Malignant Melanoma of the Conjunctiva With Intraocular Extension

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Intraocular extension of a malignant melanoma of the conjunctiva is a rare entity. A 75-year-old woman underwent repeated surgery after receiving the diagnosis of a multilocular recurrent malignant melanoma arising from a primary acquired melanosis. Treatment included 2 lamellar sclerokeratectomies and percutaneous radiotherapy. Five years after initial surgery, intraocular extension of the melanoma was observed, and enucleation was performed. Findings from histopathological examination revealed a malignant melanoma occupying part of the ciliary body, the trabecular meshwork, and the iris. Eyes with recurrent malignant melanoma of the conjunctiva should be carefully monitored for intraocular extension. Deep excision of conjunctival melanoma, including lamellar sclerokeratectomy, may abolish the natural barrier against intraocular extension of malignant melanomas of the conjunctiva.


Primary malignant melanomas of the conjunctiva arise from primary acquired melanosis (75%), melanocytic conjunctival nevi (20%-30%), or de novo.\(^1,2\) The overall tumor-related mortality rate is about 25%\(^1,2\) and multilocular tumors especially tend to produce lymphatic metastasis.\(^4\) However, intraocular extension of a malignant melanoma of the conjunctiva is rare.\(^3\) We report a case of a 75-year-old woman with intraocular extension of a recurrent multilocular malignant melanoma of the conjunctiva.

Report of a Case

A 75-year-old woman was seen at the Department of Ophthalmology of the University of Erlangen-Nürnberg, Erlangen, Germany. She had of a recurrent multilocular malignant melanoma of the conjunctiva of the left eye (Figure 1). The tumor originated from primary acquired melanosis and involved the limbal, caruncular, and fornical conjunctiva. Since June 1989, 10 excisional biopsies (some-times multiple) of conjunctival tumors (Figure 2) had been performed (8 at our institution; 2, elsewhere), including 2 lamellar sclerokeratectomies with full-thickness corneal transplants (February 1990 and October 1993) (Table). The deep histopathological margins appeared to be free of tumor cells in both specimens. Additionally, the patient received adjuvant percutaneous radiotherapy with a total radiation dosage of 175 Gy. In May 1994, the patient returned with a nonpigmented conjunctival tumor of the left eye and reported ocular inflammation for 4 weeks. Visual acuity was 20/200 OS, intraocular pressure measured 9 mm Hg, and there were pronounced dry-eye symptoms. On examination, we observed 2 slightly pigmented and prominent tumors of the conjunctiva next to the limbus at the 4- and 7-o’clock positions. The corneoscleral suture from the 4- to 7-o’clock position was tight, the transplant showed stromal vascularization, and the recipient cornea was clear. The anterior chamber was deep and showed light cellular infiltration with Tyndall phenomenon. There was iridal neovascularization originating from the chamber angle.
at the 6-o’clock position reaching to the pupillary margin. Gonioscopically, brownish-pigmented areas were seen inside the chamber angle from the 5- to 7-o’clock position (Figure 3). The lens showed a nuclear and cortical cataract, the retina was attached, the optic disc appeared normal, and there were some irregularities of the retinal pigment epithelium in the macular region. Because of the suspicion of a recurrent conjunctival malignant melanoma with intraocular extension, a modified enucleation was performed.

