to be delivered to tumour tissue while significantly lowering the dose to surrounding healthy tissues.[16] Although it has demonstrated encouraging rates of local tumour control, the lack of wide-spread availability and long-term data limit its clinical use at the present time.[16,17]

Although exceedingly rare, here we present another case of ACC as a primary orbital apex tumour in the absence of lacrimal gland involvement. Given the aggressive nature of ACC, it is paramount for clinicians to include ACC in their differential diagnoses when evaluating orbital apex tumours, even without signs of lacrimal gland involvement.

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Can J Ophthalmol 2016;51:e65–e67

http://dx.doi.org/10.1016/j.jcjo.2015.12.012

Intraocular adenocarcinoma: histopathological report of two cases with different origin

Acquired malignant tumours that involve nonpigmented ciliary body epithelium (NPCE) and retinal pigment epithelium (RPE) such as adenocarcinoma are extremely rare. Most of the histopathological changes that involve these structures are benign lesions such as adenoma, congenital hypertrophy of retinal pigment epithelium (CHRPE), and reactive hyperplasia. Although some of the benign lesions—especially CHRPE—are believed to enlarge slowly over long time, malignant changes within NPCE and RPE are extremely rare. Herein we report 2 cases of intraocular adenocarcinoma, one arising from RPE and the other from NPCE, with a description of their clinical presentation and histopathological features.

A 31-year-old male presented with a few months' history of a painful left eye, which was blind after trauma by a stick resulting in loss of vision at the age of 5 years. Visual acuity on the left was no light perception, and the intraocular pressure was 15 mm Hg. The conjunctiva was mildly injected, and the cornea showed band keratopathy with keratic precipitates that did not permit proper evaluation of the fundus (Fig. 1A). Ultrasonography revealed shrinkage of the globe, ocular wall calcification, and dense vitreous opacities. Evisceration specimen showed pleomorphic tumour cells arranged in nests as well as focal tubular and acinar patterns, separated by fine septae and invading the heterotopic bone (Fig. 1B, C). Some cells showed intracytoplasmic vacuoles. Immunohistochemical (IHC) staining showed positivity with cytokeratin AE1/AE3 (Fig. 2D), neuron-specific enolase, vimentin, CK8-18, CK19, and CK20. However, the tumour cells were negative with S-100 stain as well as melanocytic markers (HMB45 and Melan-A). A diagnosis of intraocular adenocarcinoma presumably arising from the RPE was made. Systemic workup of the brain, chest, abdomen, and pelvis did not

