



# A Rare Presentation of Retinoblastoma as a Fungating Orbital Mass: A Case Report

## Retinoblastomun Orbital Kitle Olarak Nadir Presentasyonu: Bir Olgu Sunumu

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### ABSTRACT

Retinoblastoma (RBL) arises from the precursor cells of the retinal neuroepithelium. It is the most common primary malignant intraocular tumor in children. Primary orbital RBL is an extraocular disease detected clinically or radiologically at the time of diagnosis. It is a direct metastasis of an intraocular RBL. It very rarely presents as an exuberant fungating orbital mass, like in the present case, and is found in more advanced, untreated cases. Magnetic resonance imaging (MRI) is the preferred imaging modality for the evaluation of the tumor, vital orbital structures such as the optic nerve, and intracranial involvements. Computed tomography (CT) is useful in the evaluation of adjacent bony structures and calcifications. Herein, we report the case of a 3-year-old boy who presented to our clinic with a large, rapidly growing cauliflower-like mass protruding out of the left orbit and invading the surrounding soft tissues. MRI showed a 10×8×7.5 cm<sup>3</sup> infiltrative heterogeneously enhancing left orbital mass with some necrotic and hemorrhagic components. Metastatic leptomeningeal enhancements were widespread in the intracranial region. CT revealed erosive destructive changes at the lateral orbital wall. Following left orbital enucleation, the diagnosis of RBL was made by histopathological examination, which showed sporadic Flexner-Wintersteiner type rosette formations. The patient underwent surgery and thereafter received radiotherapy and adjuvant chemotherapy. No recurrence was observed after 5 years. Although rare, orbital extension of RBL is one of the major contributors to mortality. Early diagnosis and detailed radiological evaluation are necessary to establish intracranial involvement and distant metastasis at the time of diagnosis.

**Keywords:** Primary orbital retinoblastoma, Flexner-Wintersteiner rosette, magnetic resonance imaging (MRI), leptomeningeal metastasis

### ÖZ

Retinoblastom (RBL) retinal nöroepitel öncül hücrelerinde köken alır. Çocukluk çağıının en sık görülen primer malign intraokuler tümördür. Primer orbital RBL tanı anında klinik ve radyolojik olarak tespit edilen ekstraokuler hastalık olarak tanımlanır. Intraokuler RBL nin doğrudan yayılması ile ortaya çıkar. Olgumuzda olduğu gibi mantarlaşan dev orbital kitle ile presentasyon oldukça nadirdir ve daha ileri, tedavi edilmemiş olgularda görülebilmektedir. Magnetik rezonans görüntüleme (MRG) tümörün, optik sinir gibi hayati orbital yapıların ve intrakranial tutulumlarının değerlendirilmesinde primer görüntüleme yöntemidir. Bilgisayarlı tomografi (BT) komşu kemik yapılar ve kalsifikasyon değerlendirmesinde yararlıdır. Kliniğimize başvuran 3 yaşında erkek hastamızda hızla büyüyen komşu yumuşak dokulara invaze olan dev karnıbaharimsi sol orbita kitlesini sunuyoruz. MRG de nekrotik ve hemorajik bileşenleri bulunan 10x8x7,5 cm<sup>3</sup> boyutlu heterojen kontrastlanma gösteren infiltratif sol orbital kitle ve intrakranial alanda yaygın metastatik leptomeningeal kontrastlanmalar mevcut idi. BT incelemede sol lateral orbita duvarında erozif değişiklikler izlendi. Sol orbital enukleasyonu takiben RBL tanısı Flexner-Wintersteiner tipi roset formasyonlarının gösterilmesi ile histopatolojik olarak konuldu. Hastamız operasyon sonrası radyoterapi ve adjuvan kemoterapi aldı. Beş yıl sonrasına kadar yapılan kontrollerde nuks saptanmadı. RBL un orbital uzanımı çok nadir olmakla beraber mortalitenin major nedenlerindenidir. Erken tanı ve detaylı radyolojik değerlendirme tanı anında mevcut olabilecek intrakranial tutulum ve uzak metastazın saptanması için önemlidir.

