Retrograde Metastasis of Cutaneous Melanoma to Conjunctival Lymphatics

CONJUNCTIVAL metastasis from cutaneous melanoma typically reaches the conjunctiva by hematogenous routes.1-7 We report a unique case of presumed retrograde conjunctival metastasis via lymphatic channels.

Report of a Case. A 61-year-old man developed cutaneous melanoma in the right preauricular skin. It was managed by surgical resections, skin grafts, irradiation, chemotherapy, and laser for local recurrences and cervical node metastasis. After 18 months, he was referred for progressive ipsilateral conjunctival pigmentation.

Examination disclosed cutaneous pigmentation and scarring in the right preauricular area (Figure 1A). The ipsilateral conjunctiva showed a peculiar widespread linear network of pigment (Figure 1B and C). The branching pattern was suggestive of lymphatic infiltration, and nearby conjunctival blood vessels were normal. Our clinical diagnosis was retrograde spread of cutaneous melanoma to conjunctival lymphatics.

Histopathologic analysis of a conjunctival biopsy disclosed epithelioid melanoma cells within lumina of dilated channels lined by endothelial cells, consistent with lymphatics (Figure 2A). Adjacent blood vessels contained erythrocytes but no tumor cells. The overlying conjunctival epithelium was normal without juxta epithelial activity. Immunohistochemically, the endothelium of the tumor-containing vessels was reactive to monoclonal antibody D2-40, a specific marker for lymphatic endothelial cells. In contrast, the adjacent non-tumor-containing blood vessels stained positive for CD34 and negative for D2-40 (Figure 2B and C).

The histopathologic diagnosis was retrograde conjunctival intralymphatic metastasis from cutaneous melanoma. The patient was treated with an iodine 125 plaque delivering 60 Gy to the entire conjunctiva over 7 days. Despite a favorable local response to irradiation, the patient died of disseminated melanoma after 16 months.

Comment. Metastatic melanoma to the conjunctiva is rare.1-3 Strempel1 reported a case in 1982 and found no previously reported cases. In 1989, Jakobiec et al4 described 5 cases of cutaneous melanoma metastatic to the conjunctiva. In 1996, Kriatli et al3 described 10 patients with conjunctival metastasis, in 2 of whom cutaneous melanoma was the primary site. Kwapiszeski and Savitt6

Figure 1. Recurrent cutaneous melanoma with pigment in the conjunctiva. A, Right side of the face showing an area of multiple treatments for recurrent cutaneous melanoma. Note the pigment on the temporal aspect of the conjunctiva. B, Conjunctiva with black, irregular clumps and linear strands of the pigmented lesion. Note that the blood vessels are red, apparently containing no pigment. C, Closer view of the network of black conjunctival lymphatic channels.
reported a case in 1997 and Shields et al.\(^7\) reported another case in 2004. In both of these cases, the conjunctival metastasis was the first sign of dissemination of known cutaneous melanoma.\(^6,7\)

In the aforementioned cases, the metastases reached the conjunctiva by hematogenous routes. However, Jakobiec and associates mentioned 2 patients in whom localized melanoma developed in the ipsilateral inferior conjunctival fornix years after excision of limbal melanoma.\(^4\) It is uncertain whether they represented tumor growth from surgical seeding or intralymphatic metastasis. The lesions were unlike the peculiar branching pattern seen in our case.

To confirm that the tumor-containing vessels were lymphatic channels and not blood vessels, immunostaining with lymphatic-specific endothelial cell marker D2-40 was performed.\(^8\) It has been used to demonstrate lymphatic vessels in the optic nerve sheath.\(^8\) In our case, the positive reaction confirmed that the tumor-containing vessels were lymphatics. The nearby blood vessels containing erythrocytes were nonreactive to D2-40 and reactive to CD34.

Regional metastasis from conjunctival melanoma occurs via lymphatics to regional lymph nodes, but histopathologic analysis almost never reveals tumor in lymphatics as seen in our case. Melanoma metastasis to the conjunctiva is by hematogenous routes from the primary site. One might speculate that in our patient the conjunctival metastasis developed from retrograde lymphatic flow from the preauricular tumor. The extensive scarring in that area may have forced the proliferating recurrent melanoma cells to pursue this reverse route to the conjunctiva. In summary, we report a clinicopathologic correlation of an unusual and possibly unique case of cutaneous melanoma metastatic to conjunctival lymphatics.