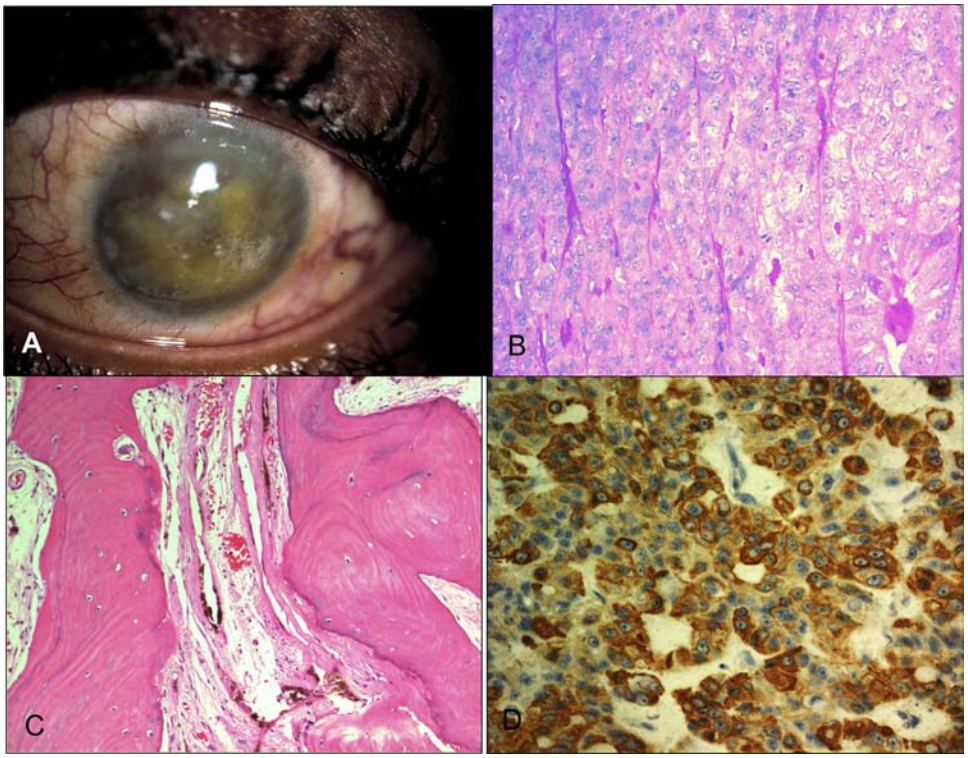

Fig. 1—(A) The clinical appearance of the left blind eye in case 1. (B) The tubular pattern of the adenocarcinoma tumour cells (original magnification ×100; periodic acid–Schiff). (C) The heterotopic bone formation in the phthisical globe (original magnification ×200; haematoxylin and eosin). (D) Tumour cells staining with CytoK AE1/AE3 (original magnification ×400)

reveal any primary tumour. The patient was last seen in the clinic 1 year postsurgery with a clean socket.

A 69-year-old male was referred with the clinical diagnosis of squamous cell carcinoma (SCC) arising from the limbus and invading the orbit. Exenteration specimen showed that the primary tumour in this case was not an SCC but rather an intraocular malignant tumour arising from NPCE with intraocular hemorrhage (Fig. 2A) The tumour showed an adjacent focus of benign lace and cribriform–like proliferation of an incidental adenoma (Fig. 2B). The malignant areas consisted of high-grade pleomorphic cells with adenoid vacuolated appearance, giant tumour cells, and frequent mitotic figures (Fig. 2C). There were intervening globules of periodic acid–Schiff–positive material between the tumour cells (Fig. 2D). Extrascleral extension near the limbus mimicking an SCC was evident. The tumour cells infiltrated the extraocular muscle (Fig. 2E). Perivascular invasion and intravascular invasion were also observed (Fig. 2F, G). The histopathological diagnosis was a high-grade carcinoma. The IHC staining of the tumour cells was positive for CK7 (Fig. 2H), CK8-18 (Fig. 2I), and AE1/AE3 as well as CAM 5.2, but negative for S-100, vimentin, HMB45, and Melan-A. A diagnosis of NPCE adenocarcinoma possibly arising from a pre-existing ciliary body adenoma was made. Metastatic adenocarcinoma was also ruled out by systemic workup. The patient was then lost to follow-up.

Adenocarcinoma of the RPE is extremely rare, with a few reported single cases in the literature. These tumours might not be easily distinguishable from choroidal melanomas. Shields et al. reviewed 13 cases of RPE tumours, 2 of which were adenocarcinomas. The youngest patient was in the mid-30s and the oldest was 79 years old.[1] Ultrasonography usually shows an elevated mass with medium to high internal reflectivity and acoustic density with 1 reported mushroom-shaped tumour.[2] On histopathology, RPE adenocarcinomas are located on the inner surface of Bruch's membrane without involvement of the uveal stroma, and tumour cells are arranged in a characteristic linear bands resting on periodic acid–Schiff–positive basement membranes.[1,2] On IHC staining, RPE tumours may express both epithelial markers (including cytokeratin, CAM 5, AE1/AE3, and epithelial membrane antigen) and melanocytic markers (including Melan-A, and HMB45). Therefore, IHC staining results should be interpreted with caution when the differential diagnosis includes choroidal melanoma.[1,3] Other IHC stains that RPE tumours may express, are: microphthalmia transcription factor 2, and S-100 protein. Although it was known that RPE tumours have no potential for metastasis, a metastatic RPE adenocarcinoma in a trisomy-21 patient with a long-standing blind eye in whom the tumour seeded into the spinal cord space has been reported.[4]

The pathogenesis of intraocular adenocarcinoma is unclear. Adenocarcinoma arising from a pr-eexisting

