Case Report / Olgu Sunumu

Clear Cell Sarcoma of the Kidney: A Remarkably Uncommon Case Report

Böbreğin Berrak Hücreli Sarkomu: Oldukça Nadir Bir Olgu Sunumu

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Abstract: Clear cell sarcoma of the kidney (CCSK) is one of the most common malignant renal neoplasms in childhood, although it is quite rare. Its incidence peaks around the age of 3 and it is twice as common in males. We present a rare case of CCSK showing a rare histopathological pattern in terms of age and gender. A 7-month-old female patient presented with complaints of vomiting, abdominal swelling, and diarrhea. Imaging analysis revealed a mass in the right kidney, and right radical nephrectomy was performed, considering Wilms tumor (WT). There was a solid gray-white mass that completely filled the kidney, with a maximum dimension of 8.5 cm, macroscopically. The samples obtained showed intratubular structures within the tumor and kidney parenchyma in limited areas at the periphery. The tumor had a normochromic monotonous nucleus with occasional clear cytoplasm and mostly exhibited a palisade-like arrangement pattern. In the differential diagnosis, with blastemal WT and Ewing sarcoma being the primary considerations, the positivity of CyclinD1 markers, negativity of other markers, and morphological characteristics were evaluated in favor of CCSK with a palisaded Schwannian pattern. The patient was put on an intensive chemotherapy process, but was lost after relaps at weet 24. CCSK is seen in a similar age group as WT but is distinguished by its rarity and relatively worse prognosis. Histopathologically, it most commonly presents in a myxoid pattern and least commonly in anaplastic pattern. The palisaded schwannian type seen in our case is recorded at a rate of 11%. No spesific diagnostic marker has been identified immunohistochemically, but the overexpression of markers such as CyclinD1, BCOR, and EZH2 is reported to be helpful in diagnosis. Due to its high metastatic potential and limited treatment options, further research is needed to understand the molecular nature of the disease.
Keywords: Clear cell sarcoma of the kidney, Case report, Rare tumor of the childhood, Malignant renal tumor of the childhood

Özet: Böbreğin berrak hücreli sarkomu (BBHS) oldukça nadir görülmekle birlikte çocukluk çağının en sık görülen malign böbrek neoplazilerinden biridir. İnsidansı 3 yaş civarında pik yapmakta olup erkek cinsiyette 2 kat daha sık görülmektedir. Nadir bir yaş ve cinsiyette nadir bir histopatolojik patern gösteren BBHS olgusu sunduk. 7 aylık kız hasta kusma, karında şişlik ve ishal şikayeti ile başvurdu. Yapılan görüntüleme analizinde sağ böbrekte kitle saptanması üzerine Wilms tümörü (WT) düşünülerek sağ radikal nefrektomi uygulandı. Makroskopik olarak en büyük boyutu 8,5 cm olan böbreğin tamamını dolduran solid gri-beyaz kitle mevcuttu. Alınan örneklerde tümör içerisinde entrape tübül yapıları ve periferde sınırlı alanlarda böbrek parankimi seçilmekteydi. Tümör normokromatik monoton nükleuslu yer yer şeffaf sitoplazmalı ve çoğunlukla palizat benzeri dizilim paterninde idi. Ayırıcı tanıda başta blastemal WT ve Ewing sarkomu da düşünülerek yapılan belirteçlerden SiklinD1 pozitifliği, diğer markırların negatifliği ve morfolojik özellikleri ile olgu palizatlanan schwannian paternde BBHS lehine değerlendirildi. Olgu yoğun kemoterapi sürecine alındı ancak 24. hafta relaps sonrası kaybedildi. BBHS, WT ile benzer yaş grubunda görülmekle birlikte oldukça nadir olması ve nispeten daha kötü prognozlu olması ile ayrılmaktadır. Histopatolojik olarak en sık miksoid, en az anaplastik paternde karşımıza çıkmaktadır. Olgumuzda görülen palizatlanan schwannian tip ise %11 oranında kaydedilmiştir. İmmunohistokimyasal olarak spesifik tanı koydurucu bir belirteç henüz tanımlanmamış olup SiklinD1, BCOR, EZH2 gibi markırların overekspresyonunun tanıya yardımcı olduğu bildirilmektedir. Metastaz potansiyeli yüksek ve tedavi alternatifi kısıtlı olması nedeni ile hastalığın moleküler doğasını anlamak için yeni araştırmalara ihtiyaç vardır.
Anahtar Kelimeler: Böbreğin şeffaf hücreli sarkomu, olgu sunumu, Çocukluk çağının nadir tümörü, çocukluk çağı malign böbrek tümörü

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1. Introduction

Clear cell sarcoma of the kidney (CCSK) is a rare kidney tumor that often appears in the early years of life. It constitutes approximately 2.8% of primary childhood kidney tumors (1). However, its incidence is reported as 0.2 per million in the overall group of childhood cancers (2). CCSK is dominant in males and more often between the ages of 2-3 years (male to female ratio of 2.63) (3). It is extremely rare in infants younger than 6 months and young adults.

