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Case report

Clear Cell Renal Sarcoma in a 2 Year Old Girl: A Case Report of a Rare Variant with Review of Literature

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Summary

Although Wilms tumor is the most common renal neoplasm in the pediatric population, other rare childhood renal neoplasms should be considered in a pediatric patient presenting with an abdominal mass. CCSK represents one of the most common tumors with "unfavorable histology" listed by the National Wilms Tumor Study Group (NWTSG). It thus deserves meticulous histopathological survey in patients treated as Wilms tumour. We report a 2 year old girl with CCSK diagnosed on histopathology after having undergone radical nephrouereterectomy for suspected wilms. Postoperatively treated with chemotherapy and is without any residual tumor or recurrence at 3 years followup.

Abstract

Malignant pediatric renal tumors include nephroblastoma, which can develop into Wilms tumor (85%), mesoblastic nephroma (5%), clear cell sarcoma (CCSK)(4%), rhabdoid tumor (2%), and other rare tumors (2%).Despite this CCSK represents one of the most common tumors with "unfavorable histology" listed by the National Wilms Tumor Study Group (NWTSG). It thus deserves meticulous hispathopatholigal survey in patients treated as wilms tumour. We report a 2 year old girl with CCSK diagnosed on histopathology having undergone radical nephrouereterectomy for suspected wilms. Postoperatively treated with chemotherapy and is without any residual tumor or recurrence at 3 years followup.

Keywords: CCSK; NWTS; Wilms Variant.

Introduction

Wilms'tumor, which accounts for 6–7% of all pediatric malignancies [1], is the most common renal tumor in children older than 6 months and younger than 12 years of age [2]. However, when a child presents with an abdominal mass, rare childhood renal neoplasms should be considered as a differential diagnosis along with Wilms' tumor. CCSK is one of these rare childhood renal neoplasms. CCSK has been reported by the NWTSG to represent 4% of childhood renal tumors [3] and is seen mainly in young children with a peak incidence between 2 and 3 years of age [4] with a male predominance [5]. It is the most frequently misdiagnosed pediatric renal tumor, attributable to its infrequency, morphological diversity, and lack of specific diagnostic markers [3]. Treatment consists of radical nephroureterectomy and chemotherapy. Reported long-term survival rate is 60–70% [5]. CT scans are invaluable in evaluating the size and extent of abdominal masses, any surrounding lymphadenopathy, and the resectability of tumors but cannot diagnose CCSK [6]. The diagnosis is made on histpoathological examination. We report a case of a 2 year old girl clinically and radiologically thought to be a Wilms' tumor, which turned out to be CCSK. She has completed adjuvant chemotherapy and radiotherapy and is without any recurrence at 3 years follow up.

Case report

A 2 year old girl presented with a large lump in the abdomen noticed by mother while she was being bathed. Clinically a large, firm mass reniform shaped was felt on the right side per abdomen. She was evaluated with an x-ray which showed a radiodense, nonhomogenous mass on right side without any calcification. Ultrasound showed a mass of size 11x10x12 cm, arising from right kidney and completely replacing it. The mass had mixed echogenecity with cystic and solid areas, without any extension into the renal vein highly suggestive of Wilms'. Contrast enhanced computed tomography was suggestive of a large mass,measuring 12 x 10 x 12 cm arising from the right kidney and entirely replacing it. It was closely related to and pressing upon the inferior vena cava and the liver though not in filtrating it. There was no extension of tumor thrombus in to the renal vein but was compressing it. The scan was reported as Wilms' tumor with enlarged ipsilateral hilar nodes. The opposite kidney was normal with no evidence of any metastasis (figure1, 2). Following the NWTSG 5 protocol the child underwent right radical nephroureterectomy. The tumor was very large 12 x 12 x 14 cm, weighing 900 grams and compressing the IVC without any extension into it (figure3, 4). Unfortunately there was localised tumor spillage intraoperative as the tumor was very friable. Lymphnodes were sampled. The histopathology diagnosed it to be a CCSK without any nodal involvement and the tumor was staged III owing to the spillage (figure 6). The child received adjuvant

