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clinical practice

A rare case of renal tumor in children: clear cell sarcoma

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SUMMARY: **A rare case of renal tumor in children: clear cell sarcoma.**

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Clear cell sarcoma of the kidney is an uncommon renal neoplasm of childhood. It represents about 4% of childhood malignant neoplasms and is generally more common in children under 5 years of age. In the present article, we describe the case of a 12-year-old male patient who came to our observation with left renal mass and with a clinical-laboratory picture indicative of inflammatory pathology.

KEY WORDS: Renal tumor - Clear cell renal sarcoma - Abscess - Ultrasound - Computed Tomography.

Introduction

Renal tumors in children are rare. According to the data AIRTUM (*Italian Association of Cancer Registry*), they constitute 5% of cases of cancer in children. The most common histotype is nefroblastoma or Wilms tumor (TW), which accounts for about 90% of all kidney cancers, while carcinoma and clear cell sarcoma (CCS) are rare (1).

CCS accounts for about 4% of childhood malignant neoplasms and is more common in children under 5 years of age with male prevalence (2-5).

The CCS in the past was considered an unfavorable histological variant of TW, whereas it is currently recognized as a separate clinical-pathological entity and is subjected to a different treatment from that of TW (4-7).

TW is bilateral and multicentric in about 5% of cases, while the CCS is almost always unilateral and unicentric. Furthermore, TW can develop in both the cortical and the renal medulla, whereas the CCS originates from the medullary and has a more aggressive clinical behavior (3, 6-8). The CCS has the propensity to spread through the renal and perirenal vascular structures and this explains the higher frequency of metastasis and the highest rate of recurrence and mortality (4, 5, 7, 9, 10).

During the presentation of the disease, the most common site of metastases are the regional lymph nodes, but it is also known as the pediatric tumor that has the peculiar potential to metastasize to the skeleton up to about 60% of patients compared to an incidence of 2% in TW (2-4, 11-13). Moreover, the CCS also has the propensity to metastasize not only to the lung and the liver, but also to the brain (2, 5-8, 11).

Therefore, the high risk of distant metastases, the propensity to late relapse up to 4 years from diagnosis and a poor prognosis require an early and correct diagnosis (2, 13, 14).

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Case report

A 12-year old male patient underwent a pediatric visit in July 2017 due to the persistence of left-sided pain, a scarcely treatable abdomen and a high fever (around 38° C) for about a week. Later he practiced laboratory tests that showed an increase in inflammation and urinalysis that was normal. At the same time, the patient underwent an ultrasound examination and a subsequent MRI in the hospital of residence. The ultrasound examination showed the presence of a voluminous mass with a mixed ecostructure, non-vascularized, about 75x65 mm. The MRI described the aforementioned expansive formation of a round appearance with a non-homogeneous content by a fluid matrix from the mixed signal referable to blood or muco-proteinaceous tissue. The MRI findings together with clinical and anamnestic data suggested the diagnostic hypothesis of pyelonephritis with abscess in the renal sinus. Therefore, on indication of the pediatrician, the patient underwent antibiotic therapy for about a month, followed by remission of the symptomatology and stability of the lesion to the ultrasound control examination (August/September 2017). In October, following the reappearance of pain on the left side associated with a scarcely treatable abdomen and high fever, he came to our observation and underwent laboratory tests, ultrasound and CT with contrast. Laboratory investigations showed an increase in the number of white blood cells (17.36x103/µL), in particular neutrophils (90%), ESR (22 mm) and C reactive protein (130 mg/L); in addition, the increase in LDH (971 U/L) was also observed, while the urinalysis was negative. The ultrasound examination showed in the left kidney a voluminous mass, devoid of vascularization and an inhomogeneous echostructure, consisting of a partly solid and partly fluid component (Figures 1 A-D). The CT scan performed with contrast agent described a left renal structure almost completely subverted due to the presence of an extensive inhomogeneous formation with a suprafluid density with peripheral enhancement. Concomitant extended thickening of phlogistic aspect of peri and pararenal spaces and left basal pleural effusion with consensual subatelectasia (Figure 2 A-C). In suspected inflammatory pathology, at the same time as antibiotic therapy (Rocefin 1g/die e.v. for about a week), a drainage tube was placed (Figure 3) and a deep eco-guided biopsy was performed with solid component trucut. The biopsy showed the presence of minute fragments with the microscopic characteristics of largely necrotic renal parenchyma cells. Microscopic examination of the drainage fluid revealed cellular elements with not well evaluated cytoplasm, rare mi-

