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Rhabdomyosarcoma in Children: About 10 Cases

Ayad Ghanam[1*], Manal Azizi[1], Hind Zahiri[1], Houssain Benhaddou[2], Imane Kamaoui[3], Amal Bennani[4], Aziza El Ouali[1], Abdeladim Babakhouya[1], Maria Rkain[1], Noufissa Benajiba[1]

[1]Department of Pediatrics, Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Mohammed First University, Oujda, Morocco
[2]Department of Pediatric Surgery, Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Mohammed First University, Oujda, Morocco
[3]Department of Radiology, Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Mohammed First University, Oujda, Morocco
[4]Department of Anatomopathology, Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Mohammed First University, Oujda, Morocco
Email: *ayadghanam@gmail.com

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Abstract

Introduction: Rhabdomyosarcoma (RMS) is a malignant soft-tissue tumor arising from striated muscle cells. It accounts for 60% - 70% of malignant mesenchymal tumors and 5% of pediatric cancers. Two-thirds of these cancers are diagnosed in children under 6 years of age, with a slight male predominance. **Materials and Methods:** This is a retrospective descriptive study of 10 cases of RMS collected in the pediatric hematology and oncology department of the Oujda university hospital, over a 5-year period, running from January 2018 to December 2022. **Results:** The median age at diagnosis was 3 years, with a sex ratio of 1. The mean time to diagnosis was 2 months. The most common site was the head and neck (50%), followed by the genitourinary tract (20%), the extremities (20%) and finally the abdomen (10%). The most frequent mode of discovery was a mass or swelling found in 90% of patients (all sites included), followed by exophthalmos in 30% of cases. At the diagnostic stage, CT scans were performed in 70% of cases and MRI in 5 patients (50%). Histological diagnosis was determined by immunohistochemical pathology in all our patients, with a predominance of embryonal (70%) versus alveolar (20%) and spindle cell types (10%). All patients underwent an extension workup, and a cervico-thoraco-abdominopelvic CT was performed in all patients (100%); MRI was performed in 2 patients (20%); lymph node involvement was present in 5 patients (50%). Metastases at the time of diagnosis were noted in only 1 patient (10%), who simultaneously presented with two metastatic sites; testicular and abdominal wall. Sixty percent of patients

presented with advanced disease (high risk) and 40% with standard risk. Chemotherapy was used in all patients (100%), with upfront tumor resection performed in 40%. Fifty percent of patients received radiotherapy at a mean dose of 43 Gy, with the orbit the most frequently irradiated area (30%). All patients underwent CTscan and/or MRI and/or ultrasound surveillance. Follow-up during and after treatment was marked by complete remission in 8patients, loss of sight in one patient, and one patient died as a result of progressive disease. **Conclusion:** RMS is a malignant tumor of striated muscle. The epidemiological and clinical features of this tumor in our study are generally similar to those described in the literature. Management of these tumors requires multidisciplinary collaboration involving oncopediatric, radiologist, pediatric surgeon, pathologist and radiotherapist.

Keywords

Rhabdomyosarcoma, Child, Chemotherapy, Surgery, Radiotherapy

1. Introduction

RMS is a malignant soft-tissue tumor arising from striated muscle cells. It accounts for 60% - 70% of malignant mesenchymal tumors and 5% of pediatric cancers. The annual incidence of RMS in children is 4.3 per million [1], and two-thirds of cases are diagnosed in children under 6, with a slight male predominance. The most frequent site is the head-neck region.

2. Materials and Methods

We present 10 cases of RMS collected in the pediatric hematology and oncology unit at the Oujda university hospital, over a 5-year period from January 2018 to December 2022.

3. Results

The median age at diagnosis was 3 years, with extremes ranging from 5 months to 7 years, with a sex ratio of 1. The mean time to diagnosis was 2 months. The most common site was the head and neck (50%), followed by the genitourinary tract (20%), the extremities (20%) and finally the abdomen (10%). The most frequent mode of discovery was a mass or swelling found in 90% of patients (all sites included), followed by exophthalmos in 30% of cases.

At the diagnostic stage, CT scans were performed in 70% of cases and MRI in 5 patients (50%).

