, it may be overlooked or its diagnosis may be delayed. Radiological examinations are extremely helpful in diagnosis and treatment. Therefore, thyroid abscess which is rare but may have fatal complications should be kept in mind in suspected patients and radiological findings should be evaluated in this respect.

Case Report

A 28-year-old female patient presented with fever, fatigue, neck pain, swelling and dysphagia for 3 days. Her fever was 38.20C. She had tachycardia and dyspnea. **She did not have any known disease.** On physical examination, there was painful swelling and redness in the area corresponding to the left lobe of the thyroid. Laboratory tests revealed leukocytosis, CRP and high sedimentation. Thyroid function tests were within normal limits. The patient with prominent dyspnea was performed ultra-sonography. A thick-walled cystic lesion with echogenic content was observed (Figure 1). When evaluated together with the current clinical findings and ultra-sonography, the patient, who was thought to have thyroid abscess was performed neck computed tomography (CT) in order to evaluate the surrounding soft tissues and abscess spread. CT examination revealed an area of hypodense abscess in the left lobe of the thyroid gland, containing air and extending towards the mediastinum (Figure 2, 3). There was significant inflammation in the adjacent soft tissues. So the patient underwent immediate surgery and operative abscess drainage and left lobectomy were performed. Staphylococcus aureus grew in blood and abscess cultures. Histopathological examination revealed the abscess cavity and surrounding benign thyroid tissue. There were no signs of malignancy. The patient was discharged with full recovery after 14 days of antibiotic treatment.

Corresponding Author: Yeşim EROĞLU **e-mail:** dryesimeroglu@gmail.com
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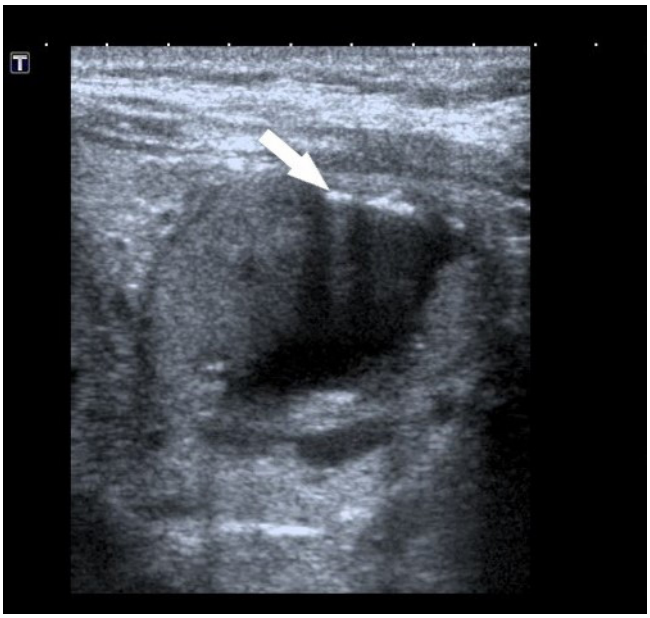

Figure 1. On cervical ultra-sonography, there was a thick-walled cystic lesion with echogenic air values in the anterior of the left lobe of the thyroid gland.

Discussion

Acute suppurative thyroiditis is a rare form of thyroid gland infections with microbial origin[1]. If the infection is left untreated, it may rarely progress to thyroid abscess[3]. It frequently develops after acute suppurative thyroiditis following upper respiratory tract infection and middle ear infection[4]. Staphylococcus and streptococcus species are the most common causative microorganisms. Staphylococcus aureus grew in the blood and abscess cultures of our case. Other agents are gram-negative microorganisms, anaeorobes and fungi[2].

It has been reported that thyroid gland is more common in women than in men and is frequently located on the left side of the thyroid gland[5]. In our case, there was an abscess located in the left lobe of the thyroid gland.

The thyroid gland is resistant to infections due to its good blood supply, good lymphatic drainage, high iodine content with bactericidal effect, and a robust capsule that provides good separation from surrounding neck structures[6]. The source of infection is thought to be mostly hematogenous[7]. Acute suppurative thyroiditis and thyroid gland abscess are mostly seen in immune-compromised patients, diabetics, and patients with congenital pathologies such as priform sinus fistula. It can also occur after fine needle aspiration biopsy [3,5]**. Our case did not have any systemic disease.**

Anamnesis, physical examination, laboratory and radiological examinations are extremely important in the diagno-

