Case Report
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Retroperitoneal Castleman Disease Mimicking Paraganglioma in a Patient with Klinefelter Syndrome: A Case Report

Klinefelter Sendromlu Bir Hastada Paragangliomayı Taklit Eden Retroperitoneal Castleman Hastalığı: Bir Olgu Sunumu

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Abstract

Castleman disease progresses with the enlargement of the affected lymph nodes and represented by a wide range of symptoms. This lymphoproliferative disease rarely affects the retroperitoneum. A patient with Klinefelter syndrome was admitted to our clinic following palpitation and sweat attacks. It was observed that the urinary catecholamine metabolites were elevated and a pararenal mass was found on the left side. The patient was directed to surgery with the paraganglioma pre-diagnosis after further examination. Histopathological examination of the excised mass confirmed the diagnosis of Castleman disease. The urinary catecholamine metabolites returned to near-normal levels at eight weeks after the surgery. We present a case of Castleman disease in a patient with Klinefelter syndrome, imitating paraganglioma as per the clinical, radiological and laboratory findings.

Keywords: Castleman disease; paraganglioma; Klinefelter syndrome; retroperitoneum

Özet

Castleman hastalığı, etkilenen lenf nodunda büyüme ile ortaya çıkar ve birçok farklı semptomla kendini gösterebilir. Bu lenfoproliferatif hastalık, nadiren retroperitoneumu etkilemektedir. Klinefelter sendromlu bir hasta, çarpıntı ve terleme atakları ile kliniğimize başvurdu. İdrar katekolamin metabolitlerinin yükselmiş olduğu gözlenip, sol pararenal bölgede bir kitle saptandı. İleri tetkik edilen hasta paraganglioma ön tanısı ile cerrahiye yönlendirildi. Eksize edilen kitlenin histopatolojik değerlendirme sonucu Castleman hastalığı tanısını doğruladı. Hastanın idrar katekolamin metabolitleri cerrahi sonrası sekizinci haftada normale yakın seviyelere geriledi. Bu çalışmada, Klinefelter sendromlu bir hastada klinik, radyolojik ve laboratuvar bulguları ile paragangliomayı taklit eden bir Castleman hastalığının sunulması amaçlanmıştır.

Anahtar kelimeler: Castleman hastalığı; paraganglioma; Klinefelter sendromu, retroperitoneum

Introduction

Castleman disease (CD) is a rare lymphoproliferative disorder with a poorly known pathogenesis. It is usually seen in young adults. CD may either present as a unicentric or a multicentric disorder. According to the etiopathogenesis of the unicentric form of the disease, excessive cytokine production, principally interleukin (IL) 6, is thought to initiate the vascular endothelial growth factor (VEGF) release and to promote angiogenesis in lymphoid cells (1, 2). CD commonly manifests with an enlarged lymph node in the cervical, axillary, mediastinal or rarely, even in the retroperitoneal and pelvic regions (3). Unicentric CD commonly presents as an asymptomatic disorder; nevertheless, different systemic symptoms may

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resemble various diseases during the onset (4). This paper reports an unusual presentation of retroperitoneal CD, mimicking paraganglioma in a patient with Klinefelter syndrome.

Case Report

A 38-year old male having Klinefelter syndrome was referred to our department due to episodic palpitation and sweat attacks. Personal history of the patient stated no chronic disease and drug use. Patient's blood pressure was measured to be 140/90 mmHg in consecutive evaluations on different days. The heart rate was recorded to be 76 beats/min and the electrocardiogram showed sinus rhythm. Physical examination showed no palpable lymph node, abdominal mass, or hepatosplenomegaly.

The hemogram revealed hemoglobin to be 13.3 g/dL, white blood cell count to be 9,100/mm^3 and platelet count to be 32,3000/mm^3. The liver and renal function test results were found to be in the normal range. Erythrocyte sedimentation rate (ESR) was 38 mm/hour, C-reactive protein (CRP) level was 9.3 mg/L and lactate dehydrogenase level was 160 U/L (normal). The thyroid hormone levels were observed to be in the normal reference range. Urine analysis yielded normal results. An elevation in the 24 h urinary catecholamine levels was determined wherein metanephrine was 585 µg/24 h (44-261 µg/24 h) while normetanephrine was 1360 µg/24 h (11-419 µg/24 h). These high measurements of catecholamine metabolites were verified by properly collected three consecutive urine tests.

Thoraco-abdominal magnetic resonance (MR) screening was performed for localization of the probable lesion. Dynamic contrast-enhanced MR images demonstrated a 47×60 mm mass as hypointense on T1-weighted imaging and heterogeneously hyperintense on T2-weighted imaging, in the retroperitoneal region adjacent to the left kidney in the anterolateral plane (Figure 1). No concomitant enlarged lymph node was detected. Positron emission tomography with fluorine-18 fluorodeoxyglucose (18F-FDG PET) revealed that the uptake of the left pararenal mass was similar to that of the liver (SUV max 2.3) (Figure 2).