Histological diagnosis was determined by immunohistochemical pathology in all our patients, with embryonal type (70%) predominating over alveolar type (20%) and spindle cell type (10%). All patients underwent an extension work-up, with Cervico-thoraco-abdominopelvic CT scan performed in all (100%) and MRI in 2 patients (20%). Node invasion was present in 5 patients (50%). Metas-

tases at the time of diagnosis were noted in only 1 patient, who presented simultaneously with two metastatic sites: testicular and abdominal wall. 60% of patients presented with advanced disease (high risk) and 40% with standard risk. Chemotherapy was used in all patients (ifosfamide, vincristine and actinomycin), with upfront tumor resection performed in 40% of patients. 50% of patients received radiotherapy at a mean dose of 43 Gy, with the orbit being the most irradiated area (30%). All patients underwent CT scan and/or MRI and/or ultrasound surveillance. Follow-up during and after treatment was marked by complete remission in 8 patients, loss of sight in 1 patient, and 1 patient died as a result of progressive disease.

4. Discussion

RMS accounts for 50% of soft tissue sarcomas in children [2], despite this frequency, RMS represents only 3% to 4% of pediatric cancers [3]. In children under 20, the incidence is 4.4/million [1]. In our study, all patients came from the Eastern region, RMS is rare and constitutes about 3.2% of all childhood cancers since the start of activity of the pediatric hematology and oncology unit of the Oujda university hospital. RMS is diagnosed in around two-thirds of cases in children under 6 years of age, with two peaks in incidence: in children under 5 years and in adolescents [4]. It is slightly more frequent in boys, with a sex ratio of 1.4 [5]. The age group most represented in our study was under 5 years (50%) with a sex ratio of 1, and the median age of our patients was 3 years.

RMS may be associated with certain familial syndromes:

Neurofibromatosis, also known as Von Recklinghausen disease, its transmission is autosomal dominant, patients with neurofibromatosis are more likely to develop embryonic-type RMS [6] [7].

Li-Fraumeni syndrome is one of the syndromes predisposing to cancer, with 7.1% of childhood soft tissue tumors and osteosarcomas occurring in families meeting the criteria for Li-Fraumeni syndrome.

Gorlin-Goltz syndrome or basal cell nevoid carcinoma syndrome , secondary to mutations in the PTCH tumor suppressor gene located on the long arm of chromosome 9 at position 9q22.3. One of these mutations has been shown to be associated with the development of embryonic RMS.

Finally, maternal marijuana or cocaine use appears to increase the risk of developing RMS [6]. In our series no predisposing factors were reported, 2 patients had a notion of consanguinity one of first degree and the other of second degree.

There are 6 seats:

- Orbit.
- Non-para-meningeal head and neck.
- Para-meningeal head and neck: nasopharynx, nasal cavities, sinuses, middle ear, mastoid, pterygo-maxillary fossa and orbit with bone lysis.
- Genito-urinary: vagina, uterus, para testicular and bladder-prostate.
- Extremities.
- Other: intra-thoracic, intra-abdomino-pelvic, wall and perineum.

The location of an RMS is a necessary element for the management of RMS and for the therapeutic strategy to be undertaken, thus the primary tumor site being an important prognostic factor [8]. A study by the German Cooperative Soft Tissues Sarcoma Study on 372 patients with RMS between 1985-1990 found the following results:36.5% of RMS cases had the head and neck region as their primary site, other localizations accounted for 26% of cases, genitourinary localization accounted for 19% of cases, RMS in the limbs accounted for 18.5% of cases [9]. In our study, head and neck were the most common locations (50%), followed by genitourinary (20%) and limb (20%). According to a study conducted by Hessissen *et al*. at the Department of Pediatric Hematology and Oncology, Rabat Pediatric Hospital, on 100 patients with RMS between January 1995 and December 2004, the average time to diagnosis was 2 months, with extremes ranging from 15 days to 3 years [10]. In our study, the mean time to diagnosis was 2 months, with extremes ranging from 15 days to 5 months. Revealing symptoms of RMS depend on the primary site of the tumor. It can be paucisymptomatic, presenting with nonspecific and minimal symptoms [11]. RMS presents as an asymptomatic mass detected by the patient himself or his family, the other clinical signs that result, vary according to the primary location of the tumor and may be secondary to the mass effect of the tumor [12]. **Table 1** below summarizes the most common clinical signs and symptoms according to the primary location of the RMS.