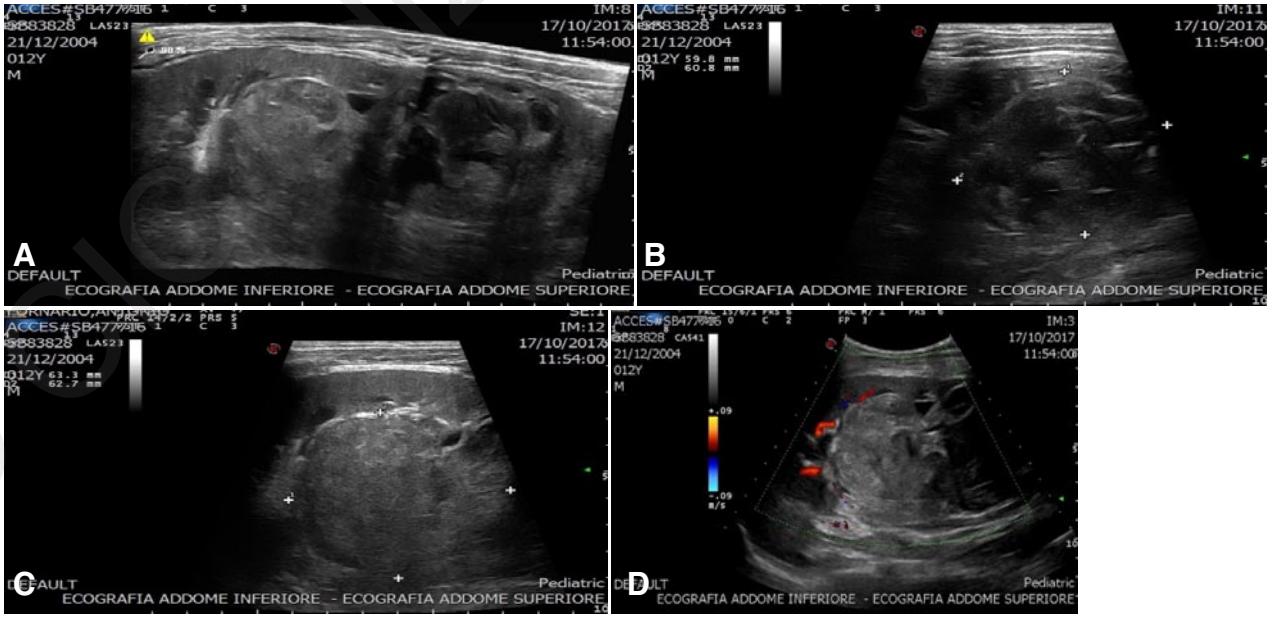

Figure 1 (A-D). Ultrasound images of the abdomen (October 2017): voluminous mass of the left kidney with inhomogeneous and mixed echostructure (A-C), without vascularization (D).

