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Orbital Rhabdomyosarcoma with a good life prognosis after surgical treatment in a 14-year-old patient

Case Report

Cristina Nicula*[1], Dorin Nicula[2], Mihai Blidaru[3], Adrian Ghițuică[4], Stefania Neamtu[5], Aniela Saplonțai-Pop[6]

1 Department of Ophthalmology, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, RO

2 Optilens Clinic, Cluj-Napoca, RO

3 Department of Pathophysiology, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, RO

4 Department of Pathology, Military Hospital, Cluj-Napoca, RO

5 Department of Pediatric Oncology, "Ion Chiricută" Oncological Institute, Cluj-Napoca, RO

6 Faculty of General Medicine, „Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, RO

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Abstract: The orbital rhabdomyosarcoma is one of the most frequent malignant orbital tumours in children. At this age, the common histological types are the embryonal and alveolar type. The onset is mainly under the age of 16. Without a recent and correct treatment it can give metastasis in lung and bone. The hereby paper presents one clinical case of a teenager presented at the ophthalmological consultation for a small tumor located in the superomedial part of the orbit. Computed tomography (CT) and magnetic resonance imaging (MRI) supported the diagnosis revealing the location and extension of the tumor. During the surgery, we discovered two small tumors and the histological examination revealed an embryonal type of orbital rhabdomyosarcoma. After the surgery, the patient followed an oncological treatment consisting of chemotherapy and local radiotherapy. The prognosis for life was favorable, linked with the recent diagnosis and treatment, the histological type and the good response at the oncological treatment.

Keywords: *Orbital rhabdomyosarcoma • Local radiotherapy • Chemotherapy*

1. Introduction

Orbital rhabdomyosarcoma is the most common primary orbital malignant tumor in children and the most common soft tissue malignancy of childhood [1], with 10% of all cases occurring in the orbit [2]. There are three histological types: embryonal (the most common type in children), alveolar (also in children) and pleomorphic (in adults). Presentation is in the first decade of life, 90% of patients presenting before age 16 [3]. Diagnosis is based on clinical signs. The tumor may involve any part of the orbit; the common location is retrobulbar, followed by superior and inferior one. Most often the first sign is the presence of the tumor with a rapidly progressive proptosis. In other cases, a palpable mass and ptosis are present in about one third of cases. Swelling and injection of overlying skin develop later, but the skin is not hot. For the positive diagnosis, we need orbital ultrasound examination, cranial tomography and magnetic resonance imaging (MRI) in order to establish

* *E-mail: niculacristina65@yahoo.com*

the presence, location, extension of the tumor and for differential diagnosis [4]. Biopsy should be performed if rhabdomyosarcoma is suspected based on clinical and radiological exams [2].

Also, for evidence of metastatic spread we need chest X-ray, bone biopsy, liver function tests, lumbar puncture and skeletal survey. The most common sites for metastasis are lung and bone [2]. The treatment consists of surgery, associated with local radiotherapy and chemotherapy [5]. The prognosis for life is dependent on the stage and location of the tumor, and the moment of the diagnosis and treatment.

2. Patient and methods

We report the case of a 14 years old girl presented for a small tumor in the superior and internal angle of the left orbit. The onset of the illness was 3 months before the presentation, because of the appearance of a small tumor localized in the superior and internal part of the orbit, which grow in dimension in time.

From the personal pathological data we retain a childhood infectious diseases.

The heredocolateral pathological data revealed healthy parents.

The ocular examination at both eyes was normal regarding the anterior and posterior segment of the eye. Ocular refraction revealed a small hyperopia at both eyes. Examination of the right orbit didn't show any pathological aspect, but at the left orbit we visualized and palpated a small tumor, in the superior and internal part of the orbit, painless and smooth. Ocular motility was normal in both eyes.

Exophtalmometry measured 12mm at both orbits. She had a normal fundus at both eyes.

Left orbital CT scan showed no bone destruction, but revealed a small space occupying lesion in the superointernal part of the orbit, with homogenous density, without bone destruction.

