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Case report

Metanephric stromal tumor with a rare incidence of squamous epithelium: A case report and a brief review of the literature

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ABSTRACT

Metanephric stromal tumor (MST) of the kidney, a rare benign pediatric neoplasm recognized for less than 20 years, is not widely known. The authors describe a case of MST with rare squamous epithelium in a 14-month-old female. A renal mass was discovered during her fetal period. After her birth, computerized tomography revealed that the mass was localized in the inferior pole of her left kidney. She then underwent nephrectomy. The tumor was an unencapsulated but well-defined mass with a white, solid and firm cut surface and had dimensions of 4 cm × 3.5 cm × 3 cm. The tumor was initially diagnosed as Wilms tumor because its frozen section exhibited spindle cells with cartilaginous and rare squamous epithelial elements. However, the paraffin-embedded section of the tumor exhibited bland stromal cells surrounding the entrapped tubules; this arrangement produced an "onion-skin" appearance. The rare squamous epithelial element appeared to originate from normal renal tubules. Immunohistochemistry results were positive for CD34 and INI1, as well as a low Ki-67 expression level, but were negative for S-100, Desmin, Actin, CD117 and Catenin-β. Fluorescence in situ hybridization analysis did not detect an *ETV6* rearrangement. Morphological characteristics, immunophenotyping and molecular genetic analysis indicated MST. No recurrence or metastases occurred during the follow-up period of 36 months. Epithelial elements should be examined carefully in pediatric patients with renal masses. MST should be included in their differential diagnoses.

1. Introduction

Metanephric stromal tumor (MST) is a rare benign stromal tumor of the kidney mostly observed in the pediatric population [1,2]. MST, first reported by Beckwith in 1998, is a pure stromal variant of metanephric adenofibroma [3]. Diagnosing MST is challenging because of its rarity and diverse and complex tumor morphology [4–8]. Here, we report the first case of MST with squamous epithelium in Shanghai, China.

1.1. Clinical history

A renal mass was discovered by prenatal check-up during the fetal period (32 weeks) of a 14-month-old female. She was delivered naturally at 39 weeks with an Apgar score of 10. After her birth, computerized tomography revealed a mass in the inferior pole of her left kidney (Fig. 1). The patient then underwent a nephrectomy when she was 14 months old. Her parents denied any family history of renal diseases. The patient did not receive chemotherapy after the surgery. No recurrence or metastases occurred during the follow-up period of 42 months.

2. Materials and methods

2.1. Morphology and immunohistochemistry (IHC)

All samples were fixed in 10% neutral formalin, embedded in paraffin, and cut into 4 μm thick slices. Then, these slices were routinely stained with haematoxylin and eosin (HE) and were stained with the EnVison method for IHC assay. A panel of antibodies against cluster of differentiation 34 (CD34), WT1, S-100, CD117,

Abbreviations: MST, metanephric stromal tumor; WT, wilms tumor; IHC, immunohistochemistry; HE, haematoxylin and eosin; CD34, cluster of differentiation 34; SMA, smooth muscle actin; PBS, phosphate-buffered saline; FISH, fluorescence in situ hybridization analysis; MAF, metanephric adenofibroma; CMN, congenital mesoblastic nephroma; CCMN, cellular CMN; CCSK, clear cell sarcoma of kidney; RTK, rhabdoid tumor of kidney.

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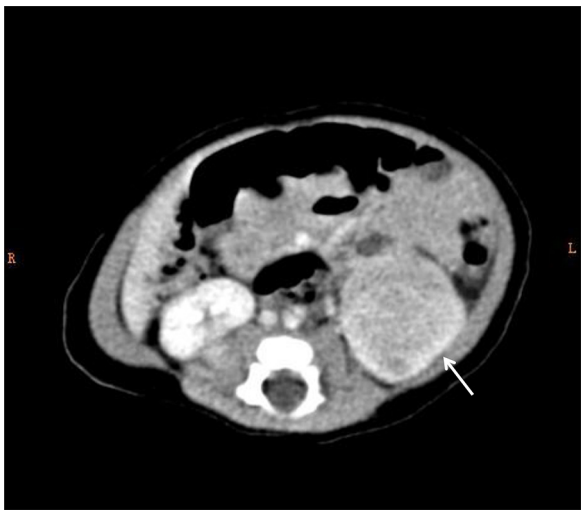

Fig. 1. Computerized tomography of abdomen revealing a mass in the left kidney (Arrow).

Desmin, smooth muscle actin (SMA), Catenin-β and Ki-67 (Dako, Glostrup, Denmark)were used. We replaced the primary antibody with phosphate-buffered saline (PBS) for the negative control and used known positive sections as positive controls.

2.2. Fluorescence in situ hybridization analysis (FISH)

FISH was performed according to the manufacture's instruction (ZytoLight, Bremerhaven, Germany). The translocations involving *ETV6* gene at 12p13.2 were detected with ZytoLight SPEC ETV6 Dual Color Break Apart Probe (PL135) (ZytoLight, Bremerhaven, Germany). An *ETV6* rearrangement was indicated by one separate green signal and one separated orange signal whereas two green/orange fusion signals implied no *ETV6* rearrangement. We used normal cells as negative control and known positive sections as positive controls.