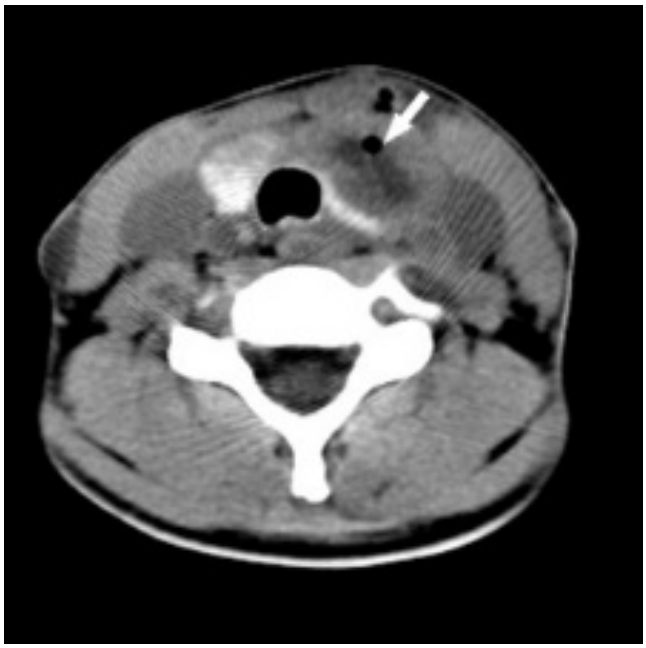

Figure 2. In axial neck CT image, the density of the left lobe of the thyroid gland was decreased and hypodense abscess containing air value was observed.

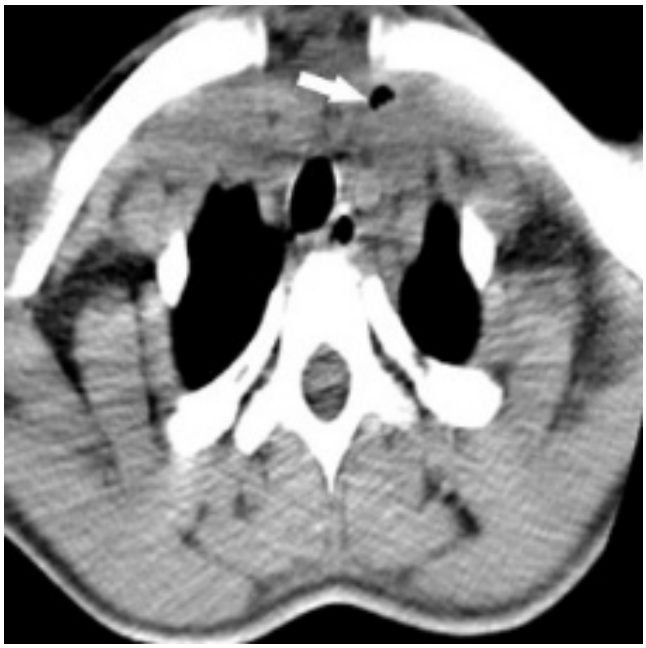

Figure 3. Inferiorly, this abscess area and air values were observed to extend towards the thoracic entrance

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sis of the disease. Symptoms include fever, neck pain, swelling, redness and dysphagia. These clinical findings can be easily overlooked by mimicking acute pharyngitis and the diagnosis may be delayed. Laboratory findings include leukocytosis, CRP and increased sedimentation. Thyroid function tests are mostly normal. However, cases of thyro-toxicosis and hypothyroidism developing secondary to thyroid abscess have also been reported in the literature[8]**.** Thyroid functional tests of our case were within normal limits.

Direct graphy reveals deviation in trachea and increased soft tissue density at this level. The solid or cystic structure of the lesion and the surrounding soft tissues are evaluated by ultra-sonography. Besides, ultra-sonography enables needle inspiration.In addition to the characterization of the abscess, the spread to the tissues and additional pathologies can be determined with computed tomography.

Complications including thyroid storm, internal jugular vein thrombosis, airway obstruction due to the spread of inflammation, and mediastinitis with high morbidity and mortality have been reported[9]. Therefore, early diagnosis of thyroid abscess and prompt initiation of appropriate treatment are extremely important.

Thyroid abscesses are treated with surgically and systemic antibiotics. As an alternative to surgery, ultrasound-guided abscess drainage can be performed. However, in the presence of underlying pathology and in significantly complicated patients, surgical treatment is more appropriate for the treatment of abscess[9]. In such cases, absorption can be used to facilitate drainage and surgical treatment.

It is extremely important to get a diagnosis as early as possible in patients coming with complaint of cervical mass. It is encountered diagnostic difficulties due to the complex structure of this region and the diversity and excess of organs. The main causes of cervical masses are congenital, infectious-inflammatory and neoplastic diseases. Congenital lesions such as thyroglossal duct cyst, branchial cyst, lymphangioma are mostly seen in children and young adults. Besides, infectious and inflammatory cervical lymphadenitis originating from bacterial, viral, fungal and parasitic is a common cause of cervical masses. Neoplastic lesions originating from salivary glands, thyroid, vascular, neurogenic and soft tissue should be considered primarily in adults coming with complaint of cervical mass[10].

