Case Report

Wilms tumour with neural differentiation: A rare histological presentation

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ABSTRACT

Wilm's tumour is the most common malignant renal tumour of childhood presenting most commonly between the age groups of 1 to 6 years. It exhibits histogenetic heterogeneity. A 4 year old female child presented with complaints of right abdominal pain and mass per abdomen for the past six months .The patient underwent right sided nephrectomy and the specimen was sent for histopathological examination .Cut surface of the tumour was variegated with extensive areas of necrosis and haemorrhage On microscopy the tumour cells were predominantly blastematous , arranged as diffuse sheets of tumor cells with focal nesting pattern in some areas. Tumour cells showed diffuse anaplasia.

These tumour cells showed positivity for WT1 ,vimentin, synaptophysin and p53. No evidence of any epithelial or stromal differentiation was noted. Findings suggested a diagnosis of monophasic variant(blastemal) Wilm's tumor with neural differentiation.

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Introduction

Wilm's tumour is the most common malignant renal tumour of childhood. It presents most commonly between the age groups of 1 to 6 years.[1] It is a complex embryonal tumour arising from metanephric blastema . Neural differentiation in Wilm's tumor suggests a possible histogenetic heterogeneity.[2]

The present case reported highlights a rare occurence of neural differentiation in Wilm's tumor.

Case Report

A 4 year old female child presented with complaints of right side abdominal pain for the last two years. Abdominal examination revealed a solid right hypochondrial and lumbar mass. The child had no other physical abnormality. Family history did not yield any contributory finding.

Computed tomography scan performed revealed a large mass with heterogenous density nearly replacing the right kidney sparing the peripheral lower pole. The other kidney showed no abnormality.

No evidence of metastasis was present.

The patient underwent right sided nephrectomy and the specimen was sent for histopathological examination.

Gross Examination: The nephrectomy specimen submitted measured 12x9x8 cms and weighed 500grams(Figure 1a). It's external surface was bosselated , encapsulated and severely congested. Cut surface showed a grey-tan tumour with extensive areas of necrosis and haemorrhage measuring 12x7x7 cms replacing almost the entire renal parenchyma and extending into the perinephric fat ,renal pelvis and renal sinus with only a peripheral rim of normal renal parenchyma. The attached ureter measures 1.5 cms in length.

Microscopic Examination: Microscopic examination showed a diffuse arrangement of predominantly blastemal tumour cells arranged in sheets(Figure 1b) with focal nesting pattern seen in some areas .These cells were small, closely packed cells with a high nuclear-to-cytoplasmic ratio and indistinct cytoplasmic borders. Their nuclei showed moderate to severe degree of pleomorphism .Diffuse anaplasia was noted with extensive areas of necrosis and hemorrhage. Mitotic activity was frequent with atypical mitotic figures . No evidence of differentiation toward epithelial or stromal cell types was noted on light microscopic .Tumor was seen to infiltrate the renal sinus,perinephric fat and renal capsule.Cut end of ureter was free of tumour.

Immunohistochemistry: Immunohistochemical study done showed tumour cells showing positivity for WT1(95% of tumour) vimentin, synaptophysin (40% of tumour) and p53 and negative for cytokeratin and LCA, S100,GFAP,CD99,chromogranin and N.S.E, myogenin. (Figure2a,2b)

A histological diagnosis of monophasic variant of nephroblastoma (blastemal predominant)with neural differentiation was rendered.

