Primary Basal Cell Carcinoma of the Conjunctiva With Intraocular Invasion

Basal cell carcinoma of the conjunctiva is extremely rare. Causative factors believed to contribute to the development of basal cell carcinoma include UV light, ionizing radiation, chemical carcinogens, predisposing genetic conditions, and possibly, infection with human papillomaviruses. Basal cell carcinoma most commonly arises in areas of long-term sun exposure. In the ocular region, common sites include the skin of the medial canthus, lateral canthus, and lower eyelid. Morpheaform basal cell carcinoma is a variant of basal cell named for its clinical resemblance to a plaque of morphea (localized scleroderma). Morpheaform tumors are firm flat lesions with indistinct borders. The small strands and cords of tumor cells in morpheaform basal cell carcinoma are embedded in a dense sclerotic stroma and are virtually untouched by curetage. Morpheaform basal cell carcinoma is noted for its subclinical spread and high recurrence rate after treatment.

Primary epithelial carcinoma of the conjunctiva is rare. It may develop from a papilloma, leukoplakia, intraepithelial epithelioma (Bowen disease), or spontaneous metaplasia. Primary conjunctival carcinoma is 10 times more likely to be squamous cell than basal cell. This report documents a rare case of intraocular extension of morpheaform basal cell carcinoma, originating from the limbal conjunctiva, in a 69-year-old man. This rare case of primary basal cell carcinoma of the conjunctiva is notable for its aggressive behavior.

Report of a Case. A 69-year-old man, who worked as a construction worker for 30 years, reported burning and stinging of both eyes for several weeks. His medical history was notable for left-sided renal cell carcinoma treated with left-sided nephrectomy, chronic obstructive pulmonary disease, right-sided basal ganglion infarct, and hypertension. His ocular history was noteworthy only for refractive error. On ophthalmic examination, the visual acuity was noted to be 20/25 OU, and the pupils were reactive without relative afferent pupillary defect. A 6 × 6-mm, slightly elevated limbal nodule at the 3-o’clock position with overlying conjunctival hyperemia was noted in the left eye (Figure 1). In addition, the left pupil was noted to be irregularly drawn to the 3-o’clock position. Gonioscopy of the left eye revealed an open angle, except between the 2- and 4-o’clock positions, where the iris was noted to bulge forward and vessels were crossing the trabecular meshwork. Indirect ophthalmic examination showed paving-stone degeneration at the 3-o’clock position without any evidence of a mass. The working diagnosis then was ciliary body mass, including melanoma. B-scan and magnetic resonance imaging (3-mm slices) showed no abnormality of intraocular tumor.

Three months later, the findings of the ocular examination were unchanged. The patient refused biopsy and was lost to follow-up. One year later, the patient returned to the clinic reporting blurred vision in the left eye. The patient’s visual acuity was 20/30 OD and 20/70 OS. Applanation tonometer measurement in the left eye was 68 mm Hg and iris-corneal adhesions were seen temporally. Treatment consisted of oral acetazolamide sodium, 500 mg, 1 tablet, twice daily, 0.3% metipranol, approximately 20 µL, 1 drop in each eye twice daily, and 2%...
pilocarpine approximately 20 µL, 1 drop in each eye 4 times daily, was instituted with a reduction in intraocular pressure. A third B-scan revealed a ciliary body mass temporally. Findings on a second magnetic resonance image were inconclusive, and the results of an oncology workup for systemic malignancy were negative.

