Recommendations for the Reporting of Tissues Removed as Part of the Surgical Treatment of Common Malignancies of the Eye and its Adnexa

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The Association of Directors of Anatomic and Surgical Pathology developed recommendations for the surgical pathology report for common malignant tumors. The recommendations for tumors of the eye and its adnexa are reported.

KEY WORDS: Basal cell carcinoma, Conjunctiva, Eyelid, Melanoma, Orbit Retinoblastoma, Sebaceous carcinoma, Squamous cell carcinoma, Uvea.

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The Association of Directors of Anatomic and Surgical Pathology named several committees to develop recommendations about the content of the surgical pathology report for common malignant tumors. A committee of persons with special interest and expertise write the recommendations, which are reviewed and approved by the council of Association of Directors of Anatomic and Surgical Pathology and subsequently by the entire membership.

The recommendations have been divided into four major areas: 1) items that provide an informative gross description; 2) additional diagnostics features recommended for inclusion in every report if possible; 3) optional features that may be included in the final report; and 4) a checklist.

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Note: Ophthalmic pathologists use the term "primary acquired melanosis with atypia" in place of the following terms: intraepithelial atypical melanocytic hyperplasia, malignant melanoma *in situ*, Level I malignant melanoma.

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The purpose of these recommendations is to provide an informative report for the clinician. The recommendations are intended as suggestions, and adherence to them is completely voluntary. In special circumstances, the recommendations may not be applicable. The recommendations are intended as an educational resource rather than a mandate.

BACKGROUND

Before the public awareness of AIDS and Alzheimer's disease as health problems, the disease feared most by Americans was cancer; the second most feared condition was blindness (The Gallup Organization, Inc., Public knowledge and attitudes concerning blindness—a survey sponsored by Research to Prevent Blindness, Inc., New York, October 1965 and April 1976, unpublished data). Patients who are confronted with a diagnosis of ocular cancer, therefore, face two of their most principal fears: shortening of their lifespan and loss of vision. Ophthalmologists who manage most patients with ocular malignancies often try to balance the patient's desire to preserve vision with the goal of eradicating the cancer. In general, the pathologist's report should catalog not only those features appropriate for estimating the natural history of the patient's disease (prognosis), but also those features that might compromise vision.

In general, it is recommended that pathologists report on malignancies of the orbit using formats either published or in development for the counterpart lesion elsewhere in the body. For example, lymphomas of the orbit should be reported according to generalized recommendations for reporting lymphomas. It is reasonable for the report for rhabdomyosarcoma (the most common primary malignancy of the orbit in childhood in the United States) to follow recommendations for reporting rhabdomyosarcomas in general. The lacrimal gland

may be considered to be a minor salivary gland for the purposes of reporting malignancies in this region, and pathology reports dealing with lacrimal gland malignancies (principally adenoid cystic carcinoma) should follow recommendations for reporting this tumor as described for the salivary gland.

Recommendations are therefore offered for three classes of ocular malignancies: conjunctival neoplasms (including those affecting the limbus—the junction between the cornea and sclera), sebaceous carcinoma (a common malignancy of the eyelid), and the two major intraocular neoplasms (retinoblastoma and malignant melanoma).

1. **General** –the Association recommends that the following features be included in the final report because they are generally accepted as being of prognostic importance, of visual importance, required for staging or therapy, and/or traditionally expected.

A. **How the specimen was received** (*e.g.*, fresh or in fixative)

B. **How the specimen was identified** (*e.g.*, labeled with the name, medical record number, and surgeon's name)

C. **Laterality of the lesion** (*e.g.*, originating from the right or left eye)

D. The exact anatomic location of the tumor

1. Conjunctiva: bulbar (by quadrant –superior, inferior, nasal, temporal), palpebral (superior or inferior), fornix (superior or inferior)