Table 1. Common clinical symptoms of rhabdomyosarcoma [11].

Localization	Symptoms
Head-neck	Asymptomatic mass, may mimick enlarged lymph node
Orbit	Proptosis, chemosis, ocular paralysis, eyelid mass
Nasopharynx	Snoring, nasal voice, epistaxis, rhinorrhoea, local pain, dysphagia, cranial nerve palsies
Paranasal sinuses	Swelling, pain, sinusitis, obstruction, epistaxis, cranial nerve palsies
Middle ear	Chronic otitis media, haemorrhagic discharge, cranial nerve palsies, extruding polypoid mass
Larynx	Hoarseness, irritating cough
Trunk	Asymptomatic mass (usually)
Biliary tract	Hepatomegaly, jaundice
Retroperitoneum	Painless mass, ascites, gastrointestinal or urinary tract obstruction, spinal cord symptoms
Bladder/prostate	Haematuria, urinary retention, abdominal mass, constipation
Female genital tract	Polypoid vaginal extrusion of mucosanguineous tissue, vulval nodule
Male genital tract	Painful or painless scrotal mass
Extremity	Painless mass, may be very small but with secondary lymph node involvement
Metastatic	Non-specific symptoms, associated with the diagnosis of leukaemia

The most frequent finding in our series was a mass or swelling in 90% of patients (all sites included), followed by exophthalmos in 30%. Diagnosis of RMS is based on an initial workup, and thus relies on clinical, imaging, histological and molecular biological findings. Local ultrasonography of the tumor site, which is mainly used for guidance in detecting signs of malignancy in any given lesion, must always be supplemented by CT scan and/or MRI.

In our study, ultrasound was performed on 5 patients (50%), all of whom showed abnormalities. Ultrasound was indicated for the following locations (cervical ultrasound: 2 cases, abdominal ultrasound: 1 case, soft tissue ultrasound: 1 case, orbital ultrasound: 1 cases). CT scan with contrast injection is also of great value, particularly for assessing bone infiltration, but is not optimal for determining tumour extent. MRI still outperforms CT in the initial workup and follow-up of patients with RMS, as it more accurately defines the tumor and its soft-tissue extensions [12] [13]. In our study, CT scan was performed in 70% of patients. Thanks to its superior ability to illustrate soft-tissue changes, MRI remains the gold standard in RMS [14]. Not only does it enable precise localization and measurement of tumor size in all 3 planes (sagittal, coronal and axial), it also allows assessment of local invasiveness and visualization of lymph node metastases, meninges and brain tissue infiltration. In our study, MRI was performed in 5 patients (50% of cases): 3 patients with orbital RMS underwent orbital MRI (30% of cases), 1 case with palmar RMS underwent wrist MRI and 1 case with cervical RMS underwent cervical MRI. Given that the main secondary localizations of RMS are pulmonary in 39% of cases, bone marrow in 32% of cases, lymph node in 30% of cases and bone in 27% of cases; the extension workup of a patient with RMS should include: [15] a chest X-ray and/or chest CT scan to look for pulmonary nodules or pleural effusion, an abdominal ultrasound scan to look for a probable secondary hepatic localization, a technetium bone scan, combined with standard X-rays or MRI if isolated bone abnormality, marrow biopsies and myelograms to look for possible extension to the bone marrow, and Cerebrospinal fluid (CSF) studies to look for tumour cells should be systematically carried out in parameningealtumours, or if parameningeal extension is suspected. In our study, cervico-thoraco-abdominopelvic CT was performed in all patients (100% of cases). Ultrasound was performed in 2 patients (20% of cases), both of whom had primary cervical RMS: an abdomino-pelvic ultrasound and a testicular ultrasound. Bone scintigraphy was performed in 2 patients (20% of cases). Myelogram and osteomedullary biopsy were performed in all patients (100% of cases). CSF examination was performed in 3 patients with orbital rhabdomyosarcoma (30% of cases). In our study, only 1 patient was metastatic at the time of diagnosis, with two simultaneous metastatic sites: testicular and abdominal from a primary cervical RMS. Alveolar rhabdomyosarcoma and embryonal rhabdomyosarcoma are the main subtypes observed in the paediatric population [3]. Embryonal rhabdomyosarcoma is more common in young children, and its most frequent site is the head and neck, whereas alveolar rhabdomyosarcoma accounts for only 31% of all forms of RMS, and has been observed

