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ISSN 2544-1361 (online); ISSN 2544-2406
doi: 10.15584/ejcem.2021.1.11

http://www.ejcem.ur.edu.pl
European Journal of Clinical and Experimental Medicine
Eur J Clin Exp Med 2021; 19 (1): 81–85

CASUISTIC PAPER

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An aggressive locoregional orbital rhabdomyosarcoma and Li Fraumeni syndrome

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ABSTRACT

Introduction. Rhabdomyosarcoma (RMS) is the most common pediatric soft tissue sarcoma with 10 % of the cases occuring in the orbit. Patients often present with a rapidly developing proptosis and globe displacement.

Aim. We aimed to present a very rare presentation of orbital RMS, with a giant exophytic orbital mass, a very rare presentation occuring in more advanced cases.

Description of the case. A 3-year old girl presented to our hospital with a rapidly enlarging tissue like ulcerative mass. Her past medical history was remarkable with the diagnosis of embryonal rhabdomyosarcoma (RMS) and treatment with chemoradiotherapy at the age of 15 months. On magnetic resonance imaging (MRI), there was a giant heterogenously enhancing mass filling the right orbit and extending to the intracranial region. Li Fraumeni syndrome (LFS) was considered due to her sister death from neuroblastoma at an early age. Cytogenetic analysis revealed mutations of p53 gene, which supported our consideration.

Conclusion. RMS is a highly malignant tumor which usually occurs sporadiacally. However, some rare syndromes are associated with increased incidence of RMS, such as LFS.

Keywords. del17p13.1, giant orbital mass, Li Fraumeni syndrome, rhabdomyosarcoma

The list of abbreviations:

LFS – Li Fraumeni syndrome, MRI – magnetic resonance imaging, RMS – rhabdomyosarcoma

Introduction

Rhabdomyosarcoma (RMS) is the most common pediatric soft tissue sarcoma with 10 % of the cases occuring in the orbit.[1,2] Most of the patients present in the first decade of life with mean age of 6-8 years.[2] Orbital RMS usually originates from eyeball but, may also be derived from other ocular adnexal structures like eye lids.[3] In primary orbital RMS, patients often present with a rapidly enlarging unilateral orbital mass associated with proptosis and globe displacement. Since the most favored location is the superonasal part of the orbit, the globe is usually displaced inferiorly or inferotemporaly.[4] Presentation with a giant exophytic orbital mass is very rare and occurs in more advanced, severe cases. Radiological imaging is important especially in the detection of local and distant extent of the disease

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Participation of co-authors: A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 21.01.2021 | Accepted: 5.02.2021
Publication date: March 2021

Erok B, Kıbıcı K. *An aggressive locoregional orbital rhabdomyosarcoma and Li Fraumeni syndrome*. Eur J Clin Exp Med. 2021;19(1):81–85. doi: 10.15584/ejcem.2021.1.11

and in the posttreatment follow up to detect recurrence and the late side effects of radiotherapy such as secondary malignancies.

Aim

We aimed to present a very rare presentation of orbital RMS with an exophytic giant orbital mass emerging from the right orbit in a 3 year old girl, which had been diagnosed as RMS previously.

Description of the case

A 3 year old girl of African origin presented with a unilateral eye protrusion in her right eye when she was 15 month old. The embryonal type RMS was diagnosed and she started on chemoradiotherapy cycles. Since she did not continue to the follow ups, there was no imaging studies to show previous state of remission. About 2 years later, she presented to our hospital with a rapidly enlarging tissue like ulcerative mass that exits the right orbit and covers most of her face (figure 1).

