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Good News in Patients Undergoing Surgery for Suspected Lung Malignancy: Unicentric Castleman Disease

Akciğer Malignite Şüphesiyle Opere Olan Hastalara İyi Haber: Unisentrik Castleman Hastalığı

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ÖZ

Castleman disease (CD), also known as angiofollicular lymph node hyperplasia, is a heterogeneous lymphoproliferative disorder. These lesions can be mistaken for malignancy in terms of size and imaging characteristics, necessitating their excision. In this report, we present cases of CD that mimicked lung malignancy, underscoring the need to consider CD in the differential diagnosis of patients presenting with suspected lung cancer. This study was retrospectively designed. It included six patients who underwent surgery due to suspected lung malignancy and were subsequently diagnosed with Unicentric Castleman Disease (UCD). Of the six patients, four were male and two were female, with a mean age of 36.5 years (range: 27-50 years). Half of the patients were lifelong non-smokers. Comorbid conditions were identified in three patients, while the remaining three were asymptomatic and had no comorbidities. Histopathological examination revealed hyaline vascular type in three patients, plasma cell type in one patient, and mixed type UCD in one patient. All patients are currently alive and have not required any additional treatment. UCD represents a rare lymphoproliferative disease with diverse clinical manifestations. Surgical intervention is the established gold standard for this disease, yielding more favourable survival outcomes compared to both MCD and malignant pathologies in the lung. Therefore, in cases where malignant lung disease is suspected, the potential presence of UCD should not overlooked.

Keywords: Castleman disease, unicentric, lung malignancy, surgery

ABSTRACT

Castleman hastalığı (CH), diğer adıyla anjiofolliküler lenf nodu hiperplazisi, heterojen bir lenfoproliferatif bozukluktur. Bu lezyonlar boyut ve görüntüleme özellikleri açısından malignite ile karıştırılabilir ve bu nedenle cerrahi olarak çıkarılmaları gerekebilir. Bu raporda, akciğer malignitesi taklidi yapan CH vakalarını sunuyoruz ve akciğer kanseri şüphesiyle başvuran hastalarda Castleman hastalığının ayırıcı tanıda göz önünde bulundurulması gerektiğini vurguluyoruz. Bu çalışma retrospektif olarak tasarlanmıştır. Akciğer malignitesi şüphesiyle ameliyat edilen ve sonrasında Unisentrik Castleman Hastalığı (UCH) tanısı konulan altı hasta çalışmaya dahil edilmiştir. Altı hastanın dördü erkek, ikisi kadındı ve ortalama yaşları 36,5 yıl (aralık: 27-50 yıl) olarak saptandı. Hastaların yarısı hayatları boyunca hiç sigara içmemişti. Üç hastada ek hastalıklar (komorbidite) saptanırken, diğer üç hasta asemptomatik olup ek hastalık bulunmamaktaydı. Histopatolojik inceleme sonucunda, üç hastada hiyalin vasküler tip, bir hastada plazma hücre tipi, bir hastada ise karma tip UCH tespit edildi. Tüm hastalar hâlâ hayatta olup, ek bir tedavi gereksinimi duymamıştır. UCH, çeşitli klinik belirtilerle ortaya çıkan nadir bir lenfoproliferatif hastalıktır. Cerrahi müdahale, bu hastalığın tedavisinde altın standart olup, Multisentrik Castleman Hastalığı (MCH) ve akciğer malignitelerine kıyasla daha olumlu yaşam süresi sonuçları sağlamaktadır. Bu nedenle, akciğer malignitesi şüphesi olan vakalarda UCH varlığı göz ardı edilmemelidir.

Anahtar Kelimeler: Castleman hastalığı, unisentrik, akciğer malignitesi, cerrahi

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INTRODUCTION

Castleman disease (CD), also referred to as giant lymph node hyperplasia or angiofollicular lymph node hyperplasia, is a highly heterogeneous clinicopathologic condition within the spectrum of lymphoproliferative disorders. The disease is stratified into unicentric Castleman disease (UCD) and multicentric Castleman disease (MCD) according to its clinical manifestations (Figure 1).