The patient remained resistant to surgical intervention for an additional year, during which his vision declined to no light perception, and his intraocular pressures became increasingly uncontrollable on maximal doses of the medications. Enucleation was performed approximately 2 years after the initial visit. Histopathologically, the highly invasive basal cell carcinoma was connected to the deep basal layer of the conjunctival epithelium (**Figure 2**) and invaded the episclera, sclera, ciliary body, trabecular meshwork, (Figures 3, 4, 5, and 6) limbus, anterior chamber, and the collector channels. In a few areas, islands of typical basal cell carcinoma with peripheral palisading columnar cells were seen (Figure 3). Most of the lesion, however, consisted of short cords and even individual tumor cells with high nuclear cytoplasmic ratio, surrounded by dense stroma, consistent with morpheaform basal cell carcinoma (Figure 5 and Figure 6). Actinic damage of the conjunctiva in the form of severe elastotic degeneration of the collagen fibers was noted. Other histopathologic findings in the enucleated eye included peripheral anterior synechiae, atrophy of the inner retinal layers, and atrophy of the optic nerve, were consistent with glaucoma.

The patient was then successfully fitted with a prosthesis. Extensive examination of periorcular tissue for a primary lesion was undertaken with the biopsy of 2 suspicious lesions of the upper eyelid and left outer canthus. Histopathologic examination, however, revealed only a skin tag of the left upper eyelid and basophilic (elastotic) degeneration of the collagen fibers at the outer canthus.

**Comment.** Basal cell carcinoma is a malignant epithelial neoplasm of the skin, most commonly arising in areas of long-term sun exposure. It is a slow-growing tumor that rarely metastasizes but is capable of causing extensive local tissue destruction. Microscopically, buds of deeply basophilic cells protrude from the epidermis and extend into the dermis, forming large nests. Morpheaform tumors are characterized by extension into thin cords that radiate peripherally. Histopathologically, these nests and cords are enmeshed in a dense stroma of thickened collagen bundles. These characteristics

**Figure 3.** Note the invasion of the episclera and sclera by the basal cell carcinoma (hematoxylin-eosin, original magnification ×20).

**Figure 4.** Higher magnification of the lesion in the episclera and sclera shown in Figure 3. The sheets of basaloid tumor cells show peripheral palisading by cuboidal to columnar cells (hematoxylin-eosin, original magnification ×100).

**Figure 5.** Ciliary body shows sheets and small nests of highly invasive basaloid tumor cells consistent with morpheaform basal cell carcinoma (hematoxylin-eosin, original magnification ×100).

**Figure 6.** Ciliary body and trabecular meshwork show highly invasive basaloid tumor cells surrounded by dense fibrous stroma, which is consistent with morpheaform basal cell carcinoma (hematoxylin-eosin, ×200).
make curettage ineffective as treatment; Moh micrographic surgery is the treatment of choice.\(^1\)

The histogenesis of basal cell carcinoma is unclear. Many researchers believe that primary basal cell carcinoma of the conjunctiva or other mucosal surface cannot exist. They assert that basal cell carcinoma is derived from basal cells of pilosebaceous structures, and therefore, mucosal surfaces, which lack adnexal structures, could never be the site of primary basal cell carcinoma.\(^6,7\) Other authors\(^8\) have held that persistent pluripotential germ cells within the deepest layers of the epidermis are somehow activated by environmental factors to produce carcinoma. In our patient, the origin of the tumor cells was the basal layer of the conjunctival epithelium. It is known that these pluripotential germ cells differentiate during embryogenesis into epithelium and adnexal structures.\(^7\) Primary conjunctival basal cell carcinoma has been rarely described in the literature. In a series of 93 comeoscleral epithelial tumors, Ash and Wilder\(^9\) described one tumor as a basal cell carcinoma. Ash\(^8\) later published the results of a larger series of 1120 patients with epibulbar tumors of which 53 tumors were listed as basal cell carcinoma. No further discussion was offered regarding the origin of the remaining limbal tumors.\(^8\) Both Aftab and Percival,\(^8\) Apte et al,\(^10\) and later Husain et al\(^11\) described primary basal cell carcinomas occurring in the nasal interpalpebral conjunctiva. Our patient had had 2 negative biopsy specimens of suspicious cutaneous lesions and has been followed up eventfully for over 8 years. Shields et al\(^12\) recently reported a case series of 5 patients with intraocular invasion of conjunctival squamous cell carcinoma.

