Anaplastic Variant of Clear Cell Sarcoma of The Kidney: A Rare Case Report

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Abstract

Clear cell sarcoma (CCSK) of the kidney is an uncommon but distinctive pediatric renal tumor with a characteristic histological pattern and marked propensity for bone metastasis. The rare anaplastic variant constitutes about 3% of cases of CCSK and carries an unfavorable prognosis, with increased tumor recurrence and resistant to chemotherapy. This variant show high frequency of p53 gene mutation and p53 over expression in comparison to the usual CCSK. We present a case of anaplastic variant of CCSK in an 10-year-old boy with both cytologic and histologic features, highlighting the importance of recognizing this rare entity.

Key words

Bone metastasis; clear cell sarcoma of the kidney; Wilms tumor.

Introduction

Clear cell sarcoma of the kidney (CCSK) is a rare malignant renal tumor mainly occurring in childhood, which was first described by Kidd et al(1) in 1970.

It was originally considered to be a variant of Wilms tumor with an unfavourable histology(1) but was subsequently separated into distinct entity(2). CCSK has many histological patterns, which include classic, myxoid, sclerosing, cellular, epithelioid, palisading, spindle, storiform and anaplastic(3). The myxoid pattern is commonest followed by sclerosing and cellular pattern. Anaplastic pattern is the rarest of all comprising 3% of overall cases of CCSK(3). It has also been seen that p53 expression is negative or mildly positive in usual CCSK, but is strongly and diffusely positive in anaplastic CCSK. Mutations of p53 gene and protein overexpression have been seen in a number of pediatric malignant tumors including anaplastic Wilms tumor, rhabdomyosarcoma and gliomas(4,5,6) but the available data on p53 protein expression in CCSK is very limited. Since this lesion is rare we report well documented case of anaplastic variant of CCSK with p53 protein overexpression.

Case Report

A 10-year-old boy was brought to the surgical outpatient department with complaints of abdominal swelling for 10 months and hematuria for 15 days. There was no history of abdominal pain, vomiting, or loss of weight. On examination, the patient had pallor and the abdomen was distended with a firm non-tender swelling in the right hypochondrial and lumbar region. Blood and urine investigations were within normal limits. Computed tomography scan showed a large mass arising from the

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Fig. 1 : Computerized tomography shows a heterogenous mass originating from the right kidney.
right kidney and filling most of the abdomen (Figure. 1). Regional lymph nodes were not enlarged. A fine needle aspiration was performed from the mass without guidance for initiating therapy.

Cytomorphology showed a malignant tumor with eccentrically placed cytoplasm and nuclei with indentations and grooves. Three types of cells were seen: cord cells, septal cells, and markedly bizarre cells (Figure. 3a). Atypical mitotic figure were identified. Based on these findings the possibilities considered were (1) Wilms tumor with unfavourable histology (2) CCSK. Preoperative chemotherapy was given to the patient which included doxorubicin and vincristine. After six months, tumor shrinkage was achieved. Subsequently, right nephrectomy was performed.

![Fig. 2 : Gross examination shows a large grey white mass replacing almost the entire kidney.](image)

**Histopathological findings**

Grossly, the nephrectomy specimen weighed 2200 gm and measured 21x17x10cm. The entire kidney was replaced by a large mass measuring 19.5x15.0x8.5cm. Cut surface was grey white, soft to firm with areas of hemorrhage and necrosis (Figure. 2).

Tissue was fixed in 10% buffered formalin, routinely processed and paraffin embedded. Five micron thick sections were cut and stained with routine hematoxylin and eosin. Immunohistochemical stains were performed by the method of avidin–biotin complex (ABC) immunoperoxidase using monoclonal antibodies to vimentin (dilution 1:100), cytokeratin (dilution 1:50), p53 (dilution 1:100).

Microscopic examination revealed a malignant tumor in classic and nodular pattern with intervening areas of fibrosis (Figure. 3b). The tumor cells were predominantly polygonal with large nuclei. Nuclear grooving and clearing were apparent. Foci of microcystic change and extracellular myxoid material were identified. In addition, bizarre anaplastic cells were seen focally and extensively in different sections (Figure 3c). These cells were markedly pleomorphic and had large irregular shape hyperchromatic nuclei. Abundant mitosis and apoptotic figures were noted throughout the lesion. On immunohistochemistry, the tumor cells were positive for vimentin and showed diffuse nuclear positivity for p53 (Figure. 3d). The tumor cells were negative for cytokeratin. Based on histological and immunohistochemical findings, the final diagnosis of "clear cell sarcoma kidney anaplastic variant" was made.