Conclusion

Thyroid gland abscess is rare and has high morbidity. Thyroid abscess should be kept in mind when radiological evaluation is performed in cases presenting with swelling and redness in the neck. Early diagnosis and appropriate treatment reduce mortality and morbidity in these cases.

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Case Report

Journal of Emergency Medicine Case Reports

Magnetic Resonance Imaging Findings in Status Epilepticus: A Case Report

Berrak Barutçu Asfuroglu[1], Yaprak Özüm Unsal YO[2], Umut Asfuroglu[1], Ali Murat Koc[3]

[1]Department of Radiology, Gaziantep Abdulkadir Yuksel Government Hospital, Gaziantep, Turkey

[2]Department of Neurology, University of Health Sciences Bozyaka Education and Training Hospital, Izmir, Turkey.

[3]Department of Radiology, University of Health Sciences Bozyaka Education and Training Hospital, Izmir, Turkey.

Abstract

Introduction: Status epilepticus (SE) is a neurological emergency in which prolonged seizures require rapid diagnosis and treatment. It is classified as convulsive, non-convulsive and electrographic patterns. Neuroimaging findings associated with status epilepticus may raise suspicion of ischemia, encephalitis, or neoplastic lesions possibly leading to additional studies and surgical treatment. Further follow-up imaging may prevent unnecessary intervention due to the fact that findings in status epilepticus may be reversible.

Case Report: We report a case of convulsive status epilepticus with electroencephalography and cranial magnetic resonance imaging (MRI) findings discussing differential diagnosis.

Conclusion: Our case highlights that clinicians should be aware of this potential fatal condition and start the treatment immediately.

Keywords: convulsive status epilepticus, seizure, magnetic resonance imaging, transient, T2 hyperintensity.

Introduction

Status Epilepticus (SE) is defined as a neurological emergency characterized by a single prolonged seizure or a series of seizures occurring close together with incomplete return to baseline. There are acute etiologies including stroke, hypoxia, systemic infection, trauma and metabolic disorders and chronic etiologies such as tumor and low concentration of anti-epileptic drugs. SE can present in convulsive, non-convulsive and electrographic patterns. Convulsive status epilepticus (CSE) is mostly recognized easily by presenting with unresponsiveness and tonic, clonic, or tonic-clonic movements of the extremities. These obvious manifestations of CSE may turn into more subtle extremity or face twitches, or saccadic eye movements[1, 2]. In addition, many neurological diseases manifest as seizure hence differential diagnosis of seizures may be challenging. Herein, we report a case of CSE with clinical and imaging features.

Case report

A 41-year-old woman admitted to emergency department with unawareness and somnolence, poor oral intake and limited cooperation nausea during the preceding week. She was known to have childhood-onset epilepsy and refuse to take her drugs (phenytoin 100mg/day, lamotrigine 50mg/day) for a week. On admission, vital signs of patient were normal. Initial neurological examination revealed drowsiness, disorientation in time and place, she was poorly cooperative. Cranial nerve examination was normal. She was able to localize painful stimulus in all extremities and had no pathological reflexes. No evidence of nuchal rigidity or meningeal irritation was present. Laboratory examination is unremarkable except high serum C-reactive protein level. Patient had evaluated in another hospital a couple of days ago because of recurrent seizures. Clear cerebrospinal fluid with a normal opening pressure, no cells, normal protein, glucose were detected on lumbar puncture performed due to suspicious neck stiffness and fever 38.5°C. She was referred to our institution for further examination and treatment, since her recurrent seizures could not be controlled. Preliminary diagnoses were encephalitis, postictal prolonged confusional state, convulsive status epilepticus, stroke. Patient underwent MRI to investigate underlying cause of clinical symptoms. MRI showed T2 hyperintensity in the grey and subcortical white matter with mild mass effect. Increased diffusion-weighted imaging (DWI) signal and low apparent diffusion coefficient (ADC) values were observed in affect-

Corresponding Author: Berrak Barutçu Asfuroglu **e-mail:** berrakbarutcu.bb@gmail.com

