



## RESEARCH ARTICLE

### MANAGEMENT OF ORBITAL RHABDOMYOSARCOMA: ABOUT 2 CASES AND LITERATURE REVIEW

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#### Abstract

Rhabdomyosarcoma is the most common primary malignancy in children. It constitutes a therapeutic emergency. The ocular region, particularly the orbital soft tissues, is an important anatomic location for RMS, which is the most common primary orbital malignancy of childhood. Radio-chemotherapy with conservative surgery allows a recurrence-free survival of 87% at 5 years. The aim of this study was to improve the understanding of the clinical features by reviewing the literature and analysing the medical records of patients who were diagnosed with orbital Rhabdomyosarcoma in our hospital. We report 2 cases of patients treated for an orbital Rhabdomyosarcoma at the radiotherapy department of the Hassan II University Hospital of FES.

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#### Introduction:-

Rhabdomyosarcoma is the most common primary malignancy in children. It is a rapidly progressive striated muscle differentiation tumor that constitutes a therapeutic emergency. The ocular region, particularly the orbital soft tissues, is an important anatomic location for RMS, which is the most common primary orbital malignancy of childhood. Radio-chemotherapy with conservative surgery allows a recurrence-free survival of 87% at 5 years.

The aim of this study was to improve the understanding of the clinical features by reviewing the literature and analyzing the medical records of patients who were diagnosed with orbital Rhabdomyosarcoma in our hospital.

#### CASE N°1:

W.E, a 6 years old boy with no significant personal history, consulted for a exophthalmia of the left eye evolving for 1 months with progressive aggravation.

The clinical examination found a patient with a non-inflammatory, nonaxial, non-painful exophthalmia of the left eye with Inferior and temporal displacement (**figure 1A, B**).

A CT scan of the left orbit has been performed showing an ocular malignant tumor (40\*35mm). An MRI was requested in favor of a left orbital tumor related to a suspicion of a rhabdomyosarcoma of the upper rectus muscle, surrounding the optic nerve without invasion or cerebro-meningeal extension (**Figure 1C**). A biopsy was made.

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After pathological examination and immunohistochemistry, the diagnosis of an embryonic rhabdomyosarcoma was confirmed (focal expression of desmine and myogenin).

Thoraco-Abdomino-Pelvic Computed Tomography (CT-TAP) and a bone scan was performed, they did not show a secondary localization.

The disease was classified as a clinical group III A, TNM stage I, with favourable histology.

The patient received IVA chemotherapy (Ifosfamide 3000 mg/m<sup>2</sup>/day, Vincristine 1.5 mg/m<sup>2</sup>, Actinomycin 1.5 mg/m<sup>2</sup>/day).

A thoraco-abdomino-pelvic CT scan was done after the 4th course, which showed a stability of the tumor.

After multidisciplinary discussion, as the tumor was not resequable, The decision was to perform radiotherapy at the 13th week of chemotherapy and to continue chemotherapy for a total of 25 weeks.

Radiotherapy was delivered within an intensity modulated radiation therapy technique (IMRT). The extent of the tumor at diagnosis determined the initial primary tumor GTV (Gross tumor Target Volume). The GTV was then expanded by an anatomically confined 2 cm to create a CTV (Clinical Target Volume). Because of a residual disease, the volume was reduced to the prechemotherapy tumor plus a 0.5 cm margin at 36 Gy, with a total dose of 50.4 Gy given at 1.8 Gy/day.

There were no significant side effects observed except moderate skin reactions on the irradiated skin and tearing of the left eye.

With a 2 years follow-up, we note a significant regression of the tumor volume with a stable imaging for over a year and without any distant localizations (**Figure 1D**).

#### **Case N°2:**

F.A is a 7 years old girl, followed for neurofibromatosis type 1 and has no other pathological history. She attended an ophthalmology consultation due to proptosis of the right eye of one month evolution.

The clinical examination found a patient with a superonasal orbital tumor, immobile, with a non-axile, non-reducible exophthalmos. The globe was deviated inferiorly and externally (**Figure 2-A**),

A CT scan of the right orbit was performed showing a superonasal extra conical, intra orbital tumor measuring 34\*31mm (**Figure 2-B**). Then he underwent a partial resection. The pathological examination and immunohistochemistry confirmed the diagnosis of an embryonic rhabdomyosarcoma.

Thoraco-Abdomino-Pelvic Computed Tomography (CT-TAP) and a bone scan did not show secondary localization.

The disease was classified as as clinical group III B, TNM stage I, with favourable histology.

The patient received IVA chemotherapy (Ifosfamide 3000 mg/m<sup>2</sup>/day, Vincristine 1.5 mg/m<sup>2</sup>, Actinomycin 1.5 mg/m<sup>2</sup>/day). After multidisciplinary discussion, it was decided to consolidate the treatment with radiotherapy at the 13th week of chemotherapy and to continue chemotherapy for a total of 25 weeks.