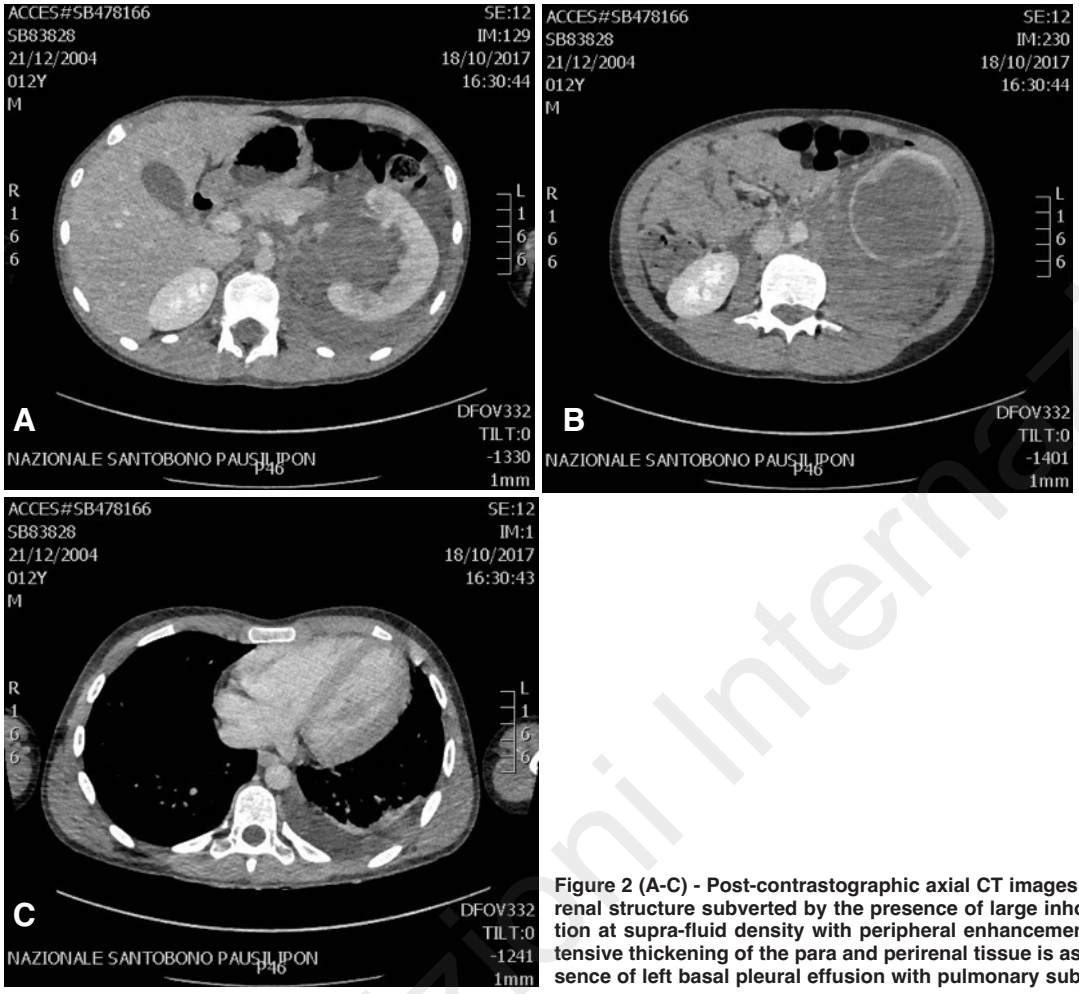

Figure 2 (A-C) - Post-contrastographic axial CT images (October 2017): left renal structure subverted by the presence of large inhomogeneous formation at supra-fluid density with peripheral enhancement. Omolaterally, extensive thickening of the para and perirenal tissue is associated (A-B). Presence of left basal pleural effusion with pulmonary subateletassia (C).