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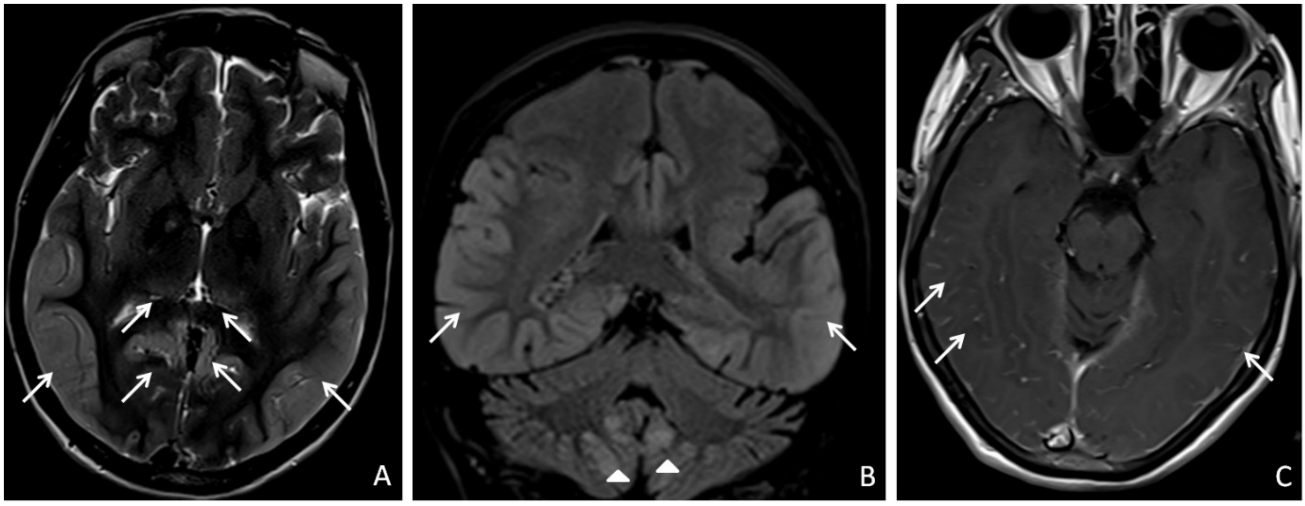

Figure 1: Axial T2W (A) and coronal FLAIR (B) MRI sequences reveal cortical and subcortical white matter (arrows), both cerebellum (arrowheads) and bilateral pulvinar nuclei hyperintensities and cortical swelling in bilateral temporo-occipital region (arrows). Axial post-contrast T1W image (C) reveal prominent bilateral occipital vessels (arrows).

ed areas. T2 hyperintensity was also detected in cerebellar hemispheres. Bilateral occipital leptomeningeal enhancement was noted on post-contrast T1 weighted (T1W) image (Figure 1 and 2). Due to unresponsiveness to treatment and ongoing seizures, she was intubated for the third-line treatment and medicated with propofol and followed up in intensive care unit. In addition to propofol infusion, phenytoin therapy (300mg/day) was maintained. Electroencephalography (EEG) showed sharp or sharp-slow wave activities in the right frontal hemisphere. Therefore, lacosamide was added for maintenance therapy. After 48 hours, no seizure activity observed clinically or electrophysiologically. Propofol was reduced and discontinued. Upon the development of seizures of a similar nature in a day, thiopental treatment was started, and valproic acid was added on to maintenance therapy. After six days, there were no seizure activity clinically or electrophysiologically. She got better and was oriented in time, place and to her own person. The final diagnosis was CSE. Control MRI performed after a month later was normal, no diffusion restriction or cortical swelling (Figure 3). She was discharged with valproic acid 1500mg/day, phenytoin 300 mg/day, lacozamide 200 mg/day treatment.

Discussion

One of the main causes of SE in epileptic patients is low blood concentrations of anti-epileptic drugs. Age, seizure duration and treatment response are prognostic factors. SE due to low serum concentrations of anti-epileptic drugs results in a usually good prognosis, with low mortality[3]. Early treat-