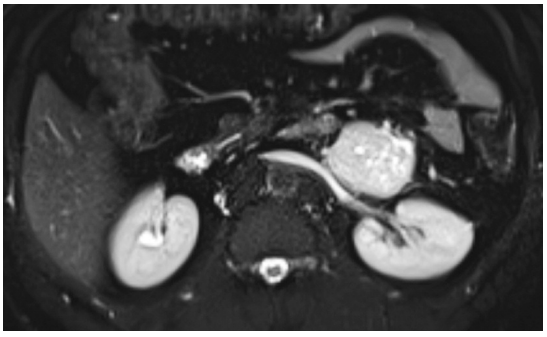

Figure 1: Dynamic contrast-enhanced MR image of a 47×60 mm mass in the retroperitoneal region adjacent to left kidney.

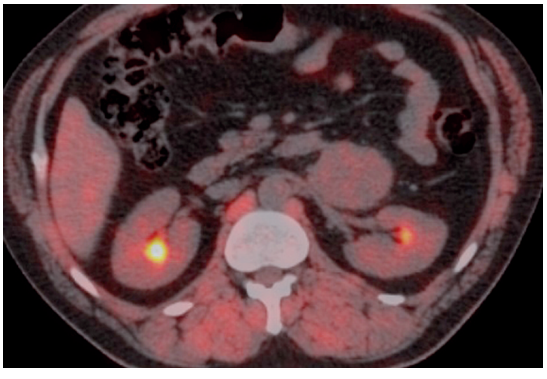

Figure 2: The similar uptake of 18F-FDG by the left pararenal mass with that of the liver on 18F-FDG PET image.

The patient was taken for surgery after the initiation of alpha blockage treatment. The retroperitoneal mass adjacent to the inferior pole of the left kidney, measuring 50×60 mm was excised with its capsule. Histological examination revealed that the structure of the lymph node was degenerated, as examined on hematoxylin and eosin (H & E) sections. The interfollicular region showed violent vascular proliferation while the vessel walls were seen to be hyalinized (Figure 3). The lollipop lesion observed at the germinal centers of the follicle is presented in Figure 4.

No complications were observed throughout the recovery period and the symptoms were disappeared after the surgery. The preoperative ESR and CRP levels that were mildly elevated were found to improve after the surgery. The controlled estimation of 24 h urinary catecholamine metabolites collected eight weeks after the surgery showed that

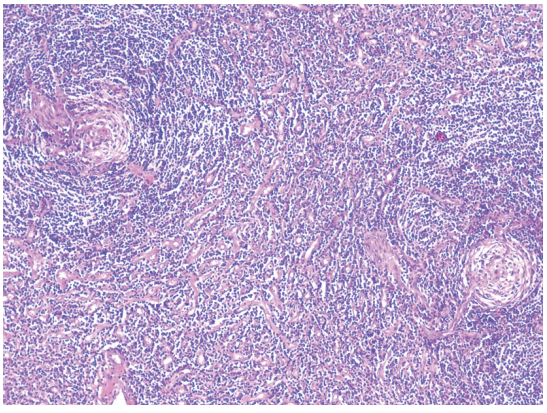

Figure 3: Violent vascular proliferation in the interfollicular region and hyalinization in the vessel wall (HE, x20 objective).

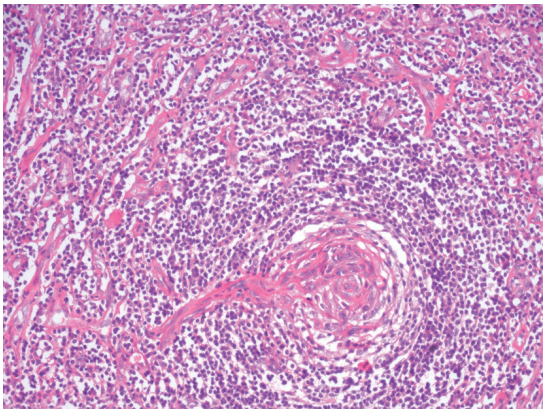

Figure 4: The lollipop lesion at the follicle germinal centers (HE, X40 objective).

the metanephrine level returned to normal (166 µg/24 h) while the normetanephrine level decreased to near-normal reference range (496 µg/24 h).

