

The Rhabdoid Tumor of the Kidney in Children—Cases Report

I. Tadmori*, S. Benmiloud, M. Hbib, M. Hida

Pediatric Department, Oncology Unit, CHU Hassan II Fez, Morocco

Email: *tadmori.ilham@hotmail.fr, benmiloudsarra@yahoo.fr, mohamed.hbib@hotmail.fr, hida63@yahoo.fr

How to cite this paper: Tadmori, I., Benmiloud, S., Hbib, M. and Hida, M. (2020) The Rhabdoid Tumor of the Kidney in Children—Cases Report. *Open Journal of Pediatrics*, 10, 600-609.

<https://doi.org/10.4236/ojped.2020.104061>

Received: September 20, 2020

Accepted: November 2, 2020

Published: November 5, 2020

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Abstract

Teratoid rhabdoid tumors are highly malignant, rare and aggressive. The prognosis is very poor, with a pejorative and rapidly lethal evolution. The objective of this study was to show diagnostic and therapeutic approach through the report of four observations of rhabdoid tumor of the kidney in children, treated in the oncology unit at the pediatric department CHU Hassan II Fez Morocco, collected over a period of 10 years. The ages of the patients varied from 8 months and 5 and a half, with 3 girls and a boy. All children have abdominal distention with the discovery of a mass on clinical examination. The patients were treated as nephroblastoma by neoadjuvant chemotherapy followed by enlarged total nephrectomy. The pathological study confirmed the diagnosis of a teratoid rhabdoid tumor. Adjuvant chemotherapy was given in all four children combined with radiotherapy in three cases. The evolution was fatal in three children. Malignant rhabdoid tumors are a particular pathological entity requiring a well codified therapeutic protocol to improve survival which does not exceed 15% to 20%.

Keywords

Child, Rhabdoid Tumor, Prognosis, Therapeutic Protocol

1. Introduction

Rhabdoid tumor Teratoid (TRT) is one of the rarest and most aggressive tumors in children, characterized by a very poor prognosis. The term rhabdoid is related to the fact that tumor cells resemble rhabdomyoblastic differentiation. TRT is considered by the World Health Organization (WHO) as a highly malignant tumor that mainly affects infants with male predominance (sex ratio 1.4 to 2). TRTs were first described in 1978, these rhabdoid tumors were initially de-

scribed in the kidney as variants of Wilms tumors, characterized by an early age of onset (first year of life), unusual aggressiveness and morphology clearly distinct from that of nephroblastomas [1]-[6]. In 1981, Haas and colleagues recognized rhabdoid tumour of the kidney as a separate tumour rather than a variant of Wilms [1]. The clinical characters are not specific and are diagnosed on histological, immuno-histochemical, and cytogenetic studies. The treatment is not well codified, and the prognosis is very poor with an overall survival rate between 20% and 25% [4] [7]. Through this publication, the authors report cases of rhabdoid tumors of the kidney in four children treated in the pediatric oncology unit at the pediatric department of CHU Hassan II in Fez, Morocco, collected over a period of 10 years (1 January 2011 to 31 December 2019). Cases of renal TRT represent 4% of all renal tumors admitted, followed in the unit during this study period, and authors specify the epidemiological, radiological, histological, and prognostic characters.

2. Cases Studied

Case N°1

A 5 and half-years-old girl presented with abdominal distension, and weight loss, complicated by the occurrence of exaggerated acute abdominal pain in the side and left iliac fossa for four weeks ago. On physical examination, she weighed 17 kg (-1 SD), afebrile, and the abdomen was distended with a large firm and fixed mass measuring 15 cm dimensions on the left hypochondrium and the epigastrium with a lumbar contact. An umbilical perimeter (PO) of 57 cm, with no other associated lesions. Blood pressure (BP) at 120/80 mmHg “hypertensive”.