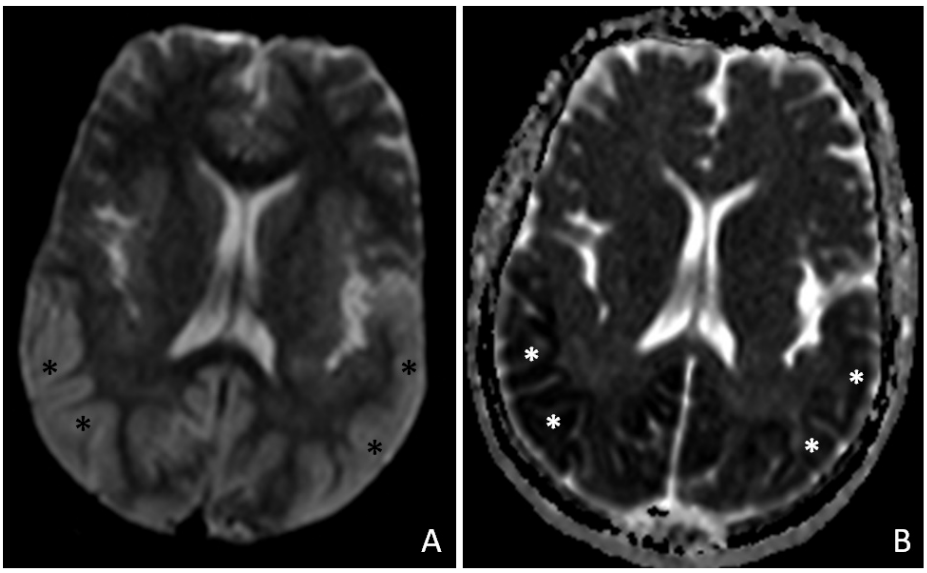

Figure 2: A diffusion-weighted axial MRI image (A, asterisk) reveals hyperintensities in the corresponding regions. The accompanying lower ADC values is noted as dark signals on ADC map (B, asteri sk).

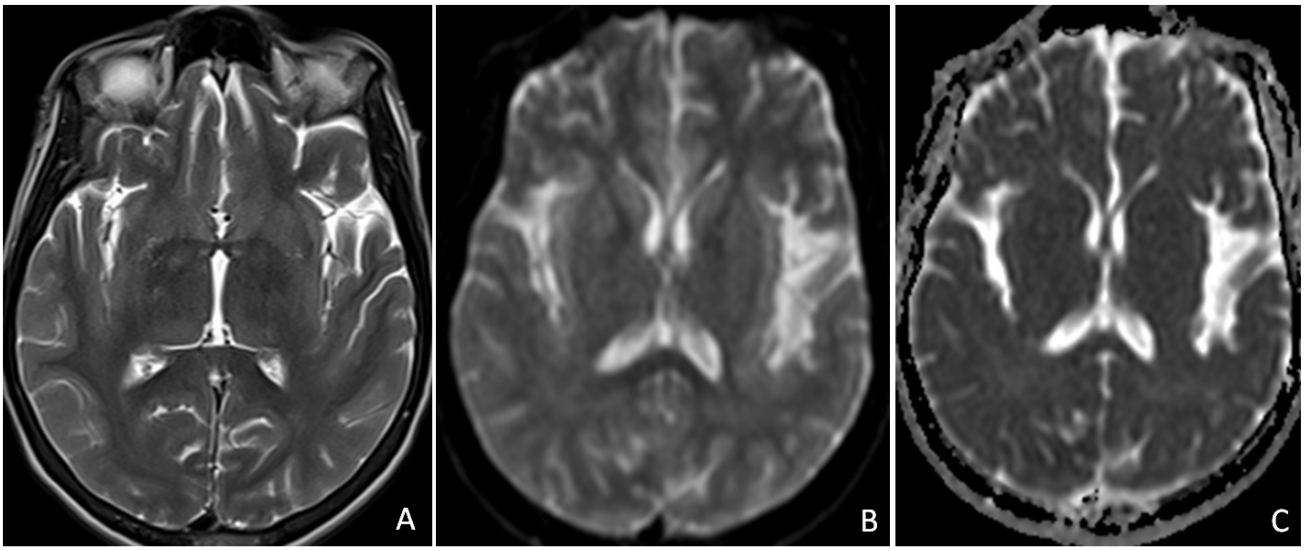

Figure 3: Axial T2W and DWI MRI obtained a month later shows resolution of abnormalities. The case report has written in an anonymous characteristic, thus secret and detailed data about the patient has removed. Editor and reviewers can know and see these detailed data. These data are backed up by editor and by reviewers.