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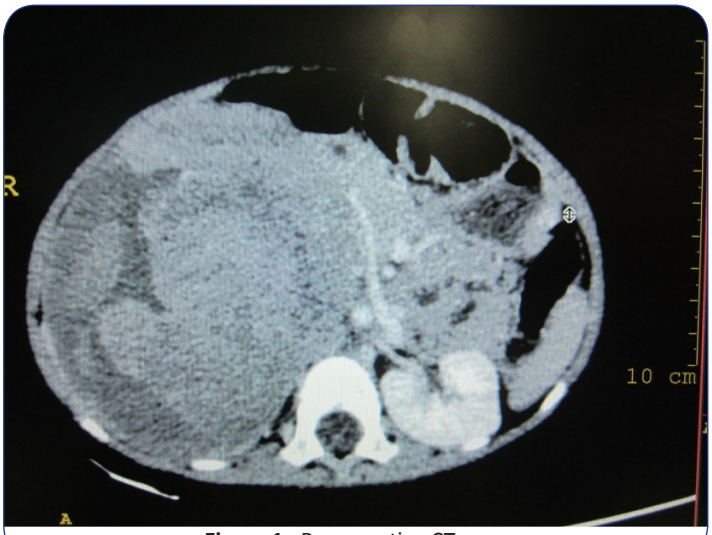