Blood investigations showed a moderate anemia (haematocrit=32.9%, Hb=10.8 g/dl) with a high Erythrocyte sedimentation rate (ESR) (60mm/h) and lymphocytes=16.1%.

The pediatric and Ear, Nose and Throat examination (ETN) was normal, including the clinical examination of the patient.

After the clinical ophtalmological examination, the paraclinical and laboratory examinations the positive diagnosis was: Left eye – Superior and internal orbital tumor, Both eyes – Small hyperopia.

At this moment it was necessary to make the differential diagnosis between the following tumors, which appears in childhood and with an internal and superior location of the orbit: deep orbital dermoid cyst (nonaxial proptosis, CT scan reveals heterogeneous well circumscribed lesion); anterior encephalocele (fronto-ethmoidal); anterior orbit capillary haemangioma (dark blue or purple through the overlying skin and displaces the glob); anterior orbital lymphangioma (soft bluish mass in the upper nasal quadrant and cystic conjunctival component) [6]; rhabdomyosarcoma (located retrobulbar superior and inferior, CT scan reveals poorly defined mass of homogeneous density; adjacent bony destruction); chloroma (a form of acute myeloid leukaemia); neuroblastoma (malignant tumor, originate from primitive neuroblasts in the abdomen).

The final diagnosis may be put after the extirpation of the tumor, accomplished with the histological exam.

Evolution of this case depends on the histological type of the tumor.

The treatment began with the surgery of the orbit which had as a goal the total extirpation of the tumor. The steps of the treatment were: cutaneous incision of 10mm, at 4mm from the orbital margin, the evidence of the tumor which was grey, cartilaginous consistency and we discovered another tumor behind the first one, tumors which were histopathologically examined.

The macroscopic examination revealed two tumors, grey, cartilaginous consistency, about 3/2 cm each.

The microscopic examination of both tumors showed: dense areas with elongated cells with a centrally located, hyperchromatic nucleus sorrrounded by a considerable amount of eosinophilic cytoplasm, with perivascular location, alternative with paucicellular areas with small cells with hyperchromic nucleii (Hematoxilin-Eosine stain) The tumor cells differentiate a long rhabdomyoblastic line forming elongated spindle cell types ("strap cells") (Figure 1).

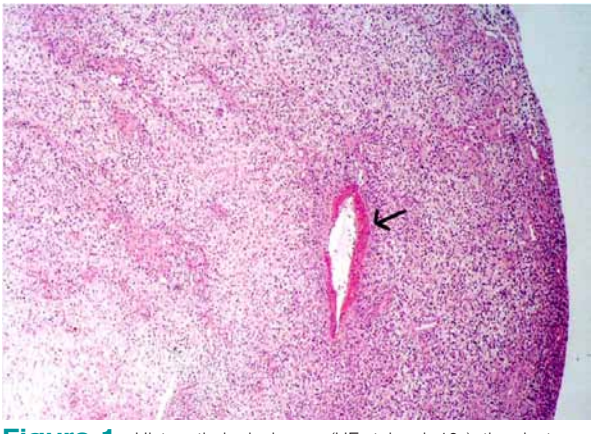

Figure 1. Histopathological exam (HE stain, ob.10x); the electron microscopic appearence of the embryonal type of rhabdomyosarcoma.

In Phosphotungstic-Hematoxilin coloration in some cells was identified striate bundles of cytoplasmic actin and myosin microfilaments (Figure 2). The microscopically aspect demonstrate the embryonal rhabdomyosarcoma type, differential degree 2.

The final diagnosis is embryonal rhabdomyosarcoma of left orbit, stage 1A (Intergroup Rhabomyosarcom Study Clinical Grouping System), TNM – T_1NoMo; Both eyes: small hyperopia.

After the surgical treatment the patient followed up the oncological treatment that consist in chemotherapy (VACA (INT protocol): *vincristine*, 1.5 mg/m2 i.v. (max, 2 mg) weekly for 7 weeks, then on week 9; *actinomycin-D*, 0.5 mg/m2 i.v. (max, 2 mg) on days 1–3 of week 4; *cyclophosphamide*, 1200 mg/m2 i.v. on day 1 of weeks 1, 4, and 7; *doxorubicin*, 30 mg/m2 i.v. on days 1 and 2 of weeks 1 and 7; for 26 weeks). Local radiotherapy applied on restricted field was 3600 cGy, one cycle/week, over 4 weeks, in order to maintain excellent survival.