Orginially called ‘’Bone-metastasizing renal tumor of childhood’’ in 1978 (4), in has a high potential for malignancy. It is known to have a worse prognosis compared to Wilms tumor (WT), which is more commonly encountered in the same age group (3). We presented an extremely rare histopathological subtype and clinical case of CCSK.

2. Case Report

A 7-month-old girl presented to the hospital with complaints of vomiting, abdominal distension, and diarrhea that had been ongoing for a month. During the physical examination, a mass was palpated in the right side of the abdomen. Abdominal ultrasound revealed a solid mass with a size of approximately 8 cm, originating from the medial parenchyma of the right kidney and showing an exophytic extension into the abdomen with widespread arterial and venous vascularity, as well as a heterogeneous internal structure and smooth contours. A mass was confirmed on magnetic resonance imaging, and compression of the inferior vena cava and right renal vein was present in the vicinity of the mass. However, no trombus was detected within the vascular lumen. Based on clinical and imaging analysis results, the patient underwent a right radical nephrectomy and was sent to the pathology laboratory with a preliminary diagnosis of WT. Macroscopically, a heterogeneous mas with smooth margins and dimensions of 8.8x8.5x8 cm was observed, consisting of gray-white and grey-brown areas that covered the entire surface of the kidney on the cut section. Capsule seemed intact. Numerous samples were taken from different areas. Histopathologically, the tumor consisted of cells with sharp borders that were separated from the renal parenchyma, which was focally selected in microscopic foci around the tumor. Most of these cells had small to medium-sized uniform nuclei with irregular nuclear membranes and focal clear cytoplasm arranged in a schwannoma-like pattern (Figure 1). There were numerous mitotic figures in the background. Additionally, angioinvasion was observed (Figure 2). Vimentin, Bcl-2, CyclinD1, CD99, CD56, INI1, and FLI1 were diffusely positive, whereas WT-1, SMA, EMA, CK AE1-AE3, PAX8, Synaptophysin, Chromogranin A, Myo-D1, CD57, Neurofilament, NSE, S100, Myogenin, Desmin, ALK-1, and CD34 were negative, indicating differential diagnosis from WT and other childhood kidney tumors. The Ki-67 proliferation index was around 40% (Figure 3). Based on the histopathological and immunohistochemical findings, the case was diagnosed as a CCSK with palisading Schwannian histological subtype. Therefore, the patient was treated according to the National Wilms Tumor Study Group 5th version (NWTS-V) protocol. Abdominal radiotherapy was administered from the 10th week of the 24-week treatment. Despite being in remission at the 6th and 18th weeks, abdominal and cerebral metastases were detected at the end of the treatment. Unfortunately, the patient, who deviated from the protocol, passed away within one month.

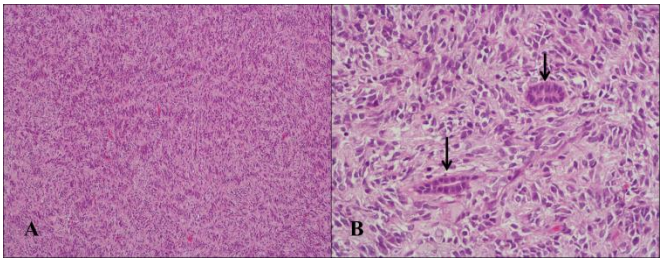

Figure 1. Verocay body-like palisading of neoplastic cells, H&E, X40 (A), abundant mitotic figures are observed in the tumoral infiltration composed of uniform hypochromatic nuclei, and there are also entrapped renal tubular structures (black arrow) in between, H&E, X200 (B)