Abdominal ultrasound revealed a large solid and cystic vascularized mass with Doppler, measuring 12 × 11 cm in the left kidney with multiple lymphadenopathy (ADPs) intra and retroperitoneal, the largest measure 2.5 cm. The thoraco-abdominopelvic computed tomography (CT-TAP) shows two heterogeneous large masses in the left kidney, one upper polar and the other lower. Containing no calcifications, delimiting large areas of necrosis, measuring respectively 170 × 75 × 144 mm and 60 × 54 × 70 mm, evoking a locally advanced bifocal nephroblastoma with retroperitoneal ADPs, the largest of which measures 13 mm, and secondary pulmonary localization, 02 micronodules in the right lower lobe (LID) and middle lobe (LM) as shown in **Figure 1**.

On the biological test, the blood count did not show any abnormality; Calce-mia: 100 mg/l; LDH: 1810 UI/l; Uree: 0.21 g/l; creatinine: 5.00 mg/l and urinary catecholamines are negative.

Case N°2

A 2 and half-years-old girl presented with abdominal distension for four weeks ago. On physical examination, she was weighing 13 kg, afebrile. Abdominal examination revealed a mass in the deep left hypochondrium measuring about 17 cm long axis with a lumbar contact and PO: 59 cm and the rest of the examination is unremarkable. Blood Pressure (BP) at 120/80 mmHg.

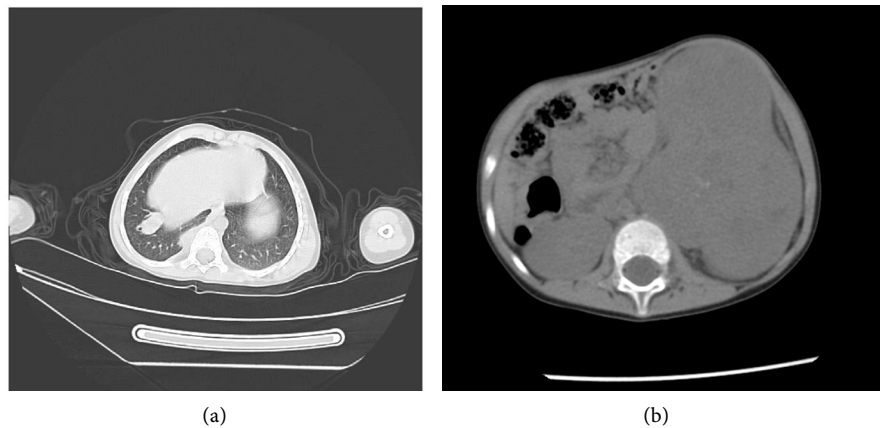


Figure 1. (a): Thoracic CT scan: Image of lung metastasis. (b): heterogeneous mass of left kidney with invasion loco regional lymph nodes its lower border extended to the pelvic.

Abdominal ultrasound revealed a large locally advanced left renal mass measured 15×11 cm with secondary abdominal lymph node localization. A thoracic-abdominopelvic CT scan (TAP CT) shows a heterogeneous voluminous left renal tissue tumor process, spontaneously hypodense with some calcifications, measuring $150 \times 120 \times 75$ mm, locally advanced (invasion of the left renal vein and inferior vena cava) to the right heart chambers with a thrombus at the level of the left ventricle and secondary abdominal lymph node localizations measuring for the largest 1.5 cm minor axis and left upper lobe (LSG) pulmonary micronodules (**Figure 2**).

Laboratory tests, the blood count showed hypochromic microcytic anemia with ferritin at 100 ng/ml; Calcemia 98 mg/l; LDH: 1320 UI/l; Uree: 0.26 g/l; Creatinine: 5.50 mg/l; and Urinary Catecholamines are negative.

The child even benefited from an osteo-medullary biopsy (2 crests), with a histological aspect of a normal marrow without tumor infiltration.

Case N°3

Infant male, 4 months and 18 days old, operated at the age of one month for hypertrophic pyloric stenosis. The family observed an abdominal mass gradually increasing in volume without other associated signs, hence the consultation in our service. Clinical examination of the infant was eutrophic, and normotense, concerning the abdominal examination, the mass dimensions are 8×14 cm in diameter at the expense of the left hypochondrium exceeding the midline, fixed, hard with a PO: 47 cm and a lumbar contact.

