

INTRA-ABDOMINAL ROUND CELL TUMOUR OF CHILDHOOD - A DILEMMA OF SITE AND ORIGIN

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ABSTRACT:

Neuroblastoma and Wilms tumor are the common intra-abdominal round cell tumours of early childhood. The treatment modalities of these malignancies are very different. Neuroblastoma arising from the kidney or an aggressive adrenal neuroblastoma invading the kidney may easily be misdiagnosed as a case of Wilms tumor preoperatively. We

report a case of small round cell tumour entirely replacing right kidney and adrenal gland. Although, the exact site of the tumour remained undetermined, immunohistochemistry confirmed the diagnosis of neuroblastoma resolving the dilemma of origin.

Key words: Adrenal gland, kidney, neuroblastoma, Wilms tumour.

INTRODUCTION:

Pediatric abdominal tumors often present in an advanced stage at first clinical examination. The primary differential diagnosis of a large palpable right upper quadrant mass in a young child includes neuroblastoma, Wilms tumor and hepatoblastoma. The location of the mass may prove useful in preoperatively identifying the origin of these lesions. A mass localized to kidney suggest Wilms tumor. The possibility of neuroblastoma needs to be considered for a mass arising within adrenal gland while a tumor localized to liver suggest a hepatoblastoma. Intrarenal neuroblastoma is very rare and originates from either adrenal rests found within the renal tissue or from intrarenal sympathetic ganglia.

CLINICAL SUMMARY:

An eight year old girl presented with distension of upper abdomen which was noticed by her mother incidentally. She also complained of dragging sensation in the abdomen. There was no history of vomiting, loose stools, constipation, fever, weight loss, joint pain, hematuria or frequency of micturition. On examination, there was a palpable mass in the right upper abdomen measuring 15x10 cm, which was vaguely nodular, firm in consistency and did not cross the midline. Hematological and biochemical parameters were normal except for an increased level of Vanillyl mandelic acid (VMA) 41.8mg/mg/creatinine (Normal value of 24 hours VMA urinary excretion-<8mg/day). Ultrasonography of abdomen showed a large well circumscribed lobulated lesion with areas of calcification and necrosis involving the right kidney, suggesting the possibility of Wilms tumor. Computed tomography (CT) of whole abdomen showed a large heterogeneously enhancing right renal mass with necrosis and amorphous calcification displacing the



Fig. 1: CT whole abdomen showing right renal mass displacing the adjoining structures with normal left kidney.

adjoining structures. Adrenal gland was not identified on CT abdomen (Fig. 1). Intraoperatively, a bosselated vascular tumor was seen occupying the upper pole and involving 2/3rd of right kidney extending up to the inferior surface of the liver and involving the inferior vena cava. Adrenal gland was not identified intraoperatively also. Right radical nephrectomy was performed and the resected specimen was sent for histopathological examination.

HISTOPATHOLOGICAL FINDINGS:



Fig. 2: Large solid, nodular, grey white tumour. Grossly no normal renal or adrenal tissue could be made out.

The nephrectomy specimen received weighed 4.5 kg and measured 19x12x7cm. Cut surface showed a grey white tumour measuring 15x11cm involving whole kidney. Adrenal gland could not be identified grossly (Fig. 2).

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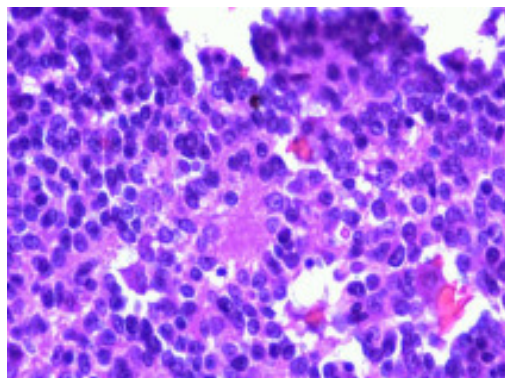


Fig 3: Sheets of small round tumor cells with rosette formation. Note the neuropil in the rosettes (arrow) (H&E 20x).

Microscopic examination showed a small round blue cell neoplasm with tumour cells arranged in lobules separated by thin fibrovascular septa. Tumour cells appeared monomorphic with hyperchromatic nuclei, scanty cytoplasm and showed prominent Homer-Wright pseudorosettes (Figure 3). Ganglionic differentiation was seen in < 5% of the neoplastic cells interspersed with focal tumor necrosis and calcification. Immunohistochemical studies with immunomarkers synaptophysin, S100 and Wilms Tumour -I (WT-1) were done for further categorization of tumour. Tumour cells were positive for synaptophysin and negative for S-100 and WT-1 immunostains. A final diagnosis of a neuroblastoma was made. Subsequently, a bone scan was done which showed evidence of skeletal metastasis.

DISCUSSION:

Primary intrarenal neuroblastoma is a rare clinical entity. It mimics Wilms tumor both clinically and radiologically. Each year two to three tumors are registered by National Wilms Tumor Study group (NWTSG) as blastemal type and are identified after central review as poorly differentiated or undifferentiated stroma-poor neuroblastoma[1]. Surprisingly, the majority of these masses are clinically confined to the kidney, and the correct diagnosis is documented only following nephrectomy[1]. Intrarenal neuroblastoma is believed to originate from either sequestration of adrenal medullary tissue in the kidney during the fetal development, from intrarenal sympathetic ganglion or extension of aggressive adrenal neuroblastoma into the kidney.