more in adolescents and patients whose primary site of RMS is generally located in the extremities, perineum, peri-anal region [16]. The botryoid variety is typically found in bladder or vaginal locations, where the tumour develops as a polypoid in a cavity [5]. The spindle-cell variety, with its pseudo-leiomyosarcomatous appearance, is paratesticular in 70% of cases, and has a good prognosis. However, in rare cases of head and neck RMS, the spindle-cell form has been observed [17]. In our study, embryonal RMS is more frequent in the head and neck location. Alveolar RMS was equally prevalent in genitourinary and extremity sites. The botryoid variety accounted for 10% of cases, with preferential localization in the genitourinary region (vagina). The spindle cell variety accounted for 10% of cases, with preferential localization in the head and neck region (orbit). This localization is inconsistent with literature data, given that this variety is rarely observed in the head and neck region, and predominates in the paratesticular region, which may be explained by the low number of cases (1 case) of this spindle cell variety in our study. Two main classification systems are used: [18]. The Intergroup Rhabdomyosarcoma Study classification, which takes into account the operability of the tumor, determined after the initial surgical procedure preceding chemotherapy and is based primarily on the size of the residual tumor after surgery, taking into account regional lymph node involvement [18]. TNM classification of rhabdomyosarcoma based on tumor description prior to treatment (clinical stages). In our study, stage III was predominant in 7 cases (70%), followed by stage II (20%) and stage I (10%). The therapeutic strategy for RMS has evolved considerably over the last five years. Close collaboration between surgeons, oncologists, radiologists, anatomopathologists and radiotherapists sometimes makes it possible to avoid the severe functional and sexual sequelae previously seen [19]. Standard treatment of RMS includes the use of chemotherapy, radiotherapy and sometimes recourse to surgery if tumour location and extension allow. Although most patients with localized RMS can be cured, results in patients with metastatic or recurrent RMS remain poor [20]. A primary resection of the tumor can only be considered if it would be carcinologically satisfactory, and otherwise without functional and/or aesthetic consequences. This is the case for certain small, easily accessible tumours, such as paratesticulartumours, certain limb tumours, and rarely wall or ENT tumours [4]. In head-neck tumours, surgery is often limited to diagnostic surgical biopsy. In the majority of limb cases, complete removal of the tumour is recommended. Amputation is reserved for severe forms with significant bone, vascular or nerve invasion [21]. At the paratesticular level, trans inguinal orchiectomy involving the spermatic cord is indicated. This procedure is often carried out laparoscopically, to minimize recovery time after surgery and bring the time of chemotherapy administration closer [22]. In the trunk, complete excision is possible. In thoracic locations, costal excision is recommended on both sides of the lesion. In pelvic, retroperitoneal or intra-thoracic localizations, excision surgery is rarely possible, given the locoregional invasion [23]. In our study, chemotherapy was used in all patients (100%), and upfront tumor resection was performed in 40% of patients.

50% of patients received radiotherapy at a mean dose of 43 Gy, and the orbit was the most irradiated area (30%). Prognosis is closely linked to tumor mass and the existence or absence of metastases. Localized forms that can be completely excised have a better prognosis, as do those occurring between 1 and 10 years of age. Embryonal histological type also has a better prognosis than alveolar type. Orbital, eyelid, non-parameningeal head and neck, genitourinary para-testicular, vulvovaginal or uterine localizations are favorable. Elsewhere, the location is considered unfavorable. The prognosis is also unfavourable in the case of tumours larger than 5 cm, or in the presence of tumouradenopathies. In our study, all patients underwent CT scan and/or MRI and/or ultrasound surveillance. Follow-up during and after treatment was marked by complete remission in 8 patients, loss of sight in 1 patient, and 1 patient died as a result of progressive disease.

5. Conclusion

RMS is a malignant tumor of striated muscle. The epidemiological and clinical features of this tumor in our study are generally similar to those described in the literature. Management of these tumors requires multidisciplinary collaboration involving oncopediatric, radiologist, pediatric surgeon, pathologist and radiotherapist.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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