ment with intravenous anticonvulsants is a significant step in the treatment of SE. Therefore, clinicians should suspect of SE and plan diagnostic assessment. Benzodiazepines are used as first-line treatment in CSE. Phenytoin and valproate are generally preferred as second-line drug. Levetiracetam and lacosamide are well tolerated popular drugs in second or third line agents. Thiopental was also added to treatment due to refractory seizures in our patient while followed in the intensive care unit. In general, EEG is not essential to start treatment, moreover, none of the ictal EEG patterns is specific to SE. The EEG in CSE shows various seizure patterns related to seizure types[1]. There is unquestionable evidence of MRI to facilitate differential diagnosis. In our case, SE was suspected by MRI findings in the first line. T2 and FLAIR hyperintensity with mild cortical swelling and corresponding restricted diffusion areas are often observed in cortex and hippocampi in SE cases. Basal ganglia, thalami, especially pulvinar nuclei, corpus callosum may also be involved. SE MRI findings may resemble that of posterior circulation ischaemic stroke[4]. It is important to know that T2 signal changes do not respect vascular territories in SE unlike stroke. These changes are suggested to be caused by a combination of vasogenic and cytotoxic edema. Ischemia and metabolic abnormalities trigger cytotoxic edema in gray matter. Increased perfusion and vascular permeability are responsible for vasogenic edema in white matter[5]. Gyral contrast enhancement, may be the reflection of impaired blood brain barrier, is another possible finding in MRI. Encephalitis may mimick SE, too. Herpes Simplex Encephalitis is the most common cause of fatal sporadic necrotizing viral encephalitis. In adults, Type 1 herpes simplex virus is more common than type 2 and involves the cortex and the subcortical white matter of bilateral temporal, frontal lobes, and insula on T2W MRI. SE typically involves in cortex and post-ictal edema affects entire hemisferic cortex. Hemorrhage is rare in SE cases[6]. Posterior reversible encephalopathy syndrome (PRES) is also a considerable differential diagnosis of SE for presenting with seizures and confusing MRI findings. It is characterized by reversible asymmetric subcortical vasogenic brain oedema, mostly in the bilateral parietooccipital region. Posterior fossa involvement is rare unless patient has an autoimmune disease[7]. Accompanying restricted diffusion and hemorrhagic foci may be seen both in encephalitis and PRES[6, 7]. Changes in the cerebellum in SE have been explained as a result of crossed cerebellar diaschisis because of prolonged excitatory synaptic activity via the cortico–cerebellar pathways[8]. Reversibility of changes in follow-up MRI is the main clue to exclude tumoral lesions. We have noticed the resolution of changes at the first month follow-up MRI of our patient. Brain atrophy, mesial temporal sclerosis and cortical laminar necrosis may be seen in long term especially in generalized convulsive SE[9].

Conclusion

Status Epilepticus (SE) is a neurological emergency that can mimic and be overlapped with multiple neurological conditions. Although T2W MRI abnormalities are mainly located in posterior regions, changes can also be focal, multifocal, hemispheric, or diffuse in SE. Knowing these findings and performing serial cranial MRI is necessary in order to adequately identify SE and distinguish it from other neurological entities. It has a remarkable mortality rate. Early recognition of these patients and early initiation of aggressive treatment is crucial and can prevent morbidity and mortality.

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Case Report

Journal of Emergency Medicine Case Reports

Acute urticaria with Angioedema in a patient with COVID-19 pneumonia: Favipiravir side effect or a rare cutaneous manifestation

Sevil Alkan Çeviker, Alper ŞENER, Cihan Yüksel, Taylan Önder, Anıl Akça, Servan Vurucu, Safiye Bilge Güçlü Kayta
Çanakkale Onsekiz Mart Üniversitesi, Tıp Fakültesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı

Abstract

Introduction: Coronavirus disease 2019 (COVID-19) has caused thousands of deaths since it was declared as a pandemic. Recently it continues to be one of the most followed topics in the world in terms of its course and treatment.Favipiravir is a broad-spectrum anti-viral agent that has been shown to be effective against various Coronaviruses in vitro. However, as with any drug use, side effects may develop with the use of favipravir treatment.

Case Report: We reported a 55-year-old female patient with acute urticarial with angioedema whom had COVID-19 pneumonia. She had no history of allergy, atopy, previous similar episodes or family history of hereditary angioedema. There is no drug or food consumption that may be suspicious in terms of allergy described by the patient other than favipravir.

Conclusion: As far as we know, it is the first case reported from our country. Since there is no specific examination for differential diagnosis, we cannot distinguish as a rare side effect due to favipiravir treatment or COVID-19 cutaneous manifestation. As a result, studies involving more cases of COVID-19 skin findings are needed.

Keywords: COVID-19, Favipiravir, side effect, cutaneous manifestations, angioedema, acute urticaria.

Introduction

Coronavirus disease 2019 (COVID-19) has caused thousands of deaths since it was declared as a pandemic and continues to be one of the most followed topics in the world in terms of its course and treatment.[1-3]

Favipiravir, a new broad-spectrum antiviral drug developed years ago for influenza virus treatment, is a pyrazine carboxamide derivative that blocks replication by selectively inhibiting influenza viral RNA-dependent RNA polymerase. It is effective against many RNA viruses including H1N1, Ebola, Arena virus and Bunyavirus.[1] Favipravir has been found to be effective in-vitro on Vero E6 cells infected with SARS-CoV-2 at high concentrations and shown in vitro against various coronaviruses.For these reasons it is one of the most widely used agents in the treatment of COVID-19 pneumonia in our country and over the world.[2,3] However, as with any drug use, side effects may develop with the use of favipravir treatment. It is reported that the most common side effect in COVID-19 patients treated with favipiravir is diarrhea. Favipravir has been shown to moderately increase liver function tests even at therapeutic doses. [4]However, sufficient literature information about skin side effects could not be reached.