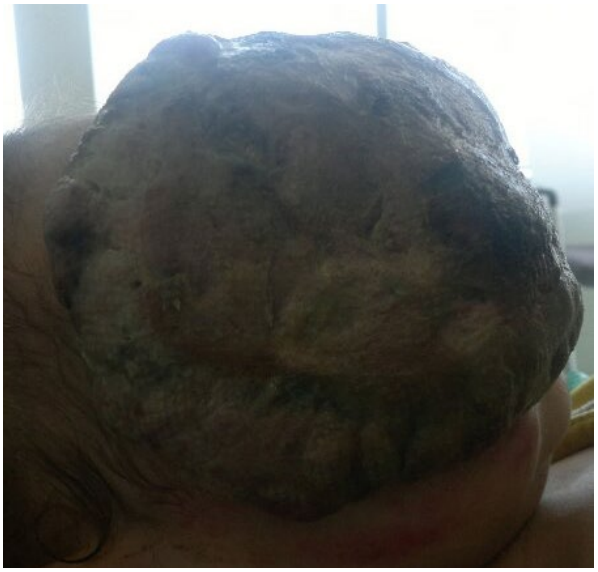

Fig. 1. Tissue like ulcerative giant mass that exits the right orbit

On magnetic resonance imaging (MRI), there was a 12x11x10 cm mass filling the right orbit and leading to invasion in its walls. The mass was heterogenously hyperintense on T2w images (figure 2) and isointense on T1w images (figure 3) as compared to the extraocular muscles.

Following intravenous (IV) contrast administration marked heterogenous enhancement was demonstrated (figure 3).

The maxillary sinuse and ethmoidal cells were also invaded with disruption of the lamina papyracea. The mass was extending from the superior orbital fissure to the intracranial area by invading the optic nerve. The right internal carotid artery was surrounded by the mass but the flow void was normal which shows vascular patency (figure 2). There were no evidence of lymph node involvement or distant metastasis on PET-CT scan. Right orbital exentration with reconstruction by flap closure was performed and followed by radiotherapy consisting of a dose of 42 Gy in 21 pulses. Peripheral blood sample analysis with FISH technique revealed mutations of p53 gene in the form of del17p13.1 in 7% of the analyzed 200 cells (figure 4).

Follow up MRI of the orbit at the first 6 th month showed complete excision and no recurrence (figure 5). Informed consent was taken from the patient's parents.

