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CASE REPORT

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Recurrent Wilms' tumour or retroperitoneal teratoma?

A challenging case

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Abstract The clinical and pathological features of a left renal tumour and a subsequent retroperitoneal tumour in a 2-year-old boy are presented. The nephrectomy specimen showed typical features of a triphasic Wilms' tumour with focal heterologous elements and intralobar nephrogenic rests. The tumour was assessed as clinical stage III and post-operative chemotherapy and radiotherapy were administered. A retroperitoneal mass, detected following completion of postoperative therapy, was mainly made up of skeletal muscle and mature adipose tissue. Nests of epithelium resembling ameloblastic nests and a unique structure reminiscent of a developing tooth were present.

Key words Differentiation · Odontogenic · Nephroblastoma · Organogenesis · Teratoma · Wilms' tumour

Introduction

Wilms' tumour (WT) is the most common renal neoplasm of childhood, arising from the metanephric blastema, which is totipotent and can differentiate into a variety of tissues. Heterologous elements are common in WT and might be mistaken for evidence of organogenesis, but unequivocal organoid differentiation (for example, bronchus, skin, and tooth) has not been described. In fact, the presence of unequivocal organogenesis in a renal tumour is considered to be pathognomonic for a renal teratoma [2].

The retroperitoneum is a common extragonadal site for teratomas, but renal teratomas are rare. We report a patient with a stage III triphasic WT, which was followed after 6 months of chemotherapy and radiotherapy by a retroperitoneal tumour showing a unique microscopic structure reminiscent of tooth development.

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Case report

A 2-year-old black male infant presented with a 10×9 cm, firm, non-tender, left upper quadrant abdominal mass. He was anaemic and malnourished, weighing 7.6 kg. A CT scan of the abdomen confirmed a partially cystic but well-encapsulated mass arising in the left kidney. The right kidney, ureter and bladder were normal, but the left kidney failed to excrete the contrast medium.

Following pre-operative chemotherapy, with actinomycin D and vincristine, surgery was performed; a large left-sided renal tumour was encountered, which had clearly penetrated the capsule at the upper pole. Tumour encased the renal pedicle and extended into the ureter. The left renal vein was thrombosed, but the inferior vena cava was clear of tumour when pre-operatively assessed with ultrasound. Total nephrectomy was performed, and a para-aortic lymph node was biopsied. The lesion was operatively staged as III according to the NWTS staging criteria. The child received post-operative radiotherapy and chemotherapy according to the SIOP protocol.

Six months after primary surgery, at completion of chemotherapy and radiotherapy, a CT scan of the abdomen showed evidence of tumour recurrence at the hilum of the right kidney. No intrarenal tumour was detected on imaging studies. At surgery a large soft tumour mass was found in the left renal bed, with extension across the midline, anterior to the aorta and in front of the right renal hilum and adrenal gland. The bulk of the tumour was close to the right renal hilum, but the right kidney was clearly uninvolved. Debulking of the mass was achieved. A CT scan done 3 months after debulking showed no residual tumour. The patient was discharged and did not return for follow-up. Genetic analysis was not performed.

Results

The nephrectomy specimen measured 14×12×6 cm and weighed 500 g. Cut sections revealed a predominantly

