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ORIGINAL RESEARCH

MALIGNANT ORBITAL TUMORS IN CHILDREN A SERIES OF 4 CASES

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ABSTRACT
Introduction: Malignant tumors in children are rare but serious conditions as they can impair function and survival. Tumors in pediatric patients can originate from the orbit. Rarely, the tumor spreads to the adjacent areas and occasionally it may metastasize.
Objectives: The objective of this study is to present the common symptoms and the clinical and radiological characteristics of most common malignant orbital tumors in children.
Materials and methods: Through the discussion of 4 clinical cases of children presenting with exophthalmos due to a tumor, the authors highlight that clinical symptoms are usually less specific, and that imaging has an important role in diagnosis, determining location, and local and regional expansion of the tumor in order to find the adequate therapy.
Results: Our patients' ages ranged from 2 to 5 years. The revealing sign in each case was a unilateral exophthalmos due to a tumor, which could only be reduced minimally or not at all. Its evolution has been rapidly progressive. Orbital imaging and histologic study, if biopsy was possible, allowed guiding the positive diagnosis of the malignant nature and its local and regional spreading, as well as the adequate treatment.
Conclusion: Orbital tumors are rare in the pediatric population. However, due to recent remarkable progress obtained through both complimentary diagnostic tools and treatments, these malignancies deserve the attention of both the ophthalmologists and the pediatricians.

KEYWORDS: Pediatric, Malignant, Tumor, Orbit.

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INTRODUCTION:
Orbital tumors in pediatric patients are relatively rare. Etiologies, which are often specific to children, include a wide range of diagnosis (1). As opposed to adults, the pathology in children is benign in the majority of cases, representing 80% of orbital tumors (2). Malignant disease is less common (20%) and includes primary tumors (retinoblastoma, rhabdomyosarcoma) and metastases (1). This latter is considered a true emergency regarding its diagnosis and treatment.
In this study we discuss the most common malignant orbital tumors of pediatric patients. Proper knowledge of these potentially life-threatening tumors allows quick diagnosis and appropriate management.
The objectives of the present study are: 1/ To present the common symptoms and clinical and radiological characteristics of the main types of malignant orbital

tumors in children through the clinical cases of 4 patients treated in the B Department of Ophthalmology of Rabat, Morocco. 2/ To differentiate between rhabdomyosarcoma, retinoblastoma and metastatic lesions of leukemia. 3/ To determine the role of imaging within the confirmation of the diagnosis and localization of the tumor, and to review local and regional tumor extension in order to find the adequate therapy. 4/ To present the follow-up, the progression and the prognosis of orbital tumors in the pediatric population.

MATERIALS AND METHODS

In the last 2 years 20 cases of non-traumatic orbital disease have been recorded in the B Ophthalmology Department of Rabat, among children younger than 10 years old. Among these, 11 cases were orbital tumors, out of the 11 cases 6 were retinoblastoma (7.84% of cases), 3 boys and 3 girls with an average age of 5 years; 4 cases of rhabdomyosarcoma and 1 case of granulocytic sarcoma. Our study reports 4 out of these cases with patients between 2 and 5 years of age, having less than 2 months between symptoms and diagnosis and the possibility of long-term follow-up.Each one of them received complete ophthalmologic and radiological examinations, assessment of tumor location and expansion, and chemotherapy with or without radiotherapy, depending on the etiology.

RESULTS

Case 1: The first patient was a 2.5-year-old Moroccan child without significant past medical history. There is no known parental consanguinity or similar case in the family. The patient was admitted to our department because of a sore inflammatory swelling of the right eye. The size of the swelling had been growing rapidly for 2 months, while a change in the general state of health was also observed. The patient underwent an ophthalmologic exam during which a firm budding tumor was discovered on the right eye, infiltrated with black tissue necrosis that developed far ahead the facial skeleton. No eye structure could be identified (Fig. 1).