CD was first described by Benjamin Castleman, who characterised the hyaline-vascular and unicentric variants of CD.[1] While UCD is localised in a single lymph node and is typically amenable to surgical excision, MCD is a systemic, progressive disorder with involvement of multiple lymph nodes, and is often fatal.[2]

Histopathologically, presentations of CD are subdivided into hyaline-vascular, plasma cell (plasmacytic and/or plasmablastic), and mixed subtypes.[3] The hyaline-vascular subtype is observed in 74–91% of UCD cases, while the plasma subtype is present in 9–26% of UCD cases.[4,5]

CASE PRESENTATION

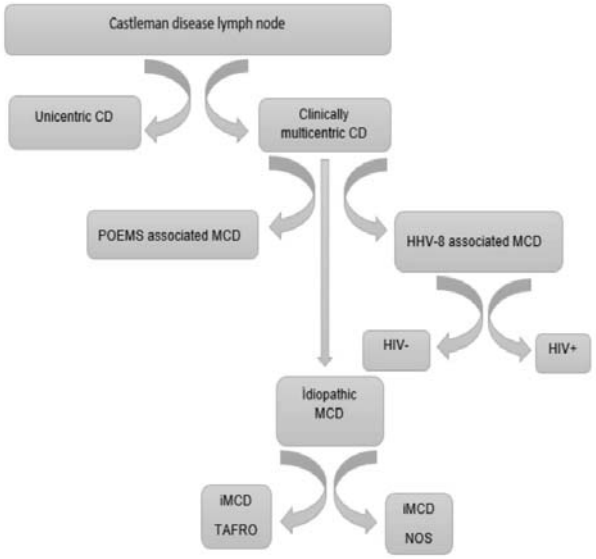
We retrospectively evaluated 6 patients who underwent surgery for suspected malignant lung disease between 2014 and 2024, all of whom were pathologically diagnosed with CD. Demographic characteristics of the patients are presented in Table 1. Preoperative thoracic computed tomography (CT) scans, preoperative and postoperative chest radiographs are illustrated in Figure 2.

Case 1

A 39-year-old woman with no significant medical history presented with complaints of chest pain, shortness of breath, cough, and sputum production for 3–4 months. No abnormal findings were detected with direct chest radiography. However, thoracic CT and magnetic resonance imaging (MRI) revealed a smoothly circumscribed space-occupying lesion of 3.5 cm in diameter adjacent to the right descending pulmonary artery. A positron emission tomography-computed tomography (PET-CT) scan showed an SUVmax of 4.5. A right posterolateral thoracotomy was performed on the patient, and the lymph node was completely excised. Postoperatively, the patient was managed in the hospital with a chest tube for 5 days and was subsequently discharged (Table 1, Figure 2).

Case 2

A 27-year-old male patient with no significant medical history or symptoms presented to the smoking cessation outpatient clinic. The thoracic CT scan revealed a 3.3 cm lesion at the level of the superior vena cava and vena azygos bifurcation. The patient initially underwent right uniportal video-assisted thoracoscopic surgery (UNI-VATS). However, due to an exposure issue, a right thoracotomy was subsequently performed, and the lymph node was completely excised. Postoperatively, the patient was managed in hospital with a chest tube for 4 days and was discharged on the 5th day (Table 1, Figure 2).



CD: Castleman disease; iMCD: idiopathic multicentric Castleman disease; MCD: multicentric Castleman disease; HIV, human immunodeficiency virus; HHV-8, human herpes virus 8; POEMS, polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin abnormalities; TAFRO, thrombocytopenia, anasarca, fever, reticulin fibrosis, and organomegaly; NOS, Not otherwise specified

Figure 1: Castleman disease classification.

Case 3

A 41-year-old male patient with no significant medical history presented with complaints of cough and sputum production. The thoracic CT scan revealed a 3 cm lymph node in the right paratracheal area. Endobronchial ultrasonography (EBUS) was performed, and a biopsy was taken, initially diagnosing a reactive lymph node. However, a follow-up thoracic CT scan performed one year later revealed that the paratracheal lymph node had enlarged to 4.5 cm. PET-CT revealed an SUVmax value for the lymph node of 6.7. Right UNI-VATS was performed, and the lymph node was completely excised. The chest tube was removed on the 2nd day of postoperative hospitalisation, and the

