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Ganglion cell differentiation in Wilms tumor: A case report

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Abstract

Classical Wilms tumor has a triphasic histological pattern consisting of blastemal, epithelial, and stromal components. A rare occurrence of heterologous elements like neurogenic tissue has been seen in this tumor. Some genes that are frequently implicated in the pathogenesis of Wilms tumor are WT1 and WT2. WT1 is also required for neural tissue formation.

An 18 month old male child presented with a history of gradual abdominal distension and intermittent low grade fever. Ultrasound examination showed multiple calcifications in a mass located within the right kidney. On admission, a diagnosis of nephroblastoma with ganglion cell differentiation was made. The index case, being under 2 years of age, with stage 1 tumor, managed with chemotherapy, and with non-atypical microscopic features, survived the disease in line with expected good prognosis. However, further studies in this field is required, to establish the role of these rare heterologous elements (in this case ganglion cells) a histologic feature, in the overall survival of patients with Wilms tumor.

Keywords

Wilms; nephroblastoma; neurone; ganglion; WT1

Introduction

Since 1814 when Rance first reported nephroblastoma, a great deal of literature about this malignancy has accumulated [1,2]. The surgeon Max Wilms' after whom this tumor was eponymously christened discovered the triphasic histologic attributes of the tumour [1,3]. The three components of the classical type of this tumor include: blastemal (small round blue cells); epithelial (abortive tubules and/or glomeruli); and stromal (mesenchymal elements) [4]. However, a rare occurrence of other tissues have been seen in this neoplasm. These heterologous elements may include neurogenic tissue [4].

Case Report

An 18 month old male child presented with a history of gradual abdominal distension and intermittent low grade fever. There was associated malaise, anorexia and weight loss. He was admitted into the Paediatric ward for investigations and treatment. Ultrasound examination showed multiple calcifications in a mass located in the right kidney. A diagnosis of nephroblastoma was made. Patient received neo- adjuvant chemotherapy comprising of courses of Vincristine and Doxorubicin for four weeks after which he had a nephrectomy. The biopsy was sent to the Histopathology laboratory where a

diagnosis of nephroblastoma (triphasic nephroblastoma with ganglionic differentiation) was made. Additional cycles of chemotherapy were given after surgery. Constant out patient monitoring and follow up was done. This case is reported after 3 years of follow up following surgery.

Macroscopy: Specimen consisted of an encapsulated firm greyish white mass measuring 14cm x 14cm x 10cm; with variegated solid and cystic cut surface with the largest cyst having a diameter of 2 cm and contain clear fluid.

Microscopy: Histologic section shows a spindle cell stroma with myxoid foci within which were seen small round cells with oval nucleus and scanty cytoplasm (blastema component). Dispersed within this background are numerous abortive tubules lined by cuboidal epithelium (epithelial component). Numerous ganglion cells with abundant eosinophilic cytoplasm and a central oval nucleus with prominent nucleolus were also seen. No evidence of cellular atypia was seen.

Immunohistochemistry: There was positivity for NSE (Neurone Specific Enolase), GFAP, and S-100 in 90%, 90%, and 75% of ganglion cells respectively (**Figure3- 5**).

Discussion

Wilms tumor is believed to develop from aberrant proliferation of pleuripotent cells in the developing kidney that falls short of differentiating into normal renal parenchymal cells [5]. This incomplete developmental process results in structures that recapitulate different stages of renal embryogenesis as seen in the triphasic Wilms [5]. Multi directional differentiation however, leads to the rare development of heterologous elements which include neurogenic tissues (neuroepithelium, neuroblasts, neuroglia, and mature ganglion cells) [4,6].

There has been reports of occurrence of neurogenic tissues in nephroblastoma [6-8]. Mature ganglion cells have also been demonstrated by works done by Llombart-Bosch et al, and Husong et al [7,8]. The later reported ganglion cells in two out of four cases of family members with Wilms tumors [8]. The former concluded that nervous tissue in nephroblastoma are matured, and should not be confused with primary ganglioneuroblastomas of the kidney [7].

The index case showed the three classical components of Wilms tumor in addition to the heterologous ganglion cells. The positivity for NSE, S-100, and GFAP exhibited by these cells indeed is indicative of neural origin.

Some genes are implicated in the pathogenesis of Wilms tumor with WT1 and WT2 being the most frequently involved [1]. Notably, WT1 distinguishes itself amongst other tumor suppressor genes owing to its requirement for organo genesis [9,10]. WT1 is required also for neural tissue formation [9,11-14]. Wagner et al. demonstrated that WT1 is necessary for the normal retina formation and has a critical role in ganglion cell differentiation [15]. In a work by Maugori et al done on human neuroblast cell lines, a role for WT1 isoforms in differentiation of neuroblastic cells into matured ganglion cells was advanced [14]. The coexistence of the histologic component of triphasic Wilms and ganglion cells in this patient could be explained by the numerous functions of the WT1 gene.

