Successful Total Resection of an Orbital Epithelioid Hemangioendothelioma with the Aid of Endovascular Embolization

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Established Facts

- Epithelioid hemangioendothelioma is extremely rare in the orbit.
- The best treatment for orbital epithelioid hemangioendothelioma is complete surgical resection if possible. However, profuse intraoperative bleeding is a possible challenge during the surgery.

Novel Insights

- Angiography and intravascular embolization before surgery helps the procedure be performed without massive blood loss.
- This case is an example of successful surgery facilitated by preoperative occlusion of the feeder vessels by endovascular intervention.

Keywords

Endovascular intervention · Hemangioendothelioma · Orbital neoplasm · Retinal vascular occlusion · Vascular lesion

Abstract

Hemangioendothelioma is rarely encountered in the orbit. We present a patient with a growing orbital mass for whom surgical excision was planned. Two previous attempts at removing the mass failed due to profuse bleeding. Endovascular embolization was performed before surgery to prevent

massive hemorrhage. After embolization, retinal vascular accident (combined central retinal artery and vein occlusion) occurred. However, surgical excision (lateral orbitotomy and transcoronal craniotomy) was successful, and the vision improved postoperatively. Histopathologic examination and immunohistochemistry study confirmed the diagnosis of epithelioid hemangioendothelioma. The combined approach by a team of specialists, including an interventional radiologist performing preoperative embolization of the feeding vessel and joint surgery by a neurosurgeon and ophthalmologist, was the key to the effective treatment of this vascular orbital neoplasm.

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Introduction

Hemangioendotheliomas are a diverse group of vascular tumors with clinical behavior and histopathologic characteristics between those of hemangiomas and angiosarcomas [1].

Epithelioid hemangioendothelioma (EHE) is a distinct variant of this neoplasm with epithelioid features, first described by Weiss and Enzinger [1]. EHE is a less malignant variant of angiosarcoma that is more frequent in young and middle-aged adults and often arises in the lower extremities. Orbital involvement has been reported in fewer than 10 cases in the literature [2].

Case Report

A 30-year-old male presented with a 1-year history of left-eye proptosis (5 mm) and hypoglobus. Corrected distance visual acuity was 20/20 for the right eye and 20/25 for the left eye. Tonometry and examinations of the anterior and posterior segments were unremarkable. Except for left small-angle esotropia, eye movements were normal. Magnetic resonance imaging showed a heterogeneous, well-defined intraconal mass in the left orbit with moderate enhancement after contrast injection (Fig. 1a). During the last year, the patient underwent lateral orbitotomy for tumor resection, but the 2 previous attempts failed due to massive intraoperative hemorrhage. Subsequently, the patient was referred for 4-vessel cerebral angiography, which described the lesion as a round, vascular mass with a diameter of 3 cm in the left retrobulbar region, supplied mainly by the left ophthalmic artery (Fig. 1b). Unfortunately, the patient did not come back within the next 2 months.

Afterwards, he returned due to progressive visual loss. Left corrected visual acuity was counting fingers at 4 m, and the relative afferent pupillary defect was positive. Left eye proptosis had increased to 10 mm, and eye movements were limited. A computed tomography (CT) scan showed tumor enlargement with a compressive effect on the left optic nerve (Fig. 1c). The patient was admitted for systemic corticosteroid pulse therapy (methylprednisolone 1,000 mg/day for 3 days). After steroid treatment, visual acuity improved to 20/200.

Then, the patient was referred to interventional neuroradiology for embolization of the feeder vessel of the tumor in hope of decreasing tumor vascularity and limiting the future intraoperative bleeding. The day after embolization, visual acuity in the left eye decreased to hand motions. Compared to the fellow eye, retinal venules were tortuous and slightly dilated. Hemorrhagic patches were evident in the temporal macula and inferior to the optic disc. Spectral domain optical coherence tomography showed a significantly increased reflectivity and loss of the lamellar structure in the inner retina. Details of the outer retinal architecture were not clear. These changes were more prominent in the central foveal area compared to the extrafoveal regions.

Surgical excision of the mass was suggested to the patient, who agreed and consented to the procedure. The patient also gave us permission for the use and publication of his photographs and pathologic and radiologic imaging results, and the consent is on

file. The tumor was totally excised via lateral orbitotomy and a concomitant transcoronal craniotomy approach. Histopathologic examination demonstrated a neoplasm composed of small nests and strands of bland epithelioid round cells with slight spindling around a few well-formed, small-sized blood vessels mostly in the periphery of the tumor. In most areas of the tumor, there were no obvious well-formed vascular channels, but some epithelioid cells showed intracytoplasmic vacuoles or lumina, with rare mitotic figures (<3 mitoses in 50 HPF). No necrosis, nuclear pleomorphism, or prominent atypia was identified (Fig. 2a, b).

Immunohistochemistry examination showed diffuse staining for vimentin, as well as diffuse and strong membranous staining for CD31 and CD34 markers in epithelioid endothelial cells (Fig. 2c, d). Staining was negative for melanocyte-A (ruling out melanoma), epithelial membrane antigen and pan-cytokeratin (excluding metastatic carcinoma), and CD68 and S100 (ruling out epithelioid nerve sheath tumors and histiocytic tumors). These findings were compatible with EHE. One week after surgery, visual acuity was counting fingers at 6 m, and an orbital CT scan revealed reduced proptosis (Fig. 3). After 2 months, visual acuity improved to 20/40, and the eye had normal fundus appearance.

