blood serum. A diagnosis of GO was made. After resolution of inflammatory symptoms, the eyelid retraction was surgically corrected.

Case 2. A 35-year-old woman with primary hypothyroidism, had subacute eyelid swelling, proptosis, eye- ball motility restriction, and pain. On CT, the right lacrimal gland appeared enlarged; biopsy of the gland revealed lymphoid cells. She was treated for IOI (dacryoadenitis) with intravenous, high-dose methylprednisolone sodium succinate. Four years later she was treated for dacryoadenitis on the left side (Figure, C) with intravenous steroids.

Four months after that treatment, she had developed diplopia and left upper eyelid retraction. Computed tomography revealed left-sided extraocular muscle enlargement (Figure, D). Thyroid antibodies were found in her blood serum, and she was diagnosed as having unilateral GO. To improve eyelid motility, she was treated with radiotherapy.

Case 3. A 30-year-old man with diabetes mellitus, Crohn disease, and hyperthyroidism, had bilateral painless proptosis, eyelid motility disturbances, and upper eyelid retraction. The extraocular muscles appeared enlarged on CT, and thyroid antibodies were found in his blood serum, which yielded a diagnosis of GO. The disease resolved itself without therapy.

At the age of 39 years, the patient developed proptosis on the left side with eyeball motility disturbances. Two months later the right side had become involved as well. Computed tomography revealed lacrimal gland enlargement, and a biopsy specimen showed chronic inflammation. A diagnosis of IOI (dacryoadenitis) was made, and the patient was treated with oral prednisone.

Case 4. A 22-year-old man, had left-sided proptosis, eyeball motility disturbances, and pain. Computed tomography revealed a mass in the medial superior orbit (Figure, E). The lesion was biopsied twice, which revealed fibrosis with some lymphocytes. He was diagnosed as having IOI and treated with radiotherapy and oral prednisone.

At the age of 27 years, he developed progressive proptosis of the left eye and extraocular muscle enlarge-
**Case 1.** An otherwise fit 53-year-old man was referred with slowly progressive left upper eyelid notching for 9 years, ipsilateral supraorbital hypoesthesia for 6 years, and diplopia for 3 years; the left eye was amblyopic from childhood squint. Results from investigations for thyroid disease and myasthenia as well as 2 magnetic resonance imaging scans had been reported as normal and—ignoring the eyelid distortion and cranial hypoesthesia—strabismus surgery was performed. The patient was referred to Moorfields Eye Hospital when his symptoms failed to resolve.

At his initial visit with us, his visual acuity was 20/20 OU and he had no optic nerve dysfunction or intraocular disease; 1-mm left relative proptosis was evident, with ipsilateral hyperphoria, reduced vertical ductions, and supraorbital, supratrochlear, and nasociliary hypoesthesia. The left upper eyelid was peaked and retracted (Figure 1A), with localized skin thickening and distorted tarsus but no madarosis. No orbital mass or lymphadenopathy was detected. Computed tomography revealed an ill-defined superolateral soft-tissue mass involving the superior rectus-levator complex and extending into the cavernous sinus through the superior orbital fissure (Figure 1B). Excision of the eyelid notch and deep orbital biopsies showed an infiltrative malignant neoplasm in a desmoplastic stroma, with nests and strands of epithelial cells showing focal perineural infiltration (Figure 2A and B). Mild cytological atypia and rare mitoses were present. With a diagnosis of MAC, the patient was referred for palliative radiotherapy.

**Case 2.** A fit 24-year-old woman was referred with progressive right lower eyelid thickening for 7 years, the lesion having been treated as a chalazion following uninformative biopsy 2 years prior to referral. Topical therapy and intralesional steroids were unsuccessful and development of eyelid retraction prompted referral.