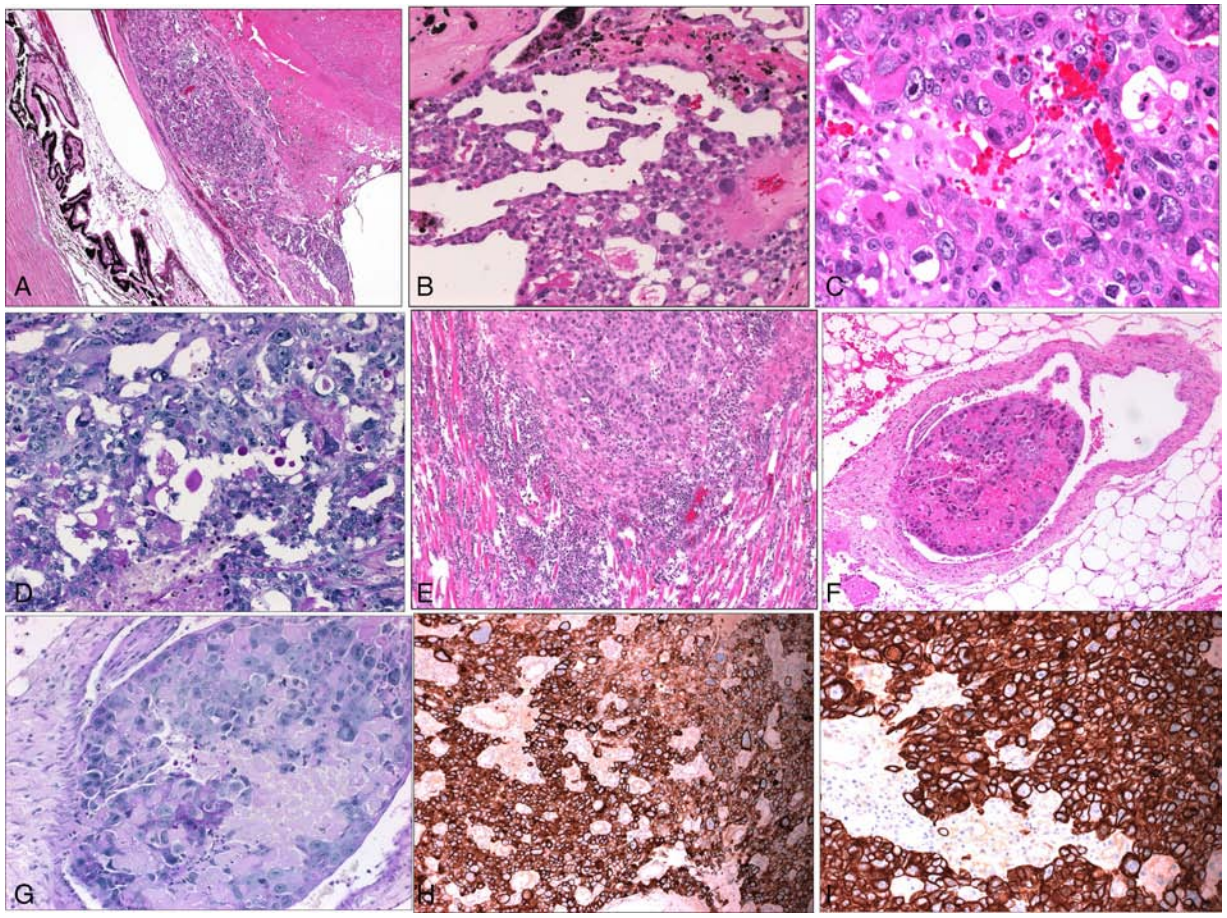

Fig. 2—(A) The histopathological appearance of the intraocular tumour in case 2 with intraocular hemorrhage (original magnification ×50; haematoxylin and eosin [H&E]). (B) The primary tumour arising from a pre-existing ciliary body adenoma (original magnification ×100; H&E). (C) Higher-power appearance of the tumour cells (original magnification ×400; H&E). (D) Tumour cells with secretory globules (original magnification ×200; periodic acid–Schiff). (E) Extraocular muscle invasion by the tumour cells (original magnification ×100; H&E). (F) Intravascular invasion (original magnification ×100; H&E). (G) Higher-power image showing the intravascular invasion (original magnification ×200; periodic acid–Schiff). (H) Immunohistochemical-positive staining of tumour cells (original magnification ×100; CK7). (I) Higher magnification of the positive tumour cells to CytoK 8/18 (original magnification ×200).

CHRPE has been reported.[5] Some experts therefore recommended observation of such lesions with careful indirect ophthalmoscopy. An elevated lesion with feeder blood vessels should attract the attention of ophthalmologists, and in this condition ultrasonography and fluorescein angiography might aid in the diagnosis. Some of the tumours described developed in association with trauma, inflammation, chorioretinal scars, and ocular phthisis. Others were noted to occur in eyes with opaque media that had been blind for many years as a result of trauma, surgery, or other conditions as in our first case.