Table 1: General information about the patients

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age	39	27	41	35	27	50
Sex	Female	Male	Male	Male	Male	Female
Syptoms	Chest pain, shortness of breath, cough	None-insidental	None-insidental	None-insidental	None-insidental	None-insidental
Smoking	Non-smoker	Smoker	Ex-smoker	Non-smoker	Ex-smoker	Non-smoker
Concomitant disease	None	None	Hepatitis B carrier	None	Myastenia gravis	Bronchiectasis
Anatomical location	Right-descending pulmonary artery neighbourhood	Right-bifurcation of vena cava and vena azygos	Right-paratracheal area	Between left subclavian artery and carotid	Anterior mediastinum	Left-above the inferior pulmonary vein
Lymph Node Size	3.5 cm	3.3 cm	4.5 cm	4.4 cm	4.0 cm	3.4 cm
PET-CT SUVmax	4.5		6.77		8.0	4.4
Surgical procedure	Right thoracotomy	Right Uni-VATS + thoracotomy	Right Uni-VATS	Left Uni-VATS	Right Uni-VATS	Left Uni-VATS
Duration of operation	60 mins	100 mins	60 mins	30 mins	120 mins	40 mins
Duration of hospitalisation	6 day	5 day	3 day	3 day	4 day	4 day
Intraoperative bleeding	100 ml	300 ml	200 ml	None	50 ml	None
Histopathological subtype	Plasma cell	Hyaline vascular	Hyaline vascular	Hyaline vascular	Mix type	Unknown
Operation year	2014	2015	2021	2018	2021	2020
Survival	Alive	Alive	Alive	Alive	Alive	Alive

patient was discharged on the 3rd day (Table 1, Figure 2).

Case 4

In a 35-year-old male patient with no significant medical history, an incidental CT scan of the thorax demonstrated a lesion of approximately 4 cm between the left subclavian artery and the left carotid artery, extending from the mediastinum into the left hemithorax. Left UNI-VATS was performed and the lymph node was completely excised. The chest tube was removed on the 2nd day of postoperative hospitalisation, and the patient was discharged on the 3rd day (Table 1, Figure 2).

Case 5

A 27-year-old patient with myasthenia gravis was examined for anaemia, during which a mediastinal lesion was detected. PET-CT revealed a 4 cm lymph node in the anterior mediastinum with an SUVmax of 8. The patient underwent a thymectomy with left UNI-VATS and total excision of the lymph node. The patient was discharged on postoperative day 4 (Table 1, Figure 2).

Case 6

A 50-year-old woman followed for bronchiectasis underwent a follow-up thorax CT scan, which revealed a 3.4

cm lesion on the left inferior pulmonary vein. A PET-CT scan showed a 4 cm lymph node with an SUVmax of 4.4. Left UNI-VATS was performed and the lymph node was completely excised. The patient was discharged on postoperative day 4 (Table 1, Figure 2).