We aimed to present a case of acute urticarial with angioedema who had COVID-19 pneumonia, that we can not distinguish as a rare side effect due to favipiravir treatment or COVID-19 cutaneous manifestation. As far as we know, it is the first case reported from our country.

Case report

A 55-year-old female patient,without a history of chronic disease, admitted to the pandemic outpatient clinic of our university hospital with tingling, swelling on the upper lip and emerging itchy maculopapular rashes on her trunk, face and abdomen for 8 hours duration (Picture 1).It was learned that, as her COVID-19 Real-time polymerase chain reaction (RT-PCR) test result was positive, favipravir treatment was started to her three days before. Except for the use of favipravir therapy, no drug, surgical, medical, and smoking history was reported.She had no history of allergy,atopy, previous similar episodes or family history of hereditary angioedema.She was not pregnant,too. There is no drug or food consumption that may be suspicious in terms of allergy described by the patient other than favipravir. Physical

Corresponding Author: Sevil Alkan Çeviker **e-mail:** s-ewil@hotmail.com
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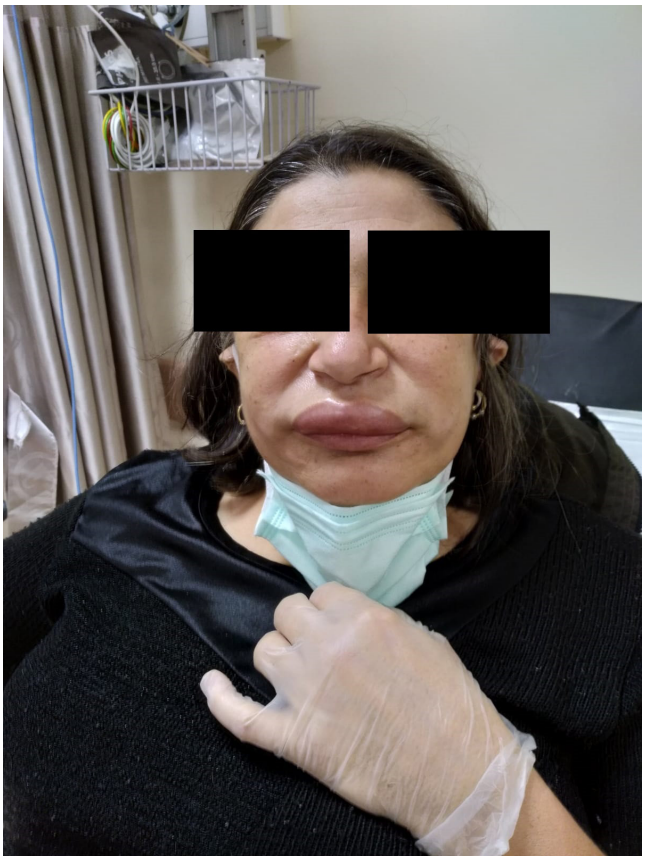
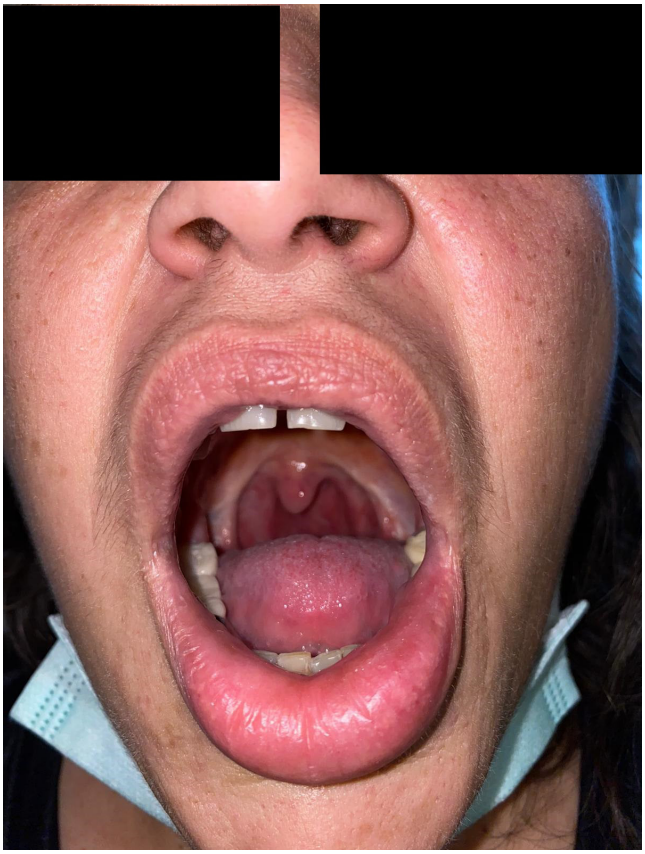