The radiotherapy was delivered within an intensity modulated radiation therapy technique (IMRT). There were no significant side effects observed during or in the end of radiotherapy.

With a 4 years follow-up, we note a complete response without any distant localizations(**Figure 2-C**).

#### **Discussion:-**

Rhabdomyosarcoma is a malignant tumor with striated muscle differentiation. It is the most common soft-tissue sarcoma of the head and neck in childhood and comprises 4% of all pediatric malignancies, with 10% of all cases

occurring in the orbit The embryonal type is the most common variety of orbital RMS; the alveolar and pleomorphic varieties occur rarely.

This rapidly growing tumor is a therapeutic emergency. The average age at diagnosis is 7 to 8 years [1, 2].

RMS with ocular involvement can be primary, secondary or metastatic. The conjunctiva, eyelids or uveal tract are rarely affected and many times are compromised by extensions of orbital RMS. The condition should be suspected in children with unilateral proptosis of sudden onset and rapid progression which is found in 71% of cases. It can often be accompanied by inflammatory signs and swelling of the eyelids. A palpable mass is present in 58% of cases [3].

Imaging must be done very quickly. It makes it possible to carry out the initial extension assessment and to guide the biopsy. Both CT and MRI *can be complimentary in evaluation, staging, and follow-up* of orbital RMS [4].

With CT, the tumor appears in the early stages as a well-circumscribed, homogeneous, round to ovoid mass that is isodense to muscle. It is usually extraconal in location and most often found in the superonasal aspect of the orbit. It is usually confined to the orbital soft tissues and does not appear to arise from the extraocular muscles or bone, although it can often cause displacement of the rectus muscles. It occasionally erodes bone. Orbital RMS shows moderate to marked enhancement with contrast agents. On MR imaging, the RMS are generally isointense to muscle on T1- and hyperintense to muscle on T2-weighted images. On T1W contrast-enhanced MR images, RMS will have moderate to marked enhancement. Meticulous search is required for assessment of local invasion into the paranasal sinuses, as well as for intracranial spread via the orbital fissures, with potential spread into the cavernous sinuses, and, at times, into the middle cranial fossa [5-8].

Orbital RMS probably arises from primitive pluripotential mesenchymal cells with a propensity to differentiate toward skeletal muscle. RMS has been traditionally classified into 3 main histologic subtypes: embryonal (ERMS), alveolar (ARMS), and Anaplastic. Additional variants have been recently identified, such as spindle cell RMS and sclerosing RMS comprising only 5% to 10% of RMS [9]. The embryonal type is most common, whereas the alveolar type appears to be the most malignant.

RMS staging is multifactorial and outcomes are reported based on 3 different classifications [10]:

1. Stage: Determined from pretreatment data based on location of primary site, tumor size (widest diameter), presence or absence of regional lymph node, or distant metastases.
2. Group: Determined by local tumor status based on postsurgical resection or biopsy, with pathologic assessment of the tumor margin and of lymph node disease.
3. Risk category: A combination of stage, group, and tumor histology.

According to The Intergroup Rhabdomyosarcoma Study, the eyelid is a favorable site and is classified as stage I. Additionally, combining the results of the CT scan of her whole body and her clinical symptoms, it is clear that our patients did not have regional lymph nodes and distant metastases. Moreover, the diameter of the tumors was under 5 cm. Thus, it was classified as T1N0M0. Regarding the clinical group, Bout of our patients had a localized tumor with a gross residual disease. Therefore, the disease was classified as group III.

Management of ocular RMS involves a collaborative decision by the ocular oncologist, pathologist, pediatric oncologist, and radiation oncologist, preferably following the guidelines of IRSG. It includes surgery, irradiation and chemotherapy depending on the stage [11-13]:

Group I are treated with chemotherapy only: VA (vincristine and actinomycin).

Group II are treated with a combination of chemotherapy (VA and cyclophosphamide; VAC) and radiotherapy (36 Gy).

Group III are treated with a combination of chemotherapy (VAC) and radiotherapy (45 Gy).

Group IV are treated with a combination of intensive chemotherapy and radiotherapy.

When treatment for orbital tumors is individualized, it is generally agreed that no surgical procedure should be used that may compromise vision or loss of function. The ultimate goal of surgery is complete removal of the tumor intact; however, that is not always possible, especially when the tumor is large and invasive into normal orbital

structures. In most patients, this means that biopsy only should be performed to provide the diagnosis. The surgical method of orbital exenteration is rarely used as a primary treatment, but can be utilized if there is recurrent deep tumor [3,14,15].