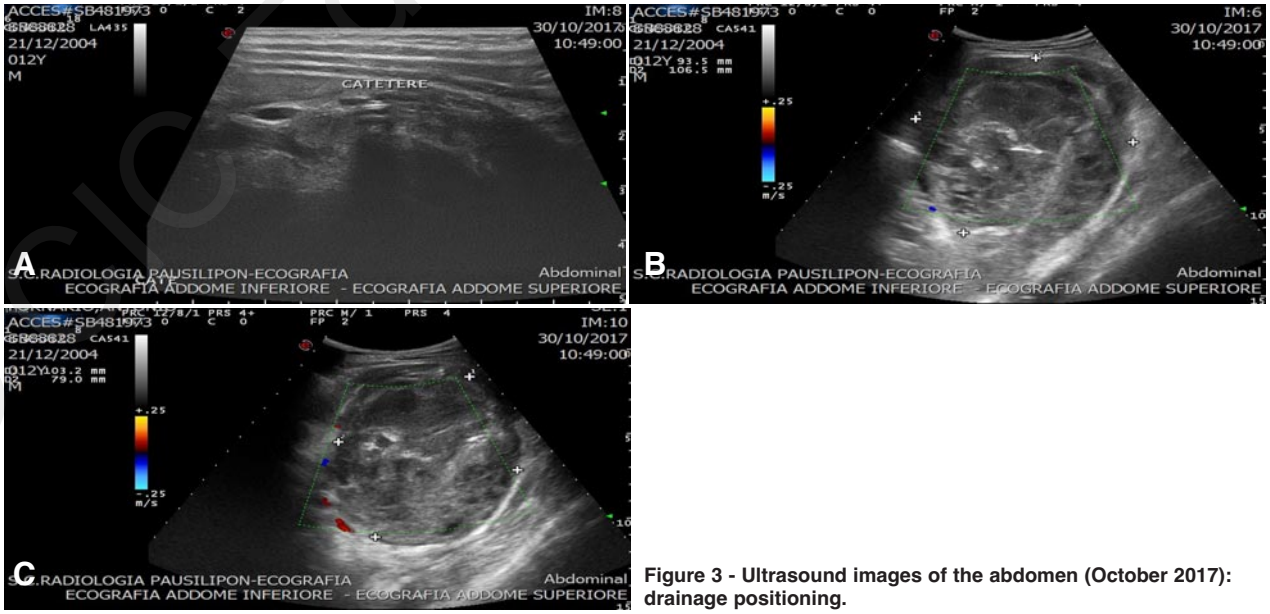

Figure 3 - Ultrasound images of the abdomen (October 2017): drainage positioning.

totic figures and multiple foci of cellulose necrosis. Also, immunohistochemical analysis of these elements was performed which revealed morphological and immunophenotypal aspects suggestive for a heteroplasic process. Therefore, for this suspicion, another eco-guided biopsy was performed in November with a trucut with an intraoperative diagnosis of the absence of neoplasia. In the meantime, the patient underwent a control ultrasound which showed the expansive formation unchanged in size and echostructure (Figure 4 A-D). At contrast CT examination the lesion appeared substantially unchanged in size, but showed inhomogeneous density, predominantly necrotic and with internal vascularized solid token-shaped. Concomitant lymphadenopathies in the left para-aortic area of the maximum diameter of about 15 mm (Figure 5 A-D). The patient also showed laboratory tests with normalization of inflammatory indices and scintigraphic examination showing regular perfusion of both kidneys, overall glomerular filtration rate within normal limits (GFR> 75 ml/min, 54% right kidney, left 46%) and regular excretory phase bilaterally (Figure 6). In consideration of the time since the onset of the disease (about 5 months), of the unchanged findings of the instrumental investigations and on the basis of the presence of neoplastic cells in the drainage fluid, it was decided to subject the patient to left nephrectomy. On the macroscopic examination the left kidney showed an external surface seat of a roundish solution of about 1.5 cm round and deformed by the presence of a mass that occupied the middle and lower third of the kidney, compressing and dislocating the pelvis; this mass measured in section about 10x6.7 cm, appeared well circumscribed, solid and largely necrotic; the ureter was not macroscopically visible (Figure 7 A, B). Microscopic analysis described the presence of a neoplasm provided for most of fibrous pseudocapsule, consisting of extensive necrotic areas and to a lesser extent by vital areas containing cells with a round-oval nucleus sometimes spliced with dispersed chromatin, with clear cytoplasm, indistinct nucleoli and abundant extracellular matrix; these cells were arranged with diffused pattern or in small nests delimited by a rich and delicate vascular network represented by thin capillaries; the mitotic figures were frequent and there was also granulation tissue and scattered flogosis even with giant cells. The immunohistochemical neoplasm expressed positivity for Vimentin, INI-1, Cyclin D1, CD56, bcl-2 and negativity for panCK, synaptophysin, chromogranin, WT-1, EMA, S100,