In summary, we report an advanced case of morphoeform basal cell carcinoma of the conjunctiva with intraocular spread and secondary glaucoma, which, to our knowledge, has not been reported. Primary basal cell carcinoma of the conjunctiva can be locally aggressive, rarely metastasize, and tend to clinically mimic papillomas. These lesions tend to occur in the actinically exposed areas of interpalpebral conjunctiva in older individuals. In our patient, we noted evidence of actinic damage in the conjunctiva and medial canthus. This finding is consistent with his job as a construction worker for 30 years with prolonged exposure to sunlight. In conjunctival tumors, ultrasonography must be performed to determine the extent of tumor spread. In the case of morphoeform basal cell carcinoma, the extent of tumor spread is difficult, but not impossible, to determine. In our patient with a blind, painful eye suspected of harboring a ciliary body tumor, enucleation seemed to be the treatment of choice.

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Bilateral Iris Neovascularization as the Initial Sign of Obesity-Hypoventilation (Pickwickian) Syndrome: Hypoxia/Hypercapnia as a Stimulus for Angiogenesis

Rubeosis iridis usually occurs secondary to decreased or absent retinal capillary perfusion (eg, diabetic retinopathy, central retinal vein occlusion, ocular ischemia). Clinical observations have established a relationship between retinal ischemia and ocular neovascularization, leading to the half-century-old hypothesis that factors produced by an ischemic retina stimulate local as well as distant blood vessel growth.\(^1\) However, it is not clear which aspect of ischemia (eg, reduced nutrient delivery, hypoxia, hypercapnia, increased metabolites) might lead to the production of an angiogenesis factor. We describe a unique case in which rubeosis iridis is seen as a consequence of systemic hypoxia/hypercapnia without retinal ischemia as part of the obesity-hypoventilation (pickwickian) syndrome.

Report of a Case. A 36-year-old man was referred for evaluation of bilateral rubeosis iridis noted shortly (4 and 6 months) after uneventful bilateral cataract surgery. There was no ocular discomfort. Visual acuity was 20/25 OU. Pupillary border rubeosis was observed (Figure 1, A) and documented by iris angiography (Figure 1, B). Fundus examination showed dilated veins and rare intraretinal hemorrhages (Figure 2, A) with prompt perfusion by fundus fluorescein angiography (Figure 2, B). Intraocular pressure was 16 mm Hg in both eyes.

The patient was not receiving any systemic medications. He had been lethargic for a few years and worked as a truck driver until 6 months prior to cataract surgery.

Medical evaluation demonstrated obesity (weight, 152 kg [338 lb]), somnolence, right ventricular failure, polycythemia, arterial blood PO\(_2\) of 32 mm Hg (normal, 75-100 mm Hg), arterial blood PCO\(_2\) of 69 mm Hg (normal, 35-45 mm Hg), and...
sleep apnea, consistent with advanced obesity-hypoventilation (pickwickian) syndrome. The patient was admitted to Johns Hopkins Hospital (Baltimore, Md) and transferred to the intensive care unit for positive pressure oxygen delivery and monitoring of respiratory and cardiac status.

With treatment of the hypoxia and a 23-kg (51-lb) weight loss, the systemic condition improved, with PO$_2$ increasing to 93 mm Hg. The rubeosis promptly involuted (Figure 1, C). Follow-up examination at 1, 3, and 6 months disclosed no recurrence of rubeosis.

**Comment.** Since there was no demonstrable retinal ischemia (decreased or absent retinal capillary blood flow) in this case, it appears that hypoxia (reduced oxygen supply to a tissue that can occur in the presence of normal perfusion of the tissue by blood) and/or hypercapnia alone may induce angiogenesis. When rubeosis iridis is secondary to ischemia, management often involves treatment of the ischemic retina with panretinal photocoagulation. It is thought that less diffusible angiogenic factor is thereby re-

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**Figure 1.** A, Iris photograph of the right eye at the time of presentation. B, Iris angiography discloses pupillary border rubeosis with diffuse fluorescein leakage in both eyes. C, Iris photograph of the right eye 3 weeks after initiation of medical treatment.