Picture 1



Picture 2

examination revealed that she had swollen lips and lower face, itchy maculopapular rashes on her trunk, the pharynx was oedematous (Picture 2) and mild crackles in the lung bases. Other system examinations were normal. She had no fever and cough. She had anosmia and ageusia. There was no periorbital or facial swelling. She was diagnosed as urticaria and angioedema afterdermatology consultation.The blood test results showed hemoglobin of 13.8 g/dl (normal range adult females, 12–16 g/dl), white blood cell count of 12040 /ul (normal range, 4000–10000/ul), platelets of 148000/ul (normal range, 165000–415000/ul), lymphocytes of 3180/ul (normal range, 800–2600/ul), C-reactive protein (CRP) 1.301mg/dL (normal range, 0 - 0,5), blood urea of 18.8 mg/dl (normal range, 15–45 mg/dl) and D-dimer of 128 (normal range, <0.5). Other investigations such as prothrombin time (PT), activated partial thromboplastin time (aPTT), international normalized ratio (INR) and liver enzymes were normal. No pathology was found in diagnostic tests for bacterial, viral and parasitic infections that could cause urticaria.Thorax tomography was compatible with viral pneumonia.The patient was hospitalized and hydroxychlorokin treatment 200 mg 2X1 per oral to treat COVID-19 pneumonia and antihistaminic treatment was started with the recommendation of consultant physician. She received intravenous methylprednisolone, ranitidine, and levocetirizine dihydrochloride. A drug side effect notification was made to the Turkish Ministry of Health. By hospital day 2, the patient's complaints markedly improved. The patient, whose clinical findings were stable during the follow-up, had no dyspne and respiratory distress, was discharged.

Discussion

When the medical literature is examined, a variety of dermatologic eruptions thought to be related to COVID-19 has been reported, but angioedema has rarely been reported[5-10]. Najafzadeh et al.[8] was reported similar case as and suggested that angioedemaas possible early diagnostic indicator of COVID-19 infection. However, while our patient had no complaints in the pre-treatment period, her complaints started on the third day of favipravir treatment.

The exact etiology of the skin findings associated with COVID-19 is not yet known. SARS-CoV-2 is thought to induce a mast cell activation, leading to histamine discharge.[5-8] Many hypotheses have been proposed in angioedema type 1 hypersensitivity reaction, often leading to an increase in vascular permeability or cross reaction between viral IgM and IgG promotes mast cell degranulation of mast cell Ig E or circulating immune complexes stimulate the production of vasoactive amines by basophils and activate com-

plement.[7-9]As general information, adverse drug reactions is divided into two groups asType A and Type B. Type A reactions are seen at a rate of 85-90%, among all drug side effects. These reactions known usually dose-dependent.[6-9] However, sufficient data on favipravir are not available yet. In the presented patient, urticaria and angioedema may be side effects due to favipravir or urticaria and angioedema due to histamine release. However, no differential diagnosis could be made. However, after favipravir was discontinued and the patient's antihistaminic treatment was arranged, the patient's complaints regressed.Urticaria and angioedema developed on the 3rd day of favipravir treatment in the patient, who had a diagnosis and symptoms of COVID-19 pneumonia before treatment but had no skin findings. Looking at the findings in the patient; both urticaria and angioedema were together, and the distinction between drug hypersensitivity reaction (Type 1 or 4) or COVID skin involvement could not be made clinically.

As seen in different case reports, COVID-19 pneumonia and urticaria/angioedema were seen in both genders. In the age group, it has been seen in patients from 30 to 60 years old.[5-10] The patient we presented was a 55-year-old female patient.

In the study conducted by Recalcati[10] in Italy, skin findings in 88 patients with coronavirus infection who did not take any new drugs within 15 days were evaluated. Skin findings developed in 18 (20.4%) of these 88 patients; Erythematous rash in 14 patients (16%), widespread urticaria in 3 patients (3.4%) and varicella-like vesicles in 1 patient (1.1%). [4] However, it was reported that photographs were not taken due to the high risk of infection.

Usually mild lip involvement, periorbital, swelling of the eyelids and tongue were reported [5-8] but in addition Hassan et al.[5] had reported a case in which hand swelling was added. The patient we presented had swelling in the hands and legs and additional urticarial plaques in the trunk and retroauricular area.

Conclusions

As far as we know, it is the first case reported from our country. Since there is no specific examination for differential diagnosis, we cannot distinguish as a rare side effect due to favipiravir treatment or COVID-19 cutaneous manifestation. As a result, studies involving more cases of COVID-19 skin findings are needed.

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Informed consent: The patient gave written informed consent for publication (both clinical information and images).

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