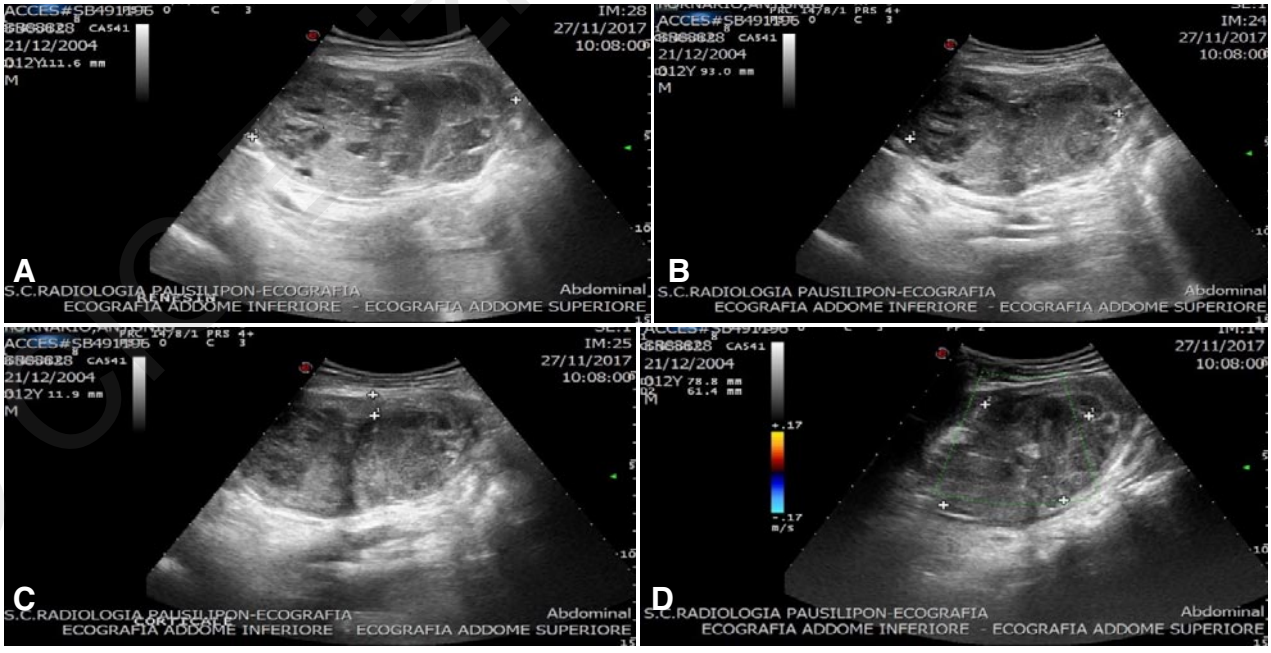

Figure 4 (A-D) - Ultrasound images of the abdomen (November 2017): voluminous mass of the left kidney with inhomogeneous and mixed echostructure (A-C), non-vascularized (D).