A favourable prognosis has been associated with Wilms' tumor occurring under the age of 2 years [16]. Also the introduction of Chemotherapy as an adjunct to Surgery, has significantly improved

prognosis from 30% to 90% between 1930 and 2000 [1]. Also patients with local and completely resectable disease (stage 1) have survival rates of 95% with current management strategy [1]. Patients who had chemotherapy over a period of 1 month before surgery have better survival outcomes [1]. Additionally, the histological characteristic of the tumor has been reported to be the most powerful prognostic tool of nephroblastoma [17]. Tumors with anaplasia, defined by the presence of cells with hyperchromasia, increased nucleo-cytoplasmic ratio, and atypical mitosis are associated with poor prognosis.

Figures

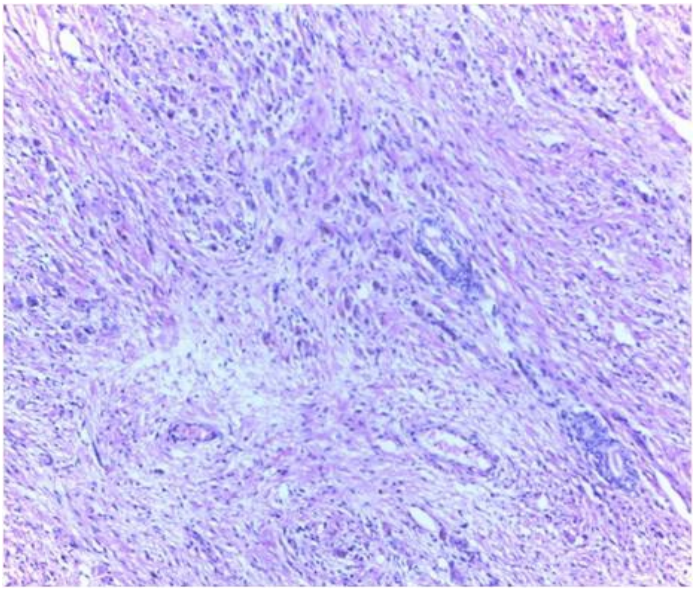

Figure 1: Photomicrograph of nephrectomy specimen biopsy: Histologic section shows a fibromyxoidstroma within which are seen numerous ganglion cells, few abortive tubules, and scanty dispersed blastema. H/E stain X4

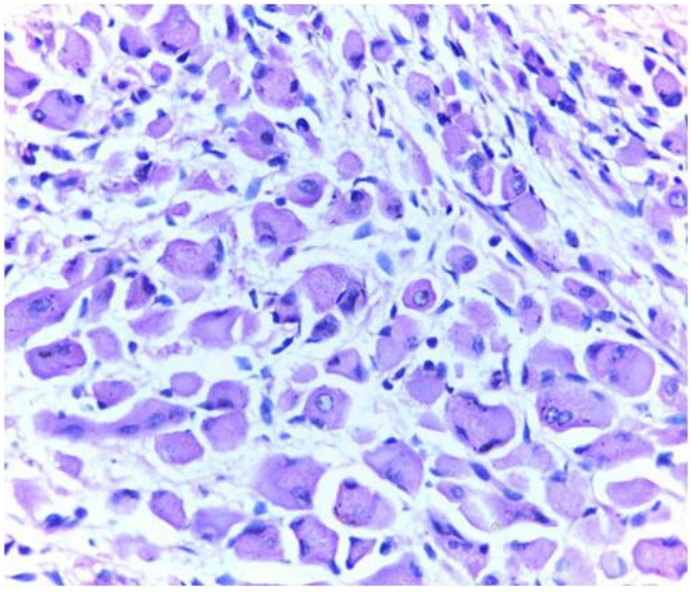

Figure 2: Photomicrograph of nephrectomy specimen biopsy: Histologic section shows ganglion cells within a fibrotic stroma. H/E Stain X40