Abdominal ultrasound shows the presence of 125 mm solidocystic mass of left renal origin. The TAP CT objectives a left renal tissue process, well limited, with regular contours, enhanced in a very heterogeneous after contrast, delimiting septate cystic areas, without calcifications or fatty islands, measuring $100 \times 115 \times 120$ mm, exceeding the midline. CT also notes an invasion of the perirenal fat and laminates the anterior and left lateral abdominal wall without invading it and rests on the homolateral psoas muscle without vertebral lysis opposite, with the presence of a locoregionallymph node location as illustrated in **Figure 3**.



Figure 2. A heterogeneous lobulated intraparenchymal large mass on the left kidney locally advanced.

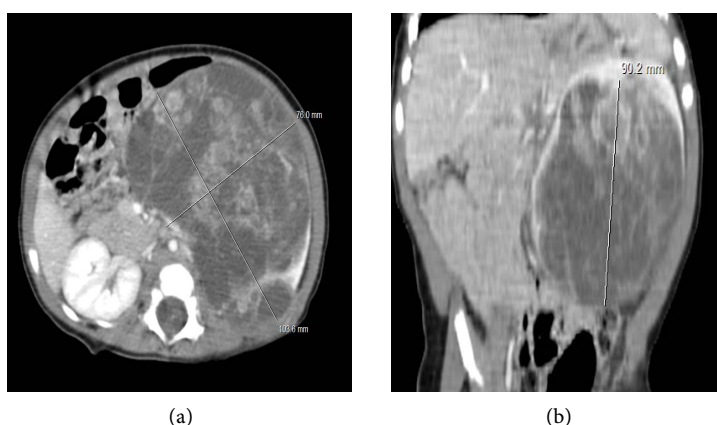


Figure 3. A heterogeneous Voluminous left kidney tumor massively necrotic refurbishing the neighborhood organs without invading them from children 4.5-months-old.

The results of the biological assessment showed that calcemia at 109 mg/l; LDH at 890 IU/l, Uree at 0.12 g/l; creatinine at 3.60 mg/l, urinary catecholamines are negative, and tumor markers are normal.

Case N° 4

A 2-years-old female child without pathological history, consulted for a mass and abdominal pain going back to 6 weeks. On clinical examination, the eutrophic child with a normal weight and height and hypertensive with a BP: 123/85 mmHg. The abdominal examination revealed a mass at the right hypochondrium measuring approximately 10 cm in the long axis with a lumbar contact of a PO: 54 cm. The rest of the examination is without particularity.

The abdominal ultrasound revealed a retroperitoneal tissue mass of heterogeneous echostructure, from the lower pole to the right kidney. It measures 9 × 8 cm without deep lymphadenopathy. A thoracic-abdominopelvic CT scan (TAP CT) found a large tumor mass of the right kidney, spontaneously hypodense with some fine calcifications, heterogeneously raised after injection of contrast material with a left necrotic area. The mass measures 105 × 114 × 113 mm, without secondary lymph node or pulmonary localization as shown in **Figure 4**.

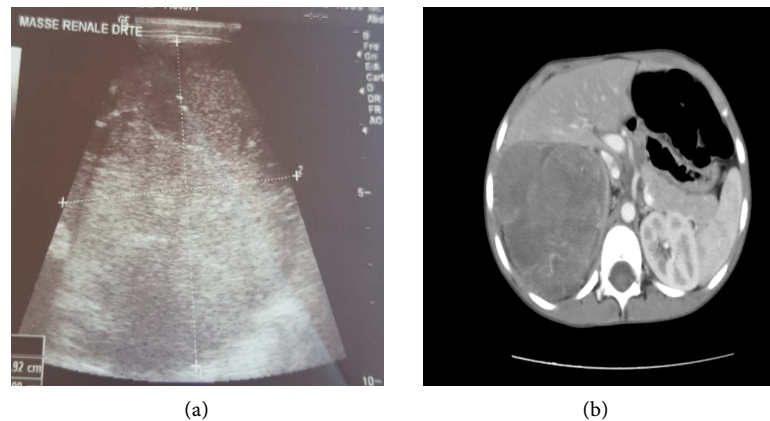


Figure 4. (a): Abdominal ultrasound: a heterogeneous large mass from the lower pole of the right kidney (b): abdominal CT scan: a heterogeneous tumor mass of the right kidney.