Orbital tumours have excellent response to chemotherapy and are considered a favourable site; because of this, neoadjuvant treatment aims to prevent the spread of neoplastic cells and reduce tumour size in order to propose a more effective consolidation treatment, which decreases post-surgical morbidity and sequelae. Primary treatment typically consists of vincristine, actinomycin-D, and cyclophosphamide (VAC) or vincristine and actinomycin-D (VA) chemotherapy. These agents are generally prescribed for 32–52 weeks [16,17].

Radiotherapy is indicated in approximately 90% of cases as it plays an important role in local control of the disease and increases survival. Radiation doses of 3600–5040 cGy over 4–5 weeks are often used over 4–5 weeks.

With a combined-modality approach, radiotherapy can be directed to the tumor plus a margin without necessarily irradiating the entire orbit. To preserve useful vision, ocular function, and appearance, new techniques are being used for radiation treatment, including proton beam therapy, intensity modulated radiotherapy (IMRT), volumetric archtherapy (VMAT) and brachytherapy. The most common complications include cataract (55%), dry eye (36%), orbital hypoplasia (24%), ptosis (9%), radiation retinopathy (90%), facial asymmetry secondary to bone hypoplasia, keratoconjunctivitis, tear duct stenosis, dental defects, growth retardation (in the case of incidental irradiation of the pituitary gland) and secondary neoplasms such as osteogenic sarcoma, lymphoblastic leukemia and melanoma. xxx [18-20].

The prognosis for orbital rhabdomyosarcomas is excellent with 5-year event-free survival of over 65% and overall survival of over 85%. Current treatment protocols must focus on reducing local complications, in particular post-radiation (bone hypoplasia in the irradiated area, cataracts, dry eyes and sometimes growth hormone deficiency) [7], but also general complications related to chemotherapy, while trying to maintain this excellent survival rate [20].

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### **Competing Interests :**

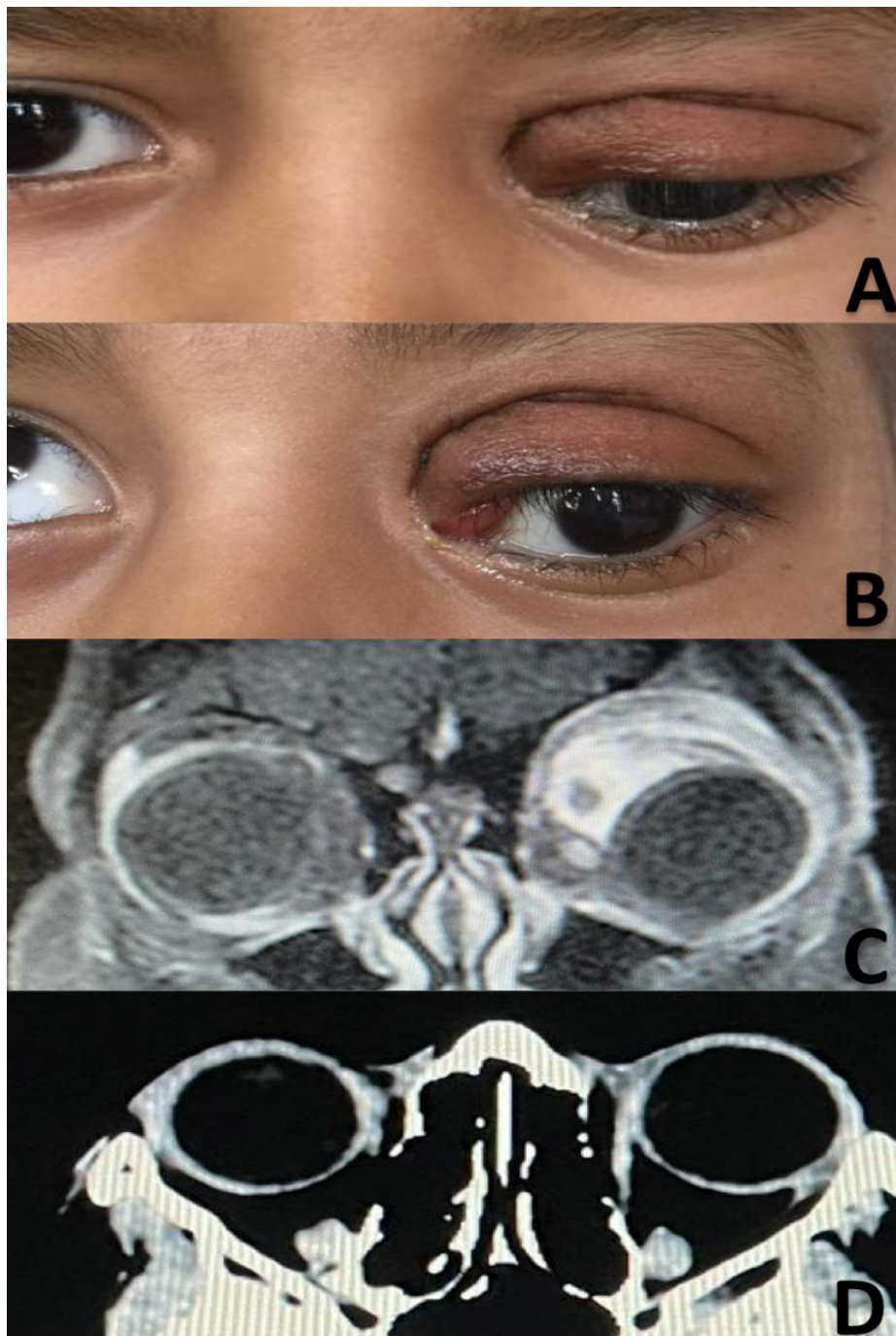
The authors have no conflicts of interest to disclose.