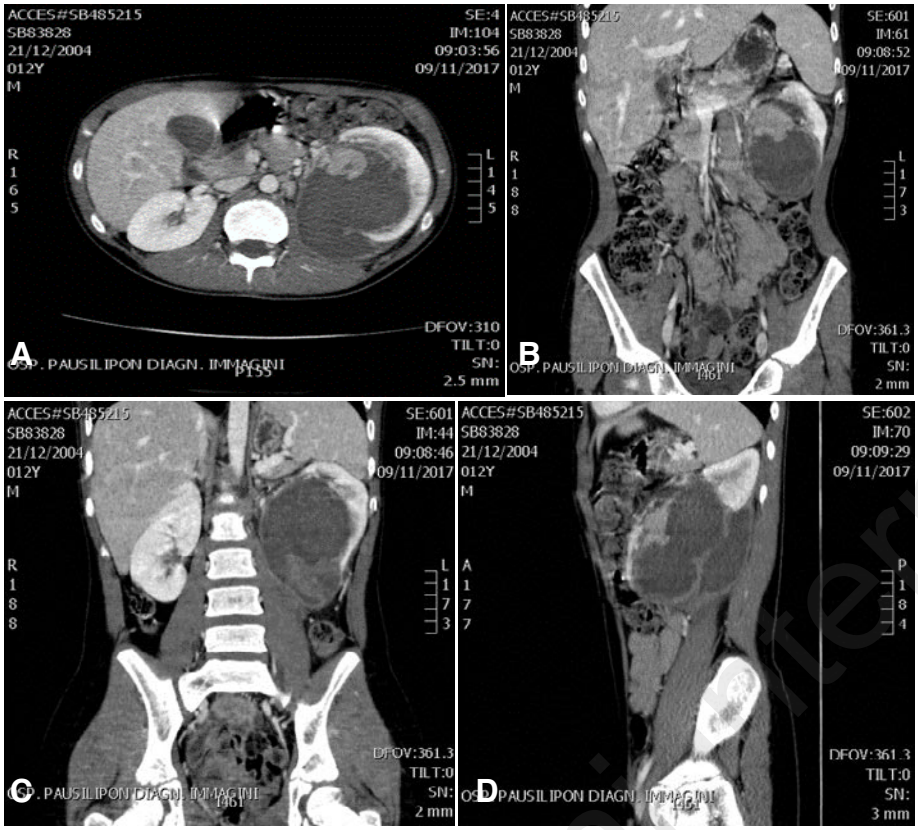

Figure 5 (A-D) - Axial CT images (A), coronal MPR (B-C), sagittal MPR (D) (November 2017): expansive formation of the left kidney, predominantly necrotic with internal vascularized solid tokens. Appreciability of lymph node elements with a max diameter of about 15 mm in the left para-aortic area (A).