In biological tests, the blood count showed microcytic hypochromic anemia with ferritin at 50 ng/ml; Calcemia 99 mg/l, LDH: 990 UI/l, and Urea: 0.15 g/l; creatinine: 3.00 mg/l, and urinary catecholamines are negative.

3. Patients Management and Evolution

All the children received neo-adjuvant chemotherapy then they were operated on by performing an enlarged total nephrectomy. The anatomico-pathological study showed a histological aspect of a renal parenchyma is the site of a proliferation of rhabdoid appearance, which is arranged in diffuse layers. It is made up of large, non-cohesive cells, with eccentric and strongly nucleolated nuclei. The cytoplasm contains eosinophilic inclusions. Frequent mitosis. Immunohistochemistry Tumor cells diffusely express Vimentin and focal length CK8/18 and EMA. Desmin and Myogenin and Chromogranin, Synaptophysin are negative. A therapeutic effect in the form of necrosis and fibrosis estimated at 70%, 25% and 45% respectively. The tumor infiltrated the sinuses in two patients. The resection limits are healthy with the presence of reactive nodes in all patients (**Figure 5(a)** and **Figure 5(b)** and **Figure 6**). The classification, according to SIOP 2002, was high risk in all patients with local pathological stages II in cases N° 1, 2 and 3 and stage III in the 4th case.

A Brain CT scan was realized in all four children looking for an associated cerebral localization, it had returned normal in three cases. In the 4 months and half old infant, it showed a spontaneously densevermian tissue lesional process containing fluid areas, heterogeneously enhanced after contrast and measuring 24.5 × 31.8 mm illustrated in **Figure 7**.

The children received chemotherapy based on Cyclophosphamide, Vincristine, Carboplatin, Etoposide. This chemotherapy is associated with intrathecal injections for the infant who had associated brain localization. Radiotherapy is at a dose of 20 Gry on 11 fractions, in the three children. The infant was operated for the cerebral process whose anatomopathological study is in favor of TRTA, and the radiotherapy was rescued by the radiotherapists due to age.

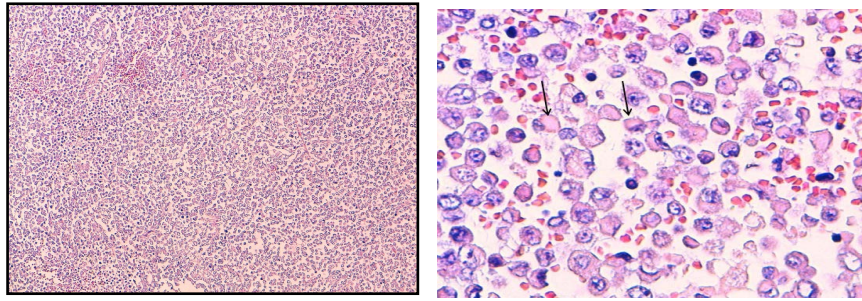


Figure 5. Rhabdoid tumor: histological appearance: (a): umorproliferation arranged in a diffuse sheet (HES $\times 100$). (b): Tumor cells show a cytoplasmiceosinophilicball (arrows).

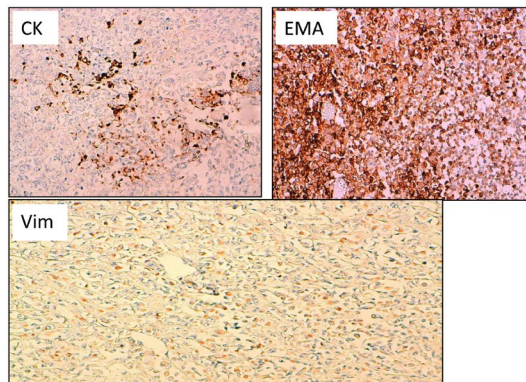


Figure 6. Rhabdoid tumor: immunohistochemical study: expression of cytokeratin, EMA and vimentin by tumor cells.