Neuroblastoma is the most common extra-cranial solid tumor of childhood and accounts for 50% of neonatal malignancies. Half of these tumors present before 2 years of age, and 75% before 4 years. It is rare in children older than ten years, however it does occur occasionally in adults. Neuroblastoma can occur anywhere along the neuroectodermal sympathetic chain, from head to pelvis, with adrenal medulla being the commonest site (50-70%). Neuroblastoma is an aggressive malignancy as compared to

Wilms' tumor and usually presents with secondaries at the time of initial presentation in approximately 75% of the patients. Renal invasion by neuroblastoma occurs by direct penetration through the renal capsule and /or lymphatic perivascular spread. Generally, the renoinfiltrative neuroblastoma (a stage III or IV disease) are extensive and have unfavourable histological features with lymph node involvement.

Bone metastasis with renal tumors is uncommon and seen mostly with clear cell sarcoma of the kidney. In our case, there was evidence of secondary metastasis to the bones at the time of presentation. The ratio of adrenal to extra-adrenal primary site is approximately 1.5 to 2:1. In about 10% of cases it is not possible to establish the primary site of origin with certainty[2]. Six of such cases were identified in the National Wilms Tumor Study Pathology Centre in 1993[3]. Adrenal neuroblastomas infiltrate the superior pole of adjacent kidney in 5% of cases. Ultrasonogram and computed tomography determines its position in relation to adrenal, kidney, and other intraabdominal and retroperitoneal organs. MRI and bone scans are helpful to detect metastases. In the index case, the adrenal gland was neither identified radiologically, intraoperatively nor microscopically. The tumor was seen extensively involving and destroying the entire right kidney. The possibilities were neuroblastoma of adrenal gland involving the kidney or a intrarenal neuroblastoma with adrenal invasion and destruction. Because of the extensive renal involvement, a renal origin was favoured in our case.

Urinary catecholamines may be negative and the imaging modalities may at times be unable to differentiate between neuroblastoma and Wilms tumor. The features of vascular (aorta) encasement, non-visualization of the kidney or its displacement, bony or muscular invasion and suprarenal location favours the diagnosis of neuroblastoma as seen in our case. However, there is always a risk of 5-10% of misdiagnosis on these imaging modalities.

Review of literature suggested that intrarenal origin or extension of neuroblastoma from adrenal gland may be confused with Wilms tumor[4,5,6,7]. In such situations radiological correlation, urinary catecholamines levels, immunohistochemistry, cytogenetics studies and bone marrow biopsy would be helpful in establishing the diagnosis[4,5,6,7]. In our case, though genetics was not performed, WT-1 negativity and synaptophysin positivity on immunohistochemistry and elevated serum catecholamine level with hot spots in bone scan clinched the diagnosis of neuroblastoma. Lall et al studied in three children between two months and four years diagnosed as intrarenal neuroblastoma and found that differentiation between Wilms tumor and intrarenal neuroblastoma is imperative as the prognosis and treatment are different for these tumors and a

correct preoperative diagnosis would be important in the management of these cases[8].

With the advent of CT and MRI, the differentiation of neuroblastoma from Wilms tumor has improved dramatically. Application of immunohistochemistry and detection of N-myc amplification and 1p deletion has greatly facilitated in differentiating neuroblastoma from other small round cell tumor of childhood. Intrarenal neuroblastoma is usually associated with a poor prognosis as the tumor presents with secondary metastasis at the time of the initial presentation.

Dactinomycin and Vincristine are the most effective drugs for Wilms tumor with favourable histology. These drugs are used in conjunction with surgery, without radiotherapy, for all patients with stage I and II lesions with favourable histology. Radiotherapy and more toxic chemotherapeutic agents are reserved for patients with stage III and IV disease. The treatment of Wilms tumor is successful with remission in 80% of children, with less than 20% experiencing serious morbidity at twenty years from diagnosis[9]. Outcomes remain poor in neuroblastoma despite intensive treatment. The bortezomib-doxorubicin combination is effective for neuroblastoma[10,11]. Neuroblastoma, because of its unique biology, continues to be a challenging tumor to treat, and many times these tumors are refractory to standard chemotherapeutic regimens. Trichostatin A (TSA) and Interferon-beta has a significant antitumor activity against neuroblastoma[12].

A high proportion of intrarenal neuroblastoma are of unfavourable histology as defined by the International Neuroblastoma Pathology Classification and have a higher incidence of anaplasia(32%) when compared to both their adrenal counterparts and to Wilms tumor. The factors that affect survival are age and health of child, extent of the disease, size, type and location of the tumor, metastasis, tumors response to therapy and overall child's tolerance to medications. Clinical, radiological and pathological correlation is very essential for diagnosis and appropriate management of this type of unusual cases.

To conclude, even though the exact site remained undetermined in this case of small round cell tumour completely replacing the right kidney and adrenal gland, immunohistochemistry played a pivotal role in confirming the diagnosis of neuroblastoma thereby, resolving the

dilemma of origin.

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