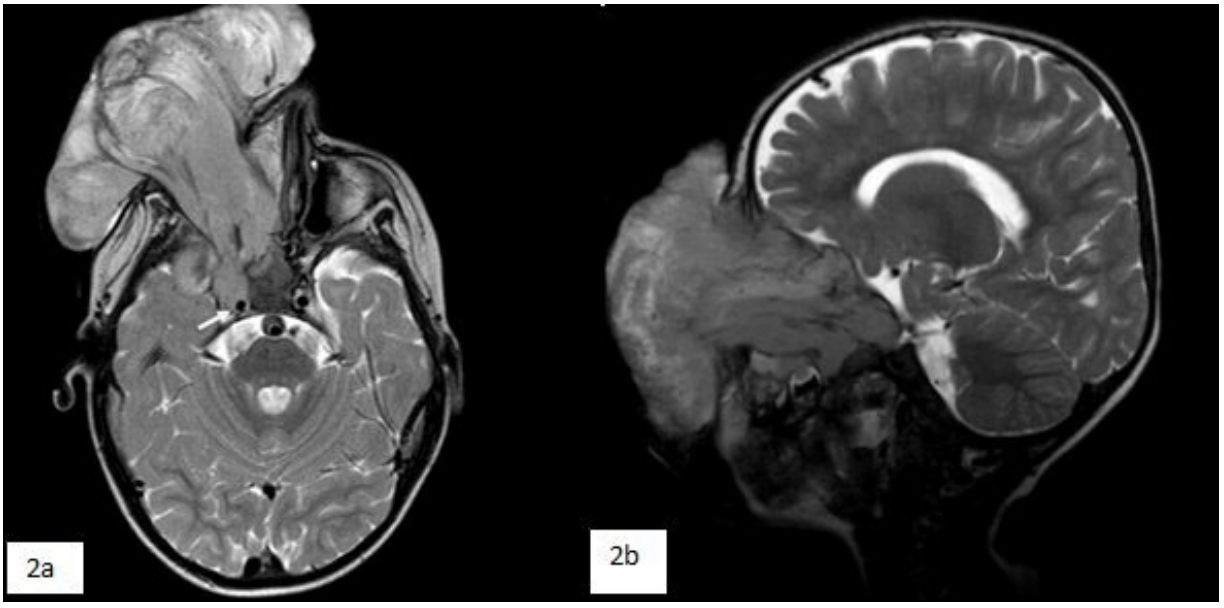

Fig. 2. Preoperative MR axial T2w image (a) and sagittal T2w image (b), showing the exophytic right orbital mass with intracranial extention, which is hyperintense as compared to the extraocular muscles. The right ICA is surrounded by the mass (a) (white arrow)

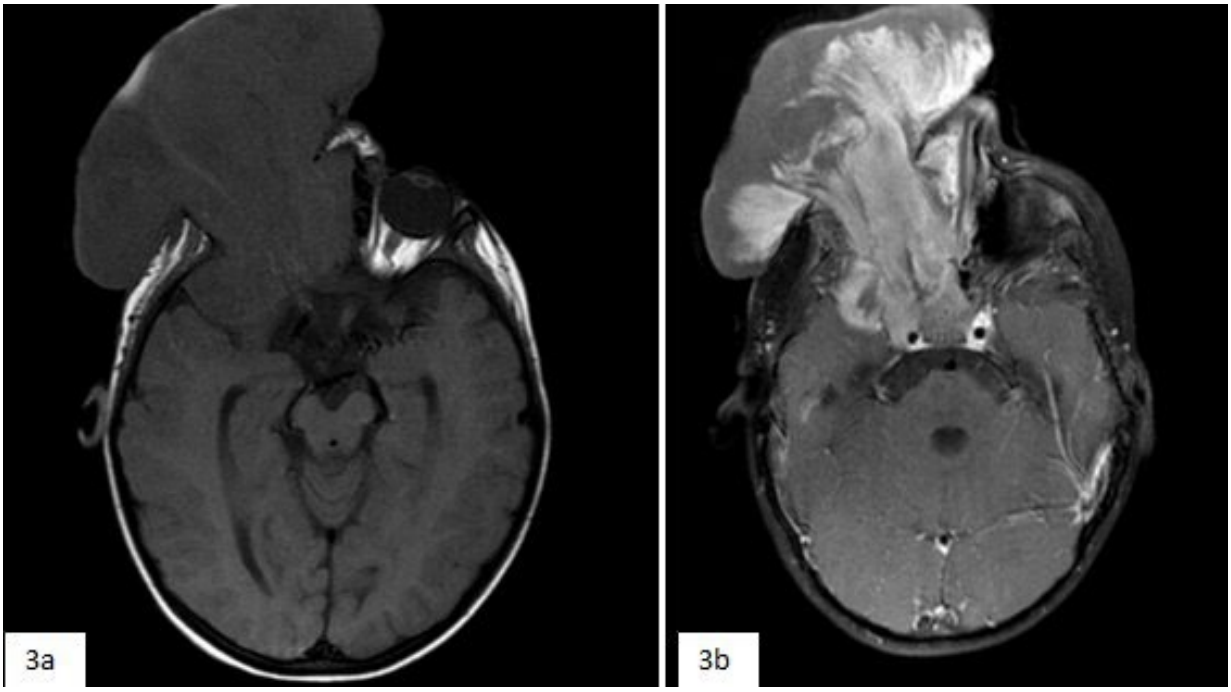

Fig. 3. Preoperative MR axial T1w image (a) showing the exophytic right orbital mass with intracranial extention, which is isointense as compared to the extraocular muscles and axial T1w postcontrast image (b) showing marked heterogenous enhancement.