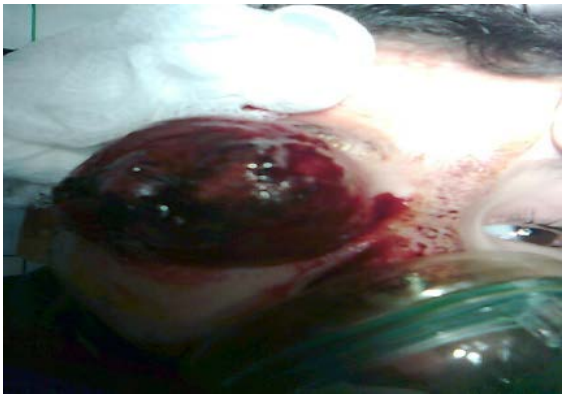

Figure 1: Firm budding tumor on the right eye, infiltrated with black tissue necrosis extensively bulging from the orbit. Ocular globe is invaded.

A thorough exam of left ocular fundus performed under general anesthesia showed no abnormalities.Since we suspected that this could be a malignant orbital tumor, the patient underwent a scan of the orbit and the brain, which revealed an intraorbital mass on the right measuring 59 x 45 mm. After the injection of the contrast agent, it showed enhancement with significant calcification, completely invading the ocular globe (Fig. 2). This presentation suggested an invasive unilateral retinoblastoma.Tumor staging (head CT, MRI of the brain and the spine, abdominal ultrasound) showed hepatic and medulla metastases. In this case, the patient suffered from a unilateral retinoblastoma with orbital invasion, and systemic metastases. Chemotherapy was started immediately based on the CEV protocol (carboplatin 18.6 mg/kg i.v., etoposide 5 mg/kg i.v., vincristine 0.05 mg/kg i.v.) in 6 cycles at 3 weeks interval with regular monitoring. The development after 2 sessions was characterized by a poor response to therapy with decline in the general state. The patient ultimately died.

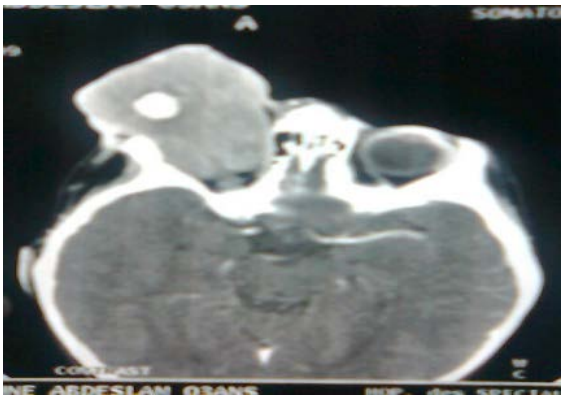

Figure 2: Scan of the orbit and the brain showing an intraorbital process on the right, enhancement together with a significant calcification was seen after injection of the contrast agent.

Case 2: The patient was a 2-year-old girl coming from the countryside of Morocco. She was the third child of the family, and there were no known similar cases in the family. She was admitted to the ophthalmology emergency department with a rapidly and progressively developing bilateral bulging mass associated with inflammatory syndrome and a serious decline in the general state for the past 3 months, during which she was not seen by a doctor. Her vision was hard to assess due to the severe decline in the general state and the fatigue of the patient. Ophthalmologic exam revealed a bilateral bulging mass, larger on the left, a swollen upper eyelid associated with chemosis and purulent secretions in both eyes. The left ocular globe was invaded, and its structures could not be identified (Fig. 3).

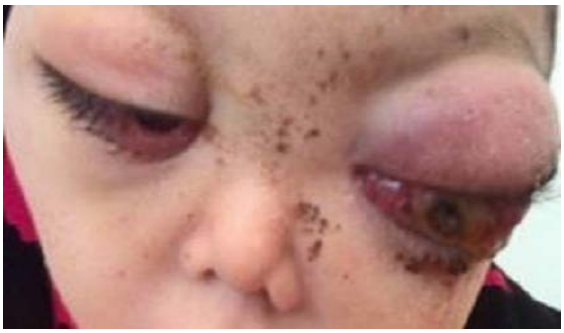

Figure 3: A bilateral bulging orbital mass, larger on the left, swollen upper eyelid associated with chemosis and purulent secretions. The left ocular globe is invaded, structures could not be identified.

