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Radiation damage following periocular radiation for basosquamous carcinoma

Clinical History

A 72 year old man was referred to our Ophthalmology Service for enucleation for a blind painful eye. He had a history of amniotic membrane transplantation in 2023 for a therapy-resistant corneal ulcer and a history of lateral tarsorrhaphy. In 2017, he was diagnosed with a large "periocular" basosquamous carcinoma involving the forehead and extending to the nose but sparing the ocular adnexae. Following an unsuccessful surgical approach, the patient received 30 sessions of radiotherapy (resulting in loss of vision OS) and was under treatment with the sonic hedgehog inhibitor Sonigedib (which had to be stopped due to severe side effects). Currently, the patient is under treatment with immune checkpoint PD1-inhibitor Cemiplimab.
Due to the complexity of the post-radiation anatomy with lagophthalmos and a deformed ocular adnexae, we assessed together with our ocularist the likelihood of a satisfying prosthesis outcome after enucleation resulting in a positive evaluation. The patient underwent successful enucleation the patient was restored with a custom-made ocular glass prothesis with a more than acceptable cosmetic result.
The fellow eye was unremarkable with a visual acuity of 20/20 with glasses. The patient denied a history of diabetes mellitus or ischemic events in the left eye.

Ocular Pathology

Gross examination.
Left globe measuring 23 x 22 x 20 mm. The cornea (11 x 11 mm) was cloudy and there was a corneal ulcer. After horizontal opening of the globe, pseudophakia became visible. A macular edema was present and a retinal tear st/p argon laser photocoagulation was visible in the retinal periphery. Choroid and sclera were unremarkable.

Light microscopy.
Cornea with only partial epithelial covering. Bowman's layer is largely absent. The limbal area is massively inflamed and gives rise to a vascularised corneal pannus. There is a neovascularisation in the anterior corneal stroma and pre-Descemet's membrane. Descemet's membrane itself and the endothelium are mainly regular. The trabecular meshwork is atrophic and the chamber angle is covered by a delicate neovascular membrane extending from the iris surface. Iris and ciliary body are otherwise regular. Pseudophakia and a secondary cataract are present. The retina exhibits a degeneration with

retinal atrophy. A macular edema is present. The optic nerve is also atrophic with thickening of pial septae. There is suspicion for retinal neovascularisation in the mid-periphery. The choroid is unremarkable without any signs of inflammation.
An infiltration of tumor cells from the basosquamous carcinoma was not observed in our sections.

Diagnosis **Corneal ulcer and corneal neovascularisation, neovascular membrane straddeling the chamber angle, radiation retinopathy with retinal neovascularisation and macular edema interpreted as complications following radiation of periocular basal cell carcinoma**

Discussion

The main goal of the surgery was to remove a blind and painful eye with an appropriate cosmetic outcome which was already quite challenging given the history of the patient. It was obvious that the corneal ulcer could be attributed to the radiation therapy. However, due to corneal clouding the intraocular structures could not be assessed. The intraocular findings with severe retinal atrophy and macular edema, focal retinal neovascularisation and a neovascular membrane covering the chamber angle were unexpected but can be attributed to an ischemic context.

Side effects of radiation include not only skin changes, keratitis and corneal ulceration but also retinopathy and glaucoma (besides cataract which is not of major relevance from an ophthalmological point of view due to the option of cataract surgery). The radiation damage is graded following the toxicity criteria of the radiation therapy oncology group (RTOG), published by Cox et al. (1). Early and late ocular toxicity from radiation are distinguished.

Our patient can be graded after histopathopathologic evaluation of the globe according to the late radiation morbidity scoring scheme as grade 3 (out of 4 grades), i.e. severe keratitis, severe retinopathy or detachment, severe glaucoma.

Although most studies report only minor complications (limited to the anterior segment) after radiation therapy for periocular tumors (2), the findings in our patient are quite characteristic for radiation damage (3, 4), in particular since other reasons for a retinopathy could be excluded. Radiation retinopathy results from a from a degenerative microangiopathy which is irreversible.

According to Jeganathan, “retinopathy has been observed within 3 months in 85% of eyes irradiated to 70 to 80 Gy. Although retinopathy has been reported after doses as low as 11 Gy, the threshold dose for retinal damage is usually considered to be 30 to 35 Gy. Furthermore, a 50% risk of ocular loss after 5 years (TD50/5) has been described in humans with a 50 Gy dose (delivered in 2 Gy-fractions) and a 5% risk (TD5/5) with a 30 Gy dose”. For our patient, the radiation dose that has been administered is not known.

References

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