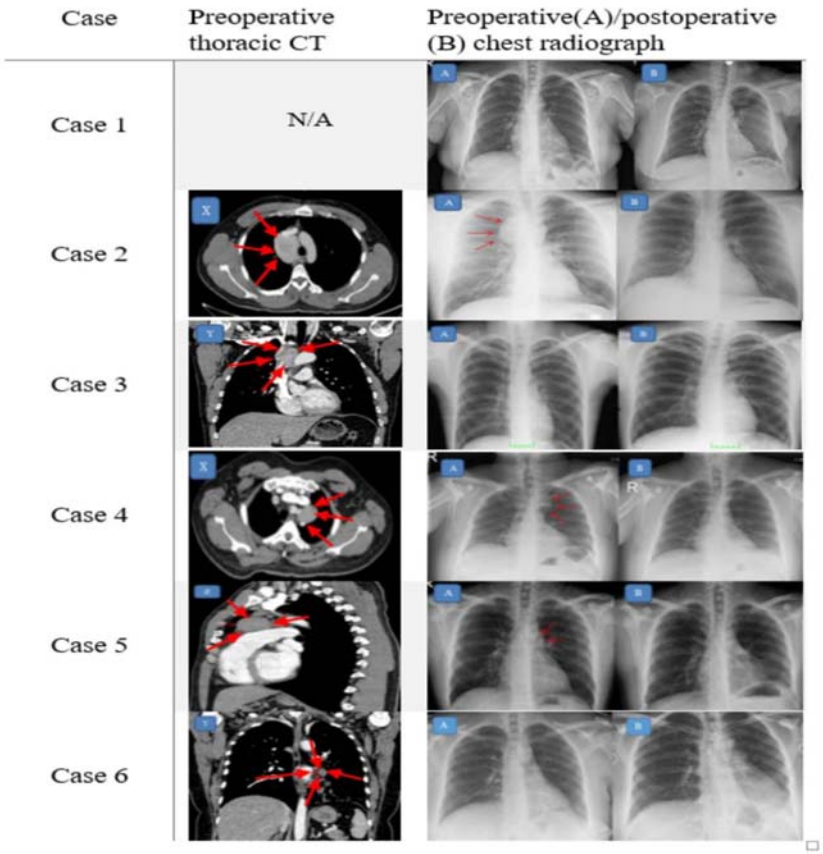


Figure 2: Preoperative and postoperative radiological images, pathological preparations and specimens of patients.

DISCUSSION

Castleman disease (CD) is a rare condition with limited cases; thus, data related to the disease have been evaluated according to guidelines, including diagnostic criteria and classification, developed by the Castleman Disease Collaborative Network (CDCN) since 2017.[6]

The incidence of UCD has been reported to be 16 per million individuals. UCD affects both sexes and can occur across all age groups, with the median onset age in the fourth decade of life.[7]

The clinical presentation of UDC typically involves an enlarged lymph node, which may cause compression-related symptoms such as local nerve compression, pain, or disruption of local structures (e.g. airways, neurovascular bundles, ureters). Laboratory abnormalities, though rare, may include hepatomegaly, splenomegaly, anaemia, signs of inflammation (elevated C-reactive protein, prolonged erythrocyte sedimentation rate), hypergammaglobulinemia, and hypoalbuminemia.[6] In our study, five patients had no primary complaints, and only one patient (Case 5) was diagnosed with UCD during a follow-up consultation for anaemia (Table 1).

Asymptomatic UCD is typically incidentally discovered during imaging procedures performed for unrelated reasons.[8] Lymph node detection and monitoring can be performed with imaging modalities including direct radiography, ultrasonography, CT, and MRI. Lymph nodes in UCD typically appear as single, well-circumscribed, and well-contrasted lesions on radiologic images (Figure 2).[9] However, the detection of a single lymph node on direct radiographs may pose challenges. In our study, three patients exhibited no abnormal findings on direct radiographs (Figure 2; Cases 1A, 3A, 6A), whereas suspicious appearances were observed on direct radiographs in the three other patients (Figure 2; Cases 2A, 4A, 5A). Thoracic CT scans confirmed the presence of enlarged lymph nodes

in all patients.

UCD can present with clinical features resembling thymoma, lymphoma, neurogenic tumour, bronchial adenoma, or lung tumour.[10,11] Therefore, the diagnosis of UCD requires complete excision of the enlarged lymph node. Consistent with existing literature, our cases initially raised suspicion of malignant lesions, leading to a diagnosis of CD post-excision.

Treatment strategies for patients with UCD vary depending on the subtype of the disease, with curative surgery being the primary approach. Recurrence following surgical intervention is rare, and the mean 5-year survival rate post-resection exceeds 90%.[12]

Asymptomatic unresectable UCD lacking compressive symptoms can be monitored without immediate intervention. However, if compressive symptoms are present, initial treatment with a monoclonal anti-CD20 antibody, with or without adjunctive steroids, is recommended. Surgical resection remains the preferred option after initial treatment, with radiotherapy recommended for cases where surgery is not viable. Patients presenting with unresectable UCD and inflammatory symptoms are managed using similar therapeutic approaches to those used for MCD (Figure 3).[13]