Figure 1 : Preoperative CT scan

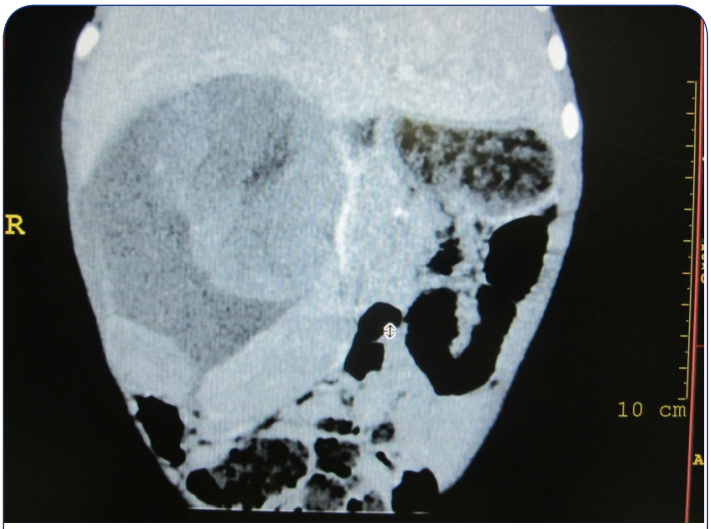

Figure 2: Preoperative CT scan

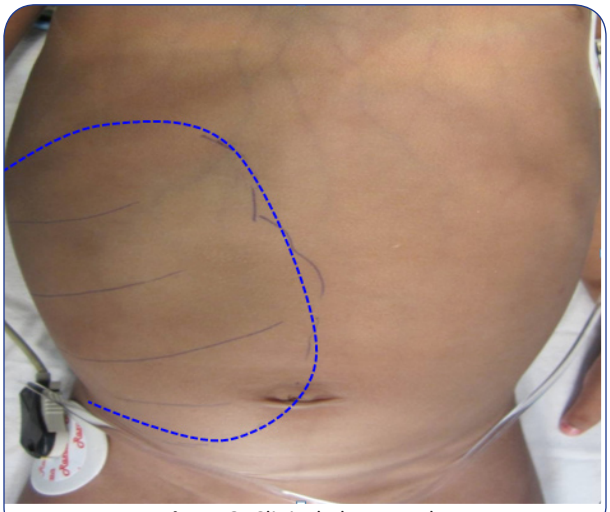

Figure 3: Clinical photograph

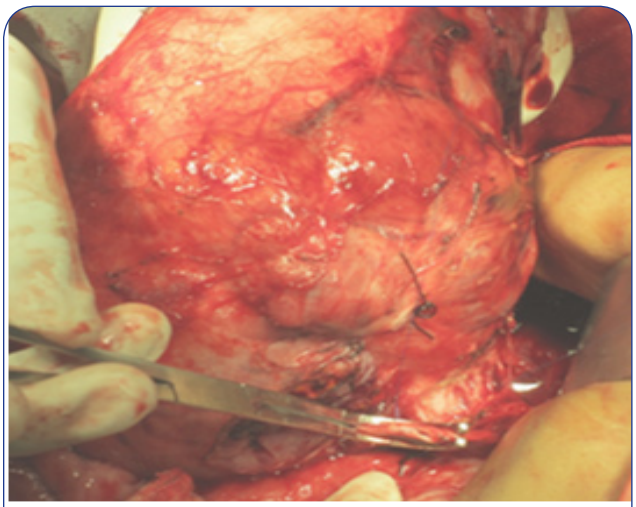

Figure 4: Intraoperative Photograph

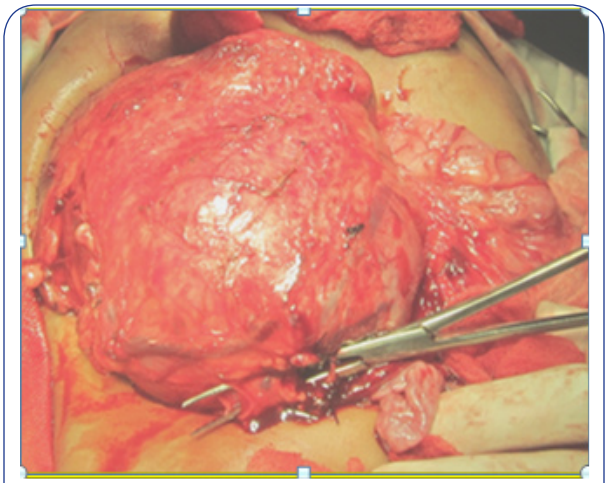

Figure 5: Intraoperative Photograph

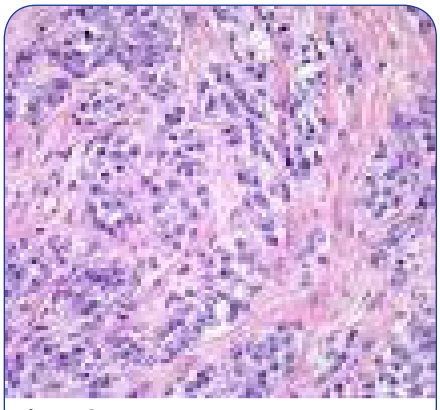

Figure 6

chemotherapy in the form of 24 cycles of Vincristine, Adriamycin and Cyclofosfamide along with 11 sittings of radiotherapy to the abdomen. Bone scan of the child is normal. She shows no evidence of recurrence or metastasis on investigations at 3 years follow up.

Discussion

In 1970, Kidd initially recognized clear cell sarcoma of the kidney as a

distinct clinicopathologic entity, noting its propensity to metastasize to bone, poor clinical outcome, and the sarcomatous nonepithelial nature of the tumor. Once thought to be an unfavourable variant of Wilms' tumor, CCSK is now considered a rare mesenchymal tumor of the kidney in children. As it is difficult to diagnose CCSK on clinical evaluation and radiological investigations, the gold standard for diagnosis is final histopathologic determination. CCSK has been reported to have a distinctive complex vascular network, classically described as "chicken-wire" pattern [6]. CCSK includes undifferentiated cells, cords and nests separated by fibrovascular septa, and abundant extracellular matrix. It has a variety of histologic patterns that includes classic, myxoid, sclerosing, cellular, epithelioid, spindle cell, palisading, and others. Nevertheless, there are no tumor specific markers for CCSK, which makes the diagnosis difficult. But immunohistochemistry can be of some help as CCSK is consistently positive for vimentin and usually negative for cytokeratin [7].

An important distinguishing feature of CCSK is its 40–60% incidence of bone metastasis, which is much higher than the 2% incidence of bone metastasis found in Wilms'tumor [4]. Other sites of distant metastases are lung, retroperitoneum, brain, and liver: unusual sites for metastasis being scalp, epidural space, nasopharynx, neck, paraspinal area, abdominal wall, axilla, and orbit [5]. Approximately 5% of patients have metastatic disease at presentation, the commonest site being the ipsilateral renal hilar lymph nodes. Skip metastases to periaortic lymph nodes have been reported as well. Its aggressiveness and risk of bone metastases, along with its propensity for late relapse (up to 4 years from original diagnosis [5]) and relatively poor outcome compared to Wilms' tumors, support the importance of early, correct diagnosis and follow up [8].