**Figure 2.** A, Fundus photographs at time of presentation are compatible with a dilated venous system (left, right eye; right, left eye). B, Intravenous fluorescein angiogram of the right eye at the initial visit discloses normal perfusion.
Pulmonary Embolism Following Head Positioning for Retinal Reattachment Surgery in a Young Patient With Factor V Leiden Mutation

Pulmonary embolism (PE) is infrequent following modern ophthalmic surgery partly because postoperative immobilization is rarely required. However, following certain vitreoretinal procedures, eg, retinal reattachment and macular hole surgery, patients who have received intravitreal gas for tamponade need to position their heads in such a way that the retinal break(s) is uppermost. Head positioning is usually required for 1 to 2 weeks and may involve prolonged bed rest. Such immobilization may predispose patients to thromboembolism, especially those with other known risk factors. We report a case to highlight this risk.

Report of a Case. A 38-year-old white woman in good general health underwent pars plana vitrectomy, endolaser retinopexy, and intravitreal sulfur hexafluoride injection under general anesthesia to treat a retinal detachment in her right eye. She was a nonsmoker and was not using oral contraceptives. She was not pregnant and had no personal or family history of thromboembolic diseases.

She rested in the prone position, facing downward, after the procedure. From the first postoperative day, she was requested to position her head for 2 weeks so that the nasal retina in the right eye was uppermost. She did this largely by lying on her right side, taking only short breaks for meals and other essential activities.

She developed pain in her calves on the fifth postoperative day. On the eighth postoperative day, she was seen with severe pleuritic chest pain on the left side and dyspnea. She did not report hemoptysis, and there was no evidence of a chest infection. She was tachypneic and in severe pain. A pleural rub was heard in the left inframammary area and left calf tenderness was demonstrable. Her electrocardiogram and chest radiograph showed no abnormalities. Perfusion-ventilation scan showed parenchymal changes in the base of the lung on the left side with perfusion and ventilation defects, and a perfusion defect in the upper lung on the right side. A diagnosis of PE was made. She was treated with intravenous heparin sodium initially, followed by oral anticoagulation with warfarin sodium for 3 months. Screening for thrombophilia disclosed activated protein C resistance caused by factor V Leiden mutation. She was heterozygous for the mutation. Her protein C, protein S, and antithrombin III levels were normal. The patient tested negative for lupus anticoagulant.

Comment. Pulmonary embolism was the leading cause of ophthalmic surgical mortality in 2 large retrospective series. Patients with retinal detachment were at significantly greater risk than other patients, with gas anesthesia at an older age and prolonged bed rest probably contributing to higher mortality.

Activated protein C resistance caused by factor V Leiden mutation is the most common inherited predisposing cause of venous thromboembolism. The mutation is highly prevalent in the general population (5%-10%). The risk for thrombosis for subjects with the mutation is increased 5- to 10-fold in heterozygotes and 50- to 100-fold in homozygotes. However, several studies have shown that factor V Leiden mutation is not independently associated with fatal PE. Besides the activated protein C resistance, we believe that the prolonged immobilization secondary to head positioning contributed

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to the development of PE in our patient.

To our knowledge, this is the first report of PE following head positioning in a young patient with a factor V Leiden mutation. We propose that patients requiring postoperative head positioning should be carefully questioned regarding family and personal risk factors for thrombosis, eg, cigarette smoking, pregnancy, and use of oral contraceptives and, when indicated, screened for thrombophilia. Ophthalmologists should encourage all patients to perform stretching exercises or to walk for 5 to 10 minutes every hour while maintaining head positioning. In addition, for patients at increased risk, they should consider perioperative deep vein thrombosis prophylaxis with compression stockings, intermittent pneumatic compression, or pharmacological agents, or the use of silicone oil tamponade to reduce the need for head positioning.

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Dr Au Eong was supported by a Tan Tock Seng Hospital Scholarship, Singapore.

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