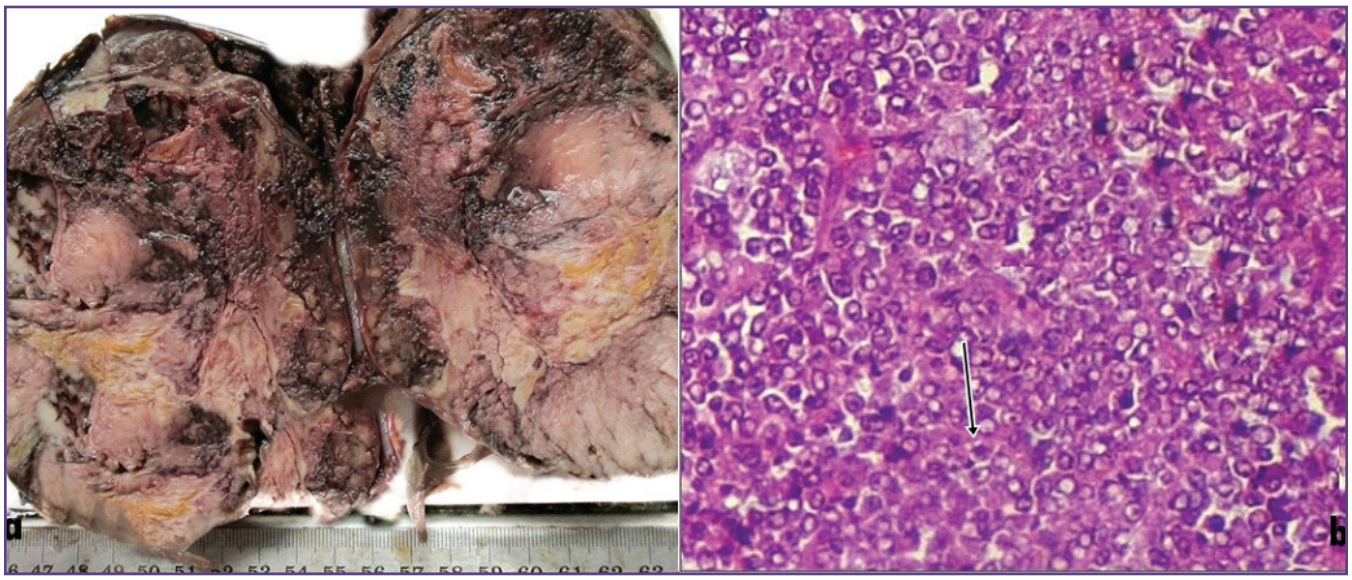

Fig. 1. a. Nephrectomy specimen showing a variegated tumor replacing almost entire renal parenchyma with areas of hemorrhage and necrosis. b. Microscopy showing sheets of blastematous tumor cells with predominantly diffuse and focal nesting pattern with diffuse anaplasia .(H&E 40X).

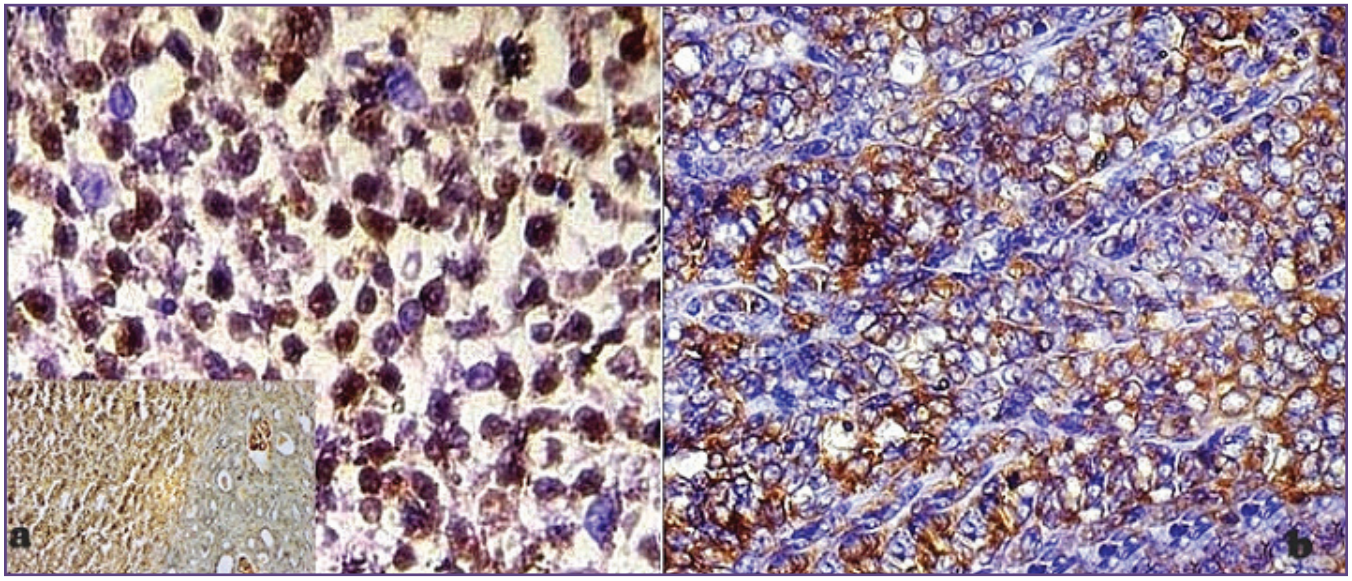

Fig. 2. a.Diffuse WT1 nuclear positivity expressed by tumour cells (IHC 40X) ,inset showing WT1 positive tumour with adjacent renal parenchyma.b.Tumor cells showing cytoplasmic positivity for synaptophysin (IHC 40 X).

Discussion

Wilm's tumor (WT) is a histologically diverse tumor .[1] It is derived from nephrogenic blastemal cells and can exhibit a wide range of histologic appearances that replicate the developing kidney. However aberrant differentiation of the metanephrogenic blastema may lead to heterologous differentiation of Wilm's tumour[3].

