Case Report

Metanephric adenofibroma in a 10-year-old boy: report of a case and review of the literature

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Received December 15, 2014; Accepted February 20, 2015; Epub March 1, 2015; Published March 15, 2015

Abstract: We reported a case of metanephric adenofibroma in a 10-year-old boy to describe the clinical, radiologic, and pathologic features and discuss its treatment and differential diagnosis. Nephrectomy was performed for the patient; final histopathologic evaluation was that of a metanephric adenofibroma. Epithelial and stromal elements were both positive for WT-1, Vimentin, PAX2, and the epithelial tumor cells were also positive for S100, AE1/AE3, PAX8, CK8/18, EMA and a few cells were positive for CK7. Larger vessel wall components were positive for SMA, Des, caldesmon while capillary components were positive for CD10, CD31, and CD34. CA-9, α-inhibin and CD-56 were negative in the neoplasm. The Ki-67 labeling index was <1%. Metanephric adenofibroma is a rare benign renal tumor; the diagnosis of it relies on pathology and immunohistochemistry. As its rarity, there is no standard treatment for this disease. The majority of patients underwent nephrectomy and had good prognosis, as it is a benign neoplasm.

Keywords: Kidney neoplasms, Wilms tumor, pathology, surgical, immunohistochemistry, nephrectomy

Introduction

Metanephric adenofibroma is a rare renal neoplasm which was thought to represent a well-differentiated, mature form of Wilms' tumor [1]. It contains both stromal and epithelial components in various proportions. The tumor appears to affect predominantly young patients [2]. In this report, we will describe the clinical, radiologic, and pathologic features of a case of metanephric adenofibroma and discuss its differential diagnosis and treatment.

Case report

A previously healthy 10-year-old boy was referred to our department because of belly-ache for one week. No remarkable abnormalities were found on physical examination. There was no weight loss or any constitutional symptoms, and no associated gross or microscopic hematuria. Blood tests were all in normal range.

Ultrasonographic examination showed a well-defined, slightly hypoechoic mass in the middle of the right kidney. Computerized tomography (CT) of the abdomen and pelvis demonstrated a 5 cm solid tumor within the renal parenchyma in the middle of the right kidney. The mass was homogeneously high density relative to the adjacent renal cortex, and had CT values between 55 Hu and 60 Hu. The tumor was enhanced heterogeneously after intravenous injection of iohexol, and had CT values between 105 Hu and 120 Hu (Figure 1). There was no evidence of extension into the adjacent adrenal gland, renal vein, or inferior vena cava. No lymphadenopathy or metastases were identified. The left kidney was unremarkable. This renal mass was clinically and radiologically thought to be a renal cancer. After appropriate preoperative counseling, a decision was made to proceed with right nephrectomy, which was performed through a subcostal incision. The tumor measured 7.0 × 5.0 × 4.0 cm and weight 75 g; it had a firm consistency with white-grey, pink cut surface (Figure 2). Tumor tissue blocks were fixed in 10% buffered formalin and embedded in paraffin. Four-micrometer sec-
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Figure 1. A 10-year-old boy with a 5 cm MAF in his right kidney. A: CT scan without IV contrast material showed a 5 cm solid tumor within the renal parenchyma in the middle of the right kidney (white arrow); B: Contrast-enhanced CT showed the tumor was enhanced heterogeneously (black arrow), and no lymphadenopathy was identified.

Figure 2. Gross appearance of the tumor: The outer surface of the tumor was smooth. Cut sections revealed a white-grey, pink and fibrous appearance. The missing part of the tumor (black arrow) was taken away for intraoperative frozen section examination.

Sections were cut and stained with hematoxylin and eosin. Upon sectioning, two distinct components were observed: epithelial and stromal (Figure 3A). The stromal component showed a hemangioma-like appearance (Figure 3B).

