context of a known heritable condition, the heparin dose can be adjusted, as was done in our patient. In highly suspicious cases (or those with a previous adverse event), treatment modalities other than OAC may need to be considered. As OAC is adopted more widely, it is important for clinicians to be aware of these prothrombotic states, the adverse events associated with them, and how to prophylactically manage them.

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Epidermal Growth Factor Receptor Inhibitors for Treatment of Orbital Squamous Cell Carcinoma

Orbital and periorbital squamous cell carcinomas (SCCs) are treated with surgical resection as the primary modality and radiation therapy as adjuvant treatment in patients with perineural invasion or concerns for microscopically positive margins. For advanced cases, extensive surgery such as orbital exenteration may be needed to fully exirpate the tumor. Orbital exenteration leads to loss of the eye and significant facial disfigurement but has the potential to produce long-term cure. The extensive surgical treatments required for advanced cases of orbital and periorbital SCC entail long periods of general anesthesia and inpatient hospitalization; thus, in patients with poor performance status, advanced age, or multiple medical comorbidities, surgery may not be the best option.

Several epidermal growth factor receptor (EGFR) inhibitors have recently been developed and have shown efficacy in treatment of non-small cell lung cancer, pancreatic cancer, colon cancer, and mucosal head and neck squamous cell carcinomas. 1-3 We herein report 2 elderly patients with recurrent advanced orbital SCC who were treated with EGFR inhibitors—erlotinib, an oral tyrosine kinase inhibitor, and cetuximab, a monoclonal antibody—and had striking initial responses to this treatment.

Report of Cases. Case 1. A 90-year-old woman with a history of SCC of the left lateral canthus that had been excised at another institution 2 years prior presented with a firm orbital mass causing proptosis, displacement of the globe, and severe orbital congestion and pain (Figure 1A). On examination, she had decreased vision, limited ocular motility, and choroidal striae. There was also a palpable mass in the parotid gland on the left side.

Computed tomography confirmed the presence of a mass with an orbital component measuring 3.2×3.1×4 cm and a zygomatic component in the masticator space measuring 4.2×2.3×2.5 cm (Figure 2A). The mass eroded through the orbital floor and inferolateral wall of the orbit and extended into the inferior orbital fissure posteriorly. Also, the patient had a mass in the parotid gland measuring 1.5×1.2 cm, consistent with a probable metastasis.

Biopsies of the orbital mass and the parotid mass were consistent with invasive SCC. We discussed with the patient the standard treatment: a wide surgical resection, including an orbital exenteration with removal of the extension of the tumor in the temporalis fossa and masticator space; a parotidectomy; an ipsilateral neck dissection; a free-flap reconstruction of the orbital socket; and postoperative high-dose radiation therapy. The patient declined surgery because of her advanced age and her multiple medical comorbidities.

She was referred to the Department of Medical Oncology for consideration of palliative chemotherapy and biologic therapies. She was prescribed 150 mg of oral erlotinib (Tarceva) daily. The patient reported that within 4 weeks of initiation of therapy, her orbital pain resolved and she experienced marked improvement in orbital congestion and ocular motility. She returned for her first follow-up visit 12 weeks after initiation of erlotinib therapy and was noted to have a remarkable improvement in her clinical findings (Figure 1B) and improved visual acuity from counting fingers before treatment to 20/80. She also had significant reduction in tumor size as measured with repeated computed tomography.
She tolerated erlotinib well and denied any significant adverse effects. The parotid metastasis, despite an initial response, started to enlarge during subsequent weeks; thus, the dose of erlotinib was increased to 200 mg daily, after which the size of the parotid mass decreased. At the time of this report, the patient had been receiving 200 mg of erlotinib daily for 11 months after initiation of therapy and had stable disease and no significant adverse effects.

**Case 2.** An 81-year-old man with a distant history of excision of a skin carcinoma on his left cheek presented with left-sided chemosis, periorbital edema, and proptosis. On examination, he had mildly decreased vision and limited ocular motility. Computed tomography confirmed the presence of a destructive orbital, maxillary sinus, and zygomatic mass (Figure 3A). A biopsy specimen of the orbital mass showed invasive SCC. We discussed with the patient the standard treatment: a wide surgical resection, including an orbital exenteration with removal of the extension of the tumor in the maxillary sinus; a skull base dissection; a free-flap reconstruction of the orbital socket; and high-dose postoperative radiation therapy. The patient declined surgery because of his advanced age, multiple medical comorbidities, and concern expressed by the neurosurgical service that the posterior extension of the mass might be unresectable.

He was prescribed intravenous cetuximab (Erbitux). He received a 400-mg/m² loading dose followed by a 250-mg/m² dose weekly. At 6 weeks after initiation of therapy, he was noted to have an improvement in his clinical findings and a decrease in the size of the orbital mass on computed tomography (Figure 3B). He had a skin reaction that necessitated a break in his treatment for 1 week, but at the time of this report, 4 months after diagnosis, the patient had denied any other significant adverse effects and had continued improvement in the size of his orbital mass.

**Comment.** The 2 patients presented in this article highlight the potential utility of EGFR inhibitors such as erlotinib and cetuximab in patients with advanced SCC of the orbit who refuse to have an orbital exenteration or in whom surgery may not be a great option because of advanced age or multiple medical comorbidities. Both patients had a dramatic reduction in the size of their orbital SCC. Both patients also demonstrated significant improvement in ocular motility and orbital congestion and demonstrated resolution of orbital pain. The reason for choosing erlotinib for one patient and cetuximab for the other was because of insurance coverage for one drug and not the other by the 2 different insurance carriers for the 2 patients described in this report.

Epidermal growth factor receptor inhibitors may make sense for ocular surface and orbital SCCs since EGFR inhibitors have shown efficacy in treatment of head and neck SCC and skin SCC. Our group has previously shown expression of EGFR in ocular squamous carcinomas. It is important for patients and their family members to understand the investigational and off-label nature of oral EGFR inhibitors for treatment of orbital SCC. While we have observed evidence of activity for EGFR inhibition in these 2 patients, overall response rates and expected response duration in this
setting are not known. Further study of this approach is indicated. There also is the potential for treatment-related toxic reactions, hypersensitivity, folliculitis, diarrhea, and fatigue. Admittedly, the follow-up time for our patients is relatively short. Nonetheless, these patients experienced a significant improvement in their quality of life, indicating that oral erlotinib or intravenous cetuximab is a reasonable option for pal-

Figure 2. Computed tomography scans of patient 1 before and after treatment with erlotinib. A, Computed tomography scan of patient 1 at presentation demonstrating a bilobed mass in the left inferior orbit and temporalis fossa. B, Computed tomography scan of the same patient following 3 months of treatment with erlotinib demonstrating significant reduction in tumor size.

Figure 3. Computed tomography scans of patient 2 before and after treatment with cetuximab. A, Computed tomography scan of patient 2 at presentation demonstrating a mass in the left lateral orbit, maxillary sinus, and zygoma. B, Computed tomography scan of the same patient following 2 months of treatment with cetuximab demonstrating significant reduction in tumor size.
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