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Original article

Ossifying renal tumor of infancy (ORIT): The clinicopathological and cytogenetic feature of two cases and literature review

Wenbin Guan[a,1], Yu Yan[a,1], Wenguang He[b], Meng Qiao[a], Yi Liu[a], Yanhua Wang[a], Bo Jiang[a], Wenwei Yu[a], Ruifen Wang (Dr.)[a,*], Lifeng Wang (Dr.)[a,*]

[a] Department of Pathology, Xin Hua Hospital Affiliated to Shanghai JiaoTong University School of Medicine, Shanghai 200092, China
[b] Department of Radiology, Xin Hua Hospital Affiliated to Shanghai JiaoTong University School of Medicine, Shanghai, 200092, China

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ABSTRACT

Ossifying renal tumor of infancy (ORTI) is a rare benign pediatric renal tumor, which has typical clinical and pathological features. In this article, the histological features, immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) assay of two cases of ORTI were performed and the literatures were reviewed. Both of the patients presented to hospital with painless gross hematuria without other symptoms. One is 6 months old male, another is 5-month-old. After several diagnostic procedures, they underwent surgery and the histological diagnosis of ORTI was finally made. Grossly, the tumor had a nodular or irregular appearance, often partially calcified and located in the renal pelvis and calyces. The cut surface of this mass was grey-white, solid and firm. Histologically, the tumor was composed of three major histologic components: osteoblast-like cells, spindle cells, and an osteoid core. Immunohistochemistry staining revealed that osteoblast-like cells were positive for EMA, Vimentin and STAB2. Spindle cells were strongly immunoreactive for Vimentin, WT-1 and focally positive for SMA, but were negative for CK, PAX8 and PAX2. The FISH studies with CEP4 probe on interphase nuclei from the two ORTIs, revealed trisomy 4 were 8.97% (case 1) and 12.23% (case 2). Our study showed that clonal trisomy 4 may be considered as a cytogenetic feature of ORTI, which makes it distinct from other pediatric renal tumor.

1. Introduction

Ossifying renal tumor of infancy (ORTI) is a rare pediatric renal tumor, which presents with painless gross hematuria and rarely with an abdominal mass. The biologic behavior of this tumor is benign, and almost all the reported patients remain well without recurrence or metastasis after operation. At present, the confirmed diagnosis of ORTI is according to its typical clinical and pathological features. However, the histogenesis of this tumor is not clear up to now and, sometimes ORTI is easily confused with calcified Wilms tumor. In this article, we report two cases of ORTI in our study and review the literature to assess the clinicopathological features of this unusual neoplasm and explore its' origin.

2. Materials and methods

2.1. Patients

The 2 cases of ORTI in this report were diagnosed at Xinhua Hospital, Shanghai Jiaotong University School of Medicine. Clinical data, imaging studies and characteristics of the tumors were obtained from hospital records.

2.2. Immunohistochemistry (IHC)

Tissue samples were fixed in 10% neutral formalin, embedded in paraffin, and cut into 4-μm-thick sections. Hematoxylin and eosin (H&E) staining and IHC were applied. The antibodies used in the IHC including cytokeratin (CK), epithelial membrane antigen

Abbreviations: CK, cytokeratin; CMN, congenital mesoblastic nephroma; EMA, epithelial membrane antigen; FISH, Fluorescence in situ hybridization; H&E, Hematoxylin and eosin; IHC, Immunohistochemistry; ILNR, intralobar nephrogenic rests; ORIT, Ossifying renal tumor of infancy; SMA, smooth muscle actin; SSC, standard saline citrate.

* Corresponding authors at: Department of Pathology, Xin Hua Hospital Affiliated to Shanghai JiaoTong University School of Medicine, 1665 Kongjiang Road, Shanghai 200092, China.
E-mail addresses: ruifen1981@163.com (R. Wang), wlf6009@163.com (L. Wang).
[1] Contributed equally.