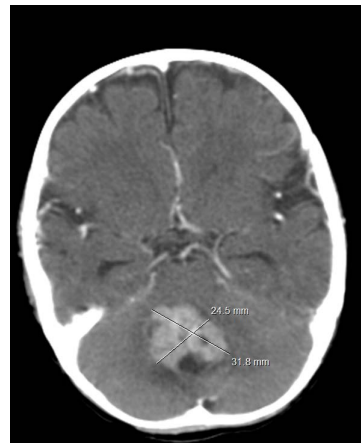


Figure 7. Brain CT scan: a tissue process in the FCP, heterogeneous after contrast for children 4 months and half old.

The evolution for the first case was favorable with a survival, without event for 2 years. The duration of chemotherapy was 34 weeks. The second case presented a post-chemotherapy infection with septic shock. The death occurred after 6 months of treatment. The infant presented, after 5 months of diagnosis, a recurrence in the kidney with secondary lung localization and died 2 months after the recurrence. For the 4th case, death occurred in their home under unclear conditions after 5 months of treatment.

4. Discussion

The teratoidrhabdoid tumors (TRTs) is one of the rarest, most aggressive, and fatal tumors for children. The term rhabdoid was assigned to it because the tumor cells resembled rhabdomyoblasts under light microscopy [2] [3] [4] [6]. The actual incidence of rhabdoid tumors remains difficult to assess. However, an estimation of the incidence could be given by Reinhardt et al, around 0.1 to 0.5 cases per million children per year [1] [6]. TRTs generally occur in children under three years of age, more rarely between three and six years of age with an average age of two years. The median age ranges from 10 to 24 months depending on the study. The sex ratio shows a male predominance of 1.37 to 2 [1.6]. Our patients were 5.5 years, 2.5 years, 4.5 months, and 2 years with an average of 31 months. We have three girls and a boy.

Rhabdoid tumor of the kidney is a rare and extremely aggressive malignant cancer. It represents 1.5% of all pediatric kidney cancers and 8% of those occurring before seven months [7] [8] [9]. It represents 2% of tumors registered with the National Wilms's Tumor Classification Group (NWTSG) [4]. It has long been considered a sarcomatous variant of Wilms' tumor, but since 1981, it has been a separate entity from nephroblastoma, a high-grade malignancy affecting infants [5] [6]. This tumor was first described for children in the kidney, and had been reported later in extra renal sites. The extrarenal localization of TRTs is multiple, brain, para-vertebral regions, thoracic wall, liver, myocardium, members, genitourinary organs, pelvic cavity, face, skin, esophagus, etc. [4] [5] [6]. The Authors report cases with renal localization in this study.

The rhabdoid tumor of the kidney has not a specific clinical symptom, it is dominated by the presence of an abdominal mass (82% of cases), hematuria (80% of cases), and pain in the flank has been described [4] [6] [9]. In more than 70% of cases, this tumor is discovered at a metastatic stage [6]. Metastases mainly affect the loco-regional lymph nodes, lungs, peritoneum, liver brain, and bones [4] [6]. The possible association with an FCP tumor suggests a neuro-ectodermal origin [2] [5] [6]. In the case of our patients, the clinical examination has shown an abdominal mass. Metastases were lymph node and pulmonary revealed on radiological examination in two cases and one case an association with a tumor of the FCP.

The laboratory test can reveal non-specific abnormalities such as anemia or hypercalcemia (4% to 18% of cases). In addition to bone metastases, this hypercalcemia is linked to hypersecretion of parathormone by tumor cells [6]. The markers for blood tumors in pediatric oncology (alpha-fetoprotein, beta-HCG) are negative [9]. In all four cases, there was a tendency for hypercalcemia and two children had anemia.