After the oncological treatment (after 1 month) the blood investigations showed a decrease in ESR (30mm/h) and slightly increase in the haematocrit value (34.2%), leucocytes were 3700/mm3 and none lymphocytes. The CT scan showed a left normal orbit and the tumor was completely removed (Figure 3).

The patient showed up constantly every year at the medical check performed by a panel of experts (ophthalmology, oncology, neurology) and every time it was performed the cranial MRI to show the aspect of left orbit. The cranial MRI at 4 years after the treatment was normal (Figure 4).

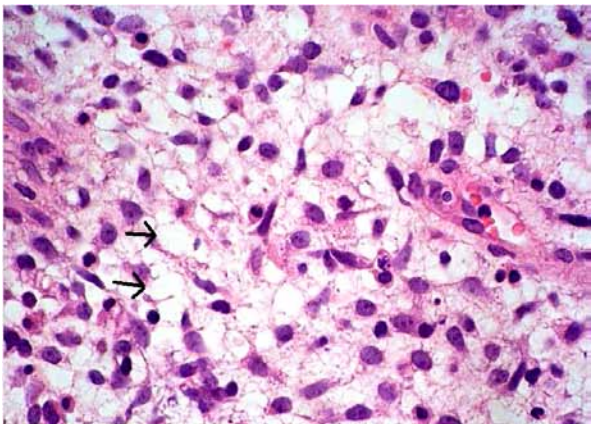

Figure 2. Histopathological exam (Haematoxylin Phosphotungstic stain, ob.40x); the electron microscopic appearence of the embryonal type of rhabdomyosarcoma with cytoplasmic microfibrils (arrow).

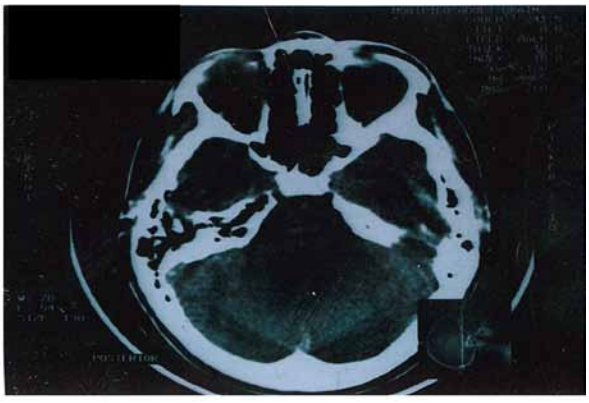

Figure 3. CT scan - one month after surgery.

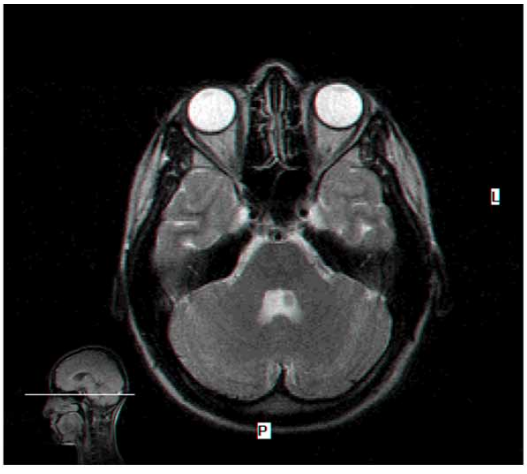

Figure 4. Cranial MRI - 4 years after surgery (normal aspect).

3. Discussion

In our case, the location of the tumor was in the supero-nasal part of the orbit without proptosis because of the small dimension of the tumor. Usually, two-thirds of orbital rhabdomyosarcoma have this location [1,3-5].