**Anahtar kelimeler:** Primer orbital retinoblastom, Flexner-Wintersteiner roset, magnetik rezonans görüntüleme (MRG), leptomeningeal metastaz

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## INTRODUCTION

Various neoplasms can arise from orbital structures. Retinoblastoma (RBL) is a neoplasm that arises from the retina, affecting the precursor cells of the retinal neuroepithelium. It is the most common primary malignant intraocular tumor in children. It is exclusively found in young children, and most cases were diagnosed before the age of five (1). RBL may be sporadic or secondary to a germline mutation associated with the inactivation of the RBL protein tumor suppressor gene, which is usually inherited. The hereditary form, which constitutes approximately half of the cases, tends to occur bilaterally at younger age (2,3). Affected children are also at increased risk of developing trilateral RBL (unilateral orbital RBL and pineoblastoma) and osteosarcoma (4). Sporadic disease forms usually occur in older children and are typically solitary (1). Primary orbital RBL is diagnosed as an extraocular disease and a direct extension of intraocular RBL. It is very rarely reported in developed countries due to early diagnosis and treatment. However, in developing and underdeveloped countries, extraocular extension of RBL is not an unusual presentation and is one of the major factors of poor prognosis. It is different from secondary orbital RBL, which is defined as orbital recurrence several weeks to years after enucleation for intraocular RBL. The most frequent manifestations are leukocoria (a white pupil), similar to that in intraocular RBL or proptosis (5). In more advanced and untreated cases, massive extraocular tumor spread very rarely results in a fungating giant orbital mass, as in the present case. Diagnosis is made by histopathological examination. In patients with extraocular extension of RBL, radiological imaging is important to determine the exact size and extent of the tumor. Herein, we report a case of a primary orbital RBL with intracranial involvement at the time of diagnosis in a 3-year-old boy.

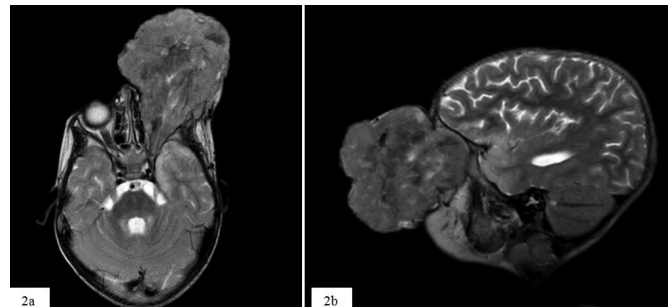
## CASE PRESENTATION

In August 2013, an otherwise healthy 3-year-old boy presented to our clinic with a giant, rapidly enlarging cauliflower-like mass protruding out of the left orbit and invading the surrounding

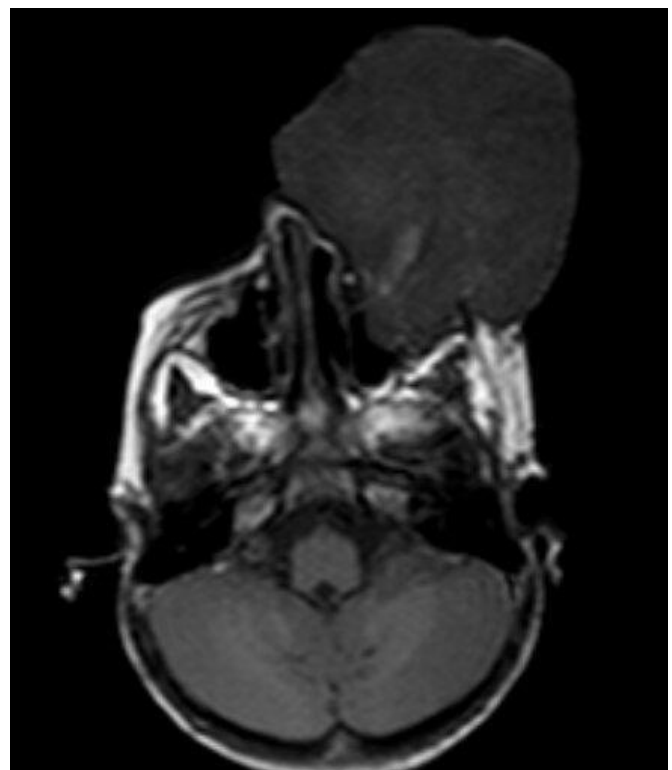


**Figure 1.** A large, cauliflower-like mass protruding out of the left orbit and invading the surrounding soft tissues in a 3-year-old boy

soft tissues (Figure 1). He recalled that the lesion appeared approximately 6 months earlier and started to grow rapidly for the last 3 months. On physical examination, no regional lymph node enlargement or organomegaly was detected. Magnetic resonance imaging (MRI) of the orbit showed a 10x8x7.5 cm<sup>3</sup> solid infiltrative left orbital lesion obliterating the superior orbital fissure. The globe and retro-orbital structures lost their normal morphology. The left optic nerve (ON) was indistinguishable (Figure 2). There were some areas of necrosis on T2-weighted images (T2-WI) (Figure 2) and some linear hemorrhagic components on T1-WI (Figure 3). The mass extended into the left ON through the orbital apex into the optic chiasm, which