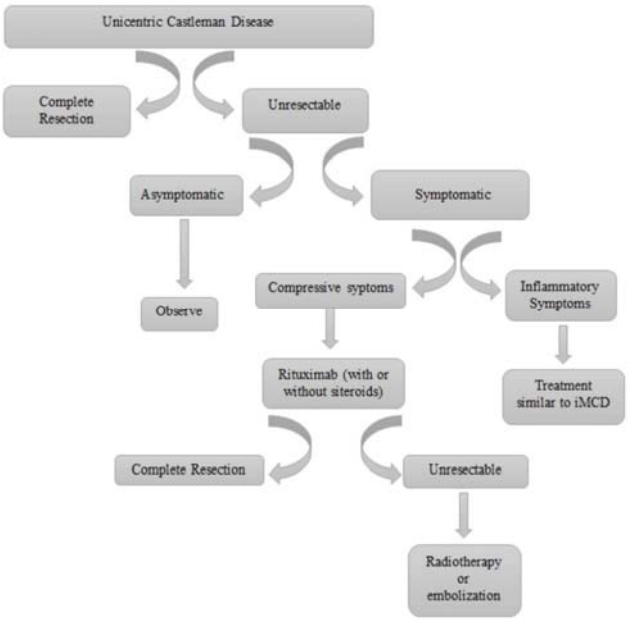


Figure 3: The treatment of Unicentric Castleman Disease. iMCD, idiopathic multicentric Castleman disease.

In conclusion, surgical intervention is the established gold standard for this disease, yielding more favourable survival outcomes compared to both MCD and malignant pathologies in the lung. Therefore, in cases where malignant lung disease is suspected, the potential presence of UCD should not overlooked.

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REFERENCES

1. Castleman B, Towne VW. Case records of the Massachusetts General Hospital: Case No. 40231. *N Engl J Med*. 1954;250(23):1001-1005. doi:10.1056/NEJM195406102502308
2. Kessler E. Multicentric giant lymph node hyperplasia. A report of seven cases. *Cancer*. 1985;56(10):2446-2451. doi:10.1002/1097-0142(19851115)56:10<2446::aid-cncr2820561020>3.0.co;2-4
3. Carbone A, De Paoli P, Gloghini A, Vaccher E. KSHV-associated multicentric Castleman disease: A tangle of different entities requiring multitarget treatment strategies. *Int J Cancer*. 2015;137(2):251-261. doi:10.1002/ijc.28923
4. Yu L, Tu M, Cortes J, et al. Clinical and pathological characteristics of HIV- and HHV-8-negative Castleman disease. *Blood*. 2017;129(12):1658-1668. doi:10.1182/blood-2016-11-748855
5. El Hussein S, Evans AG, Fang H, Wang W, Medeiros LJ. Unicentric Castleman Disease: Illustration of Its Morphologic Spectrum and Review of the Differential Diagnosis. *Arch Pathol Lab Med*. 2024;148(1):99-106. doi:10.5858/arpa.2022-0404-RA
6. Dispenzieri A, Fajgenbaum DC. Overview of Castleman disease. *Blood*. 2020;135(16):1353-1364. doi:10.1182/blood.2019000931
7. Simpson D. Epidemiology of Castleman Disease. *Hematol Oncol Clin North Am*. 2018;32(1):1-10. doi:10.1016/j.hoc.2017.09.001

8. Boutboul D, Fadlallah J, Chawki S, et al. Treatment and outcome of Unicentric Castleman Disease: a retrospective analysis of 71 cases. *Br J Haematol*. 2019;186(2):269-273. doi:10.1111/bjh.15921

9. Pitot MA, Tahboub Amawi AD, Alexander LF, et al. Imaging of Castleman Disease. *Radiographics*. 2023;43(8):e220210. doi:10.1148/rg.220210

10. Keller AR, Hochholzer L, Castleman B. Hyaline-vascular and plasma-cell types of giant lymph node hyperplasia of the mediastinum and other locations. *Cancer*. 1972;29(3):670-683. doi:10.1002/1097-0142(197203)29:3<670::aid-cncr2820290321>3.0.co;2-#

11. Ko SF, Hsieh MJ, Ng SH, et al. Imaging spectrum of Castleman's disease. *AJR Am J Roentgenol*. 2004;182(3):769-775. doi:10.2214/ajr.182.3.1820769

12. Talat N, Belgaumkar AP, Schulte KM. Surgery in Castleman's disease: a systematic review of 404 published cases. *Ann Surg*. 2012;255(4):677-684. doi:10.1097/SLA.0b013e318249dcdc

13. Gündüz E, Özdemir N, Bakanay ŞM, Karakuş S. A Rare Lymphoproliferative Disease: Castleman Disease. *Turk J Haematol*. 2021;38(4):314-320. doi:10.4274/tjh.galenos.2021.2021.0440