Intravitreal bevacizumab (avastin) for circumscribed choroidal hemangioma

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Circumscribed choroidal hemangiomas are rare ophthalmic entities that cause diminution in vision due to accumulation of subretinal and/or intraretinal fluid in the macular area. Various treatment options ranging from conventional laser to photodynamic therapy have been employed to destroy the tumor and reduce the exudation; however, either the inability to penetrate through the exudative fluid or the collateral retinal damage induced by these treatment modalities make them unsuitable for lesions within the macula. We evaluated the role of intravitreal bevacizumab, a pan-vascular endothelial growth factor (VEGF) inhibitor, in reducing the sub- and intraretinal fluid in three patients with circumscribed choroidal hemangiomas. All the patients had complete resolution of the serous retinal detachment that was maintained till at least 12 months after the first injection. Intravitreal bevacizumab may be used in combination with thermal laser or photodynamic therapy in treating circumscribed choroidal hemangiomas with subretinal fluid.

Key words: Bevacizumab, circumscribed choroidal hemangiomas, photodynamic therapy, transpupillary thermotherapy

Choroidal hemangiomas are benign vascular tumors that sometimes present with visual impairment due to cystoid macular edema (CME), exudative retinal detachment, retinal pigment epithelium alterations or subretinal fibrosis. Circumscribed choroidal hemangiomas (CCH) are usually located in the macular and peripapillary region. Various modalities like cryotherapy, laser photocoagulation, plaque radiotherapy, proton beam irradiation, transpupillary thermotherapy (TTT), and photodynamic therapy (PDT) have been reported in literature for the treatment of CCH. Of late, bevacizumab has come up as a new treatment option in many retinal and choroidal vascular diseases. In this report we present our long-term experience with three cases of CCH treated with intravitreal bevacizumab.

Case Reports

Case 1

A 35-year-old man presented with gradual diminution of vision in his right eye in October 2005. His best corrected visual acuity (BCVA) was 20/200 in the right eye and 20/20 in the left eye. On examination he was found to have CCH in the macular area with serous retinal detachment involving the fovea, which
was confirmed with optical coherence tomography (OCT). As the patient could not afford PDT, TTT was performed. TTT was repeated in February 2006, with no improvement in the serous detachment and CME [Fig. 1a, b, and e]. After taking informed written consent, 1.25 mg of bevacizumab (Avastin) was injected intravitreally and was repeated after six weeks. Three months later, his BCVA improved to 20/100, with a marked decrease in the serous detachment and CME on OCT. At the 12-month follow-up, fundus fluorescein angiography (FFA) demonstrated only staining, without any leakage, and BCVA was maintained at 20/100 [Fig. 1c, d, and f].

Case 2
A 36-year-old man presented with gradual diminution of vision in his right eye since the past one month. His BCVA was 20/100 in the right eye and 20/20 in the left eye. On examination he was found to have CCH superotemporal to the fovea [Fig. 2]. As the lesion was extrafoveal, conventional laser photocoagulation was performed over the lesion. At the three-month follow-up, the patient had no improvement in BCVA, and FFA showed persisting leakage. OCT also demonstrated serous retinal detachment and CME. Intravitreal bevacizumab (1.25 mg) was injected twice, six weeks apart. Three months after the first injection his BCVA improved to 20/80, which was maintained at the 12-month follow-up. Similar to the previous case, OCT demonstrated a disappearance of the serous detachment, but showed persisting cystic changes, nasal to the fovea.

Case 3
A 40-year-old man presented with gradual diminution of vision in his right eye for the past five months. His BCVA was hand movements close to face in the right eye and 20/20 in the left eye. On examination he was found to have a large CCH, superonasal to the disc. OCT demonstrated serous detachment and intraretinal cystic spaces involving the macula [Fig. 3a-c]. He was treated with intravitreal bevacizumab (1.25 mg) injection as the primary treatment. At six weeks BCVA was unchanged and OCT demonstrated the absence of the serous detachment [Fig. 3d], but persisting intraretinal cystic spaces [Fig. 3e]. A second intravitreal injection of bevacizumab
Figure 3: Large choroidal hemangioma located superonasal to the disc in patient 3 (a) with subretinal fluid and intraretinal cysts seen more nasally on the OCT line scan (b). The lesion shows a characteristic mottled appearance on angiography (c). At the six-month follow-up, post injection, the macular edema has disappeared with the consolidation of macular exudates (d). The 12-month OCT shows absence of any subretinal exudation although intraretinal cysts are still present (e).

(1.25 mg), in combination with conventional laser photocoagulation was performed at that time. At the 12-month follow-up, [Fig. 3c], there was no further improvement in BCVA.

Discussion
Circumscribed choroidal hemangiomas are composed of endothelial cell lined thin-walled vessels that rarely increase in size and may remain quiescent for months or years.[3] As a result, treatment is usually considered when the patient suffers from vision loss. Confluent laser photocoagulation probably causes tumor destruction and a decrease in the serous retinal detachment.[5] However, visual complications from intense photocoagulation have essentially ruled it out as a modality to treat CCH involving the macular area.[6] TTT has also been reported to decrease both tumor size and the associated exudation, but the visual benefits in treated patients have been disappointing.[7] PDT has been shown to cause atrophy of the hemangioma vessels, thereby decreasing the leakage and associated vision loss in a series of patients.[8] Although PDT is emerging as the treatment of choice for circumscribed choroidal hemangiomas, the high expenses involved, limit the number of patients that can afford it, particularly in developing countries. In addition, PDT may not provide the desired results in larger tumors as well as significantly high retinal detachments overlying the tumor mass, due to limited penetration of the laser beam.