2. Limbus (by clock hour)

3. Caruncle or plica semilunaris

4. Eyelid (upper, lower, medial canthus, lateral canthus)

5. Intraocular tissue (iris, ciliary body –by clock hour)

E. **The type of surgical procedure**

1. Incisional biopsy, excisional biopsy, shave biopsy (conjunctiva, eyelids)

2. Iridectomy (removal of iris tissue), iridocyclectomy (removal of iris and ciliary body tissue)

3. Enucleation (removal of eye)

4. Exenteration (removal of the eye and orbital contents, with or without eyelids, not covered in this report)

2. **Gross Description**

A. **Conjunctival and Eyelid Biopsy**

1. Dimensions of the specimen (length, width, thickness)

2. Maximum diameter of any visible lesion

3. Measurement of minimum distance between edge of lesion and surgical margin (minimum clearance)

4. Presence or absence of ulceration

5. Color of the lesion and adjacent tissue

6. Description of attached tissue (episclera, cornea)

7. Orientation of the lesion if provided by the surgeon

1. Some surgeons will identify surgical margins of interest by applying a suture to an edge of the specimen, by painting certain margins with dyes, or attaching the specimen to a piece of filter paper and making notations on the specimen mount

B. Iridectomy/iridocyclectomy

1. Dimensions of the specimen (length, width, thickness)

2. Description of tissue received (iris only, iris and ciliary body, iris, ciliary body and peripheral cornea and/or sclera including location by clock hour)

3. Dimensions of lesion (length, width, height)

4. Measurement of minimum distance between edge of lesion and surgical margin (minimum clearance)

1. Relevant surgical margins include the lateral margins and the posterior margin (the anterior margin is the pupillary border and is not a true surgical margin)

C. **Enucleation**

1. Dimensions of the eye (anterior-posterior, horizontal, vertical)

2. Length of optic nerve attached

3. Examination of the surface of the eye for gross evidence of extraocular extension of tumor

4. Dimensions of the cornea (horizontal and vertical)

5. Clarity of the cornea

6. Color of the iris (describe lesions if present)

7. Shape and diameter of the pupil

8. Transillumination of the eye with dimensions of any shadows

1. Transillumination of the eye may be performed with a fiberoptic light source to locate a tumor within the eye by the shadow that it casts during this procedure

1. Location of transillumination shadow(s) relative to the limbus and optic nerve (distance of shadow borders from limbus and optic nerve)

2. Location of the shadow relative to clock hour

9. Describe the section plane used to open the eye

10. Obtain cross section of the optic nerve

1. Retinoblastoma

1. Obtain a section from either the surgical margin of the optic nerve (the transected edge) or the cut surface of the optic nerve as it inserts in the eye

1. If the cut section of the optic nerve adjacent to the eye is negative for tumor, then one may conclude that there is no involvement of the nerve posterior to the eye (tumor extends through the nerve without skip lesions)

2. Frequently, the surgical margin of the optic nerve (the cut edge of the nerve) is crushed by enucleation scissors

11. Describe the cut surface of the eye

1. Retinoblastoma
1. Number and size of lesions
2. Location of the lesion(s)
3. Gross evidence of choroidal invasion or extraocular extension
4. Presence or absence of vitreous seeding
5. Presence or absence of retinal detachment
2. Uveal melanoma
1. Tissues involved (choroid only, choroid and ciliary body, ciliary body only, iris and ciliary body, iris only)
2. Location of the melanoma relative to clock hour
3. Dimensions from cut surface (maximum zone of scleral contact, dimension perpendicular to maximum zone of scleral contact, elevation measured from top of lesion to interface with sclera)
4. Color of the surface lesion
1. Color of the lesion may provide important clinicopathologic correlations to the ophthalmologist
1. A white plaque over the surface of the lesion may indicate fibrous metaplasia of the overlying retinal pigment epithelium
2. Orange pigment over the surface of the tumor (lipofuscin) is considered by some ophthalmologists as clinical evidence of an aggressive tumor
5. Color of the cut surface of the lesion (melanotic, amelanotic, variegated)
6. Presence or absence of retinal detachment or hemorrhage
7. Presence or absence of extraocular extension or involvement of intrascleral emissary channels