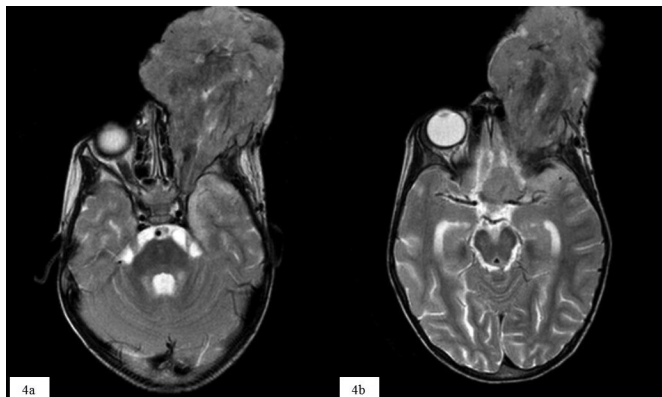


**Figure 2.** (a) Axial and (b) sagittal T2-weighted magnetic resonance images of the left orbit showing exophytic left orbital mass, which is heterogeneously isointense to the cortical gray matter with some areas of necrosis. The superior orbital fissure is obliterated, and the left optic nerve is indistinguishable

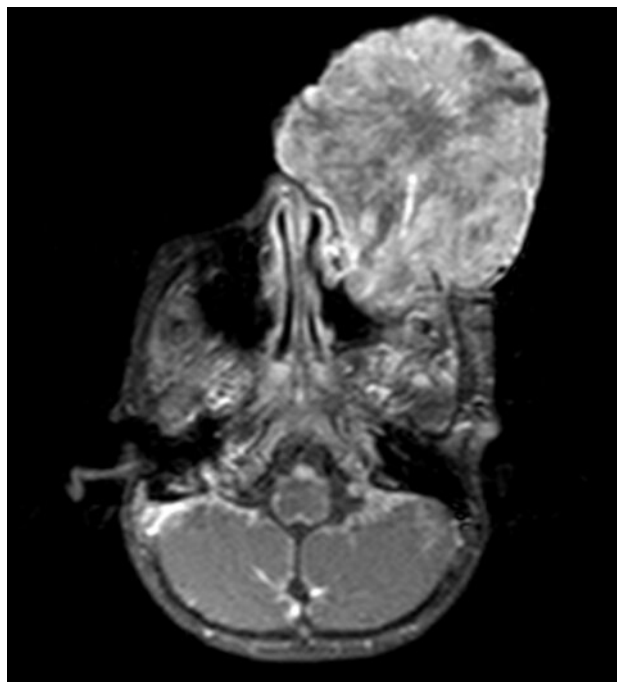


**Figure 3.** Axial T1-weighted magnetic resonance image showing some linear hyperintense hemorrhagic components

was occupied by a nodular component of the mass (Figure 4). Following contrast administration, non-necrotic areas of the mass showed moderate to marked enhancement (Figure 5). In the intracranial region, enhanced metastatic meningeal lesions were detected in both supratentorial and infratentorial regions. The lesions were the widest at the left middle cranial fossa on the temporal lobe (Figure 6). On computed tomography (CT), the lesion was isodense compared with the vitreous, and there were erosive destructive changes at the lateral orbital wall, with no extension into the maxillary and ethmoid sinuses. There were some hemorrhagic foci, but no calcification was detected