Due to the extensive character of the clinical picture and the severely declined general health, malignancy was strongly suspected. Thus, a scan of the orbit was

immediately performed and it showed a mass with soft tissue density, on the left side invading the ocular globe, the optic nerve, the wall of the orbit and the soft tissue of the eyelid, with the presence of intraocular macro and microcalcifications. We found an intraocular mass with microcalcification on the right and we concluded that the diagnosis was invasive bilateral retinoblastoma (Fig. 4). Tumor staging (brain MRI, CT of the facial skeleton, abdominal ultrasound) revealed multiple secondary lesions in the brain, in the parietal and occipital bones and in the mandibula. The pediatric oncologist suggested no therapy given the severely declined general health of the child and the very poor prognosis of the invasive bilateral retinoblastoma also affecting the brain. One week after the diagnosis the child died.

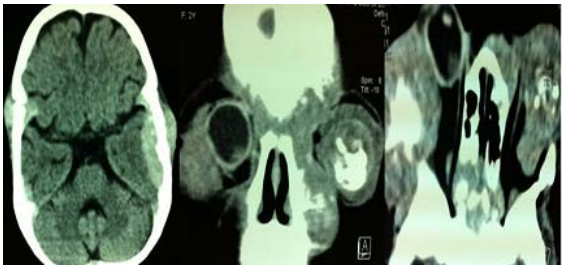

Figure 4: Scan of the orbit and the brain showing bilateral retinoblastoma, which is more developed on the left, with bone metastases.

Case 3: A 5-year-old Moroccan child with no past medical or contributory family history was seen for a sore unilateral exophthalmos in the right eye, which had been rapidly progressing for 2 weeks (Fig.5).

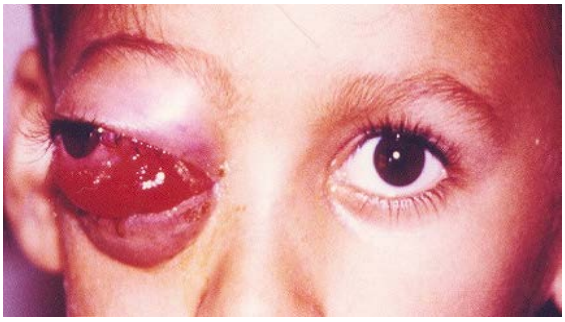

Figure 5: Exophthalmos on the right with eyelid retraction and significant inferior chemosis.

The ophthalmologic exam revealed a painful, asymmetric and inflammatory exophthalmos with ptosis in the right eye and a diffuse keratitis. The rest of the eye was hard to examine. The left eye was normal. A CT performed immediately showed an advanced tumor process destructing the medial rectus muscle. It was isodense compared to the other muscles in the area, causing grade II exophthalmos without bone lysis (Fig. 6). This suggested an orbital rhabdomyosarcoma. A biopsy by partial excision of the mass was performed to confirm histology (Fig. 7). After that, chemotherapy was started for 2 cycles, with 3 sessions at a dose of 1.5 mg/m2 of vincristine, 1.5 mg/m2 of actinomycin D and 3 g/m2 of ifosfamide. Between the sessions there was a rest period of three weeks. The total duration of the treatment was 9 weeks. Renal and hematologic toxicity was monitored using basic metabolic panel, complete blood cell and platelet count. After two sessions the progress was favorable and vision and physical ophthalmological exam started to show improvement.

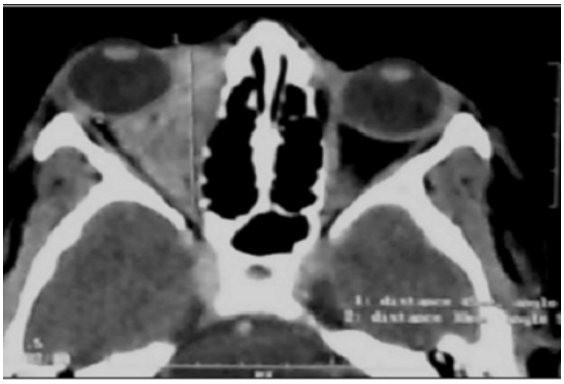

Figure 6: Advanced tumor process destructing the medial rectus muscle; isodense when compared to the muscles with grade II exophthalmos.