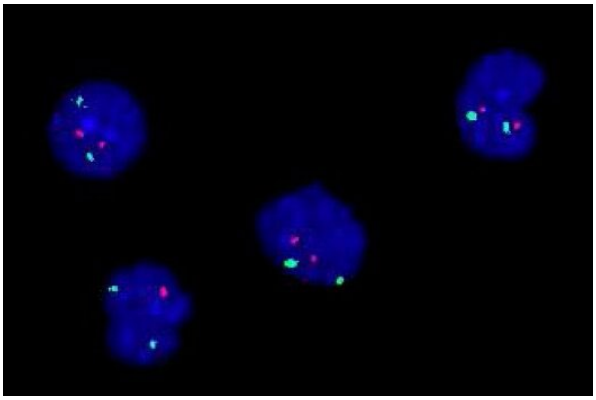

Fig. 4. Cytogenetic analysis with FISH technique showing mutations of p53 gene in the form of del17p13.1

Discussion

Majority of the cases of orbital RMS are sporadic and there is no known specific genes responsible for direct hereditary trasmission. However, RMS has been noted to occur more commonly in some familial cancer syndromes such as LFS, which is a rare inherited familial predisposition to wide range of malignant tumors with early occurance.[5,6] It is caused by a germline autosomal dominant mutation in the tumor suppressor gene; TP53, resulting in a malfunctioning p53 protein.[7] The syndrome was first recognized and named in honor of two American physicians, Frederick Pei Li and Joseph F. Fraumeni, Jr. after they review the medical records of 648 childhood RMS cases.[8] A modified diagnostic criteria was proposed by Chompret et al.for maximum clinical utility.[9] Approximately 70 % of the patients with LFS contain germline mutations in the p53 gene on chromosome 17p13.1.[10] Our patient was diagnosed as RMS by histopathological examination when she was 1.5 year old and her sister was died due to neuroblastoma. Therefore, LFS was considered according to the Chompret criteria and supported by the cytogenetic analysis.[9]

Previously, RMS was believed to be originated from skeletal muscle cells. However, since it can occur anywhere in the body even where the skeletal muscle is not present, now it is thought that it originates from pluripotent mesenchymal cells that go on to differentiate into striated muscle.[11] Therefore, contrary to the early belief, orbital RMS do not arise from extraocular muscles but rather develop from pirimitive mesenchymal cells**.** RMS is one of the small round blue cell tumors and is classified histologically into 3 main subtypes: embryonal, alveolar and pleomorphic. Embryonal RMS which accounts the majority of the cases (80%) of orbital RMS, affects more frequently children than adults and generally has a favorable prognosis. The alveolar variant which is less frequent in the orbit, is the most anaplastic type and has a poor prognosis.[12]

The principle imaging modality in the assessment of the primary tumor and intracranial involvement is MRI with its multiplanar imaging capacity, excellent soft tissue resolution, the advantage of bone marrow assessment and the lack of radiation. It is highly effective in determining the epicenter of the tumor and the intracranial extent. However, CT is also useful with its superiority in cortical bone assessment and detection of calcifications. Orbital RMS is usually extraconal or both