In this case, the diagnosis was established in an early stage. A detailed history (pain visual loss, signs of sinusitis) is essential in any child suspected to have orbital rhabdomyosarcoma [3], in order to exclude other differential diagnosis [3,6].

Usually, orbital rhabdomyosarcoma is extraconal (37-87 %) or both intra and extraconal (13-47%) and more commonly supero-nasal in location, especially for embryonal rhabdomyosarcoma [5,7-10], as we had in our case. Because it was detected in an early stage, the tumor was well circumscribed, but it is known that, in later stages where there is pseudocapsular invasion, the borders are irregular [3].

Cranial CT scan and cranial MRI are important for the preoperative evaluation staging, bone involvement and detection of intracranial spread, regarding the follow-up of orbital rhabdomyosarcoma [7,8,11].

The favorable prognosis for life depends of the tumor extension (limited at the orbit), complete surgical extirpation (showed on the cranial CT scan made one month after the surgery) and of postoperative survival.

Previously, rhabdomyosarcoma was believed to arise from extraocular muscles, but now it is thought that it originates from pluripotent mesenchymal cells that have the ability to differentiate into skeletal muscle [3,7,12]. There are three histological subgroups: pleomorphic, embryonal and alveolar type [3]. The embryonal type comprises 50-70% of orbital rhabdomyosarcoma [2]. In our case, the histopathlogical exam showed the embryonal type.

Malignant fibrous histiocytoma (MFA) was considered the most soft tissue sarcoma in adults [13]. Nowadays this term has been supplanted by undifferentiated pleiomorphic sarcoma (UPS) [14]. Further in the diagnosis, frequency of UPS may arise by using array-comparative genomic hybridization [Kelleher]. Rhabdomyosarcomas are categorized in the second molecular subclasses of sarcoma, which have numerous non-reccurent chromosomal alterations leading to complex Karotypes [13].

In 2010, a different classification for sarcoma was introduced based on clinical, pathological and molecular features [13]. Regarding this classification, rhabdomyosarcoma is included in the pleiomorphic sarcoma category with complex karyotypes and gene expression profiles. There are studies [13] which showed that the spindle and pleiomorphic sarcomas were found to have a similar gene expression profiles compared to the other tumors (normal cell liposarcoma, etc).

Literature [15-20] showed 5 year survival in 86.3% of cases in the embryonal rhabdomyosarcoma type. This histopathological type has a favorable evolution comparable with the other types [21]. Some authors [22], observed on their cases the association of the embryonal rhabdomyosarcoma with neurofibromatosis type 1.

On the other hand alveolar orbital rhabdomyosarcoma is rare. Some authors [23] showed that this tumor can simulate a sinusitis and early diagnosis and treatment is very important in such cases.

Of course, the differential diagnosis is very important. In this sense granulocytic sarcoma (chloroma) can have the supero-nazal orbital location, but also other ones. It was reported a case [24] with an alveolar granulocytic sarcoma of the mandible in a patient with HIV with a complete remission after chemotherapy.

Overall survival was about 25-30% (with historical recommended treatment) and with the introduction of surgery combined with adjuvant chemotherapy as well as radiotherapy, overall survival improved to around 90% [1,5,9,25-29].

Other authors reported [30] no relationship between early response and survival, and that an early response to therapy among patients with rhabdomyosarcoma, does not predict any outcome.

Metastatic spread of orbital rhabdomyosarcoma is uncommon, although if untreated left rhabdomyosarcoma has a property to metastasize to the lung, bone and bone narrow mainly hematogenously (because orbital lymphatics are scarce [2,3].

Current management includes surgery, irradiation and chemotherapy depending on the stage [3,31,32]. In our case we applied all three types of treatment with a good evolution of the patient.

Favorable prognosis was reflected in tumor size (under 5cm), age onset (upon 9 years old), histological type (embryonal rhabdomyosarcoma) and oncological treatment. The literature [9] showed that 5 year survival was better in groups of orbital rhabdomyosarcoma that received high doses chemotherapy (58.4%), compared with the same group without this therapy (18.2%).