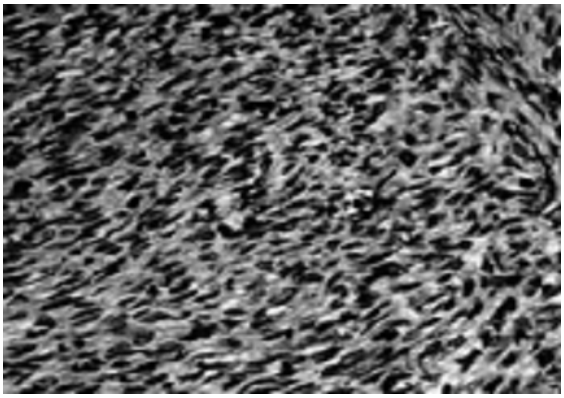

Figure 7: Embryonal rhabdomyosarcoma: highly cellular tumor without specific organisation.

Case 4: A 2.5-year-old Moroccan child without significant past medical history, and in good general health was admitted to our department with bilateral protrusion of the ocular globe. The protrusion was larger on the right and it grew aggressively over a few days period showing inflammatory signs and purulent secretions (Fig. 8).

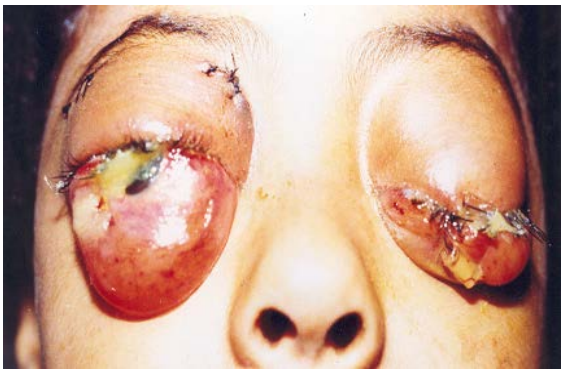

Figure 8: Bilateral exophthalmos, larger on the right, with chemosis and purulent secretions.

The initial exam revealed bilateral exophthalmos, which was larger on the right. It was symmetric, irreducible and sore, associated with an annular chemosis with significant inflammation preventing us from examining the anterior chamber. A CT was immediately performed and showed a peribulbar tissue infiltration invading the whole orbit in both eyes, while respecting intraorbital structures (Fig. 9). We suspected a malignant tumor due to its heterogeneous and osteolytic characteristic and the rapidly progressive

growth of the infiltration. Biological examination showed a circulating blastosis in the blood cell count, which was confirmed by the myelogram. After cytology and cytochemical studies acute myeloid leukemia (AML-2) was revealed. The association of clinical, radiological and hematologic signs was alone enough to diagnose an orbital granulocytic sarcoma. Since treatment of this malignant leukopathy was urgently needed, as well as the hemorrhagic risk related to the severe thrombocytopenia was high, we decided not to perform an initially planned tumor biopsy. The patient was sent to the hematology department for therapy. The protocol proposed for him consisted of an allogenic bone marrow transplant from an HLA-identical family member as donor, applying a pre-transplant chemotherapy conditioning with busulphan (480 mg/m²) and cyclophosphamide (50 mg/kg/day x 4 days). However, we lost track of the patient and have no information about the progress of his disease.

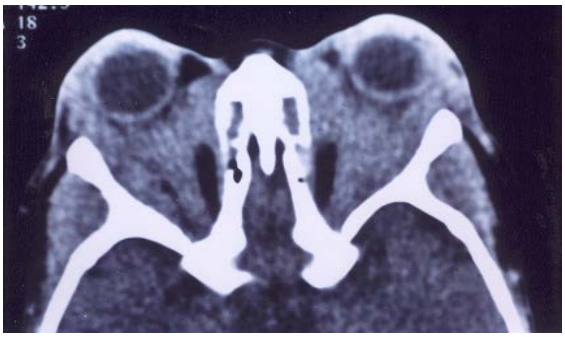

Figure 9: Peribulbar tissue infiltration invading the whole orbit in both eyes, while respecting intraorbital structures.

