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Unexpectedtumour recurrence after endoresection and adjuvant ruthenium-brachytherapy of a choroidal melanoma

Clinical History

A 48-year-old female patient first presented to our clinic in June 2002. She reported perceiving a veil over her left eye since January 2002. By April, she noticed progressive visual deterioration and a nasal visual field defect. The cause of the visual impairment was a choroidal melanoma located in the upper mid-periphery. The tumor was treated with endoresection and adjuvant ruthenium brachytherapy, and the patient was monitored regularly during follow-up visits in the tumor consultation clinic.

By February 2008, visual acuity in the left eye had decreased to the perception of hand movements, and since August 2009, intraocular pressure had been relatively low, ranging between 3 and a maximum of 8 mmHg. In April 2019, for the first time, a prominent reddish lesion was observed in the resection area, which was barely measurable sonographically. Over time, this lesion increased in size. In June 2020, a dome-shaped, relatively hyperreflective mass measuring 4.25 × 4.56 × 4.01 mm was identified sonographically. Due to a vitreous hemorrhage, fundus examination was no longer possible.

We discussed with the patient that, given the growing mass, the possibility of a tumor recurrence existed, which could only be clarified through exploratory vitrectomy and biopsy. Alternatively, considering a visual acuity limited to hand movements and the onset of phthisis bulbi, enucleation was also presented as an option. The patient opted for enucleation of the left eye.

Ocular Pathology

Gross microscopy. Globe (left eye: 22x21x21mm, cornea 11x10mm, optic nerve 1mm). Diaphanoscopy: Shadow temporal superior of the optic nerve. Opening through the shadow. Resection area superior to the optic nerve with a small pigmentedtumour. The artificial lens is removed.

Light microscopy.
Advanced degenerative changes in the eye. The corneal epithelium can be traced along the entire section length. Layering is somewhat irregular, with an extended thinning to two or three cell layers. Predominantly basal epithelial edema. The Bowman layer is essentially intact. The stroma appears unremarkable, without significant alterations. The Descemet membrane is generally thickened. Peripherally, Hassall-Henle warts are present, with no significant guttata formations. The endothelium is rarefied, partially displaying vacuolated cytoplasm. There is also a focal impression of fibrous endothelial metaplasia.

Access to the chamber angle is unobstructed, except for a localized anterior synechia. The trabecular meshwork contains some pigmented cells, but no tumor cells are apparent. No clear evidence of rubeosis iridis. The ciliary body remains relatively well-preserved, with a two-layered epithelial structure. Remnants of the lens capsule with regenerative posterior cataract.
In the pars plana region, fibrovacular proliferation is observed, resembling a cyclitic membrane. There are also distinct round cell infiltrates. The retina is severely degenerated and appears extensively absent at the posterior pole, similar to the choroid, according to the resection area. At the posterior pole, a spherical neoplasm is observed at the level of the retina, featuring wide-lumened, thin-walled blood vessels filled with erythrocytes, with partial extravasation of erythrocytes into the adjacent connective tissue. The optic nerve demonstrates a glial atrophy.

Immunohistochemistry. The vascular endothelial cells are positive for Von Willebrand Factor (VWF). The tumour is surrounded by a thin capsule of glial cells (GFAP positive) in continuation ot the retina. The reaction is negative for alpha smooth muscle actin (SMA).

Diagnosis Cavernous hemangioma of the retina.

Discussion

Retinal hemangiomas are rare. They are classified into capillary, cavernous, and racemose forms. Cavernous hemangiomas are uncommon, typically congenital vascular anomalies that are most often discovered incidentally in asymptomatic patients. They were first described as a distinct entity by Gass in 1971.[1] They consist of multiple venous aneurysms in the peripheral retina and, less commonly, are located epi- or juxtapapillary.[2]Fibrogliotic tissue is often associated. Most cavernous hemangiomas are asymptomatic but can cause visual disturbances due to secondary gliosis with vitreoretinal traction or as a result of vitreous hemorrhage. In fluorescein angiography, cavernous hemangiomas exhibit a pathognomonic pattern. During the filling phase, the caverns remain hypofluorescent, and in the late venous phase, the aneurysmal dilations begin to fill until the upper half is filled with fluorescein. The lower half remains hypofluorescent due to blood filling, creating a characteristic mirror-like effect.[2]
Cavernous hemangiomas usually occur in isolation, but they can also be found in association with cutaneous and cerebral cavernous hemangiomas as part of an autosomal dominant hereditary neuro-oculo-cutaneous syndrome. Mutations in the *CCM1* gene (7q), which encodes the KRIT1 protein (Krev interaction trapped-1), are known to be associated with this condition. Abnormal forms of KRIT1 have been identified in families with cavernous hemangiomas of the retina, central nervous system, and skin.[3,4]
The pathogenesis of the cavernous hemangioma in our patient remains unclear. This is not a congenital but an acquired hemangioma, which developed over the long term following endoresection and adjuvant radiation therapy, ultimately leading to vitreous hemorrhage. Whether the cavernous hemangioma is radiation-induced and can therefore be considered a complication of "radiation retinopathy" cannot be definitively determined. The vitreous hemorrhage likely developed as a result of traction in the area of the hemangioma surface.[5] The differential diagnosis of a choroidal melanoma recurrence is not always straightforward. Vitreous hemorrhages are inherently suspicious for choroidal melanoma recurrence. Congenital cavernous hemangiomas typically do not grow; however, in this case, the mass increased in size over time. Congenital cavernous hemangiomas are classically characterized by grape-like clusters of aneurysms. In this case, the endothelial-lined vessels of the acquired hemangioma formed a compact, dome-shaped lesion. Sonographically, choroidal melanomas with hemorrhages are not always easy to distinguish from subretinal hemorrhages or other highly reflective solid masses. A definitive diagnosis could only have been established through biopsy.

Literature cited:

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