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Urachal rhabdomyosarcoma in childhood: a rare entity with a poor outcome

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ABSTRACT

Backgroud/Purpose: Rhabdomyosarcoma (RMS) of the urachus is rare and gathered in the "abdominal and other locations" group for oncological treatment purpose, and therefore not well characterized. Our aim was to assess the clinical and prognostic specific features of urachal primary RMS in childhood.
Methods: We retrospectively reviewed the charts of 8 patients with an urachal RMS treated between 1984 and 2013 in two Pediatric Oncology Departments. Median follow-up was 42 months (18–100).
Results: Urachal RMSs were embryonal in 6, alveolar in 1, and not otherwise specified in 1. Age at diagnosis was 4.4 years (2.6–6). All patients had advanced locoregional extension (IRS IIIIV) and 1 had distant metastasis. All had chemotherapy and surgical resection. Six had external radiotherapy. Four had extensive peritoneal recurrence including 2 with distant metastasis, within a median of 25 months (11–82) after the end of treatment. One had metastatic progression under primary treatment. Four of them died between 18 and 57 months after diagnosis, and 1 is still under treatment for a late recurrence. Only 3 are free of disease after 3.3 to 7.9 years of follow-up.
Conclusions: Pediatric urachal cancer is rare and poorly identified. In our series, RMS was exclusive in this location. Locoregional extension was always advanced. Prognosis was poor despite current multimodal therapy. We underline the need for new therapeutical strategies.

Urachal diseases in childhood result mainly from an abnormal delayed closure of its lumen, and are usually non-malignant. They include persistent patency with umbilical urine discharge, infection either urinary or urachal, or abdominal pain. In adults, the majority of urachal diseases are malignant, with adenocarcinoma being the most frequent tumor in this location, and of a poor prognosis [1]. In children, urachal tumors are rare and poorly identified. Most reports in the literature are single-case reports of various tumors including rhabdomyosarcomas (RMS) [2], and other types of rare tumors (leiomyosarcoma [3], inflammatory myofibroblastic tumor [4], neuroblastoma [5] and yolk sac tumor [6]), but no adenocarcinoma. However, pediatric series of RMS do not clearly identify cases with the urachus as a primary, and in the RMS international classification, urachal primary is usually classified within the large so-called "others" group gathering all trunk primaries.

We hereby report eight cases of urachal RMS in childhood, which is the largest series reported until now. Our aim was to assess the specificity of this location, in terms of clinical presentation, management and outcome.

1. Methods

1.1. Patients

The pediatric oncology databases of two large national reference centers were reviewed retrospectively, to identify patients with RMS arising specifically from the urachus during the period of 1984–2013.

The urachal origin was primarily suspected at diagnosis when the tumor arose from the dome of the bladder, in between umbilical arteries, and extending to the umbilicus. In some cases, the tumor was too large at diagnosis to define its primary origin. Urachal primary RMS was confirmed at surgery after neoadjuvant chemotherapy reduced the size of the tumor.

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Patients with a tumor arising distantly from the urachus (i.e. umbilical artery) were not included in the study.

1.2. Data analysis

The clinical characteristics, the histology and the invasiveness of the tumor, its treatment and outcome were retrospectively studied in the medical charts of the departments of pediatric oncology and pediatric surgery. Lymph nodes were evaluated clinically and by imaging (ultrasonography and CT-scan) in all patients. If nodal involvement was doubtful, cytological or histological biopsies were performed during surgery. However, systematic lymph node dissection was not done for diagnostic purposes only. Postsurgical staging was presented according to the Intergroup Rhabdomyosarcoma Staging (IRS) grouping system as follows: IRS I (complete resection), IRS II (microscopic residual disease), IRS III (macroscopic residual disease) and IRS IV (metastatic disease). Patients with extraregional lymph nodes, peritoneal nodules or positive cytology in abdominal fluids and/or extra-abdominal involvement were considered having metastatic disease. Histological subtypes were identified as alveolar, embryonal, or not otherwise specified (NOS) [7].

1.3. Statistical analysis

Quantitative data were expressed as median and range, as the small number of patients did not allow the study of overall survival and event free survival.

1.4. Ethics

Institutional ethics board approval was obtained for all participating centers according to the rules established over the years, as all patients were on clinical trials at the time.