Epithelial and stromal elements were positive for WT-1 (Figure 4A), Vimentin (Figure 4B) and PAX2 (Figure 4C), and the epithelial tumor cells were also positive for S100, AE1/AE3, PAX8 (Figure 4D), CK8/18 and EMA, and a few cells were positive for CK7. Larger vessel wall components were positive for SMA, Des, caldesmon while capillary components were positive for CD10, CD31, and CD34 (Figure 4E). CA-9, α-inhibin and CD-56 were negative in the neoplasm. The Ki-67 labeling index was <1%.

Chromosomal analysis of peripheral lymphocytes revealed a normal male karyotype (Figure 5). SNP microarray experiment of the blood detected no copy number variations or loss of heterozygosity (Figure 6).

Discussion

Metanephric adenofibroma, formerly designated nephrogenic adenofibroma, was first described by Hennigar and Beckwith in 1992 [2]. Since then a few cases have been reported in literature [3-7]. It is a rare, biphasic, benign tumor containing both stromal and epithelial components in various proportions. This tumor is classified among the metanephric neoplasms, which also include metanephric adenoma and metanephric stromal tumor. Metanephric adenoma is a purely epithelial lesion and...
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metanephric stromal tumor is a purely stromal lesion while metanephric adenofibroma is between of them.

Metanephric adenofibroma appears to affect predominantly children and teenagers. Patients commonly present with gross hematuria, occurring when central lesions penetrate the renal collecting system, but a significant proportion of patients are asymptomatic [1, 2]. Few patients with polycythemia resolved on excision [2, 3]. Physical examination usually cannot reveal any abnormalities, but larger tumors are palpable on the body surface. The tumors can achieve substantial size, as reported by Piotrowski et al, who performed robotic assisted partial nephrectomy for a 19 cm metanephric adenofibroma [5]. The radiologic appearances are nondiagnostic and indistinguishable from other solid pediatric renal tumors. Some patients with metanephric adenofibroma are given an initial diagnosis of Wilms’ tumor, accepting adjuvant chemotherapy, which makes it difficult to assess the inherent biologic potential of the tumor. The most common gross description of metanephric adenofibroma is that of a solitary tumor with indistinct borders centered in the renal medulla. The lesions sometimes are partially cystic or nodular and have tan, white-grey or yellow cut surface.

The histological appearances of metanephric adenofibroma are variable. The tumors contain a variable amount of a bland spindle cell stroma, which is essentially identical to the recently described metanephric stromal tumor. The epithelial components of these lesions contain at least focally an inactive embryonal epithelium identical morphologically to metanephric adenoma, and hence could be classified as metanephric adenofibroma. The epithelial nodules are unencapsulated and composed of tightly packed glandular and papillary structures. The epithelial component may show different subtypes. Arroyo et al. [3] in their series of 25 cases observed that metanephric adenofibromas could be divided into 4 subgroups: the usual metanephric adenofibroma, metanephric adenofibroma with mitoses, composite metanephric adenofibroma/Wilms’ tumor and composite metanephric adenofibroma/tubulopapillary carcinoma. They have speculated that these tumors are interrelated lesions. The spindled stromal component features angiodysplasia, concentric cuffing around entrapped tubules (“onion skinning”), and heterologous differentiation. Psammoma bodies (eosinophilic extracellular concentric calcified structures) are a common microscopic finding in metanephric adenofibroma.

The epithelial component is typically positive for AE1/3 and WT-1. The stromal component is frequently positive for Vimentin and CD34 [2, 5, 6]. But at this point in time, no immunohistochemical profile exists to characterize metanephric adenofibroma, the correct diagnosis can be established on the basis of clinical, morphologic, and immunohistochemical features.

The differential diagnosis was congenital mesoblastic nephroma, Wilms’ tumor or Wilms’ spectrum benign variant (mesenchymal metanephric stromal tumor, epithelial metanephric ade-
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According to the World Health Organization classification, metanephric tumor family includes metanephric adenoma, metanephric stromal tumor and metanephric adenofibroma. Metanephric adenofibroma is a biphasic tumor that spans the morphologic spectrum between pure stromal and pure epithelial lesions. They can be distinguished by histological and immunohistochemical examination.