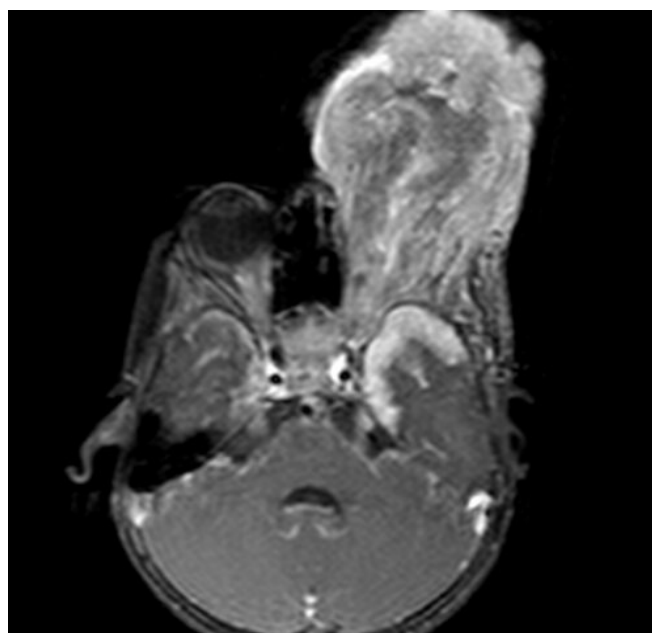
**Figure 4.** Axial T2-weighted magnetic resonance image showing (a) the extension of the mass into the left optic nerve through the orbital apex into the optic chiasm and (b) a nodular component of the mass occupying the optic chiasm



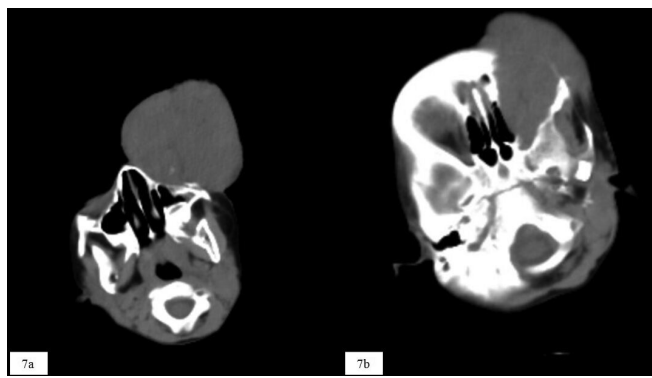
**Figure 5.** Axial T1-weighted fat-saturated magnetic resonance image with gadolinium showing moderate to marked enhancement in non-necrotic areas of the mass

(Figure 7). Further systemic evaluation revealed neither systemic metastasis nor adrenal mass or paravertebral lesion suggesting orbital metastasis of neuroblastoma (NBL). Primary orbital NBL, primary orbital RBL, and orbital rhabdomyosarcoma (RMS) were considered in the differential diagnosis. Following left orbital enucleation, the diagnosis of orbital RBL was made by histopathological examination, which showed orderly proliferation of neoplastic cells with trabecular and insular pattern, occasionally presenting as Flexner-Wintersteiner type rosette formation (Figure 8). After surgery, the patient received radiotherapy and adjuvant chemotherapy. The patient was seen again in 2018, but no recurrence was observed.

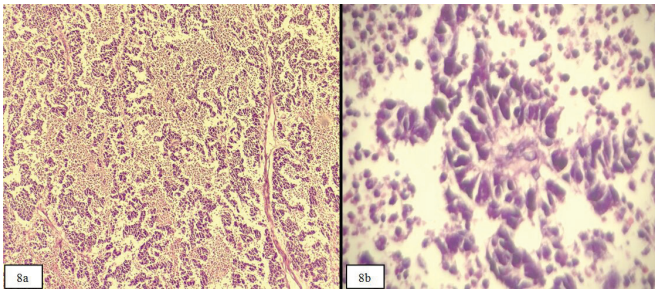
Informed consent has been taken from the family of our patient.



**Figure 6.** Axial T1-weighted fat-saturated magnetic resonance image with gadolinium showing metastatic leptomeningeal enhancement at the left temporal pole



**Figure 7.** Axial computed tomography scan showing (a) the left orbital mass with some hemorrhagic foci but no calcification and (b) erosive destructive changes at the lateral orbital wall



**Figure 8.** Histopathological examination showing (a) orderly proliferation of neoplastic cells with trabecular and insular patterns, occasionally forming rosettes (hematoxylin-eosin, x40). (b) Sections show a close-up view of a Flexner-Wintersteiner type rosette formation (hematoxylin-eosin, x400)