The case particularities consist of the aspect that the diagnosis was established in an early stage, the tumor was small with location possible to be mistaken with the benign tumor [20], the surgery as the first step of treatment was complete, chemotherapy was optimal (as doses, rhythm protocol), local radiotherapy was done on a restricted field and no adverse effects appeared. The patient remained in complete continuous remission after the end of the treatment and no recurrence appeared in time.

The case has a favorable life prognosis.

4. Conclusions

In our case, early diagnosis contributed to prevent dissemination. Good life prognosis was linked to histological type – embryonal rhabdomyosarcoma, and with an early surgical treatment.

The oncological treatment (chemotherapy and radiotherapy) as adjunctive therapy induced also a positive life prognosis.

Conflict of interest statement

Authors state no conflict of interest.

References

[1] Rootman J, Neoplasia, Diseases of the orbit: a multidisciplinary approach, Lippincott Williams and Wilkins, Philadelphia, 2003, 54, 262–268

[2] Jurdy L, Johanus HM, Pieters B, Mourits M, Kloos R, Strackee S, Saeed P. Orbital rhabdomyosarcomas: A review, Saudi J Ophthalmol. 2013, 27(3), 167–175. doi: 10.1016/j.sjopt.2013.06.004

[3] Shields JA, Shields CL, Rhabdomyosarcoma: review for the ophthalmologist, Surv Ophthalmol, 2003, 48, 39–57

[4] Turner JH, Richmon JD, Head and neck rhabdomyosarcoma: a critical analysis of population-based incidence and survival data, Otolaryngol Head Neck Surg, 2011, 145, 967–973

[5] Conneely MF, Mafee MF, Orbital rhabdomyosarcoma and simulating lesions, Neuroimaging Clin N Am, 2005, 15, 121–136

[6] Koopman JH, van der Heiden-van der Loo M, van Dijk MR, Bijlsma WR, Incidence of primary malignant orbital tumours in The Netherlands Eye (Lond), 2011, 25, 461–465

[7] Terezakis SA, Wharam MD, Radiotherapy for rhabdomyosarcoma: indications and outcome, Clin Oncol (R Coll Radiol), 2013, 25, 27–35

[8] Sohaib SA, Moseley I, Wright JE, Orbital rhabdomyosarcoma-the radiological characteristics, Clin Radiol, 1998, 53, 357–362

[9] Neudorfer M, Leibovitch I, Stolovitch C, Dray JP, Hermush V, Nagar H et al. Intraorbital and periorbital tumors in children-value of ultrasound and color Doppler imaging in the differential diagnosis, Am J Ophthalmol, 2004, 137, 1065–1072

[10] Boparai MS, Dash RG, Clinical, ultrasonographic and CT evaluation of orbital rhabdomyosarcomas with management, Indian J Ophthalmol, 1991, 39, 129–131

[11] Staibano S, Franco R, Tranfa F, Mezza E, Lo Muzio L, Strianese D et al. Orbital rhabdomyosarcoma: relationship between DNA ploidy, p53, bcl-2, MDR-1 and Ki67 (MIB1) expression and clinical behavior, Anticancer Res, 2004, 24, 249–257

[12] Viswanathan S, George S, Ramadwar M, Shet T, Arora B, Laskar S et al. Extraconal orbital tumors in children – a spectrum, Virchows Arch, 2009, 454, 703–713

[13] Kelleher FC, Viterbo A. Histologic and genetic advances in refining the diagnosis of “undifferentiated pleomorphic sarcoma, Cancers (Basel). 2013, 22, 5(1):218-33. doi: 10.3390/cancers5010218

[14] Goldblum JR. An approach to pleomorphic sarcomas: can we subclassify, and does it matter?, Mod Pathol., 2014, 27, suppl 1:S39-46. doi: 10.1038/modpathol.2013.174

[15] Kanski JJ, Clinical Ophtalmology, 4th ed., Butterworth Heinemann, Oxford, 1999, 581-582.