3. Results

The surgical specimen was an unencapsulated but well-defined mass in the inferior pole of her left kidney. The mass had dimensions of 4 cm × 3.5 cm × 3 cm. The cut surface was white, solid and firm. Examination of an intraoperative frozen section revealed a spindle-cell tumor with cartilaginous and rare squamous epithelial elements. Thus, the tumor was initially considered as Wilms tumor (WT) based on these features. However, the microscopic examination of the paraffin-embedded tumor section under a low-power field revealed a nodular appearance (Fig. 2A). The spindle tumor cells were distributed around the entrapped renal tubules or vessels. This arrangement created an "onion-skin" appearance (Fig. 2B). The inner layer of the "onion skins" was hypocellular when compared with peripheral spindle cells with mucoid degeneration. However, the inner layer sometimes was hypercellular while the peripheral layer was hypocellular. In addition, angiodysplasia (vascular wall structure disturbance and muscle fiber degeneration) was detected (Fig. 2C). Some entrapped tubules exhibited juxtaglomerular hyperplasia (Fig. 2D). Cartilaginous (Fig. 2E) and squamous epithelia (Figs. 2 F, 3 A) were present, whereas neoplastic embryonic components were absent.

Immunohistochemically, the tumor cells were positive for CD34 (Fig. 3B) and INI1 and showed a rare expression of WT1, but was completely negative for S-100, Desmin, Actin, CD117 and Catenin-β. Moreover, Ki-67 labeling of less than 5% of the tumor cells suggested low cellular proliferation. Fluorescence in situ hybridization analysis did not detect an *ETV6* rearrangement (Fig. 3E). Thus, after carefully evaluating tumor morphology and the results of immunohistochemical assay and molecular genetic analysis, a diagnosis of metanephric stromal tumor was pronounced.

4. Discussion

Metanephric stromal tumor (MST) is a part of a spectrum of well-differentiated nephroblastic lesions known as "metanephric tumor family" [1,2,9]. These primary renal tumors also include purely epithelial metanephric adenoma at opposite ends and a biphasic metanephric adenofibroma (MAF) in between [1,2,9]. Given that these tumors share the same morphology of differentiated elements of the WT, the tumors appear to be related to WT [1,2,9]. MST is commonly seen in children (the mean age at diagnosis is 13 months, range from 2 days to 13 years) [1,2,9]. The clinical presentation is not specific and invariably shows an abdominal mass [1,2,9]. Microscopic examination of this tumor shows that it is characterized by an unencapsulated, nodular appearance [1,2,9]. The tumor is predominantly composed of spindle or stellate cells, which always surround entrapped renal tubules or blood vessels, thereby showing a characteristic "onion-skin" appearance [1,2,9]. Other features include angiodysplasia-type changes of intratumoral vessels, juxtaglomerular hyperplasia, and heterologous differentiation such as glial or cartilaginous elements [1,2,9]. Immunohistochemically, the tumor cells demonstrate varying degrees of CD34 positivity [1,2,9]. The molecular genetic analysis of MST shows no characteristic abnormality, and only one study reports that partial triplication of the segment between bands 17q22 and 17q24.3 that originates from a complex homogeneous gain between bands 17q22 and 17q25.3 is detected in MST [1,2,9–11]. The diagnosis is essentially based on the morphological examination. Most patients receive good prognosis after nephrectomy or heminephrectomy [1,2,4–6,9].

The morphological differential diagnosis includes a diverse group of spindle cell renal tumors, such as MAF and congenital mesoblastic nephroma (CMN) [1,2,9]. Histologically, MAF includes two components, namely, epithelium and stroma [1,2,9]. In the stromal component, the spindle tumor cells of MAF are distributed around the renal tubules or arterioles, producing a "fibroblast"-like form, which closely resembles certain areas of MST [1,2,9]. However, MAF also includes the epithelial component, which MST lacks [1,2,9]. The epithelial component of MAF is always hypercellular and displays immature morphology, showing round or oval hyperchromatic nuclei and less cytoplasm [6,12,13]. These tightly packed cells form tubules or show a papillary appearance [1,2]. Nodules of different sizes are always shown [1,2,9]. These tubules are embedded in the tumor stromal component [1,2,9]. Different from the morphology of MAF epithelial component, the entrapped renal tubules in MST are diffusely distributed single ducts [1,2,9]. In this case, all tumor cells were spindle cells apart from the single entrapped renal tubules. The structure of entrapped renal tubules was similar to that of the adjacent residual normal renal tubules. Thus, MAF was ruled out from the differential.

CMN is the most common kidney tumor that develops in children under 3 months old [1,2,9,10]. Similar to MST, CMN is a spindle cell tumor localized in the renal medulla [1,2,9,10]. Owing to the infiltrative growth pattern of CMN, the large-scale normal renal tissue could be entrapped, producing a "renal tissue island" within the tumor cells [1,2,9,10]. Monomorphic tumor cells are evenly distributed and arranged in an "infantile myofibromatosis"-like architectural pattern [1,2,9,10]. The tumor cells are also arranged in a characteristic "herringbone" or "feather"-like architectural pattern in cellular CMN (CCMN) [1,2,9,10]. In several areas of this case, the "feather"-like architectural pattern could be found. However,