Additional Information: A subset of the participants was ascertained while Dr Pericak-Vance was a faculty member at Duke University, Durham, North Carolina.

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Periorbital and Ocular Necrobiotic Xanthogranuloma Leading to Perforation

Necrobiotic xanthogranuloma (NXG) is a rare granulomatous disease of unknown cause often associated with paraproteinemias, particularly IgG monoclonal gammopathies, including multiple myeloma. Cutaneous involvement is universal with a predilection for the periorbital region; typical lesions are indurated, yellow papules and plaques accompanied by central ulceration and atrophy. We report an unusual clinical course of NXG involving periorbital and ocular tissues that resulted in corneal perforation.

Report of a Case. A 73-year-old woman was initially diagnosed with NXG after biopsy of a periorbital lesion by her ophthalmologist. A corneal ulcer from exposure keratitis related to poor eyelid closure had been successfully treated in the right eye. When examined at Mayo Clinic, best-corrected visual acuities were 20/60 OD and 20/50 OS (Figure 1). Hematologic evaluation including bone marrow biopsy revealed multiple myeloma, and treatment with lenalidomide and dexamethasone was begun.

Two months later, the patient returned with a 2-week history of worsening vision, pain, and corneal ulceration. The right eye had no light perception and the left eye had light perception with projection. Examination showed extensive progression of the cutaneous NXG with loss of preseptal tissue but sparing of pretarsal tissue; the tissues were secondarily infected with multiple microbes. All eyelids were immobile, resulting in exposure keratopathy. The right cornea was superin-

Figure 1. Clinical photographs. A, At the initial consultation, necrobiotic xanthogranuloma of the periorbital tissues was evident with mild exposure keratopathy. Palpebral fissures measured 7 mm in both eyes, and there was 3 mm of lagophthalmos in the right eye and 2 mm of lagophthalmos in the left eye. B, Two months later, the periorbital necrobiotic xanthogranuloma had markedly progressed, with necrosis of the preseptal tissues and sparing of the pretarsal tissues. The right malar eminence and left orbital rim were exposed. The eyelids were immobile, resulting in severe bilateral exposure keratopathy. C, The right globe was perforated with endophthalmitis. D, The left eye was finally treated by a buccal membrane graft and a Boston type II keratoprosthesis after multiple procedures to manage exposure of the ocular surface had failed.
fected and perforated, and the left cornea was opacified inferiorly, presumably from infection (Figure 1). After beginning systemic and topical antibiotic treatment, the right globe was enucleated and the periorbital tissue debrided. The left eye required several procedures to cover the exposed cornea, including conjunctival flaps and amniotic membrane grafts; finally, a buccal mucosal graft was required because the conjunctival flaps became necrotic. Adjuvant systemic therapy throughout this course included 2-chlorodeoxyadenosine (or cladribine) and hyperbaric oxygen, with significant improvement of the cutaneous disease. The left eye received a buccal mucosal graft with a Boston type II keratoprosthesis 10 months after her initial visit to us, resulting in best-corrected visual acuity of 20/60 (Figure 1).

Histologic examination of the periorbital tissues confirmed NXG. The enucleated right eye showed extensive necrobiosis of the sclera, surrounded by palisaded and multinucleated giant histiocytes with occasional multinucleated giant cells (Figure 2). The cornea was perforated and endophthalmitis was present. The left cornea, excised during keratoprosthesis surgery, showed focal necrobiosis with minimal acute inflammation suggestive of NXG).

Comment. Necrobiotic xanthogranuloma is a rare disease that was first described by Kossard and Winkelmann in 1980.

Necrobiotic xanthogranuloma affects both sexes equally and typically manifests in the sixth decade of life. The disease has a predilection for the periorbital region and in 80% to 90% of patients is associated with paraproteinemias. The pathogenesis remains unknown. The differential diagnosis for NXG includes necrobiosis lipoidica, xanthogranuloma, Erdheim-Chester syndrome, erythema induratum of Bazin, foreign body granuloma, and sarcoidosis.

Previous reports of NXG suggest a broad spectrum of ocular involvement including scleritis, episcleritis, and keratitis, but none have documented such involvement by histopathologic analysis. The histopathologic analysis in our case showed NXG extensively involving the sclera of the enucleated right eye; although not diagnostic, left corneal involvement by NXG was suggested by the presence of necrobiosis without significant acute inflammation. Involvement of the ocular tissues by NXG might have contributed to failure of the conjunctival flaps. Our case demonstrates that aggressive periorbital and ocular NXG can result in loss of vision and the eye. Visual rehabilitation was complex and required multiple procedures prior to placement of a Boston keratoprosthesis, and systemic treatment with cladribine was associated with significant improvement and control of the disease.

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