2. Results

Eight patients were found in the databases with urachal cancer, all RMSs. There was no other patient with non-RMS urachal tumor. Their clinical presentation, tumor characteristics, treatment and evolution are detailed in Table 1. Median age at diagnosis was 4.4 years, and sex ratio was 1:1. Previous familial history of cancer was found in two patients: glioma in a cousin (patient 5), and multiple familial stomach, lung and breast cancers history (patient 2). No patient had previous urachal symptoms such as umbilical discharge or urachal infection.

2.1. Clinical presentation

Patients were poorly or not symptomatic at diagnosis, except in two cases. One presented with symptoms of peritonitis misleading for a complicated appendicitis. Surgery revealed a hemoperitoneum with a ruptured urachal tumor which was completely resected. The second patient presented with an extreme poor general status because of advanced metastatic disease. Only three had urological complications, which were not the revealing symptoms.

Most patients presented with a very large tumor with a median size of 10.3 cm (range 5–21), in a supravesical preperitoneal medial location (Fig. 1). Five patients had nodal involvement. Six patients had metastatic disease: five with peritoneal tumor extension (nodules) including the patient with vertebral and sacral metastasis, and one with isolated distant iliac lymph nodes. All patients had peritoneal fluid (ascitis), including one hemorrhagic. However, no documentation about the existence of malignant cells was available, as cytology was not performed at diagnosis in a regular manner.

2.2. Pathology

Diagnosis of RMS was performed after biopsy (six patients), or at initial resection (two patients). Patient 1 who had the “not otherwise specified” (NOS) RMS was the oldest patient of the series, at a time when molecular analysis of the tumor was not available. Patient 2 had a fusion positive alveolar RMS.

2.3. Treatment

Patients 1 and 2 underwent macroscopically incomplete surgical resection at diagnosis. Both of them received adjuvant chemotherapy. Patient 2 had a second look surgery after six courses of chemotherapy by laparoscopy and a suprapubic incision. A bladder dome cuff was resected, and there was no residual viable tumor at pathology.

The remaining six patients received neoadjuvant chemotherapy after a tumor biopsy, performed either percutaneously (4 cases) or by a small paraumbilical laparotomy (2 cases who were managed initially in a general hospital). Patients 4 and 5 had a primary diagnosis of lymphoma, and received a cyclophosphamide/vincristine/prednisone (COP) course until diagnosis was corrected. All six patients had a tumor partial response after chemotherapy and underwent surgery for residual tumor resection.

Two patients had a laparoscopic exploration before laparotomy, which was done by a midline incision (infraumbilical in 4 cases, supra and infraumbilical in 1 case), or a suprapubic incision (1 case). In all cases, careful mobilization of the tumor was performed, with “en bloc” resection including some parietal tissue of the abdominal wall (peritoneum, aponeurosis and muscle), and a bladder dome cuff. Two patients also had a larger but partial cystectomy (patients 3 and 6), one had a resection of a 20 cm-small bowel segment because of tight adhesions to the tumor (patient 5), and one had a partial omentectomy (patient 8). Surgery was macroscopically incomplete in patient 8, microscopically incomplete in patients 3, 4 and 6, and microscopically complete in patients 5 and 7. Viable cells were found in four patients (patients 4, 5, 7, and 8).

All patients received postoperative chemotherapy. Six received external abdominal radiotherapy, associated to ovarian transposition in the recent female patients. No patient had complications of radiotherapy. One patient was reoperated because of intestinal obstruction with severe inflammatory sheathing of the small bowel, which was related to chemotherapy and not radiotherapy.

2.4. Evolution and prognosis

Seven patients were in complete remission at the end of treatment. The patient with initial distant metastatic disease progressed on metastatic sites during maintenance therapy and died despite a second line therapy. In four patients, tumor relapsed within a median time of 25 months (range 11–82) after the end of treatment, including two with distant metastases. All died between 18 and 57 months after diagnosis except the one who presented the latest recurrence (Fig. 2). He recently underwent surgical resection associated with hyperthermic intraperitoneal and intrathoracic chemotherapy, and is still alive with eight weeks follow-up. Three patients are alive in first complete remission, 40, 45 and 95 months after diagnosis, including both most recent patients.

3. Discussion

We report eight cases of urachal cancer in childhood, all RMSs, referred to two large national reference centers of pediatric oncology, covering a population of 10^7 inhabitants, during a period of 28 years. As this location is poorly described in the RMS classification, some cases could however have been lost in our review among the other patients identified as presenting abdomino-pelvic RMS. Our major