Table 1—The differentiating clinical and histopathological features of intraocular adenocarcinoma

Feature	NPCE adenocarcinoma	RPE adenocarcinoma
Colour	Grey to yellow	Dark brown to black, can be nonpigmented
Associated clinical features	Inflammation, focal cataract, and sentinel blood vessels	Abruptly elevated mass, feeder retinal blood vessels, exudation and/or exudative retinal detachment
Transillumination	Transmits light	Blocks light
B-scan	High internal reflectivity	Moderate to high internal reflectivity
Microscopic appearance	Strands of epithelial cells that may infiltrate the ciliary body smooth muscles	Atypical epithelial cells with linear arrangement separated by fibrous septa
	Possible inflammatory cells and extracellular mucopolysaccharide	Cells can be vacuolated. Prominent periodic acid–Schiff–positive basement membrane
Immunohistochemical staining	Moderate reactivity to S-100 and mild reactivity to vimentin	Can co-express epithelial markers (cytokeratin, CAM 5, AE1/AE3, and epithelial membrane antigen) and melanocytic markers (Melan-A and HMB45)
	May show positivity with CAM 5.2 and CK7	

NPCE, nonpigmented ciliary body epithelium; RPE, retinal pigment epithelium.

Primary tumours of the ciliary body include adenoma, Fuch's adenoma, and adenocarcinoma. The adenoma can be easily distinguished by lack of infiltrative behaviour and relatively rare mitosis.[6] Similarly, ciliary body adenocarcinomas—including those arising from NPCE—are rare and have been reported in all age groups.[7] It has been believed that these arise as a reactive proliferation secondary to trauma or inflammation. These ciliary body masses are nonpigmented and irregular, have the tendency to cause localized cataract changes, and can be associated with sentinel vessels.[7] Differential diagnosis of this tumour includes medulloepitheloma, adenoma, melanoma, and metastasis. IHC studies have shown that these tumours stain positive with S-100 protein and vimentin as they originate from NPCE. They can show positivity with Kermix, CAM 5.2, and CK7.[7,8]

Since we have encountered the aforementioned 2 cases in which the adenocarcinoma had originated from 2 different intraocular structures, we have summarized the differentiating features between those tumours arising from the NPCE and the ones arising from RPE in Table 1.

In conclusion, intraocular adenocarcinomas may constitute diagnostic challenge to the ophthalmic pathologist. Good knowledge of the characteristic features and careful examination of routine evisceration tissue are a must to avoid overlooking such tumours or misdiagnosis especially when an underlying neoplasm is unsuspected.

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Can J Ophthalmol 2016;51:e67–e70

http://dx.doi.org/10.1016/j.jcjo.2015.12.010

IgG4-related orbital disease mass lesion

IgG4-related disease (IgG4-RD) is a systemic, tumefactive, inflammatory disease. It is increasingly recognized in the orbit (IgG4-related orbital disease [IgG4-ROD]), where it may affect the lacrimal glands, extraocular muscles, orbital fat, trigeminal nerve branches, orbital septum, sclera, optic nerve, eyelid, nasolacrimal drainage system, and bulbar conjunctiva.[1–3] We present a case of a solitary posterior orbital mass, histologically proven to be IgG4-RD.

A 42-year-old male presented with a 3-month history of increasing, painless reduction of vision in his right eye. The presenting right visual acuity was 6/60 unaided, 6/24 with pinhole, and 6/5 unaided in the left eye. Ishihara colour vision testing was 10/11 both eyes, with subtle right red desaturation. There was no globe displacement. Funduscopy found choroidal folds, confirmed on optical coherence tomography (Fig. 1). Magnetic resonance imaging (MRI) demonstrated a well-demarcated, contrast-enhancing lesion spanning the intra- and extraconal spaces in the right superotemporal orbit (Fig. 2). The extraocular muscles, optic nerve, lacrimal gland, and supra- and infraorbital nerves were normal. The findings of an MRI of the head and orbit performed 2 years previously for an unrelated condition were normal.

A latera orbitotomy was used for surgical excision. A large, firm, spherical lesion was excised intact. Histopathology revealed a densely sclerotic lesion with storiform fibrosis and obliterative fibrosis. The average IgG4 count per high-power field was 78, and the IgG4:IgG cell ratio was 41.4% (10 fields counted) (Fig. 3).

No other foci of disease were identified on computed tomography scan of the chest, abdomen, and pelvis. The findings of blood tests, including inflammatory markers and serum IgG4, were all normal. Six months postoperatively, the vision had improved to 6/24 unaided and 6/12 pinhole despite persistent choroidal folds, and there was no clinical or radiological evidence of disease recurrence.