Discussion

The term EHE was suggested by Weiss and Enzinger for the description of a biologically borderline vascular tumor with epithelioid appearance. This tumor is an intermediate entity between hemangioma and angiosarcoma and can be differentiated from these tumors clinically and histologically [1]. EHE often involves the deep soft tissues of adult patients and does not contain large, well-formed vascular channels, in contrast to epithelioid hemangioma [1]. EHE is usually angiocentric, with a low metastatic tendency and good prognosis. These characteristics distinguish EHE from angiosarcoma, which is associated with nuclear pleomorphism, a complex vascular pattern, necrosis, and high mitotic figures [1]. The most predictive feature for malignancy in EHE is the number of mitotic cells identified in histopathologic examination (higher risk in those with >3 mitotic figures in 50 HPF). However, the depth of the tumor and intravascular location are not reliable indicators for malignancy [1]. Because of the nesting and epithelioid appearance of the tumor in EHE, differential diagnoses such as epithelioid nerve sheath tumors, histiocytic tumors, metastatic carcinoma, and melanoma must be considered. In our case, immunohistochemistry findings excluded these alternative diagnoses.

The proposed treatment for EHE is complete resection with surgery. Extended surgery should be considered based on the location of the lesion, morbidity of radical surgery, and cosmetic result of the operation [1].

Fig. 1. **a** Magnetic resonance imaging showing a well-defined intraconal mass in the left orbit. **b** Angiography showing a round vascular mass, supplied mainly by the left ophthalmic artery. **c** Computed tomography scan showing a large intraconal tumor that has threatened the left optic nerve.

Fig. 2. **a, b** Hematoxylin-eosin-stained slides showing short strands and small nests of bland looking cells ($\times 100$ magnification) (**a**) and a small nest of epithelioid to spindle cells ($\times 400$ magnification) (**b**). **c** Immunohistochemical (IHC) staining shows diffusely positive reaction for CD31. **d** IHC staining shows diffuse positivity for vimentin.

Fig. 3. Orbital computed tomography scan 1 week after the last operation, showing considerable decrease in proptosis. The residual heterogeneous orbital lesion was hematoma, which resolved in the following weeks.

In a study that included 49 cases of EHE between 1989– and 2005, only 6 cases had lesions involving the head and neck region. Of these patients, 31 were treated with surgery alone and 15 were treated with chemotherapy and/or radiotherapy plus surgery. The results of this study indicated that pathologic findings including mitotic rate and tumor size can predict patient outcome and help physicians decide which patients require aggressive treatment [3].

Recently, a case of EHE was reported in a 22-year-old female that originated in the palpebral lobe of the lacrimal gland. The patient was treated by total tumor resection without adjunctive therapy [4].

An aggressive type of EHE has also been reported by some authors. In 1 case report, a 27-year-old patient pre-

sented with a large intracranial EHE that extended to the cavernous sinus and orbital apex. Despite wide tumor resection, the patient died 8 months later [5].

Chang et al. [6] reported an orbital tumor suspected to be EHE. Orbital exenteration was performed due to evidence of malignancy in the first pathology report [6].

Similarly, a 3.5-month-old infant was reported with a rapidly growing EHE causing involvement and destruction of the orbital bone. Transconjunctival biopsy was performed that led to significant blood loss (80 mL) during the procedure [7].

It seems that orbital EHE has more malignant presentation (including a faster growth rate and extension to orbital tissues) in comparison to EHE in other sites of the body.

Wallace et al. [8] reported a case of orbital hemangiopericytoma for whom endovascular embolization with n-butyl cyanoacrylate glue before surgery facilitated total resection of the tumor with minimal hemorrhage. In another case report, Puca et al. [9] presented an intracranial EHE whose first attempt for surgical tumor resection failed due to excessive bleeding. In the second surgery, 4 days after endovascular embolization and closure of the feeding arteries with special material, tumor resection was successful without significant hemorrhage.

Based on previous data, it seems that the best treatment for orbital EHE is complete surgical resection if possible. Angiography and intravascular embolization before surgery helps the procedure be performed without massive blood loss. However, the effectiveness of chemoradiation in orbital EHE has not been proved.

A major limitation of this study is the short-term follow-up of the patient. Due to the known potential of late recurrence of hemangioendotheliomas [10], long-term follow-up is typically recommended to assess the effec-

tiveness of the treatment. However, the patient did not follow the schedule of postoperative visits, and longer follow-up was not feasible.

Another significant problem in our case was retinal vascular accident. A reasonable scenario is that increased inflammation following embolization might have resulted in optic nerve compression with subsequent combined retinal vein and artery occlusion. However, there was excellent visual recovery, which is in favor of etiologies such as inflammatory compression rather than embolus with the glue used for endovascular intervention. An alternative possibility is that the occlusion has had a transient and incomplete nature and led to a favorable outcome.

In conclusion, this case was reported due to the rarity of EHE in the orbit, retinal vascular accident following intravascular embolization, and visual improvement without retinal sequela. In addition, the use of interventional endovascular treatment of the primary vascular supply of this tumor was an effective measure in the prevention of massive intraoperative bleeding.

Statement of Ethics

The Review Board and Ethical Committee of the Eye Research Center, Tehran University of Medical Sciences, Tehran, Iran, approved the study. We also state that it conforms to the provisions of the Declaration of Helsinki in 1995 (as revised in Edinburgh, 2000). Written informed consent was obtained from the patient following a complete explanation.

Disclosure Statement

The authors declare that they have no conflicts of interest to disclose.

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