A 77-year-old woman consulted an ophthalmologist because her left eye had “turned black” during the last 6 to 9 months. In addition, she felt that her eye was “sinking in the orbit.” Visual acuity was reduced to 20/30. The right eye was normal with 20/20 vision. The nasal, temporal, and especially, the upper conjunctiva (Fig 1A) of her left eye contained literally myriad dark brown pigment deposits that also extended to the eyelid skin at the upper lid margin (Fig 1A; arrowheads) and to the cornea (Fig 1A; double arrowhead). On eversion of the upper eyelid, the tarsal conjunctiva was found to be involved (Fig 1B). In its central area, the pigment deposits formed a confluent, nonelevated patch (Fig 1B; arrowhead). One month later, an ocular oncologist confirmed that the melanosis was confined to the conjunctival epithelium and had not caused conjunctival thickening. The eyelid crease was inconspicuous, suggesting ptosis. The diagnosis was primary acquired melanosis of the conjunctiva with atypia. Close follow-up was recommended. The patient was reviewed for conjunctival thickening at 2- to 6-month intervals for a year and a half, during which time the melanosis progressed with waxing and waning; the deposits decreased in some areas (Fig 1C; arrowheads) and increased in others (Fig 1D; arrowhead). Because of the extent of the melanosis, it could not be removed by surgery. Cryotherapy and irradiation were also impractical. Topical chemotherapy, 0.2 mg/mL mitomycin diluted in commercial artificial tears four times a day, was consequently started. Two-week-long courses separated by an interval of 3 weeks were planned. The eye became irritated during the second course, which was stopped after 1 week. The irritation disappeared quickly with a topical corticosteroid preparation. The melanotic areas gradually regressed and the pigment deposits rarefied. The patient was reviewed for the last time 14 months after start of chemotherapy, by which time the bulbar conjunctiva and cornea were almost free of melanosis (Fig 1E), which had also disappeared from the nasal eyelid margin (Fig 1E; arrowheads). The confluent patch in the tarsal conjunctiva was also smaller.
conjunctivitis was breaking down into smaller pigmented deposits (Fig 1F). The patient died 8 months later as a result of unrelated causes.

Primary acquired melanosis (PAM) of the conjunctiva may develop without or with atypia as a benign or premalignant proliferation of melanocytes, respectively. The former is characterized by large melanocytes with prominent nucleoli, which spread and form nests in the basal layer, and eventually throughout the epithelium. In advanced cases like the tarsal conjunctiva of our patient, the epithelium is replaced by atypical melanocytes. This is known as conjunctival melanoma in situ. PAM with atypia usually appears after the age of 45 years in whites. In addition to age and race, ultraviolet radiation is suspected to be a risk factor analogous to conjunctival melanoma. The incidence of PAM is not known in detail, but it is estimated to be comparable to the incidence of conjunctival melanoma, or about 0.5 per million inhabitants. Like that of cutaneous melanoma, the incidence of conjunctival melanocytic tumors is increasing. PAM typically appears as an accumulation of pigmentation deposits giving the conjunctiva a brownish, speckled appearance. These resemble grains of pepper and they typically wax and wane. The pigmentation can be moved over the underlying sclera, unlike congenital oculus melanosis, which is confined to the episclera and sclera. More than one patch may be present in the same eye. This is probably because pigmentation varies, and in most if not all cases nonpigmented atypical melanocytes are present as well. PAM with atypia progresses to invasive malignant melanoma in 50% of patients. Conversely, 50% to 80% of conjunctival malignant melanomas are estimated to develop from PAM. Any thickened areas are highly suggestive of progression into invasive melanoma and are best biopsied, although occasionally thickening is caused by secondary lymphocytic infiltrate. PAM of the conjunctiva was traditionally managed by observation, unless it was extensive, multifocal (probably with amelanotic skip areas), confluent, or progressive because of complications from large excisions, widespread cryotherapy, and beta irradiation. These included adhesions, dry eyes, corneal scarring, and secondary glaucoma. More recently, it has been found that PAM responds to topical chemotherapy with mitomycin. The advantage of topical chemotherapy is that the entire conjunctiva is spared, and that the drug also penetrates to the lacrimal passages, which may be involved by PAM. Mitomycin is applied in concentrations from 0.2 to 0.4 mg/mL 1 to 5 times per day, most often in 2-week courses, or as a single course of 4 to 6 weeks. Histopathologic studies document the disappearance of atypical melanocytes. Treatment is well tolerated although conjunctival injection and a transient inflammatory reaction are common, and conjunctival atrophy as well as dyskeratosis can occur. Mitomycin is now also used as an adjuvant treatment in combination with excision of invasive conjunctival melanomas.

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REFERENCES

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