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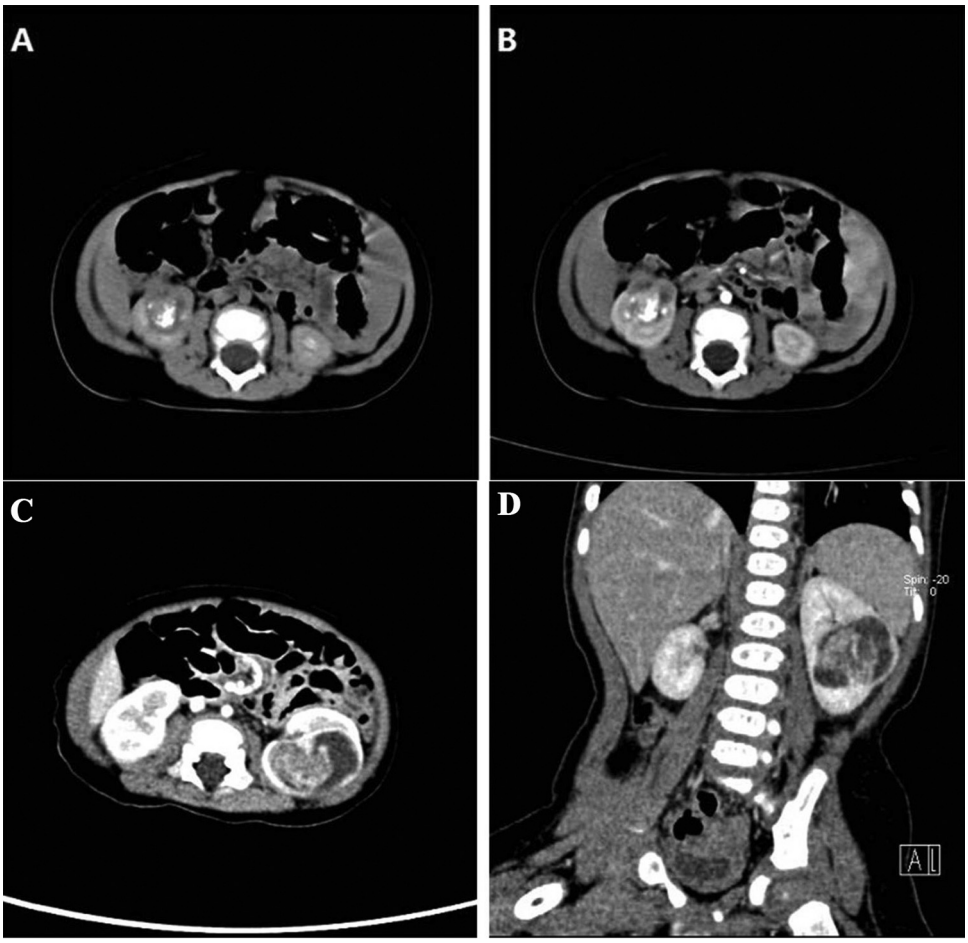

Fig. 1. CT images of ORTI in two cases(A and B, case 1; C and D, case 2). (A) Axial nonenhanced CT image shows a calcified soft tissue mass located in the lower pole of the right kidney and extended into the collecting system, (B) with poor contrast enhancement contrast medium injection. Axial (C) and coronal (D) contrast-enhanced CT images show a solid and cystic mass located in the left kidney with fairly heterogeneous enhancement.

(EMA), Vimentin, smooth muscle actin (SMA), Ki67, S100, CD34, WT-1, CD56, PAX8, PAX2, STAB2 and Desmin. STAB2 antibody was obtained from Abcam, others were obtained from DAKO. Appropriate positive and negative controls were simultaneously evaluated.

2.3. Fluorescence in situ hybridization (FISH) assay

FISH analysis on the tumor samples of each case was performed using Vysis CEP 4 (α-satellite) Spectrum Green probe (Vysis, Abbott Park, IL) at the 4p11q11 centromere region of chromosome 4, and ETV6-NTRK3 dual color break apart probe (ZytoVision). Briefly, 4-μm tissue sections from the tumor samples were de-paraffinized and hybridized with the probe, overnight, according to the manufacturer's protocol. Next day, the slides were washed three times in 2 × standard saline citrate (SSC) (Sigma-Aldrich, St Louis, MO) for 1 min at room temperature, followed by 2 × SSC for 1.5 min at 72 °C, and then washed in 2× SSC for 1 min at room temperature. Finally, the slides were counterstained with DAPI I (Vysis, Abbott Park, IL). Hybridization signals were captured and analyzed using the CytoVison Image Analysis System (Applied Imaging, Santa Clara, CA). Only non-overlapping nuclei with strong and well-defined signals were examined. Small, irregular, pale and ambiguous fluorescent deposits in the nuclear area were disregarded. The positive of trisomy 4 was confirmed if the number of nuclei with three hybridization signals for the centromere probe. The positive of ETV6-NTRK3 gene fusions was confirmed if more than 10% nuclei can be seen signals breaking apart.

2.4. Literature review

Previous cases of ORTI were obtained from the PubMed-MEDLINE database, using the term 'ossifying renal tumor of infancy'. A total of 21 cases of ORTI were searched from the English literatures. An effort was made to identify the cases that had been reported more than once and only the cases with the most recently updated information were included in this report.

3. Results

Patient#1, a 6-month-old male, has been reported in 2013 [1]. The patient presented with intermittent painless gross hematuria for 2 months without other symptoms. Physical examination showed that the abdomen was soft with no painful abdominal mass. Blood samples showed WBC of 7600/mm^3, CrP of 6.0 mg/dL, and Hb of 9.9 mg/dL. Urine analysis revealed numerous red blood cells per high-power field, a corpuscular hemoglobin level of 250/μL and a urine protein level of 25.0 mg/dL. During abdominal ultrasonography, the patient was found to have a solid mass with inhomogenous echoes in the right kidney. The CT scan showed that a partially calcified soft-tissue mass was located in the lower pole of the right kidney and extended into the collecting system (Fig. 1A and B) [1]. Therefore, the patient was performed a partial nephrectomy of right kidney. Frozen section showed a renal ossifying tumor with safe surgical margins. There was no evidence of recurrence or metastasis by 6 months follow-up after the operation.