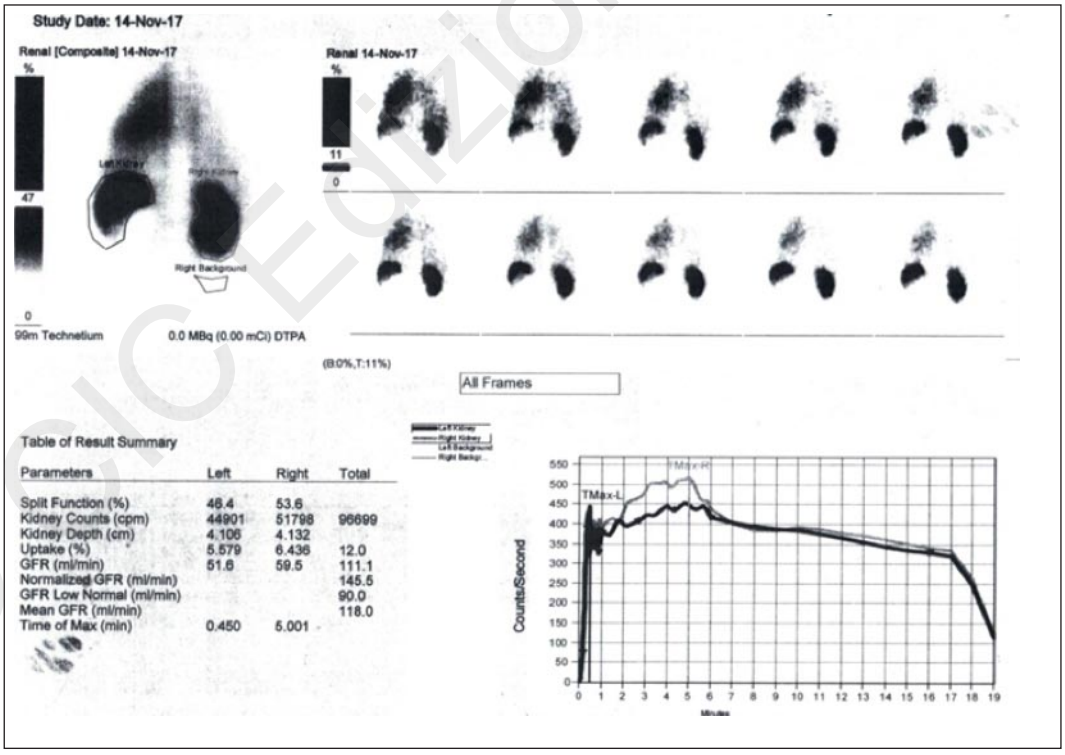

Figure 6 - Renal scintigraphy: regular perfusion and excretory phase of both kidneys with overall glomerular filtration rate within normal limits.

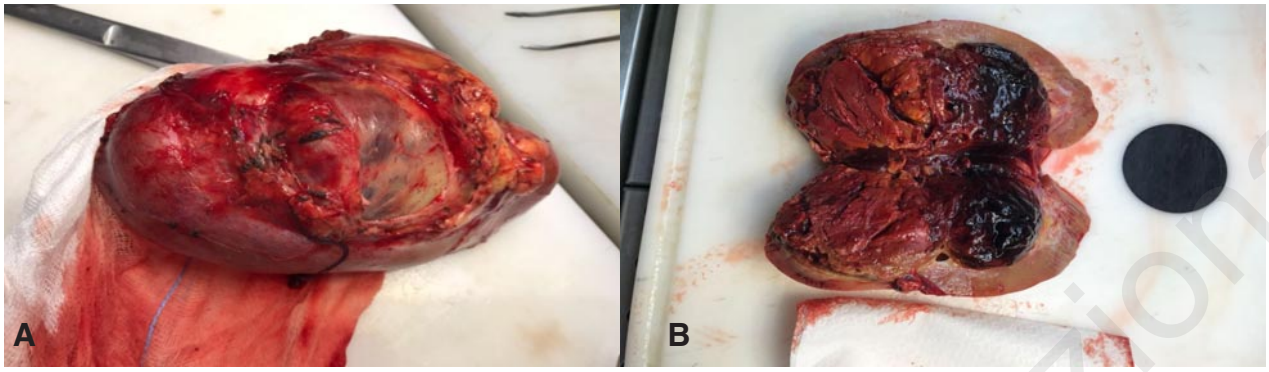

Figure 7 (A, B) - Images of the left nephrectomy: macroscopic aspect of the kidney and tumor, in (A) outer surface, in (B) inner surface.

Desmin, PAX-8 and CD34; CD99 was not contributive, while there was a plurifocal and weak expression for p53. The neoplasm infiltrated the fibrous pseudocapsule and focally the renal sinus and the soft tissues adhered. The pelvis and margins of hilar vessels were free of neoplasia. The residual renal parenchyma was free from significant changes. In conclusion, the histological and immunohistochemical examinations reported findings compatible with the presence of a CCS.

Discussion and conclusions

The CCS is a rare cancer that affects predominantly male children aged 2-3 years and has a non-specific clinical presentation that makes differential diagnosis difficult, presenting itself, in most cases, only as abdominal mass (2, 10-13). Small patients with CCS often show clinical symptoms similar to those of TW that include not only the distension of the abdomen due to the presence of expansive formation, but also macroscopic hematuria and abdominal pain. Other symptoms, less frequent, are vomiting, fever, constipation, loss of appetite and hypertension (6, 7, 9). The case presented concerned a patient, who came to our observation with left renal mass and with a clinical picture indicative of an inflammatory disease in the absence of hematuria. After antibiotic therapy the patient showed remission of symptoms with normalization of inflammatory indices.