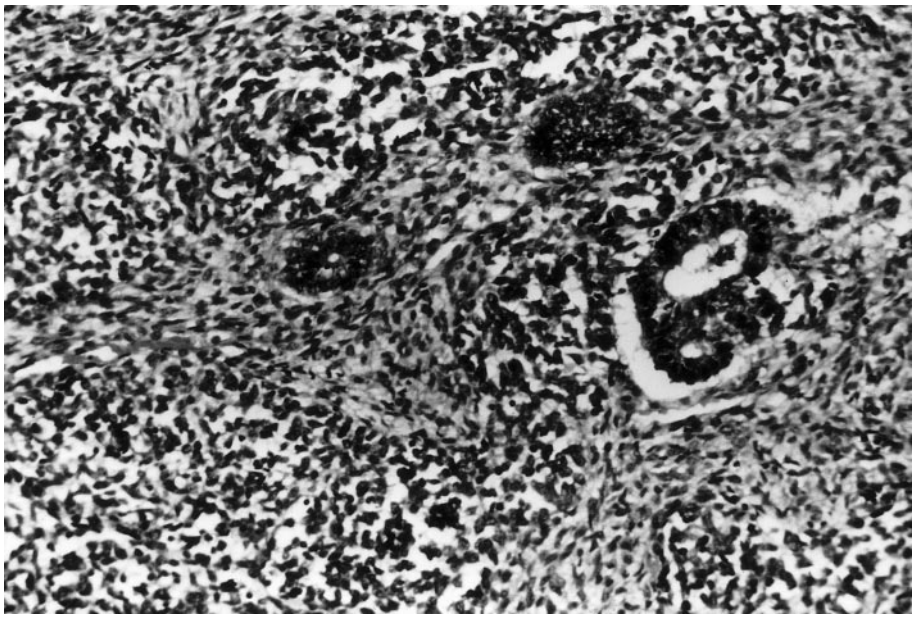

Fig. 1 Renal neoplasm composed mainly of blastema with immature tubules and undifferentiated mesenchyme. ×250

solid tumour with focal cystic change, necrosis and haemorrhage. Histology showed a large component of blastema with embryonal tubules and undifferentiated mesenchyme (Fig. 1). Focal skeletal muscle tissue and adipose tissue were present, but they were not enough to warrant diagnosis of a teratoid WT, so that a diagnosis of triphasic WT was recorded. Intralobar nephrogenic rests were noted. Despite extensive sampling of the specimen, no evidence of organogenesis was identified. The tumour extended into the pelvicalyceal system and the renal hilum. There was also extension into perinephric fat, and tumour was present at the resection margin. The paraaortic lymph node showed reactive sinus histiocytosis.

The second specimen, removed after completion of post-operative therapy, measured 4×4×4 cm. The tumour consisted mainly of skeletal muscle tissue with intervening fibrous stroma and mature adipose tissue. In addition, there were small nests of epithelium with central loosely arranged cells and peripheral columnar cells whose nuclei were orientated away from the basal lamina (Fig. 2). A small focus of squamoid cells was present in the centre of one of the nests (Fig. 2). These nests resemble ameloblastic epithelium similar to that present in an ameloblastoma. There was also an intriguing and unique structure, which was reminiscent of a developing tooth (Fig. 3a, b). Although the features are not unequivocally those of odontogenesis, we will attempt to illustrate the similarities. The structure had the form of an inverted “chalice” or “cup”, which is open at the bottom. The sides of the cup were lined with two layers of columnar epithelium (Ex, In), which were separated by stellate cells that extend into the base of the cup. At the base the stellate cells were loosely arranged and resembled the stellate reticulum of odontogenesis. The open end of the cup was composed of cellular mesenchyme mimicking the dental papilla. Within the concavity of the cup there were deposits of uncalcified hyaline material lined

