Propranolol for Isolated Orbital Infantile Hemangioma

Infantile hemangioma is the most common benign solid tumor of the ocular adnexa of children, causing significant functional and cosmetic deformity, with a 43% to 60% incidence of astigmatic or occlusion amblyopia when either the eyelid or orbit is affected.1,2 In cases involving the orbit, there can be proptosis, displacement of the globe, exposure keratopathy, compressive optic neuropathy, and strabismic amblyopia.3 Numerous modalities have been used to treat infantile hemangioma, but no single uniformly safe and effective method has yet been found. Léauté-Labréze et al3 recently discovered that propranolol can inhibit growth and cause regression of segmental infantile hemangioma without any serious adverse effects. We report the successful use of systemic propranolol in an infant who had an isolated, extensive, and deep orbital infantile hemangioma.

Report of a Case. A healthy 4-month-old female infant had experienced progressive painless protrusion of the right eye for 3 months. Examination revealed axial proptosis of the right globe along with fullness of the eyelids (Figure 1A). A relative afferent pupillary defect was not detected. Magnetic resonance imaging revealed a predominantly intracanal mass replacing the orbital fat, pushing the globe forward but not distorting the optic nerve (Figure 1B). A biopsy was obtained through an inferior transconjunctival orbitotomy. A hypercellular tumor was composed of variably sized lobules replacing most of the orbital fat except for a scattering of surviving adipocytes (Figure 2A and B); the endothelial cells also expressed glucose transporter isoform 1, a marker for infantile hemangioma (Figure 2D). Propranolol treatment was initiated at a dosage of 2 mg/kg/d intravenously for 5 days and then continued at home at the same dosage by oral administration. At the 6-week follow-up visit, there was no obvious proptosis (Figure 1C). Repeated magnetic resonance imaging at the 3-month visit revealed complete resolution of the orbital tumor with restoration of an unremarkable retrobulbar fat pattern (Figure 1D). Our patient was treated with propranolol until 1 year of age (treatment for 8 months). Propranolol was then tapered over a 1-month period, and the patient experienced no adverse effects or regrowth at the 9-month follow-up.

Comment. Direct interventional treatments for infantile hemangioma such as local corticosteroid injection,
laser therapy, embolization, and surgery, while suitable for superficial and subcutaneous lesions, are sometimes problematic in deep orbital cases primarily because of poor access and risk of injury to the optic nerve and extraocular muscles. Traditional pharmacologic treatment with systemic corticosteroids can be efficacious but may be accompanied by significant systemic adverse effects. Other agents such as vincristine sulfate and cyclophosphamide are less predictable and potentially more dangerous than corticosteroids; we have abandoned interferon alfa altogether in this patient population because of neurotoxicity. Propranolol could represent a new pharmacologic approach to the treatment of deep orbital and/or periocular infantile hemangioma with many potential advantages.

Of 11 patients with infantile hemangioma described by Léauté-Labrèze and colleagues, 7 displayed periocular disease, 1 of whom had orbital involvement. This patient failed to show regression after the earlier administration of systemic corticosteroids (discontinued after 4 months). Within 3 days of the introduction of propranolol, blanching, softening, and early regression of the visible cutaneous lesions occurred. Propranolol was maintained for 3 months in this patient. All of the patients in the series experienced resolution of their hemangiomas without any rebound growth on cessation of propranolol.1

In rare instances, propranolol can cause transient hypoglycemia, bradycardia, and hypotension; bronchospasm can be seen in patients with underlying reactive airway. These risks can be managed anticipatorily by obtaining a pediatric pretherapy evaluation, by monitoring vital signs and blood glucose levels at initiation and throughout therapy, and by maintaining frequent pediatric follow-ups. Doses of propranolol can be administered intravenously or orally. Treatment responses are typically determined by clinical examination, but deep isolated lesions may require repeated magnetic resonance imaging. Discontinuation of therapy through tapering of propranolol over a 2-week period is said to be unnecessary but may minimize the risk of a hyperadrenergic withdrawal response. As exemplified in this case, propranolol is highly promising as an alternative pharmacologic agent and, based on nonophthalmic experience, may emerge as the preferred tool for the treatment of deep orbital and other inaccessible infantile hemangiomas.

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Ocular Involvement by Epstein-Barr Virus-Positive Diffuse Large B-Cell Lymphoma of the Elderly: A New Disease Entity in the World Health Organization Classification

The new World Health Organization classification of lymphoma places great emphasis on the definition of real biological disease entities in the category of diffuse large B-cell lymphoma (DLBCL). Epstein-Barr virus (EBV)–positive DLBCL of the elderly is a new subtype of DLBCL according to the 2008 World Health Organization classification. This is an extremely rare tumor, and no case of ocular EBV-positive DLBCL of the elderly has been reported to our knowledge. Here we describe the first case of EBV-positive DLBCL of the elderly with involvement of the eyelid and orbit.

Report of a Case. An 83-year-old woman was referred with an eyelid tumor of her left eye. Serologically, human immunodeficiency virus antigen and anti–human T-cell lymphoma virus 1 antigen were both negative. The left upper and lower eyelids were affected by a hyperemic tumor with a rough surface and a small scab, which caused ectropion (Figure 1A and B). Physical examination revealed that her left submandibular, parotid, and cervical lymph nodes were enlarged. Staging examination showed that she had stage III B-cell malignant lymphoma according to the Ann Arbor classification. Orbital magnetic resonance imaging revealed a cystic mass in the left periorbital region, invading the orbit and anterior ethmoid sinus (Figure 1F and G). Incisional biopsy of the left eyelid lesion was performed, revealing a tumor composed of pleomorphic large cells and marked by the presence of mononuclear Hodgkin-like cells and multinucleated Reed-Sternberg–like cells (Figure 2A and B). Immunohistochemistry revealed that the tumor cells expressed CD20 (Figure 2C), Pax-5 (Figure 2D), CD30 (Figure 2E), and multiple myeloma oncogene 1 protein (not shown). The tumor cells were also positive for latent membrane protein 1 (Figure 2F) but negative for EBV nuclear antigen 2 (not shown), indicating that the EBV infection pattern in this case was type 2 latency. Staining results for CD5, CD10, and the follicular B-cell lymphoma marker bcl-6 were negative (not shown). Based on these findings, a diagnosis of EBV-positive DLBCL of the elderly was made according to the new World Health Organization lymphoma classification. Cervical lymph node involvement was also confirmed by biopsy. Immediately after the biopsy, the patient received standard chemotherapy with rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone, followed by rituximab and

Figure 1. Images from a patient with Epstein-Barr virus–positive diffuse large B-cell lymphoma of the elderly. A and B, Before starting chemotherapy. C and D, After completion of chemotherapy. E, Positron emission tomography confirms marked left orbital uptake. There is also uptake in the spleen, mediastinum, and involved lymph nodes. F and G, Orbital magnetic resonance imaging shows a cystic mass in the left periorbital region that invades the orbit and anterior ethmoid sinus and is accompanied by eyelid ulceration. The mass shows heterogeneous low signal intensity on a T1-weighted axial image (F) and high signal intensity on a T2-weighted axial image (G).