Specific genetic loci have been implicated in Wilm' tumorigenesis including the *WT1* tumor suppressor gene at chromosome 11p13, *WT2* at chromosome 11p15,and loci at chromosomes 1p13 and 16q[4] .

Wilm's tumor (WT) tumour typically exhibits a triphasic differentiation. In blastemal predominant WT light microscopy reveals small, round or oval cells, which are densely packed in diffuse or nested patterns. WTs do not exhibit a specific immunophenotype. The blastemal component is typically reactive for vimentin and usually shows desmin reactivity and shows nuclear positivity for WT1 in the blastemal predominant tumor cells . [5]

This histologic pattern alone is most likely to cause diagnostic difficulty especially in small biopsies as it simulates many other small round cell neoplasms .[6] The differential diagnosis includes lymphoma, Ewing's sarcoma/peripheral neuroectodermal tumor(EWS/PNET), rhabdomyosarcoma(RMS) and desmoplastic small round cell tumour(DSRCT).[7]

WT are distinguished from the above mentioned differential diagnosis by the presence of nephrogenic tissue as a major component and with immunohistochemical analysis.[8] In the present case the blastematous tumour cells expressed WT1 along with vimentin and synaptophysin.The absence of CD99, N.S.E ,CD45,myogenin expression in tumour cells and presence of nuclear positivity of WT1 helped to distinguish blastemal predominant WT from 's Ewing's sarcoma (EWS) /PNET, lymphoma, rhabdomyosarcoma.[7] The present case can be differentiated from desmoplastic small round cell tumour by histological findings which reveals clusters of small to medium sized cells with hyperchromatic nuclei and increased nuclear/cytoplasm ratio, surrounded by a dense desmoplastic stroma. [9] Immunohistochemical findings suggest a trilinear coexpression including the epithelial marker keratin, the mesenchymal markers desmin and vimentin.[10]

The role of neural differentiation in renal tumorigenesis was well described and theorized by Pierre Masson,who had postulated that Wilms tumors (or "embryonal adenosarcomas")arose from the neural crest[11]. However the metanephrogenic blastema theory may account for the origin of the cells found in most cases of Wilm's tumor suggesting the capability of these tumor cells towards multidirectional differentiation[3].

Neural elements such as glial tissue, pseudorosettes, primitive neuroblastema, ganglion cells, and neuroendocrine cells have been described previously in Wilm's tumour [8]but in the present study no stromal differentiation towards any of these elements was noted .The tumor cells showed focal nesting pattern which has been described in blastematous areas of Wilm's tumour[12]. Neural differentiation in WT has been also associated with

reactivity for chromogranin, and synaptophysin along with WT1 but staining for S -100 and glial fibrillary acidic protein protein (GFAP) has been found to be variable. [1,13]

Orazzi et al in 1988 described neuroendocrine differentiation in Wilms tumor in which 90% of the blastematous cells showed strong positivity for Grimelius stain along with immunohistochemistry showing NSE, vimentin and low molecular weight cytokeratins and electron microscopy also favouring the same.[14]

In the present case also histology is not conclusive to point out neural differentiation in the blastematous WT cells and only by immunohistochemical analysis synaptophysin expression in tumor cells were confirmed.

Neural differentiation in WT needs to be differentiated from other renal tumors such as primary renal teratoma and anaplastic sarcoma of the kidney (ASK),and malignant ectomesenchymoma (MEM)[15]. Primary renal teratomas also show heterotopic organogenesis such as skin adnexa, intestinal mucosal epithelium, and neuroglial tissue .[2] MEMs are characterized by both neuroectodermal (neuroblastoma, ganglioneuroblastoma, ganglioneuroma, peripheral primitive neuroectodermal tumor) and mesenchymal components (usually rhabdomyosarcoma) [16].ASK are composed of small primitive mesenchymal cells coexisting with a spindle cell component exhibiting anaplastic nuclear changes .[17]

Presence of larger areas with blastema-like cells, positive immunohistochemical staining of WT-1 in the blastema-like foci along with synaptophysin expression in the tumour cells favoured the diagnosis of Wilm's tumor with neural differentiation and was not reported in the latter mentioned lesions.

In the present case as theWT1 and synaptophysin positive WT showed predominantly diffuse blastemal predominant ,it was associated with marked aggressiveness, but with a high survival rate due to the good response to chemotherapy as reported by Beckwith [18].

However there is a need for further evaluation of these tumour cells by electron microscopic analysis and cytogenetic analysis to know the debatable origin of neural expression in blastemal predominant Wilm's tumour .

Conclusion

The present case reported highlights a rare histological variant of Wilm's tumor and emphasizes the ability of nephroblastoma tumor cells for a multidirectional differentiation.

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Competing Interests

None

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