The suspicion of the presence of a renal tumor derived from the persistence of the mass at about 5 months from the initial finding, from the presence of neoplastic cells in the drainage fluid and from the findings of the imaging, in particular the presence on the CT examination of vascularized solid token-shaped all inside the mass. The most probable diagnostic hypothesis could be that of TW, being the most frequent renal neoplasia in pediatric age (1), but in our case the patient was 12 years old and the TW has a higher incidence in the age range between 3-4 years. Furthermore, on the CT examination the renal mass had no specific characteristics and neither showed the typical inhomogeneity of a TW, which in most cases is very heterogeneous due to the presence inside of hemorrhagic, fat, necrotic and calcification areas. Also, the TW tends to thrombose the inferior vena cava and the renal veins, findings not present in our case (7, 8, 10). Finally, no renal nodal lymph nodes were visible at the imaging site and the pulmonary parenchyma showed no metastatic lesions, whereas both the lymph node involvement and the pulmonary metastases were frequent in the TW presenting the disease (5, 7, 10, 12). Conversely, a CCS was a diagnostic hypothesis that was not easily done due to its rarity, but also to the patient's age, as the TW is more frequent in children under the age of 5 (2-5). Furthermore, the clinical suspicion of the presence of CCS could arise in the presence of bone metastases, rare in TW and not present in our patient (2, 7, 11). At imaging the findings were not characteristic, in particular the finding of little tissue component within the renal mass did not support the diagnostic hypothesis of a CCS, which, in most cases, presents itself as a predominantly solid expansive formation and only occasionally composed of cystic, hemorrhagic and/or necrotic areas (2, 6, 8, 15). Furthermore, vascular infiltration and hilar pathological lymph nodes were not found ho-

molateral to the lesion, findings often present in the CCS (2, 4, 5, 7, 9), but on the CT examination only the enlarged lymph node elements in the left paraaortic site were evident, which in the CCS can be the exclusive venue for metastatisation (2). Ultimately, ultrasound and CT scan do not provide findings useful for the differential diagnosis between CCS and other renal tumors, particularly with TW (9-11, 15). Miniati et al. in their study show that the CT scan in detecting the presence of a TW has a sensitivity of 92%, but a very low specificity, of about 55%. Therefore, the Authors argue that in clinical practice in many cases the CT findings are erroneously indicative of the presence of a TW, being eventually diagnosed with a histopathological examination a renal tumor other than Wilms (12). In our case the histological examination using a deep eco-guided biopsy with trucut did not show the presence of neoplasia twice. On the other hand, according to the 2001 European Protocol of the SIOP (International Society of Pediatric Oncology), percutaneous biopsy of a renal tumor is not systematically recommended (9). Biopsy findings are easily misinterpreted due to sampling errors and the histopathological features of CCS may mimic or be imitated by other pediatric renal neoplasms, especially TW, which makes CCS the childhood renal tumor most frequently subject to an incorrect diagnosis (16). In our case the diagnosis of CCS was only possible after nephrectomy. The histopathological examination showed typical findings of a CCS represented by cells with a round-oval nucleus sometimes fused to dispersed chromatin, with clear cytoplasm, indistinct nucleoli and abundant extracellular matrix; moreover, some cells showed a small-nided arrangement delimited by a rich and complex vascular network described in the "chicken-wire" pattern (2, 4, 6-9, 11, 14). Immunohistochemical analysis was useful to distinguish CCS from other childhood renal tumors, as the CCS showed positivity for Vimentin and bcl-2 and negativity for cytokeratin, WT-1, EMA, S100, Desmin, CD34 and CD99. However, no single immunohistochemical reaction is universally diagnostic for CCS, therefore, the study is mainly used to exclude other renal tumors (2, 6, 8, 9, 11, 13). Ultimately, the diagnosis of CCS may be difficult, but the identification of CCS as a different entity from other renal tumors, especially from TW, is of considerable importance, differing in prognosis and treatment. Furthermore, an early diagnosis of CCS is essential because it is a particularly aggressive tumor with high potential for metastasis, especially in the skeleton (3, 4, 7).

In conclusion, in children with renal mass in the differential diagnosis the presence of a CCS must also be considered, although it is rare, since the correct identification of this neoplasm allows an appropriate treatment.

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