[16] Kaliaperumal S, Tiroumal S, Rao V, Orbital rhabdomyosarcoma: a case series, Indian J Cancer., 2007, 44(3), 104-107

[17] George JL, Marchal JC, Orbital tumors in children: clinical examination, imaging, specific progression, Neurochirurgie, 2010, 56(2-3), 244-248

[18] Forstner D, Borg M, Saxon B, Orbital rhabdomyosarcoma: multidisciplinary treatment experience, Australas Radiol., 2006, 50(1), 41-45

[19] Silvana G, Roberto De B, Domenico P, Giuseppina S, Ciracì L, Antonio C, Orbital cavitary rhabdomyosarcoma: a diagnostic dilemma, Orbit., 2010, 29(1), 45-47

[20] Hosoi H, Et Al, A review of 331 rhabdomyosarcoma cases in patients treated between 1991 and 2002 in Japan, Int J Clin Oncol., 2007, 12(2), 137–145

[21] Hayes-Jordan A, Andrassy R, Rhabdomyosarcoma in children, Curr Opin Pediatr., 2009, 21(3), 373–378

[22] Shome D, Honavar SG, Reddy VA, Vemuganti GK, Orbital embryonal rhabdomyosarcoma in association with neurofibromatosis type 1, Ophthal Plast Reconstr Surg., 2007, 23(2), 147–148

[23] Sanz-Marco E, España E, Alamar A, Pérez-Rojas J, López-Prats MJ, Díaz-Llopis M. Orbital alveolar rhabdomyosarcoma masked by ethmoid sinusitis in a 25-year-old, Arch Soc Esp Oftalmol., 2012, S0365-6691(12)00538-2. doi: 10.1016/j.oftal.2012.10.012

[24] Colović N, Jurišić V, Terzić T, Jevtovic D, Colović M. Alveolar granulocytic sarcoma of the mandible in a patient with HIV, M. Onkologie, 2011, 34, 55-8. doi:10.1159/000317351

[25] Breneman JC, Lyden E, Pappo AS, Link MP, Anderson JR, Parham DM et al. Prognostic factors and clinical outcomes in children and adolescents with metastatic rhabdomyosarcoma – a report from the intergroup rhabdomyosarcoma study IV, J Clin. Oncol., 2003, 21, 78–84

[26] Olivier Pascual N, Calvo JM, Abelairas Gómez JM, Orbital rhabdomyosarcoma: difficulties with European treatment protocol, Arch Soc Esp Oftalmol, 2005, 80, 331–338

[27] Raney RB, Maurer HM, Anderson JR, Andrassy RJ, Donaldson SS, Qualman SJ et al., The Intergroup Rhabdomyosarcoma Study Group (IRSG): major lessons from the IRS-I through IRS-IV studies as background for the current IRS-V treatment protocols, Sarcoma, 2001, 5, 9–15

[28] Wharam MD, Hanfelt JJ, Tefft MC, Johnston J, Ensign LG, Breneman J et al., Radiation therapy for rhabdomyosarcoma: local failure risk for clinical group III patients on intergroup rhabdomyosarcoma study II, Int J Radiat Oncol Biol Phys, 1997, 38, 797–804

[29] Shields CL, Shields JA, Honavar SG, Demirci H, Primary ophthalmic rhabdomyosarcoma in 33 patients, Trans Am Ophthalmol Soc, 2001, 99, 133–143

[30] Rosenberg AR, Anderson JR, Lyden E, Rodeberg DA, Wolden SL, Kao SC, Parham DM, Arndt C, Hawkins DS. Early response as assessed by anatomic imaging does not predict failure-free survival among patients with Group III rhabdomyosarcoma: A report from the Children's Oncology Group, Eur J Cancer, 2013, S0959-8049(13)01027-7. doi: 10.1016/j.ejca.2013.11.031

[31] Breneman J, Meza J, Donaldson SS, Raney RB, Wolden S, Michalski J et al., Local control with reduced-dose radiotherapy for low-risk rhabdomyosarcoma: a report from the children's oncology group D9602 study, Int J Radiat Oncol Biol Phys, 2012, 83, 720–726

[32] Tyl JW, Blank LE, Koornneef L, Brachytherapy in orbital tumors, Ophthalmology, 1997, 104, 1475–1479