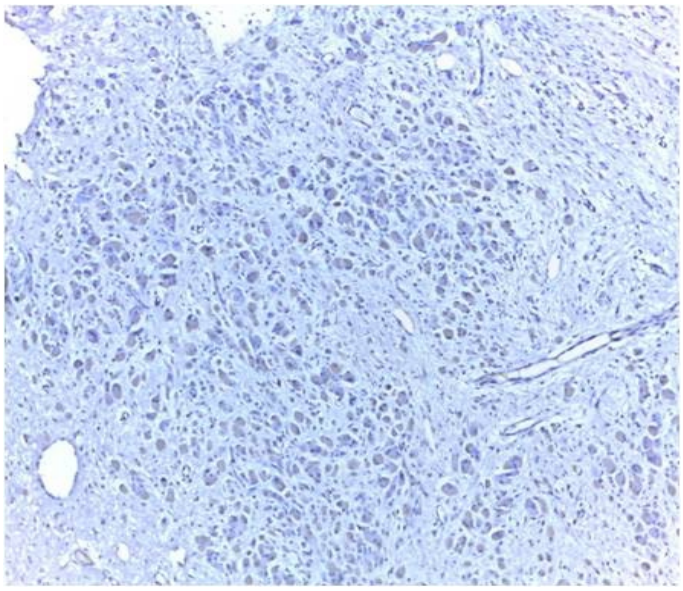

Figure 3: Nephrectomy biopsy staining for NSE Stain X10: Section shows strong cytoplasmic staining of ganglion cells with NSE immuno-stain.

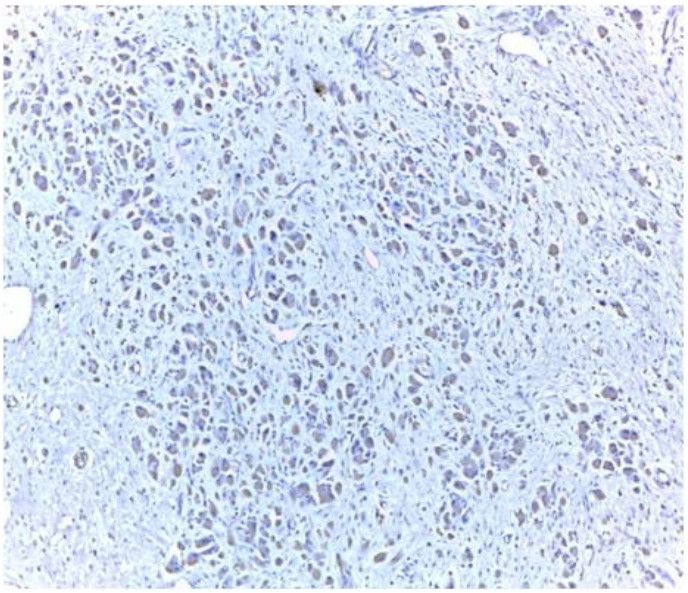

Figure 4: Nephrectomy biopsy staining for GFAP Stain X10: Section shows strong cytoplasmic staining of ganglion cells for GFAP immuno-stain.

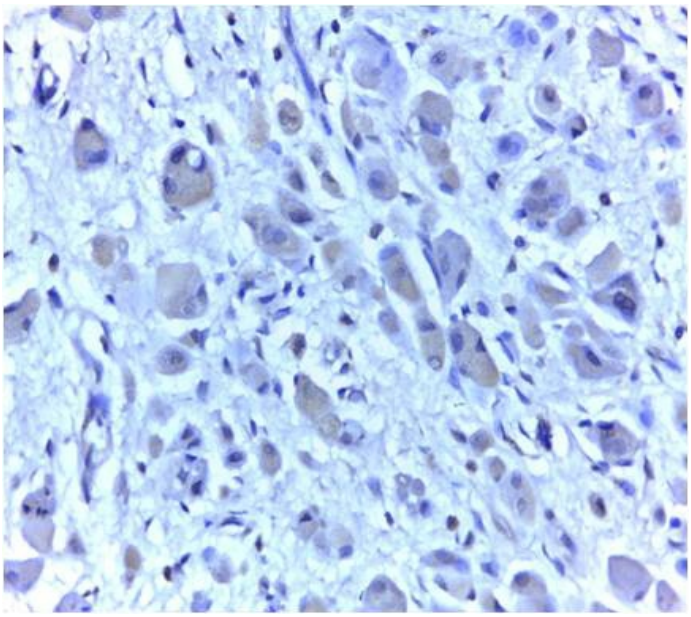

Figure 5: Nephrectomy biopsy staining for S-100: Section shows strong cytoplasmic staining of ganglion cells with S-100 immuno-stain.

Conclusion

The index case, was under 2 years of age, with stage 1 tumor having non-atypical microscopic features, and managed with chemotherapy and surgery, survived the disease inline with expected good prognosis. However, further studies in this field is required to establish the role of these rare heterologous elements-in this case ganglion cells, a histologic feature, in the overall survival of patients with Wilms tumor.

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