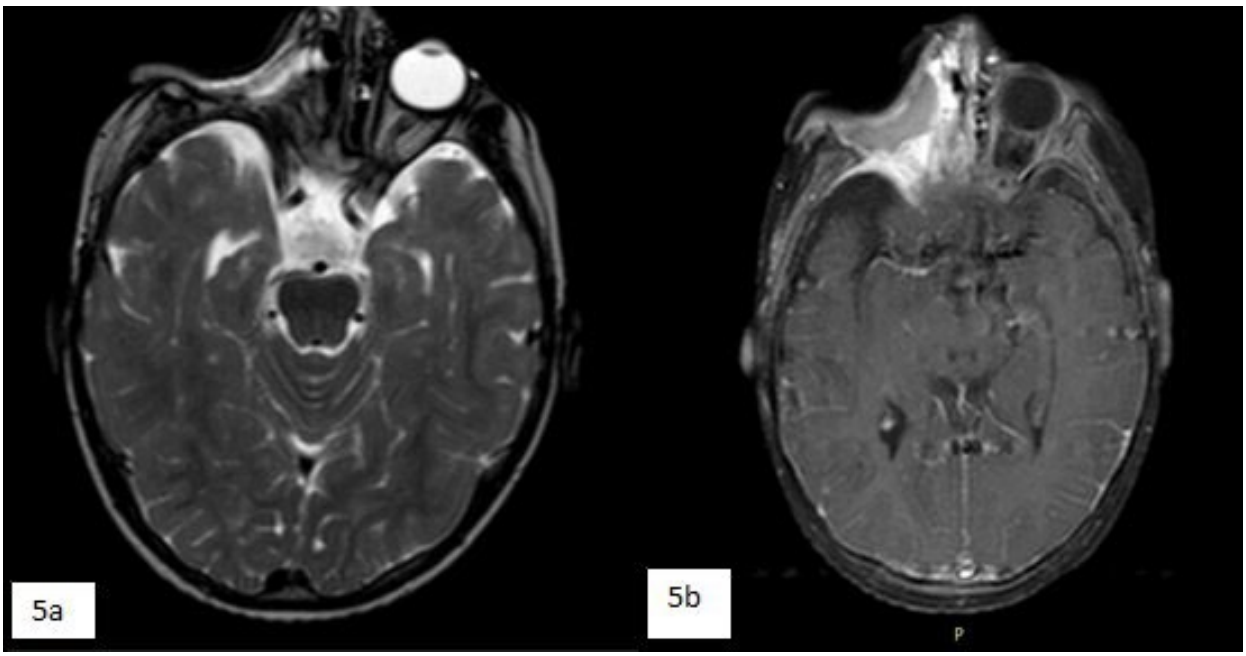

Fig. 5. Posttreatment MR at 6 th month, axial T2w image (a) and axial T1w postcontrast image (b) showing complete excision and no recurrence

intra and extraconal. The epicenter of the embryonal subtype is usually the superonasal part wheras the alveolar subtype is more common in the inferior part of the orbit.[4] The tumor is well defined in early stages but later with the invasion of the pseudocapsule, the borders may become ill defined. On nonenhanced CT, the mass is usually seen as an irregular shaped soft tissue lesion that is isodense to the extraocular muscles. Calcification is rare in untreated tumors and occur only with bony destruction.[13] On MRI, the mass is isointense compared to extraocular muscles and hypointense with respect to the orbital fat on T1w images. On T2w images, the mass shows typical bright T2w signal with respect to both extraocular muscles and orbital fat. Following IV contrast administration moderate to marked heterogenous enhancement is observed, which is best seen with fat suppression. Although, the alveolar and pleomorphic subtypes demonstrates large areas of necrosis and hemorrhages, it is uncommon for an embryonal RMS.[12] However, it may be seen also in embryonal RMS as a posttheraupeutic change or as a result of fast growing like in any other tumor. The mass distort the globe and extraocular muscles but rarely invades these structures. At advanced stages, because of the rapid growth and aggressive nature of the tumor, adjacent bone and soft tissue invasion is frequent, however intracranial extention is relativelly uncommon.[13] The differential diagnosis based on radiological findings include orbital metastasis of neuroblastoma (NBL), primary orbital NBL and orbital RMS. Moreover, extremely rarely, primary orbital retinoblastoma RBL has been reported to be presented as a giant orbital mass.[15] For differentiation, further systemic evaluation and histopathological examination is needed.

In orbital RMS recurrence was reported in about 17% of the cases with 92% being local and 8% being distant recurrence occured at a median time of 18 months.[16] However, in our patient since we could not be able to obtain posttreatment follow up imagings to show her remission state, we could not say this is a recurrent tumor. Therefore, it is possible that this is a residual mass rapidly grown in size. Treatment of orbital RMS is composed of combinations of surgery, radiotherapy and chemotherapy depending on the stage of the disease.

Conclusion

RMS is a highly malignant tumor which usually occurs sporadiacally. However, some rare syndromes are associated with increased incidence of RMS, such as LFS. Prognosis is favorable for localized orbital RMS with the help of current advances in the diagnosis & treatment especially in the embryonal subtype. Since the most important factor having positive influence on survival is more localized disease, follow up of patients with imaging after treatment is essential and MRI is the preferred imaging modality due to lack of exposure to ionizing radiation.

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