An increasing number of articles have reported favorable anatomic and functional results following the use of intravitreal bevacizumab in various choroidal and retinal vascular pathologies.[9] Being a pan-VEGF inhibitor it causes both regression of abnormal vessels as well as reduction of leakage from them. As the vision loss in choroidal hemangiomas is usually caused by sub- as well as intraretinal accumulation of fluid rather than by the tumor itself, any treatment modality that causes resolution of the fluid for a prolonged period of time will lead to a better functional gain.[9] Sagong et al, have recently documented sustained improvement in visual acuity using intravitreal bevacizumab in three cases of CCH, with serous retinal detachment involving the fovea.[9]

All three patients were given intravitreal injections within two weeks of decrease in vision and two patients further underwent PDT after one week, with good visual recovery and restoration of normal foveal architecture. In our series, the first injection of bevacizumab was administered after the macula had been detached for at least five months, due to either delayed presentation by the patient or initial treatment failure with conventional laser or TTT. Although there was complete resorption of the subretinal fluid in these patients, the intraretinal cystic changes were still present on the last visit, suggesting irreversible anatomic and functional damage to the fovea, precluding restoration of near normal visual acuity.

In conclusion, the results of the three patients treated so far suggest that intravitreal bevacizumab can cause complete resolution of leakage from a choroidal hemangioma that is sustained for a significant period. It may be used as a primary mode of treatment, especially for subfoveal lesions, or as a means to decrease the height of the overlying fluid so as to make laser photocoagulation or TTT more effective in extrafoveal tumors. Further studies with larger number of patients and longer follow-up are required to confirm these findings.

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A 16 year old girl with no contributory medical illness presented with irritation and watering of the right eye for 3 months. She had noticed a progressively increasing black mass above her right eye for 6 months prior to presentation. There was no history of pain, redness, discharge or sudden increase in the size of the mass. The history of trauma with a stick, absence of history of any dermatological disease and lack of any pre-existing ocular pathology were noted.

Clinical examination revealed a right eyelid mass measuring 8 × 10 mm with incarceration of uveal tissue. The right eye was hypotropic. Her cornea had a 9-mm vertical meridian astigmatism (Ds) and 20/20 (L). Elevation of the right eye was mildly restricted and the eye was hypotropic. She did not complain of diplopia. Other ocular movements were normal. Her cornea was clear. The superior perilimbal area showed ectatic sclera with a 1 mm margin except at the limbus where it was cut off at a distance of 5 mm from the limbus. The remainder of the anterior segment and fundus was normal. Keratometry was not done. Clinical examination and slit-lamp examination of the right eye revealed a marked bulbar conjunctival involvement. Lacrimal fossa showed no visible mass and syringing of the nasolacrimal duct was normal. Left eye examination was normal. Rigid nasal endoscopy of the nasal cavity showed normal nasal mucosa with no lesions.

The presumptive diagnosis was upper respiratory infection. The presence of spumous material on the nasal mucosa was noted. A biopsy of the nasal mucosa for histopathological examination was done and it showed subepithelial spherules of sporangia containing numerous endospores, suggestive of rhinosporidiosis. Diathermy was applied to flatten the staphyloma. The ectatic area was covered with a corneal patch graft. The patient was started on antimicrobial therapy using verteporfin. Arch Ophthalmol 2001;119:1606-10. Thermotherapy for circumscribed choroidal hemangiomas. Ophthalmology 2000;107:351-6.

It was regarded as a sporozoan by Malbran in 1892, as Mesomycetozoa. Through molecular biological analysis of the ribosomal DNA, Herr et al, classified the organism into a new clade named Rhinosporidium seeberi. It has been described in the literature. There have been 12 cases of scleral melt associated with bulbar conjunctival involvement. Bulbar conjunctival involvement has been described in 7.3% and 12.4% of cases.

Intraoperatively, the involved conjunctiva was excised to a probable diagnosis of ocular rhinosporidiosis. Hence, she was advised conjunctival biopsy and patch graft over the involved conjunctival area. A Tectonic corneal graft for conjunctival rhinosporidiosis with scleral melt was performed. The incision was performed along the limbus in the involved area and was cut to a depth of 1.5 mm. A 9-mm button of donor cornea was chosen from the temporal side of the right eye. The button was cut to fit the recipient bed. The host cornea was cut to a depth of 1 mm using a 7-mm trephine. The host bed was then cut as an annulus to the donor button size. The donor button was sutured to the recipient bed using interrupted 10-0 nylon sutures. The graft was well incorporated and conjunctivalized by 3 months. Since the graft was not seen within the palpebral aperture, there was good cosmetic result. The corneal graft had no recurrence at 6 months.

Key words: Rhinosporidiosis, scleral melt, tectonic graft.