DISCUSSION

Malignant orbital tumors are rare in the pediatric population (20%) (3). Most of them are primary tumors, essentially retinoblastomas and rhabdomyosarcomas. Rarely, secondary tumors are also observed, such as granulocytic sarcoma, which is a myeloid leukemia found in the orbit. Retinoblastoma is the most common malignant orbital tumor in children. In our study, it represents 55% of orbital tumors, which is in line with the literature, with an average age of 18 months at the time of diagnosis (4). In this study, retinoblastoma was diagnosed at a very advanced stage invading the orbit with inflammatory exophthalmos in both cases. This clinical appearance is rare in developed countries, and it ranges from 6.3% to 7.6% (4). CT is the first exam to perform, since it shows calcifications that are present in 80% to 95% of cases (1, 4), as it was the case in two of our patients. These calcifications are the most important factor for diagnosis. Therapy depends on the stage of retinoblastoma. In case of extraocular extension with guarded prognosis, we perform enucleation before chemotherapy (1). This is well demonstrated in our case reports where retinoblastoma was diagnosed at a very advanced stage with orbit invasion and systemic metastases. Their death in the following few months confirmed the extremely unfavorable character of this disease.

In the third clinical case, our patient was seen for inflammatory and painful unilateral exophthalmos with ptosis. This is a classic case reported in the literature at the age of 5, with an average age of 8 years (5). Radiological check-up performed with CT revealed an isodense mass when compared to muscle, destructing the medial rectus muscle, without bone lysis. This condition suggested rhabdomyosarcoma, according to the results of published studies (6). Immediate treatment combines multidrug therapy and radiotherapy, allowing a survival of patients of 5 years at a ratio superior to 80% (6). Our patient has embryonic rhabdomyosarcoma with good prognostic factors and is showing good response to chemotherapy alone, according to the medium-term follow up.Diagnosis of granulocytic sarcoma, which can present in different ways (7), in our patient was based on typical clinical presentation of the orbital tumor syndrome leading up to hematological problems. This is described in the literature in 88% of patients with an average of 5 months of latency period (8).

In our patient, the orbit scan showing the peribulbar tissue infiltration invading the whole orbit in both eyes, while respecting intraorbital structures, was not specific but the subsequent biological examination of the blood revealing a circulating blastosis greater than 5% allowed us to confirm the hematologic origin of this tumor syndrome.

Granulocytic sarcoma, like AML, is treated with chemotherapy. It is combined with cytostatic agents administered orally. The plan for our patient was the following: he was treated by a hematologist to achieve complete remission, and an ophthalmologist who monitored his symptoms via serial clinical examinations and scans of the orbit. Prognosis for granulocytic sarcoma has different aspects, visual function due to optic nerve disease, and life-expectancy due to pancytopenia (8). We lost track of our patient and no information can be reported at the moment.

CONCLUSION

Although malignant orbital tumor is rare in children, it can be associated with a significant morbidity and a high risk of mortality. It is therefore of great importance to correctly identify and treat patients who suffer from it. This is why clinical consultation and imaging methods have an important role in diagnosing tumors, specifying their location and confirming diagnosis with histology exams in order to find the proper therapy.

ABBREVIATION

AML : Acute Myeloid Leukemia
CEV: Carboplatin, Etoposide, Vincristine.
CT: Camputerised Tomograpghy.
HLA: Human Leukocyte Antigen.
MRI; Magnetic Resonance Imaging.

SOURCE OF SUPPORT:
Declared none.

COMPETING INTERESTS
The authors declare no competing interests.

AUTHORS' CONTRIBUTIONS
The participation of each author corresponds to the criteria of authorship and contributorship emphasized in the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals of the International Committee of Medical Journal Editors. Indeed, all the authors have actively participated in the redaction, the revision of the

manuscript and provided approval for this final revised version.

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