Discussion

CD is a rare, lymphoproliferative disease having ill-defined pathogenesis. Although the etiology of the unicentric variant of CD remains unclear, human immunodeficiency virus (HIV) and human herpesvirus 8 (HHV-8) have been found to be associated with the development of the multicentric variant of this disease (5). Previous studies have shown that increased levels of cytokines such as IL-6 and VEGF may play a principal role in the pathogenesis of the unicentric disease and lead to different systemic symptoms (2). The diagnosis of CD is based on histopathologic evaluation. Three main histopathological variants of unicentric CD have been recognized: the hyaline vascular, plasma cell, and mixed types (6, 7). The case reported here is of a unicentric hyaline vascular variant of the disease, which is the most common histopathological type (6). The multicentric form of the disease commonly presents with extensive peripheral lymphadenopathy and systemic symptoms like fever, weight loss, and night sweats (8). On the contrary, unicentric CD frequently presents with the asymptomatic manifestation of an enlarged lymph node (9). This paper reports the case of a patient who presented with episodic palpitation and sweating with no peripheral lymph node enlargement. Laboratory findings revealed elevated ESR and CRP levels, and hemogram abnormalities including anemia and thrombocytopenia. Although mild elevation in the ESR and CRP levels were detected in the patient; nevertheless, this elevation was not so high as to consider a malignancy. Elevated urinary catecholamine metabolites and a visible pararenal mass during the MR screening enthralled about a paraganglioma in the patient. The patient was advised surgical treatment to excise the identified retroperitoneal mass. The surgery was completed successfully and no complication was seen during the recovery period. Histopathological evaluation of the mass demonstrated the presence of degenerated lymph node with hyalinized vessel walls and lollipop appearance of germinal centers, leading to the diagnosis of Castleman disease. The patient's symptoms subsided after the surgery. Also, the level of urinary catecholamine metabolites came to near-normal level.

Retroperitoneal localization of CD is not commonly seen and comprises only 11% of all the cases (10). The gold standard treatment for unicentric CD involves complete surgical resection of the lesion (3).

Atypical presentation of CD has been reported in previous case reports. Kim et al. reported an unusual presentation of the pararenal CD by mimicking systemic lupus erythematosus with persistent tongue ulcers and positive antinuclear antibody and anti-double-strained DNA (11). Some other atypical presentations of CD have been reported as urosepsis (12), papilledema (13), and hypercalcemia (14).

Many growth factors and cytokines including IL-6, localized in paragangliomas and pheochromocytomas, and immunoreactive characteristics of these disorders have been described earlier (15). Clearly increased IL-6 levels was reported in a case of pheochromocytoma characterized by symptoms of inflammatory response including fever and malaise; the authors commentated that excessive IL-6 secretion may be associated with increased normetanephrine level (16). Some other catecholamines secreting pheochromocytomas with over-production of IL-6 have been demonstrated in the literature previously (17-19). Most of these cases presented with inflammatory symptoms and a demonstrative decrease in IL-6 levels was seen after the patients were being treated either surgically or medically. However, the literature reports only limited cases of IL-6 over-production in paraganglioma. Sokabe et al. reported a case in a patient with the systemic inflammatory syndrome, having increased IL-6 level due to a jugular paraganglioma, without any detectable hormone secretion including catecholamines (20). Another case report in the literature presented the coexistence of Castleman disease and pheochromocytoma possibly by linking up to the expression of IL-6 by the tumor mass (17). Although we could not estimate serum IL-6 levels of the patient, a similar cause and effect relationship may explain the elevation in the levels of catecholamines in the present case.

In summary, this case report deals with a patient with Klinefelter syndrome. However, its accompaniment with the CD is exceptional. Although malignancies like extragonadal germ cell tumors or breast cancer are commonly seen in patients with Klinefelter syndrome, they are seldom seen in association with lymphoproliferative diseases (21). The literature reports only one case presenting Klinefelter Syndrome and CD concomitantly in an 11-year-old boy and the authors commented that Klinefelter syndrome may make a patient susceptible to CD (22). However, this relationship still remains a hypothesis without sufficient evidence.

The diagnosis of the unicentric CD may be difficult for the clinician in some cases since the disease does not present typical symptoms. In this paper, we have reported a different presentation of the disease which mimics the clinical and laboratory findings of paraganglioma in a patient with Klinefelter syndrome. Castleman disease as a rare cause of retroperitoneal lesions should, therefore, be kept in mind in patients presenting with clinical and laboratory findings of retroperitoneal paraganglioma.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Sema Hepşen, Erkam Sencar; Design: Sema Hepşen, Pınar Akhanlı, Erman Çakal; Control/Supervision: Erman Çakal, Mustafa Özbek; Data Collection and/or Processing: Sema Hepşen, Erkam Sencar, Ata Türker Arıkök, Duray Şeker; Analysis and/or Interpretation: Sema Hepşen, Pınar Akhanlı, İlknur Ünsal; Literature Review: Sema Hepşen, İlknur Ünsal, Erkam Sencar; Writing the Article: Sema Hepşen; Critical Review: Sema Hepşen, Pınar Akhanlı, Erman Çakal; References and Fundings: Erman Çakal; Mustafa Özbek; Materials: Ata Türker Arıkök, Duray Şeker, Sema Hepşen.

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