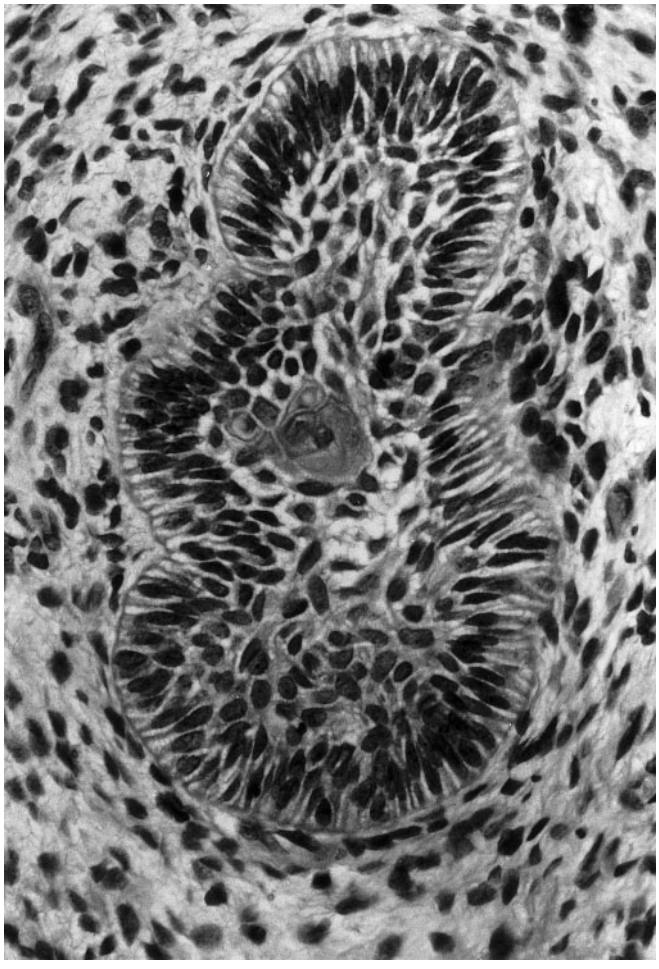

Fig. 2 Epithelial nest with peripheral columnar cells, central stellate reticulum and surrounding undifferentiated mesenchyme resembling ameloblastic nests. ×250

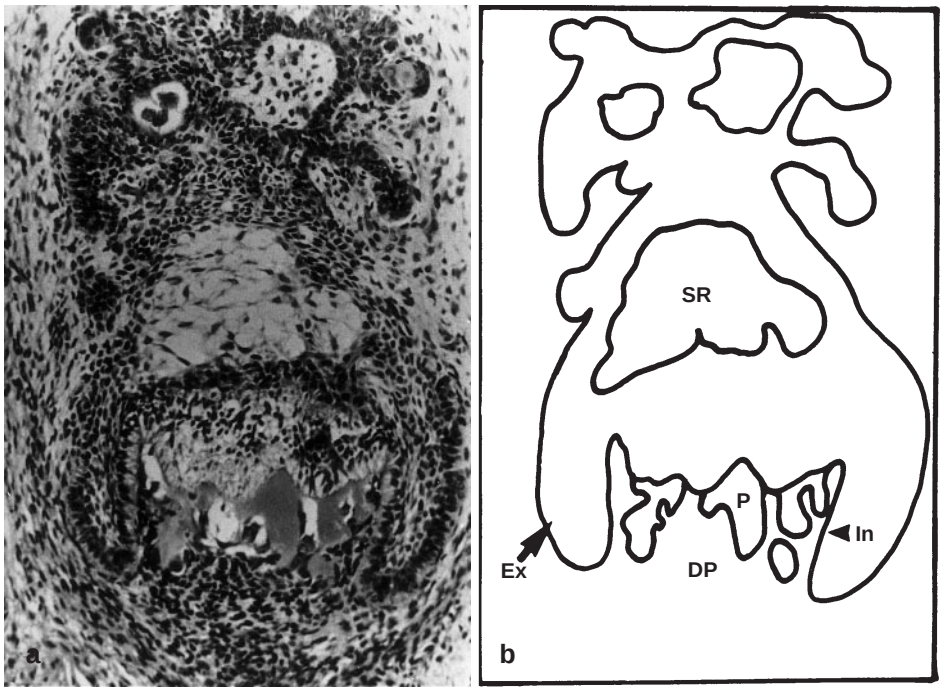

Fig. 3a Microscopic structure reminiscent of a developing tooth. ×50. **b** Line drawing of structure depicted in **a**: internal enamel epithelium (*In*); external enamel epithelium (*Ex*); dental papilla (*DP*); stellate reticulum (*SR*); predentine (*P*)

focally with large epithelioid cells. The hyaline material lacked the tubular appearance of mature dentine, but was consistent with its precursor form, predentine. A zone of undifferentiated mesenchyme (Figs. 2, 3a) surrounded both the epithelial nests and the "developing tooth" structure. There were no immature neuroectoderm, blastema, tubular or glomeruloid structures within the tumour.