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3. Strempel I. Metastatic conjunctival tumor originating in a primary cutane-
cked by iridocyclectomy, which obscured a view of the tumor (Figure, B). Ultra-
sound biomicroscopy revealed a well-defined ciliary body mass 3 mm in thickness (Figure, C). The differential diagnosis included ciliary body melanoma, acquired neoplasm of the NPCE, tumor of the pigment epithelium, and leiomyoma; ARH-NPCE was not considered. The tumor was removed by iridocyclectomy (Figure, D). Three years after surgery, visual acuity in the affected eye was 6/15 owing to continued enlargement of the cataract into the visual axis.

Gross examination revealed a well-circumscribed white mass arising from the ciliary body measuring 3 × 3 mm in diameter. Histopathologic evaluation disclosed linear segments of nonpigmented, benign, ciliary epithelial cells encompassing large amounts of avascular, amorphous, periodic acid–Schiff–positive extracellular matrix (Figure, E and F). There was no evidence of malignancy. The final diagnosis was ARH-NPCE.

Comment. Age-related hyperplasia of the NPCE (Fuchs adenoma or coronal adenoma) occurs in an occult location in the pars plicata of the ciliary body. In their study of eyes mostly at autopsy, Iliff and Green found 7 cases of ARH-NPCE among 11 patients older than 80 years compared with 1 lesion in 17 eyes from patients younger than 50 years. Bateman and Foos, in a similar series, also found a relationship with age. Age-related hyperplasia of the NPCE can be solitary or multiple and unilateral or bilateral, and usually it is confined to 1 ciliary process. When it is larger, it can simulate a cyst or a solid neoplasm. Single lesions removed by iridocyclectomy were included in the series by Iliff and Green and Bateman and Foos. Another lesion removed by iridocyclectomy was reported by Zaidman et al in 1983. Our literature search disclosed no additional cases that were recognized clinically. Rarely, ARH-NPCE can assume tumorous proportions as occurred in our case.

In summary, we report a case of ARH-NPCE that enlarged, caused a secondary cataract, and grew through the iris root to appear as a mass in the anterior chamber angle. It is important to realize that ARH-NPCE rarely can grow to sufficient size to simulate a malignant neoplasm of the ciliary body.

Report of a Case. A 54-year-old woman was referred because of a suspected ciliary body melanoma. Her corrected visual acuity was 6/6 OU and intraocular pressures were normal. The left eye was healthy. Slit-lamp biomicroscopy of the right eye disclosed a tan mass arising from the ciliary body measuring 3 × 3 mm in diameter. Histopathologic evaluation disclosed linear segments of nonpigmented, benign, ciliary epithelial cells encompassing large amounts of avascular, amorphous, periodic acid–Schiff–positive extracellular matrix (Figure, E and F). There was no evidence of malignancy. The final diagnosis was ARH-NPCE.

Comment. Age-related hyperplasia of the NPCE (Fuchs adenoma or coronal adenoma) occurs in an occult location in the pars plicata of the ciliary body. Although it is extremely common in enucleated eyes, it generally is unapparent clinically because it is small and asymptomatic. It is believed to represent a proliferation of the NPCE that is associated with aging. In their study of eyes mostly at autopsy, Iliff and Green found 7 cases of ARH-NPCE among 11 patients older than 80 years compared with 1 lesion in 17 eyes from patients younger than 50 years. Bateman and Foos, in a similar series, also found a relationship with age. Age-related hyperplasia of the NPCE can be solitary or multiple and unilateral or bilateral, and usually it is confined to 1 ciliary process. When it is larger, it can simulate a cyst or a solid neoplasm. Single lesions removed by iridocyclectomy were included in the series by Iliff and Green and Bateman and Foos. Another lesion removed by iridocyclectomy was reported by Zaidman et al in 1983. Our literature search disclosed no additional cases that were recognized clinically. Rarely, ARH-NPCE can assume tumorous proportions as occurred in our case.