**Clinical and Histopathological Findings From Biopsy Specimens of Conjunctival Tumors***

<table>
<thead>
<tr>
<th>Date</th>
<th>Conjunctival Findings</th>
<th>Intraocular Findings</th>
<th>Treatment</th>
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</thead>
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<tr>
<td>Jun 1989</td>
<td>Pigmented tumor (2- to 6-o’clock position)</td>
<td>MM</td>
<td>Tumor excision</td>
</tr>
<tr>
<td>Jul 1989</td>
<td>Pigmented tumor (2- to 5-o’clock position)</td>
<td>Scarring conjunctiva with inflammation</td>
<td>Tumor excision</td>
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<td>Feb 1990</td>
<td>Multiple pigmented tumors (4- to 7-o’clock position) involving plica and limbus (6- to 8-o’clock position)</td>
<td>MM with acquired melanosis</td>
<td>Lamellar keratotomy and sclerectomy with tectonic lamellar keratoplasty</td>
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<td>Jul 1990</td>
<td>Pigmented tumors involving the fornix (5- to 8-o’clock position)</td>
<td>MM with acquired melanosis</td>
<td>Tumor excision, radiotherapy, 45 Gy</td>
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<td>Mar 1991</td>
<td>Multiple pigmented tumors (12- to 3.5- and 5- to 8-o’clock position)</td>
<td>MM with acquired melanosis</td>
<td>Tumor excision, radiotherapy, 40 Gy</td>
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<td>Oct 1991</td>
<td>Multiple pigmented tumors (2-, 6-, and 8-o’clock position)</td>
<td>MM</td>
<td>Tumor excision, radiotherapy, 44 Gy</td>
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<tr>
<td>Apr 1992</td>
<td>Multiple pigmented tumors (5- to 7.5-o’clock position)</td>
<td>MM with acquired melanosis</td>
<td>Tumor excision</td>
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<td>Oct 1992</td>
<td>Pigmented tumor involving the limbus (4- to 7-o’clock position)</td>
<td>MM with acquired melanosis</td>
<td>Tumor excision, radiotherapy, 46 Gy</td>
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<td>Jun 1993</td>
<td>Pigmented tumor (8-o’clock position)</td>
<td>MM with acquired melanosis</td>
<td>Tumor excision with cryotherapy</td>
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<td>Oct 1993</td>
<td>Pigmented tumor (3- to 6- to 8-o’clock position)</td>
<td>MM with acquired melanosis</td>
<td>Lamellar keratotomy and sclerectomy with lamellar sclerokeratoplasty</td>
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<tr>
<td>May 1994</td>
<td>Multiple pigmented tumors (4- and 7-o’clock position)</td>
<td>MM with acquired melanosis</td>
<td>Modified enucleation</td>
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*MM indicates malignant melanoma; ellipses, none.

**HISTOPATHOLOGICAL REPORT**

Findings from histopathological evaluation revealed an intact conjunctival epithelium. Focally, the epithelium had areas of primary acquired melanosis with cellular atypia. In the subepithelial tissue, nests of slightly pigmented, uniform-looking tumor cells were surrounded by a chronic, nonspecific lymphoplasmacytic-cellular infiltration. Nests of tumor cells were seen within the sclerocorneal graft as well as inside the underlying cornea, reaching almost to the middle of the cornea. The chamber angle showed neovascularization and was partly invaded by tumor cells growing on the corneal and iridal surfaces with invasion of iris and trabecular meshwork. The ciliary body was partially thickened with collateral retinal detachment. There was a diffuse in-

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*Figure 1. Clinical photograph of the left eye (October 1991) after sclerokeratoplasty with multifocal recurrence of malignant melanoma of the conjunctiva at the 2- and 6-o’clock positions and from the 7- to 9-o’clock position.*

*Figure 2. Histopathological appearance of conjunctival biopsy specimen (February 1990) with uniform-looking pigmented cells spread within the epithelium and the subepithelial tissue (hematoxylin-eosin, original magnification ×480).*
vasion of the ciliary body by mainly epithelioid tumor cells (Figure 4). Single sections showed tumor cells in the scleral emissaria connecting the tumor cell masses inside the sclera and the cornea with the ciliary body (Figure 5). The choroid, attached retina, and optic nerve appeared normal. All different parts of the tumor of conjunctiva, cornea, sclera, and ciliary body expressed the same immunohistochemical-staining pattern (positive for S100 antigen and HMB-45 antigen) and showed polygonal nuclei, prominent nucleoli, and a small cytoplasmic rim.

