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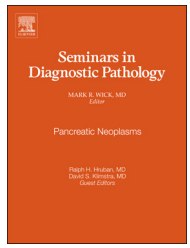

Macroscopic techniques for ophthalmic tumor specimens

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ABSTRACT

This article explores the range of tumor specimens that may be submitted to ophthalmic pathology. The handling of complex enucleation and exenteration is described along with smaller eyelid, conjunctival and corneal specimens. The importance of a good understanding of the unique anatomy of the ocular region and detailed clinical information is emphasized as this results in the taking of appropriate blocks for histology and consequently clinically helpful reports. Recommendations for handling specimens where further tissue is required for molecular studies is discussed.

In ophthalmic pathology, tumors of various types may be seen because that discipline also encompasses such areas of pathology as dermatopathology and soft tissue pathology, along with diseases of the conjunctiva, cornea, intraocular structures, optic nerve, lacrimal gland, and lacrimal apparatus. In certain countries such as the United Kingdom, published guidelines exist for the reporting of tumor specimens in ophthalmic pathology.[1] However, that situation is not present in all countries, and, for some general pathologists, such specimens may therefore constitute bewildering rarities. This article aims to provide a practical approach for the handling of gross specimens of ophthalmic tumors.

Enucleation for a tumor

Enucleation for a tumor is most commonly undertaken for primary malignancies such as retinoblastoma[2] in children and uveal melanoma[3] in adults. Unless the lesion is advanced at presentation, removal of the eye is done only after previous treatments, such as irradiation, have been given. Morphological changes that are related to the initial intervention may alter the eventual appearance of the tumor.[4] Other neoplasms that may necessitate enucleation include tumors of the ciliary epithelium (adenomas or adenocarcinomas; medulloepitheliomas), lesions of the retina (retinocytoma and other astrocytic tumors), and proliferations of the retinal pigment epithelium (adenocarcinoma). Enucleation may uncommonly be done for lymphomas (both primary and secondary), metastatic tumors, or choroidal vascular neoplasms.

External examination

Globes should be submitted intact, in a volume of formalin sufficient to cover the specimen; they should then be fixed for at least 24 h. The eye should be oriented prior to dissection by looking for the muscular insertion of the inferior oblique muscle on the temporal aspect of the globe posteriorly and the fibrous insertion of the superior oblique muscle superiorly.[5] If the muscles have been cut off close to the globe, the ciliary arteries may be used for identification in the horizontal plane. The eye is traditionally measured in the following order—antero-posterior × horizontal × vertical, using an engineer's callipers or a small ruler. The normal size of each dimension is 22–23 mm.

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Uveal melanoma

Until recently, it was not uncommon to submit eyes containing uveal melanomas in the fresh state, to remove tumor for cytogenetic studies. However, almost all required techniques for that purpose can now be applied to formalin fixed tissue.

In cases of uveal melanoma, the vortex veins should be identified as they pass obliquely through the scleral canals. The veins may be obscured by blood clot, which can be removed with a fine forceps. They are located by drawing an imaginary line at 45° from the center of the optic nerve, and searching in the area 6–9 mm from the nerve. The venous canals are oblique slits that will admit the tip of a pair of fine forceps. The veins should be cut close to the sclera, and then removed and processed separately for histological examination. If they are not identified, a slice of sclera across the venous canal is an acceptable substitute. The optic nerve should also be sampled before opening the globe. A razor blade is useful in removing small structures such as the vortex veins or the optic nerve resection margin.

Signs of previous treatment may be evident, such as tantalum markers sutured to the globe as used in proton beam therapy or a surgical coloboma caused by prior local resection (Fig. 1A). Other features in this category include rubeosis iridis and extraocular spread (Fig. 1) or expansion of the optic nerve by tumor (Fig. 1B).