## DISCUSSION

Primary orbital RBL is defined as an orbital extension of an intraocular RBL detected clinically or radiologically at the time of diagnosis (1). The term, microscopic orbital RBL, is used when an enucleated eye with intraocular RBL demonstrates ON invasion, evident scleral infiltration, or extrascleral extension on histopathological evaluation (6). Clinical presentation with an exuberant fungating orbital mass, as in the present case, is very rare and found in more advanced, untreated cases due to massive extraocular tumor spread through the ON or sclera. Both MRI and CT are used to assess the exact size and extent of the tumor. MRI, with its excellent soft tissue contrast, is the preferred imaging modality for the orbits and brain and for the evaluation of the tumor, vital orbital structures like the ON, and intracranial involvements. In addition, MRI enables diffusion-weighted imaging (DWI) that is valuable in monitoring treatment response. CT is useful in the evaluation of adjacent bony structures and calcifications. Following contrast administration, moderate to marked enhancement is seen in non-necrotic parts of the tumor. The rapid growth of the tumor results in necrosis and heterogeneous enhancement. On DWI, the enhancing viable part of the tumor tissue shows restricted diffusion associated with apparent diffusion coefficients lower than those of non-viable necrotic tissues. However, since these imaging features are not specific for RBL, histopathological examination is needed for exact diagnosis. In the present case, the differential diagnosis included embryonal RMS, primary orbital NBL, and primary orbital RBL, all of which share similar histology that basically consists of small round blue cells. RMS is the most common primary orbital malignancy in children (7). Clinical presentation is a typical rapidly growing mass, often in the upper inner quadrant of the orbit (8). On histopathological examination, embryonal RMS, which accounts for the majority of orbital RMS cases, is differentiated by the presence of rhabdomyoblasts. By contrast, NBL is the most common metastatic orbital tumor in children, with the primary focus in the adrenal medulla or paravertebral sympathetic/parasympathetic tissue of the abdomen and chest. In our patient, CT of the chest and abdomen did not reveal remarkable findings.

Very rarely, NBL may be found as a primary orbital NBL without any systemic disease (9). Histologically, the undifferentiated part of the RBL demonstrates small blue cells with large hyperchromatic nuclei and scant cytoplasm. Homer Wright Pseudorosettes and Flexner-Wintersteiner Rosettes may be seen. Homer Wright Rosettes are differentiated tumor cells grouped around a central region containing neuropil and are therefore associated with tumors of neuronal origin and found in other tumors like pancreatic neuroendocrine tumors. On the contrary, Flexner-Wintersteiner Rosette is a relatively unique characteristic of RBL. In our patient, occasional Flexner-Wintersteiner type rosette formation was found and the tumor was differentiated from NBL. Since the orbital extension of the intraocular RBL increases the risk for regional and systemic dissemination of the disease compared with patients without extraocular disease, detailed evaluation is mandatory (10). The most common metastatic dissemination of RBL occurs intracranially via the ON in which the subarachnoid space of the ON sheath is infiltrated by the tumor cells with dissemination into the cerebrospinal fluid (5). Therefore, MRI of the brain and spinal cord should be performed at the same time to assess leptomeningeal metastases in patients with extraocular extension of RBL. Brain MRI is also necessary to rule out trilateral RBL. In the present case, both supratentorial and infratentorial leptomeningeal metastases were found on the brain MRI at the time of presentation. In RBL, lymphatic spread to regional lymph nodes depends on the involvement of the conjunctiva or eyelids due to the absence of lymphatics in most of the globe and the orbit. Preauricular lymph nodes are most commonly affected in these patients (1). Therefore, they should be carefully palpated in clinical examination, and fine-needle aspiration biopsy should be done in case of suspicion. Metastasis to the lungs, bone, bone marrow, and liver may occur hematogenously. Skeletal metastases are best evaluated by bone scintigraphy or fluorodeoxyglucose positron emission tomography, because the highly hematopoietic bone marrow in infants makes it difficult to detect bone marrow involvement on MRI. On post-treatment follow-up, MRI is the preferred modality for the assessment of treatment response and detection of local and distant recurrences because of the increased long-term risk for malignancy in young patients who undergo repetitive CT. Currently, there are no standard treatment protocols for orbital RBL. Good long-term survival results have been reported with multimodal treatment, including high-dose chemotherapy, orbital enucleation, radiotherapy, and additional adjuvant chemotherapy over the last years. However, extraocular extension of RBL is still a major contributor to mortality, and patients have a poor prognosis (5).

## CONCLUSION

Despite its rare occurrence in developed countries due to early diagnosis and treatment, primary orbital RBL is one of the major contributors to mortality. Early diagnosis and detailed radiological evaluation are essential to establish intracranial involvement and distant metastasis at the time of diagnosis. MRI, with its high tissue contrast and improved spatial resolution, is the mainstay in

the diagnosis and follow-up of patients. Survival can be increased with early multimodal treatment and close radiological follow-up.

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