Intraocular extension of a conjunctival malignant melanoma is an extremely rare entity. Much more frequently, uveal melanomas lead to pigmented epibulbar lesions by extraocular extension. Therefore, the coincidental finding of epibulbar and intraocular pigmented lesions in our patient primarily suggests a uveal melanoma with intraocular extension. The clinical and histopathological appearance of the ciliary body changes especially seemed to indicate a primary epithelioid malignant melanoma of the ciliary body (Figure 4). The presumed ciliary body tumor showed collateral retinal detachment and invasion of chamber angle, trabecular meshwork, iris, cornea, and sclera and, most likely, extraocular extension. Indeed, there is no way to directly prove whether the tumor in our patient was originating from the conjunctiva or the ciliary body because there is no method to differentiate between conjunctival or uveal melanocytes.

However, we present 6 arguments supporting our hypothesis of a primary conjunctival melanoma with intraocular extension. (1) Acquired melanosis with cellular atypia was seen inside the conjunctival epithelium in close relationship to the tumor. This finding is not consistent with an epibulbar growth originating from a primary intraocular tumor. (2) During a follow-up period of more than 5 years, malignant melanomas and epithelial changes were seen in almost all parts of the conjunctiva, including the plica, fornix, and caruncula far from the ciliary body tumor. (3) Pigmented lesions were also seen at the limbus (Figure 1), which is rarely seen in extraocular extension of uveal melanoma. (4) Despite multiple previous examinations, intraocular changes did not occur until the last time the patient was seen. (5) Looking at the histological sections, tumor cells were seen within a scleral emissaria connecting the tumor cell masses inside the sclera and the cornea with the tumor in the ciliary body. This seems to represent the pathway of intraocular invasion. (6) Finally, there was a clear immunohistochemical identification of a melanocytic tumor in contrast to other tumors more frequently invading the intraocular structures, such as a mucoepidermoid or a squamous cell carcinoma. S100 Antigen and HMB-45 antigen were detected in all parts of the tumor (within conjunctiva, sclera, cornea, anterior chamber, and ciliary body).

The appropriate treatment for conjunctival malignant melanomas is still controversial and not satisfactory, looking at the overall tumor-related mortality rate of more than 25%. Additionally, there are no exact data concerning the radiosensitivity of the conjunctival malignant melanoma and the advantages of an adjuvant radiotherapy. In our patient, local tumor control had been intended by multiple excisions of the tumor and adjuvant radiotherapy. Nevertheless, there was recurrent tumor growth with partially deep scleral and corneal extension. This extension of the tumor led to a deep excision by lamellar sclerokeratotomy. Despite treatment, tumor cells persisted deep inside the sclera and cornea underneath the transplant and were able to invade the eye. Compared with the technique published by Shields et al, the deep scleral extension of the tumor in our patient demanded deeper scleral incisions of 0.5 and 1.0 mm; therefore, a corneal graft was required for wound coverage. Perhaps the preceding limbal surgery with partial removal of the Bowman membrane in our patient reduced the natural barrier against intraocular tumor invasion, as discussed by Gow and Spencer. The case reported by Gow and Spencer also had intraocular extension of a conjunctival malignant melanoma after lamellar keratotomy and sclerectomy. This could in-
dicate that the scleral and corneal barrier is normally resistant to penetration by an epibulbar malignant melanoma but may lose this function after lamellar surgery.

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Figure 5. Magnification of the histopathological section of the enucleated eye showing nests of tumor cells in the extraocular tissue spreading through the sclera toward the ciliary body (periodic acid–Schiff stain, original magnification ×240).

A look at the past . . .

SUMMARY.—In a series of experiments made upon seventy-eight eyes in the rabbit, with a view of testing the safety and efficiency of the suture of the wound in cataract operation, it was found that by a modification of the methods hitherto practised, loss of the vitreous and intraocular hemorrhage could be prevented, the wound could be readily and firmly closed, and the prolapsed iris could be returned to the anterior chamber, and this without aseptic treatment. Primary healing occurred in 80 per cent of the cases, with a clear, circular, and nearly central pupil.