Discussion

The presence of heterologous elements in a WT is not an infrequent finding, and the extent of such elements has been used as a feature in the classification of WTs. Various heterologous elements have been reported, including cartilage, muscle, bone, squamous epithelium, mucinous epithelium, ciliated columnar epithelium, neuroepithelium, neuroblasts, ganglion cells and neuroglial epithelium [2]. The term teratoid WT was introduced by Variend et al. [6] to describe a variant of WT in which heterologous elements predominate. Teratoid WTs are not aggressive tumours, and metastases have not been reported. This variant has a relatively poor response to chemotherapy [5, 7]. As with other variants of WTs, the prognosis seems to be dependent on stage at presentation and the presence or absence of anaplasia.

The main differential diagnosis of a teratoid WT is a renal teratoma, which also contains an abundance of heterologous elements. The two criteria essential for the diagnosis of a renal teratoma are an unequivocal intrarenal origin and unequivocal organogenesis with clear attempts at formation of some other organ(s) than the kidney [2]. Extragonadal teratomas are most frequently situated in midline structures, viz. mediastinal, retroperitoneal, presacral and coccygeal regions and midline intracranial sites. Furthermore, both retroperitoneal and sacrococcygeal teratomas may contain a predominance of nephroblastomatous tissues [4, 8].

The interpretation of the histological features and the diagnosis of the second specimen present a challenge. The hyaline material seen in the "odontogenic" structure may be interpreted as osteoid. Similar hyaline "osteoid" material is not an uncommon component of teratoid WT (J.B. Beckwith, personal communication). However, we feel that the relationship with adjacent cells and its situation in the cup-shaped structure support a dentigerous origin and most probably represents predentine. We have alluded to the similarities of the structure with normal tooth development, and these have been independently confirmed by an oral pathologist (M. Altini, personal communication).

The possible diagnoses include: (1) metachronous contralateral WT, (2) retroperitoneal teratoma, and (3) a recurrent WT. A metachronous contralateral WT is favoured by the presence of intralobar nephrogenic rests (ILNR) in the left kidney [3]. Tumours arising from ILNR tend to be centrally situated, often contain heterologous tissues, especially skeletal muscle, and extend into the pelvicalyceal system. All these features are present in the left renal tumour. Against a contralateral WT, however, is the total absence of intraparenchymal tumour in the right kidney. Furthermore, tumour was present on both sides of the midline, including the left renal bed. This we believe favours a recurrent tumour. The second possibility, of a retroperitoneal teratoma, is dependent largely on evidence of unequivocal organogenesis. Although it is very unusual for a teratoma to consist almost entirely of

skeletal muscle and adipose tissue, this can be explained by the prior administration of chemo- and radiotherapy. Induction of differentiation in the primitive nonepithelial elements by irradiation and ablation of the more chemo- and radiosensitive primitive tissues may be the reason for the absence of immature elements in the second neoplasm [1, 9]. Similar reasoning would explain the predominance of heterologous elements in a recurrent WT. A diagnosis of retroperitoneal teratoma also implies that these are two separate neoplasms. However, at primary surgery no evidence of such a tumour was noted. Although we cannot be entirely certain, after assessing and analysing the possibilities we feel that the second tumour is best diagnosed as a recurrent WT with teratoid elements.

This case raises the question of what should be regarded as unequivocal organogenesis. Various histological appearances in WTs that can easily be misinterpreted as evidence of gut, respiratory tract, brain or other organ differentiation are frequently encountered. Alternative explanations for these appearances should be considered and excluded before they are accepted as unequivocal evidence of organogenesis**.**

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