Congenital mesoblastic nephroma is a rare low-grade malignant renal tumor, which exhibits spindle cells in histomorphology. Congenital mesoblastic nephroma typically affects babies before the age of 3 months, whereas metanephric adenofibroma tends to involve older children and young adults [2]. Metanephric adenofibroma is usually well demarcated; however, congenital mesoblastic nephroma has an infiltrative growth pattern. Immunohistochemically, the spindle cells in metanephric adenofibroma are also different from those in mesoblastic nephroma; the former are negative for actin and desmin and the latter are positive [8]. Cytogenetics and molecular genetics show that

Figure 4. Immunohistochemical profile of the tumor (200×). A: Epithelial component of metanephric adenofibroma was positive for WT-1 and a small amount of stromal cells was positive for WT-1. B: Stromal component of metanephric adenofibroma showed vimentin expression and a small amount of epithelial cells showed vimentin expression. C: Epithelial component of metanephric adenofibroma was positive for PAX2 and a small amount of stromal cells was positive for PAX2. D: The epithelial component was PAX8 positive. E: Capillary components were positive for CD34.
most cellular congenital mesoblastic nephromas have chromosomal abnormalities, especially triploid of chromosome 11 and bear the t(12;15)(p13;q25) translocation with ETV6-NTRK3 (EN) fusion gene [9]. In our case, chromosomal analysis revealed a normal male karyotype.

Metanephric adenofibroma can potentially be mistaken as Wilms’ tumor; both neoplasms are biphasic, containing spindle cells of mesenchymal origin and discrete nodules of embryonal epithelium. It is very important to distinguish between the two for management purpose. Metanephric adenofibroma is a benign neoplasm whereas Wilms’ tumor is fully malignant which requires chemotherapy. More than 80% of patients with Wilms’ tumor are diagnosed before 5 years of age, with a median age of 3.5 years, while metanephric adenofibroma is 10.2 years [7, 10]. Classic Wilms’ tumor includes three histological cell types in varying proportions: blastemal, epithelial and stromal components [11]. Tumors with predominantly epithelial differentiation have low aggressiveness, but high mitotic activity, while those with blastemal predominance are highly aggressive [12]. The main difference between them hinges on an increased presence of active mitosis found in Wilms’ tumor but not metanephric adenofibroma. LOH at chromosome 16q occurs in 20% of Wilms’ tumors [13]. Similarly, 10% of cases have been found to have LOH at chromosome 1p [14]. Currently, there are no reports of loss of heterozygosity for chromosome associated with metanephric adenofibroma. This is consistent with our microarray results. WT-1 mutations are present in 10-15% Wilms’ tumor cases; patients with WT-1 abnormalities have a higher predisposition for developing nephroblastoma [15, 16]. The p53 tumor suppressor gene is not involved in the pathogenesis of Wilms’ tumor and less than 5% of Wilms’ tumors have a mutation in this protein [17]. However, it is present in 75% of tumors with anaplasia and predicts a poor prognosis [18]. Although genetic testing can not fully distinguish the two diseases, but they are helpful clues. The final diagnosis needs to consider various factors.

The radiologic appearances of metanephric adenofibroma are nondiagnostic and impossible to distinguish from other solid pediatric renal tumors. It is not logical to recommend partial nephrectomy preoperatively because there are no features on ultrasound or CT scan sufficiently reliable to justify a less aggressive management plan. If the diagnosis of meta-
Metanephric adenofibroma is confirmed by initial biopsy or frozen section at the time of surgery and the tumor locates at the upper or lower pole of the kidney with the largest diameter smaller than 4 cm, nephron sparing surgery is recommended. Because it is a benign course and no recurrences following surgical resection by radical or partial nephrectomy have been reported in the literature. Very rare cases of metastatic metanephric adenoma and adenosarcoma at presentation have been reported and long term behavior is unknown due to lack of follow up in the literature, therefore, it is necessary to accept periodically review [19, 20].

Disclosure of conflict of interest

None.

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References


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