Staging of CCSK is essentially same as that for Wilms' (Table 1) CCSK being a rare childhood renal tumor; only a few homogeneously treated CCSK cohorts have been reported. Multivariate analysis by Argani et al on reviewing 351 cases of clear cell sarcoma of the kidney (CCSK), including 182 cases entered on National Wilms'Tumor Study Group (NWTSG) trials revealed four independent prognostic factors for survival: treatment with doxorubicin, stage, age at diagnosis, and tumor necrosis. Of note, stage 1 patients had a remarkable 98% survival rate. No other histologic or clinical variable independently correlated with survival [9]. Approximately 20% of documented clear cell sarcoma of the kidney metastases occurred at least 3 years after diagnosis; some occurred as long as 10 years later [6].

According to current Children's Oncology Group protocol (AREN0321), all patients with clear cell sarcoma of the kidney, except patients with stage IV, continue treatment as in NWTS-5. However, patients with stage I who undergo lymph node sampling do not undergo radiation therapy to the tumor bed. Any patient with stage I who has not undergone lymph node sampling is upstaged to stage II. Patients with stage IV undergo treatment with irinotecan and vincristine in an upfront window approach before treatment with cyclophosphamide, etoposide, vincristine, doxorubicin, and cyclophosphamide [9]. The approach for treating clear cell sarcoma of the kidney (CCSK) is different from the approach for Wilms' tumor because the overall survival of children with clear cell sarcoma of the kidney remains considerably lower than that of patients with favorable-histology Wilms' tumor [10] Patients who have stage I tumors, are aged 2-4 years, and have no tumor necrosis tend to have a better prognosis. Patients who present with distant metastases or multifocal disease have a poor prognosis, with a 50% long-term 6-year survival rate. Treatment with doxorubicin has resulted in a 66% reduction in the tumor-related mortality rate [11,10].

In the largest SIOP cohort described so far which is by AR. Furtwangler et al analysed a total of 191 CCSK patients. Pre-

Table 1

Stage	Description
Stage I	Tumor confined to the kidney and completely resected. The renal capsule is intact and the tumor was not ruptured prior to removal. No renal sinusextension. There is no residual tumor.
Stage II	Extracapuslar penetration, but is completely resected. Renal sinus extension or extrarenal vessels may contain tumor thrombus or be infiltrated by tumor.
Stage III	Residual nonhematogenous tumor confined to the abdomen: lymph node involvement, any tumor spillage, peritoneal implants, tumor beyond surgical margin either grossly or microscopically, or tumor not completely removed
Stage IV	Hematogenous metastases to lung, liver, bone,brain, etc.
Stage V	Bilateral renal involvement at diagnosis.

operative chemotherapy was administered to 169/191 patients. All patients underwent total nephrectomy and 189/191 patients received post-operative chemotherapy. Radiotherapy was used selectively. Factors such as gender, tumor volume and type of initial treatment were not found to be prognostic for event free survival and overall survival. As further intensification of treatment is hampered by direct and late toxicity, future directions should include the development of targeted therapy based on specific molecular aberrations of CCSK [12].

The indexed child was treated as stage III CCSK and received 24 cycles VDC and 11 sittings of radiation to abdomen without any morbidity and is recurrence free at 3 years follow up. Sagar Dhamne et al used the morphoproteomic approach to analyze clear cell sarcoma of kidney (CCSK), and proposed that cyclin D1 may be a central molecule and inclusion of relatively less toxic but effective therapies in the form of statins, 13-cis retinoic acid, curcumin, and 17-AAG in the combinatorial treatment strategies, which can target the involved subcellular pathways, may be considered [13].

The ideal follow up schedule has not been established particularly for the length of follow up. Generally, these visits occur every 1-3 months for the first year, every 3-6 months for the second and third years, then yearly there after. Investigators in Europe and in North America have reported an increase in number of CNS recurrences of clear cell sarcoma of the kidney (CCSK). The brain should be routinely scanned with other areas like lungs. Patients with recurrent CCSK that involves the brain have responded to treatment with ifosfamide, carboplatin, and etoposide (ICE), coupled with local control consisting of either surgical resection and/or radiation.

Conclusion

Although Wilms' tumor is the most common renal neoplasm in children other rare childhood renal neoplasms like CCSK should be considered as its differentials. Stagewise treatment for CCSK differs, it alters the prognosis and requires thorough Workup and rigorous follow up.

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