Severe Periorbital Edema Secondary to Imatinib Mesylate for Chronic Myelogenous Leukemia

A 70-year-old man developed severe periorbital edema secondary to imatinib mesylate (Gleevec; Novartis Pharmaceuticals Corp, East Hanover, NJ). Imatinib mesylate is a tyrosine kinase inhibitor with a high degree of specificity for the BCR-ABL, KIT, and platelet-derived growth factor receptor β tyrosine kinases. It is thought that inhibition of platelet-derived growth factor receptor β results in disruption of fluid homeostasis in the eyelids, resulting in the development of periorbital edema.

Report of a Case. A 70-year-old man developed mild periorbital edema within 2 weeks of starting imatinib mesylate at 400 mg per day for treatment of BCR-ABL–positive chronic myelogenous leukemia. Three months later, the patient developed accelerated-phase chronic myelogenous leukemia and his imatinib mesylate dose was increased to 600 mg per day. His periorbital edema became significantly worse and visually disrupting. The patient was unresponsive to conservative therapy, including following a low-salt diet, restricting fluid intake, elevating the head of his bed, and using hydrocortisone cream, and was subsequently referred for bilateral upper and lower eyelid blepharoplasty.

At the time of his first examination, his visual acuity was 20/25 OD and 20/40 OS. His intraocular pressure was 18 mm Hg bilaterally. There was no clinical evidence of intraocular involvement by his leukemia. The anterior septal tissue of the upper and lower eyelids was markedly distended bilaterally (Figure 1 A). There was a visually disrupting superior field defect that disappeared with taping of the eyelid bilaterally. The patient illustrated a functional field defect that was treated definitively with bilateral upper and lower eyelid blepharoplasty. Postoperative bleeding was extensive, requiring blood transfusion, and was attributed to thrombocytopenia secondary to his leukemia.

By light microscopy, the lower eyelid skin was edematous (Figure 2 and Figure 3). There was a mild increase in dermal epithelioid histiocytic cells and dermal dendrocytes. Immunoperoxidase studies were performed on paraffin-embedded tissue sections with antibodies to KIT (Dako, Carpinteria, CA), S100 (Dako), and CD1a (Immunix, Marseille, France). The dermal dendrocytes were immunoreactive with antibodies to KIT. S100 immunostain highlighted dermal nerve twigs. CD1a immunostain highlighted Langerhans cells. The diagnosis was marked periorbital edema associ-
ated with the use of imatinib mesylate.

Treatment with imatinib mesylate for BCR-ABL–positive chronic myelogenous leukemia was continued following blepharoplasty. Seventeen months following blepharoplasty, the patient continued treatment with imatinib mesylate at 600 mg per day. There has been no recurrence of periorbital edema (Figure 1B).

Comment. Imatinib mesylate is a selective signal transduction inhibitor showing a high degree of specificity to the pathologic BCR-ABL tyrosine kinase as well as normal KIT and the platelet-derived growth factor receptor tyrosine kinase family. This drug inhibits proliferation and promotes apoptosis in BCR-ABL cell lines. A promising treatment for chronic myelogenous leukemia and gastrointestinal stromal tumors, imatinib mesylate is generally well tolerated. Fluid retention, superficial and periorbital edema, nausea, vomiting, myalgia, fatigue, skin rashes, diarrhea, and hepatotoxicity are reported as the most common clinical adverse effects of imatinib mesylate. Periorbital edema has been reported in up to 70% of patients treated with imatinib mesylate.

Platelet-derived growth factor receptor β is thought to regulate tissue fluid properties and is avidly expressed on the dermal dendrocytes of periorbital tissue. Studies have shown that inhibition of platelet-derived growth factor receptor β in dermal dendrocytes by imatinib mesylate increases interstitial fluid pressure in the dermis, predisposing to edema. The lack of structural support in periorbital tissue, particularly the lower eyelids, makes it exceptionally vulnerable to localized edema.

Our patient was treated definitively with bilateral blepharoplasty, rather than biopsy, because of a significant field defect. Immunohistochemical studies showed that dermal dendrocytes were positive for KIT, suggesting the periorbital edema in this patient was secondary to imatinib mesylate.

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During the past century this country has passed through five important wars, but separate ophthalmic departments in medical services were organized only in the two world wars. The ophthalmologists who manned these departments in each war were volunteers, not draftees. For the great sacrifices these men made, it cannot be said that on their return to civilian life they were overwhelmed by the gratitude of those who had remained at home. A truthful account of the efficiencies and inefficiencies of the ophthalmic services in the two world wars would no doubt be of considerable interest, but is beyond the scope of this address, since these services contributed nothing of importance to the advancement of ophthalmic science, greatly as they contributed to the welfare of our armed forces.