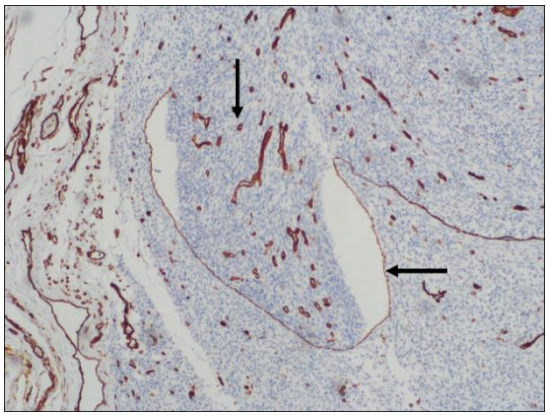

Figure 2. Vascular invasion of tumor cells, CD31, immunohistochemistry, X100

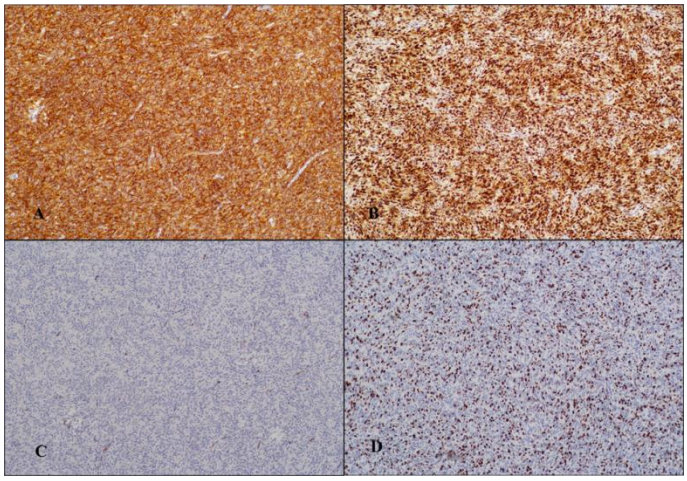

Figure 3. The tumor shows positivity for CD56 (A) and Cyclin D1 (B), negativity for WT1 (C), and Ki-67 proliferation index of 40% (D), immunohistochemistry, X40

3. Discussion

CCSK ranks second among childhood kidney malignancies. Approximately 90% of tumors in this group are composed of WT (1, 5). The most common symptoms observed in patients are abdominal pain, distension or mass, nausea, vomiting, weight loss, subfebrile fever, hamaturia, and anemia. It is known for its aggressive clinical behavior and late recurrence (6). WT is the most important differential diagnosis for CCSK. While WT shows different incidences according to ethnic groups, such a characteristic has not been

identified for CCSK. Genetic factors are thought to play a major role in its pathogenesis.

CCSK can present with a wide range of histopahological morphologies. The described patterns and frequencies include myxoid (50%), sclerosing (35%), cellular (26%), epitheloid (trabecular or acinar type) (13%), palisading verocay bodies (11%), spindle cell (7%), storiform (4%), and anaplastic (2.6%), with patterns frequently coexisting within the tumor (7). Classical morphology consists of cell nests or cords separated by thin and branching fibrovascular septa, giving a ‘’chicken-wire’’ appearance. Cord cells contain clear cytoplasm and monotonous round-to-oval-shaped nuclei with fine chromatin and indistinct nucleoli. Hypochromatic finely dispersed chromatin is an important cytologic feature helpful in distinguishing this tumor from mimickers (8). Differentiating CCSK, especially blastemal WT, congenital mesoblastic nephroma, rhabdoid tumor, primitive neuroectodermal tumor, extra-skeletal Ewing's sarcoma and neuroblastoma is important for the correct treatment protocol and prognostic approach (9). WT has an early tendency to metastasize, classically spreads to lymph nodes, lungs, and liver, but bone metastasis is rare. WT can have a bilateral onset in 5% of cases, but such a feature has not yet been reported for CCSK. In contrast to WT, no relationship has been shown between CCSK and congenital anomalies (10).

There is no spesific immunohistochemical marker identified for CCSK. It shows positivity with Vimentin and weak positivity with Actin. Negativity for EMA, Desmin, S100, WT1, CD56, CD99, Synaptophysin, CKAE1-AE3, CAM5.2 supports the diagnosis (8, 11). The overexpression of CyclinD1 has been detected in recent times and it is recommended as an auxiliary diagnostic tool (12). Although BCOR positivity has been suggested to be supportive, negative cases with molecularly proven diagnosis have also been reported (13). In some recent molecular studies, it has been found that the tumor exhibits overexpression of EZH2 messenger RNA (14).

The treatment protocol consists of systemic chemotherapy and local radiotherapy in addition to radical surgery (15). The prognosis has improved in recent times with the application of more intensive chemotherapy or radiotherapy, but the need for alternative targeted therapies persists due to the toxic effects of intensive therapy. Relapse is observed in approximately 16% of patients within 17 months of diagnosis. The most common sites of relapse are the brain, lungs, and bones, and the prognosis after relapse is quite poor (16).

This case was in a rarer age group and gender compared to the cases in the literature, and it had a rare histopathological pattern, palisaded variant like schwannoma. It is a challenging diagnosis clinically, radiologically, and histopathologically, and it is necessary to differentiate it from mimickers due to its poor prognostic features. Molecular investigations are recommended for cases that cannot be ruled out with immunohistochemical markers for clarification of the diagnosis.

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Ethics

Informed Consent: The authors declared that informed consent form was signed by the patient.

Copyright Transfer Form: Copyright Transfer Form was signed by the authors.

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