3. **Microscopic Description**

A. **Conjunctival squamous cell carcinoma**

1. State presence or absence of invasion into underlying tissues (episclera, corneal stroma)
2. State presence or absence of tumor at resection margins, including the deep margin and all lateral margins
3. State degree of differentiation (well differentiated, moderately differentiated, poorly differentiated)
4. State type (ordinary squamous cell carcinoma, spindle cell variant of squamous cell carcinoma, mucoepidermoid carcinoma)
5. Mention presence or absence of vascular, lymphatic, perineural, intraocular, or intraorbital invasion

B. **Conjunctival malignant melanoma**

1. State presence or absence of invasion into underlying issues (episclera, corneal stroma)
2. State presence or absence of tumor at resection margins, including the deep margin and all lateral margins (description of margins should include presence or absence of intraepithelial primary acquired melanosis with atypia, see note)
3. Thickness of the tumor in millimeters and tenths of millimeters as measured by the Jakobiec modification of the Breslow method using a calibrated ocular micrometer. The tumor thickness is measured from the top of the epithelium (there is no granular layer in the normal conjunctival epithelium).
1. Some pathologists consider a depth of invasion of 0.8 mm to be significant in separating patients at high risk for metastasis from those at low risk.
4. Intralymphatic invasion by tumor
5. Optional criteria
1. Mitotic figures/mm^2; proliferation indices using markers such as MIB-1 or Ki67

C. **Sebaceous carcinoma of the eyelid**

1. Location of the tumor (upper eyelid *versus* lower eyelid)
2. Size in millimeters
1. Some pathologists consider this measurement to be optional
3. Gland of origin (Meibomian *versus* Zeis gland)
4. State presence or absence of infiltrative growth pattern
5. Differentiation
1. Some pathologists consider the differentiation of sebaceous carcinoma to be an optional feature of the report
6. Multicentricity
7. Intraepithelial (intraepidermal) pagetoid involvement in conjunctiva, cornea, or eyelid skin
8. Tumor involvement of lymphatics or blood vessels or intraorbital invasion
9. State presence or absence of tumor at resection margins, including the deep margin and all lateral margins (description of margins should include presence or absence of intraepithelial pagetoid spread)

D. **Retinoblastoma**

1. Growth pattern (diffuse, unifocal, multifocal)
2. Bilaterality and trilaterality (bilateral with involvement of the pineal gland)
3. Differentiation (presence of Flexner-Wintersteiner rosettes, Homer Wright rosettes, and fleurettes)
4. Invasion into the optic nerve by layer (prelaminar, laminar, retrolaminar, to optic nerve resection margin)
5. Extraocular extension
6. Some pathologists and oncologists consider choroidal invasion to be a significant risk factor for metastasis although this feature is not universally accepted as prognostically significant
7. Optional features of the tumor
A. Endophytic vs. exophytic, presence and degree of tumor necrosis, calcification, DNA deposition around blood vessels, vitreous seeding, anterior chamber seeding (pseudohypopyon)
8. Effects of the tumor on the eye
A. Retinal detachment; iris neovascularization

E. **Uveal malignant melanoma**

1. Location (confined to the iris, involving the iris and ciliary body, confined to the ciliary body, involving the ciliary body and choroid, involving the iris, ciliary body and choroid, or confined to the choroid)

2. Extraocular extension

3. Growth pattern: diffuse melanoma, ring melanoma, focal melanoma

4. Cell type (McLean's modification of the Callender classification)

5. Mitotic figures per 40 high-power fields

6. Presence or absence of 100 tumor infiltrating lymphocytes per 20 high-power fields

7. Matrix-rich microcirculation-associated loops, networks or parallel with cross-linking structures (some pathologists have suggested that microvascular density is also a prognostic feature)