Retinoblastoma

Globes removed because of retinoblastoma may be sampled in the fresh state for molecular analysis to determine whether the tumor is hereditary or sporadic in nature. International guidelines have defined a consensus approach for this procedure,[6] in which the optic nerve resection margin should be sampled before opening the globe to prevent contamination by tumor. Thereafter, a window can be made in the sclera at the edge of the intraocular lesion with a trephine or sharp blade. Additional features that can be seen in retinoblastoma enucleation specimens include leukocoria,[7] pseudohypopyon,[7] rubeosis iridis,[7] tumoral expansion of the optic nerve, and foci of extraocular spread.[8]

Internal examination

Transillumination/retroillumination

In these procedures, a fiber-optic light is placed behind the globe that is rotated and shielded with the fingers so that light passes through the specimen. The normal globe is translucent; hence, internal shadows may indicate the outline of a tumor. These can be outlined on the sclera with indelible ink after the surface has been dried.

Sectioning of the entire eye

The plane of sectioning of the globe depends on observations made during external examination and transillumination. The aim is to obtain a plane in which the pupil, optic nerve and the main tumor mass are represented.[5] Although horizontal sectioning is usually the method of choice, because this allows for examination of the optic nerve and macula in one plane, oblique sectioning is usually required for mass lesions. Upon removing the calotte, the interior of the eye is examined and described, and, if appropriate, photographed. A restraining cup fashioned from pins or needle tips projecting from a black plastic sheet can be useful to hold the globe in position for gross examination or photography. Examining the globe in a black-walled container under water is helpful to eliminate highlights.

For uveal melanomas, the following features should be recorded: the structures involved (iris: ciliary body or choroid), largest basal dimension and thickness of the tumor in mm, size of any extrascleral extensions, and macroscopic growth pattern.

Iris melanomas have a more favorable prognosis than do choroidal melanomas, but the converse pertains to ciliary body melanomas[9]. Size is an important prognostic factor for uveal melanoma. Small tumors (base 5 mm; thickness up to 3 mm) have a 5-year mortality of 16%. Medium-sized lesions (base <16 mm; thickness up to 10 mm) have a 5-year mortality of 32%. Large tumors (thickness >10 mm or base >16 mm) have a 5-year mortality of 53%.[10] Most uveal

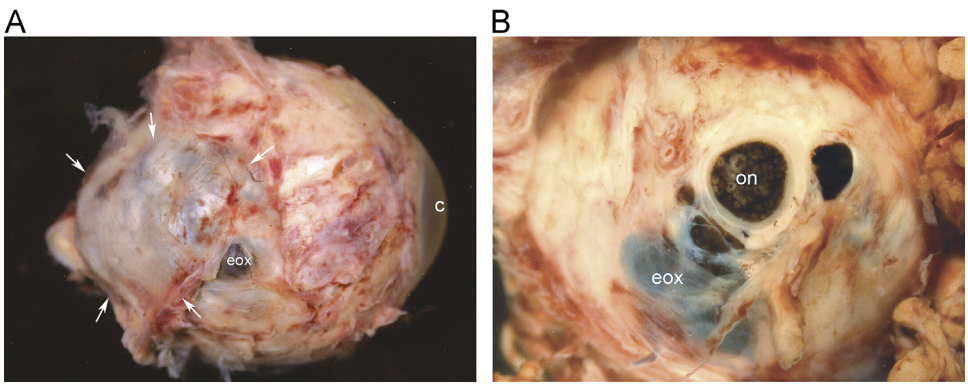

Fig. 1 – (A) This eye was enucleated for recurrent choroidal melanoma after previous local resection. The cornea (c) allows orientation. The arrows indicate the scleral thinning in the region of the surgical coloboma. Tumor has recurred at the edge of the local resection site and formed a small extraocular extension (eox). (B) This is the posterior aspect of a globe enucleated for melanoma (with no history of prior treatment). The tumor has invaded the optic nerve (on) which is expanded by pigmented brown tumor. The tumor also forms an extraocular extension (eox) around the nerve.