![Fig. 3 : Aspirate shows tumor cells with eccentric and grooved nuclei. Numerous atypical bizarre hyperchromatic cells and atypical quadripolar mitosis also identified (papincoulaou original magnification x400).](image)

**Fig. 3 :**

a. Aspirate shows tumor cells with eccentric and grooved nuclei. Numerous atypical bizarre hyperchromatic cells and atypical quadripolar mitosis also identified (papincoulaou original magnification x400).

b. Classic pattern of clear cell sarcoma of the kidney characterized by cells with fine nuclearchromatin, palecytoplasm separated by fibrovascular stroma (H&E x100).

c. Anaplastic bizarre hyperchromatic cells seen within the tumor (H&E x400).

d. Tumor cells show intense immunoreactivity for p53 (H&E x400).
Postoperatively the patient died after 9 months due to bony metastasis.

**Discussion**

CCSK comprises 1.6-4.1% of all primary pediatric renal tumors\(^7\text{-}^8\). The tumor is more prevalent in males rather than females in the ratio of 6.7:1\(^7\). There is increased frequency of bone metastasis (42-78%)\(^9\) and the overall distant metastasis is seen in 4% of patients at presentation\(^3\). Due to several distinctive features CCSK has been classified separately from Wilms tumor. Unlike Wilms tumor, there is no known genetic association in CCSK and no association with hemihypertrophy and sporadic aniridia. CCSK has wide spectrum of histological patterns including classic, myxoid, sclerosing, cellular, epitheloid, palisading, spindle, storiform, and anaplastic. Anaplastic variant of CCSK is characterized by nuclear hyperchromasia, nuclear gigantism and atypical mitosis. Anaplasia can be focal or diffuse. Anaplastic pattern is slightly less common (3%) in CCSK, than anaplasia among Wilms tumor (5%)\(^3\text{-}^10\).

It has been postulated that p53 tumor suppressor gene (TSG) mutations play an important role in the tumorigensis of CCSK\(^3\text{-}^11\). The information regarding p53 gene mutation and protein expression in CCSK is remarkably scant. Moreover unlike Wilms tumor, genetic studies regarding p53 mutation on CCSK have not shown any consistent findings\(^12\). The reported incidence of p53 mutations in anaplastic WT ranged from 25% to 73%\(^10\text{-}^13\text{-}^14\). A study by Cheah et al\(^11\) in all 8 cases of CCSK showed p53 immunohistochemical expression but the molecular evidence was lacking. In one of the largest study of 351 cases of CCSK\(^9\), IHC staining for p53 was done in 29 non-anaplastic and 3 cases of anaplastic CCSK. Among the 29 non-anaplastic CCSK, 25 showed minimal staining, <5% of nuclei and 4 cases had intermediate staining, ranging from 11% to 40%. In contrast, 66% of anaplastic CCSK showed intense diffuse staining >75% of nuclei for p53. In another study eight cases of CCSK were analyzed for p53 mutations in the region of exons 4 to 8 by polymerase chain reaction–single-strand conformational polymorphism (PCR-SSCP) method and DNA sequencing analysis\(^15\). Histopathologically, no CCSK showed anaplastic features. Only two cases harbored p53 mutation and none of them showed protein overexpression. However it was concluded that p53 gene mutations were infrequent along with lack of protein expression in usual cases of CCSK\(^15\).

It is important to distinguish anaplastic CCSK from anaplastic Wilm’s tumor because of differences in treatment. A comparative study showed that addition of doxorubicin to the combination of vincristin and actinomycin-D improved six year relapse free survival of children with CCSK\(^16\). In the NWTS-5 protocol CCSK at all stages is treated with radical nephrectomy followed by chemotherapy with doxorubicin, cyclophosphamide, VCR, etoposide for 24 weeks and radiotherapy. Multivariate analysis has shown four independent significant prognostic factors for survival: treatment with doxorubicin, revised stage, patient age, and presence of tumor necrosis\(^3\).

**Conclusion**

Anaplastic Wilms tumor is associated with high incidence of p53 gene mutation and protein expression thus leading to high resistance to chemotherapy and poor prognosis. This lesion assumes importance that p53 overexpression plays role in pathogenesis of CCSK especially anaplastic variant. However, whether the presence of anaplasia in CCSK is related to p53 mutations and a poor prognosis remains uncertain. Because of the prognostic significance and treatment implication, it is important to diagnose anaplastic variant of CCSK.
References