8. Optional features

A. Pertaining to the tumor: presence of absence of nevus, necrosis, intrascleral invasion, invasion into the trabecular meshwork, or invasion into the vortex veins; cytomorphometric measurement of nucleolar diameter (mean of the largest nucleoli or standard deviation of nucleolar area), proliferation indices, cytogenetic abnormalities (especially chromosomes 3 and 8)

B. Effects of the tumor on the eye: retinal detachment, Bruch's membrane rupture, retinal invasion, iris neovascularization, angle closure, cataract

TABLE 1. Checklist for Conjunctival Squamous Cell Carcinoma

1. Site (circle all affected)
Conjunctiva
Bulbar, palpebral, fornix
Caruncle
Plica semilunaris
Limbus
Cornea
2. Procedure
Excisional biopsy
Incisional biopsy
Debridement of corneal epithelium
3. Involvement of the (circle all that apply)
Corneal stroma
Episclera
Orbital fat
4. Type (circle one)
Squamous cell carcinoma, common type
Spindle cell variant, squamous cell carcinoma
Acantholytic variant, squamous cell carcinoma
Mucoepidermoid carcinoma
5. Excision (circle one)
Complete
Not complete laterally (indicate affected margins) but complete in depth
Not complete in depth but complete laterally
Not complete either laterally or in depth
6. Vascular invasion (circle one)
Absent
Blood vessels
Lymphatics
Blood vessels and lymphatics

TABLE 2. Checklist for Conjunctival Melanoma

1. Site (circle all affected)
Conjunctiva
Bulbar, palpebral, fornix
Caruncle
Plica semilunaris
Limbus
Cornea
2. Procedure
Excisional biopsy
Incisional biopsy
Debridement of corneal epithelium
3. Involvement of the (circle all that apply)
Corneal stroma
Episclera
Orbital fat
4. Thickness: ____.____mm
5. Mitotic rate: ____/mm^2
6. Excision (circle one)
Complete
Not complete laterally (indicate affected margins) but complete in depth
Not complete in depth but complete laterally
Not complete either laterally or in depth
7. Vascular invasion (circle one)
Absent
Blood vessels
Lymphatics
Blood vessels and lymphatics

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TABLE 3. Checklist for Sebaceous Carcinoma, Eyelid and/or Conjunctiva

1. Site
2. Procedure (circle one)
   Excisional biopsy
   Incisional biopsy
   Shave biopsy
   Map biopsy (conjunctiva)
3. Lesion is: unifocal multifocal
4. Origin (circle one)
   Zeis gland
   Meibomian gland
   Both Zeis and Meibomian glands
5. Size (mm)
6. Infiltrative growth pattern (circle one)
   Absent
   Present
7. Pagetoid spread (circle one)
   Absent
   Present

TABLE 4. Checklist for Retinoblastoma

1. Site
   Right eye, left eye
2. Growth pattern (circle one)
   Diffuse
   Unifocal
   Multi focal
3. Extraocular extension (circle one)
   Absent
   Present
4. Invasion into the optic nerve (circle one)
   None
   Prelaminar
   To the lamina scleralis (cribrosa)
   Retrolaminar
   Posterior resection margin
5. Differentiation (circle all that apply)
   Poorly differentiated
   Flexner-Wintersteiner rosettes
   Home Wright rosettes
   Fleurettes

TABLE 5. Checklist for Uveal Melanoma

1. Location (circle all involved)
   Iris
   Ciliary body
   Choroid
2. Extraocular extension: yes no
3. Growth pattern (circle one)
   Diffuse
   Ring
   Focal
4. Dimension of largest diameter in contact with the sclera:
   ____.____mm
5. Cell type (Callender classification - circle one)
   Spindle cell type
   Mixed cell type
   Epithelioid cell type
   Necrotic
6. Number of mitotic figures per 40× field: ____.
7. Presence of more than 100 tumor infiltrating lymphocytes per 20 high power field (circle one)
   Present
   Absent
8. Matrix-rich microcirculation-associated patterns (circle all that apply)
   Nevus-like (normal, avascular, straight, parallel)
   Loops
   Networks
   Parallel vessels with cross-linking

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