The radiological examination does not bring pathognomonic elements diagnostic. CT revealed evocative but inconstant elements of rhabdoid tumor of the kidney including calcification, sub-capsular hematoma, and the lobular appearance of a large, centrally located, heterogeneous mass and the spontaneously

hyperdense nature of the lesion, areas of hypodense necrosis are often noted [1] [4] [6].

Histologically, the tumor is made up of sheets of typical rhabdoid cells that are not very cohesive, ovoid or round to polygonal cells with vesicular nuclei and prominent nucleoli and large round eosinophilic cytoplasmic inclusion-like structures. Mitosis is frequent. Sometimes cells have a less atypical nucleus and a pale, fine-grained eosinophilic cytoplasm. Immuno-histochemically of great interest for diagnostic confirmation, the rhabdoid cells stain diffusely positive for vimentin and focally positive for cytokeratin, EMA neuron-specific enolase (NSE), and S-100 protein (s-100). The intracytoplasmic hyaline inclusion of typical rhabdoid cells strongly expresses vimentin (95% of cases) and EMA (epithelial membrane antigen) (75% of cases). The positivity of cytokeratin was reported in 60% of cases and of smooth muscle actin in 50% of cases. This positivity is variable for GFAP (Glial Fibrillary Acidic Protein), Neuron specific enolase (NSE), protein S100, and Synaptophysin [1] [4] [6]. All of our patients under study immunohistochemistry of tumor cells diffusely expressing Vimentin and focally CK8/18 and EMA which confirms the diagnosis of renal TRT. No case has benefited from a genetic study.

In the cytogenetic examination, an abnormality of chromosome 22q11-12 (hSNF5/INI1) is present in half of the cases. [2] [4] [5] [6].

The therapeutic protocol for the rhabdoid tumor of the kidney is not unanimous. For the NWTS (the National Wilms Tumor Studies), rhabdoid tumors kidney is treated by an enlarged nephrectomy, followed by chemotherapy (carboplatin; cisplatin, and cyclophosphamide) for 24 weeks and radiotherapy. However, for the SIOP (International Society of Pediatric Oncology), the treatment consists of first chemotherapy followed by surgery, then postoperative chemotherapy (etoposide, carboplatin, ifosfamide, and epirubicin) for 34 weeks and radiotherapy postoperative [6]. In the series reported by Hilden *et al.* (reference missed) Patients who benefited from a complete excision presented a better survival than those who had a partial excision. Treatment should be supplemented with aggressive chemotherapy and intensive radiotherapy. Chemotherapy is based on the administration of various combinations of some or all of the following drugs: cyclophosphamide, cisplatin, etoposide, vincristine, carboplatin, ifosfamide, and methotrexate [4] [5] [10]. Current therapy seems to be reaching the maximum levels of tolerable intensification without bringing a significant change in outcomes, and new approaches are desperately needed to advance therapy. Our patients were treated according to the SIOP protocol with chemotherapy then enlarged nephrectomy followed by chemotherapy and radiotherapy.

These tumors are extremely aggressive, and their prognosis is poor. It is a grade IV tumor according to the latest WHO classification. The average survival varies according to the studies is 11 to 17 months [1]. The prognosis is very grim with 80% to 90% of deaths, despite intensive treatment. The overall survival in the NWTS-1 to NWTS-4 trials is 23.6%. The main factors of the poor prognosis

are in stage three and four (III-IV), age < 1 year. However, it has been noted that children over the age of three have longer survival. The evolution is marked by local recurrences in 60% of cases [1] [2] [5] [6]. For our cases, the evolution of which was fatal in three cases (75%). Local recurrence was noted in one case and the two-year survival concerned the 5½ years old girl.

5. Conclusion

The rhabdoid tumor of the kidney is a rare and very aggressive tumor mainly affecting the infant. It is characterized by its rapid growth, and the occurrence of early metastases giving them a diagnostic and therapeutic urgency and the need for a well-coded therapeutic protocol to improve survival which does not exceed 15% to 20%.

Conflicts of Interest

Authors declare that there are no conflicts of interest related to this paper.

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