Visual functions, globe positions, and ocular ductions were normal on referral. The right lower eyelid margin was thickened medially with pearly changes, telangiectasia, and mild eyelash distortion. There was a subcutaneous mass overlying the lower eyelid retractors (Figure 3A) and MAC was favored on clinical grounds: eyelid and retractor biopsies revealed a dense desmoplastic stroma pervaded by numerous small ducts with occasional tadpole-like morphology and accompanied by bland epithelial cells located within the superficial dermis (Figure 2C). No cytological atypia or mitotic activity was present, but there was an infiltrative growth pattern with early perineural involvement; tumor cells were positive for the epithelial markers BerEP4 and CK7. After Mohs micrographic excision, the area was repaired with a hard palate mucosal graft and a Mustardé cheek rotation flap. Neurogenic ptosis developed 10 months after surgery, with ipsilateral mydriasis and decreased eye movements (Figure 3B). Computed tomography showed patchy opacification from the right cheek to the orbital apex (Figure 3C) and biopsies confirmed extensive tumor infiltration. The patient underwent orbital exenteration and fractionated external beam radiotherapy; tumor was present at the posterior margins of resection.

**Case 3.** A 70-year-old man had slowly progressive right lower eyelid thickening for several years. There were 2 firm intradermal nodules in the medial part of the eyelid but no madarosis, telangiectasia, ulceration, or periocular sensory loss. Right upgaze was reduced and computed tomography revealed an enhancing soft-tissue mass involving the cheek, lower eyelid, and inferior oblique and rectus muscles. Biopsy showed MAC with a slightly hyalinized desmoplastic stroma containing fine sheets and aggregates of epithelial cells with large, atypical nuclei and prominent nucleoli but no mitotic activity; the epithelial cells stained with BerEp4 and CK7. The patient underwent orbital exenteration.
Comment. Microcystic adnexal carcinoma is a rare skin tumor of pilar and eccrine differentiation; the etiology is unknown, although cases have been described after radiotherapy or immunosuppression. As in our cases, MAC progresses insidiously and is often missed for years before diagnosis. The tumor may manifest as yellow or flesh-colored nodules, as ill-defined plaques, or with relentless eyelid distortion; skin telangiectasia may be present but ulceration or madarosis is rare. Microcystic adnexal carcinoma often shows intraneural and perineural infiltration, and eyelid distortion with pain or periorcular numbness should alert the clinician to this diagnosis. Likewise, progressive multiple cranial nerve deficits over years (as in case 1) should always alert a physician to the likelihood of an insidious malignant neoplasm such as MAC.

Histological confirmation of MAC is difficult—the minimal cellular atypia giving it a bland appearance—and such tumors may be thought to be benign or may be missed entirely (as in case 2 before referral). Inadequate tissue sampling may result in less than 10% diagnostic yield. Eyelid distortion and retraction are caused by an eosinophilic desmoplastic reaction containing eccrine ducts or keratinized cysts that resemble commas or tadpoles, and perineural invasion is an important diagnostic feature. Although MAC does not have a unique immunophenotype, staining with BerEP4, CK15, and CK7 helps differentiate MAC from desmoplastic trichoepitheliomas, infiltrative basal cell carcinoma, and squamous ductal carcinoma.

Treatment options for periorcular MAC include wide local excision, Mohs micrographic surgery, and radiotherapy. Perhaps reflecting the infiltrative nature of MAC, small series using Mohs surgery have shown a lower recurrence rate (0%-12%) as compared with en bloc ex-
cision (30%-47%). Toluidine blue staining during Mohs clearance helps highlight tumor strands and perineural invasion. Exenteration is advised for perineural or orbital infiltration, and palliative or adjunctive high-dose radiotherapy may be used. Despite its invasive nature, periorcular MAC has a fairly good prognosis, with only 7 cases of metastasis and 1 death reported. Intracranial invasion has been reported, and its presence in 2 of our patients must limit their chance of cure (cases 1 and 2).

Relentless eyelid retraction (in the absence of thyroid dysfunction) or distortion should always be regarded as tumor-induced fibrosis until proven otherwise. Adequate biopsy specimens must be taken and the histopathologist should be alerted to the diagnosis of MAC. In particular, there should be a specific request to search for sparse epithelial cells within deep tissues or dense fibrosis—the presence of which is likely to confirm this diagnosis.

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