### **Consent:**

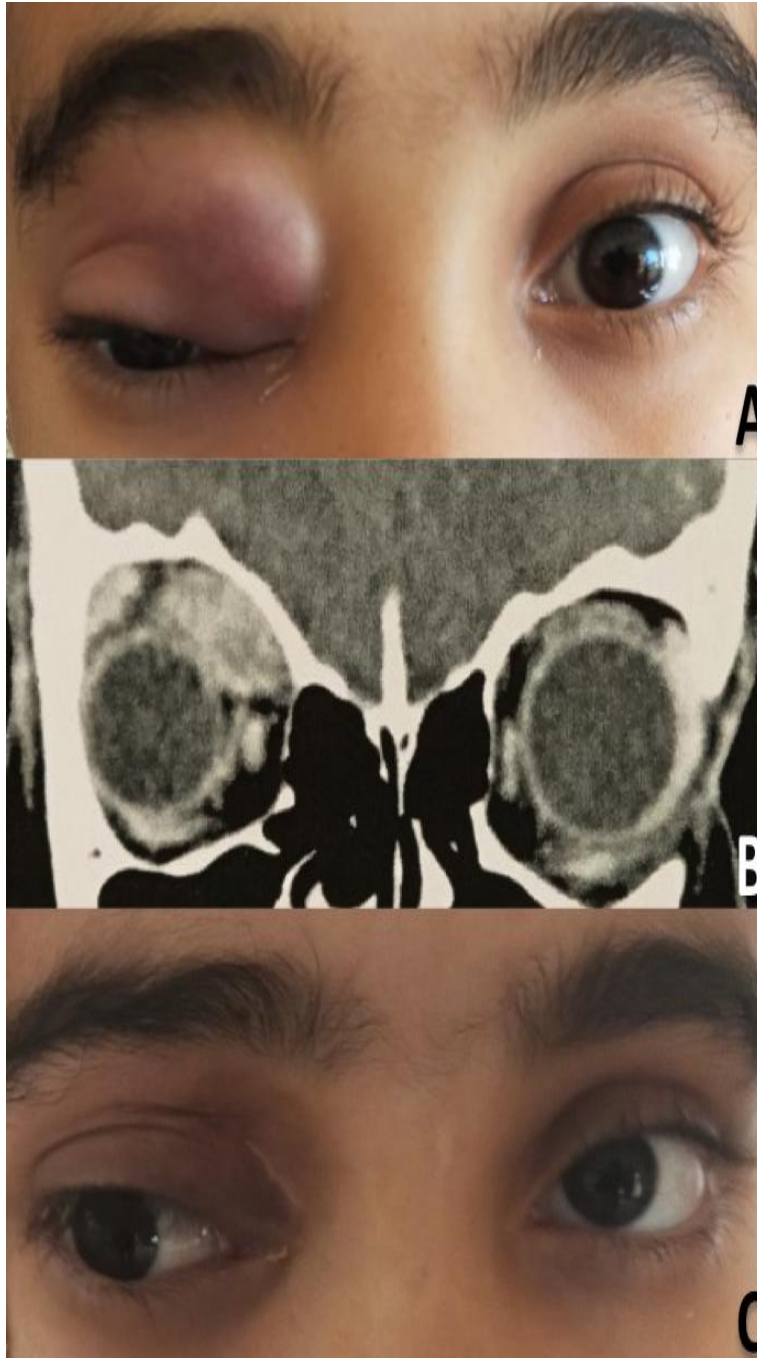
As per international standard, patient's written consent has been collected and preserved by the authors.

### **Ethical Approval:**

It is not applicable.



**Fig 1:- A, B** initial clinical image after chemoreduction. **C** MR image showing the presence of a superonasal intraorbital tumor mass. **D** clinical image after 2 years follow-up.



**Fig 2:-** **A** initial clinical image after chemoreduction. **B** CT image showing the presence of a superonasal intraorbital tumor mass. **C** clinical image after 1 year follow-up.

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