Ocular Malignancies in the Elderly

E. Rand Simpson, MD, Associate Professor of Ophthalmology, University of Toronto; Director, Ocular Oncology, Princess Margaret Hospital, Toronto, ON.

Larry Ulanski II, MD, Ocular Oncology Fellow, University of Toronto, Princess Margaret Hospital, Toronto, ON.

Ocular malignancies in the elderly are often difficult to diagnose and manage. The five main cancers found in association with the eye are basal, squamous and sebaceous cell carcinomas, uveal melanoma and malignant cancers to the orbit. These include malignancies from breast, lung, GI, prostate and myelogenous proliferations. This article briefly reviews the most common forms of ocular cancer and brings the general practitioner up to date on the most current data from the Collaborative Ocular Melanoma Study (COMS). We use clinical photos to demonstrate specific clinical signs of cancerous disease. By maintaining a high level of suspicion when treating patients with acute visual symptoms, unnecessary morbidity and mortality may be avoided.

Key words: ophthalmology, cancer, radiotherapy, malignancy.

Cancer of the eye and surrounding tissue presents with varied frequency and significance in the aging population. Malignant disease of the eyelids, the eye and orbit is often challenging to detect and manage. Although certain cancers carry a high risk of mortality, current therapeutic principles can provide favourable outcomes for preservation of vision and overall survival for most forms of ocular neoplastic disease. The five cancers primarily associated with the eye and its surrounding tissue are basal, squamous and sebaceous cell carcinomas, uveal melanoma and malignant cancers to the orbit.

Basal Cell Carcinoma

Basal cell carcinoma (BCC) is the most common malignant tumour of the eyelid, with 95% of cases occurring between the ages of 40 and 79 years; average age of onset is 60 years. BCC comprises 85–90% of all malignant epithelial eyelid tumours, and occurs on the lower eyelid in two-thirds of cases. Ultraviolet light exposure and light skin pigmentation are important risk factors, and 99% of these cancers occur in Caucasians.1

BCC has a predilection for occurring in medial canthal region, appearing as a flat, indurated yellow-pink plaque on the eyelid margin with telangiectatic vessels. The morpheaform or sclerosing type of BCC may simulate blepharitis or dermatitis. Nodular BCC is well circumscribed or irregular, and may be ulcerated with a central crater. Pigmented BCC is similar to noduloulcerative type in morphology, but with black or brown pigmentation.2 Generally, BCC is painless, slow growing and may become quite disfiguring if left untreated (Figure 1).

The diagnosis of BCC is made by clinical appearance; however, definitive diagnosis can only be made by histopathologic examination of a biopsy specimen. The goal of therapy is complete removal of tumour cells with preservation of unaffected eyelid and periorbital tissue. Morpheaform and multicentric types of BCC may extend far beyond the area that is clinically apparent, and may require excisional biopsy with frozen section control. Recurrence rates of up to 50% have been reported when simple excisional biopsy is performed without frozen section control.3

Radiation therapy, while not recommended as primary therapy, may be used as an adjunct to surgical excision. Doses of 4,000–7,000 cGy to the tumour may be given; however, radiation is associated with a higher recurrence rate and surgical therapy is more difficult after radiation. Cryotherapy may be used for lesions less than 100mm in diameter, although this treatment also is associated with a higher rate of recurrence. Overall, the incidence of malignancy is very low, and tumour-related death is usually caused by direct orbital extension.

Squamous Cell Carcinoma

While squamous cell carcinoma (SCC) is 40 times less frequent than BCC, it is seen more commonly on the upper lid and lateral canthus.2 Furthermore, while rarer than BCC, SCC has a higher potential for malignancy. SCC may spread by lymphatic mechanisms to the preauricular or submandibular lymph nodes or by perineural invasion. Invasion into deep orbital tissues may require orbital exenteration for control.

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actinic lesions. Ultraviolet radiation exposure, ionizing radiation, arsenic ingestion, psoralen plus ultraviolet A (PUVA) therapy for psoriasis and the human papilloma virus may contribute to the development of SCC. Chronic skin dermatoses, ulceration and scarring also may contribute to the development of this tumour. Typically, SCC presents as an erythematous, indurated, hyperkeratotic plaque or fungating nodule with irregular keratin on its surface, giving a crusty appearance (Figure 2). They have a tendency to ulcerate, and may be confused easily with keratoacanthoma, which is a benign condition. Actinic keratosis, a premalignant form of SCC, has a flaky, white, scaly surface and may be slightly elevated and slightly erythematous. Actinic keratosis may evolve to SCC in 12% of cases.4

Sebaceous Gland Carcinoma

Sebaceous gland carcinoma (SGC) is a rare but highly malignant form of ocular cancer. It may arise from meibomian glands along the eyelid margin, or from glands of Zeis or those associated with the caruncle. SGC accounts for 1–5.5% of all eyelid cancers, and usually presents in the sixth to seventh decade of life, affecting the upper eyelid in two-thirds of cases. Younger patients may develop SGC if they have a prior history of radiation exposure.5 This tumour often presents as a firm, yellow nodule that resembles a chalazion. Often there is associated madarosis (loss of eyelashes) due to tumour invasion into the eyelash follicles. SGC may mimic chronic blepharitis, meibomianitis or a chalazion that does not respond to usual therapies (Figure 3). Due to a tendency for pagetoid spread, full thickness wedge biopsy of central lesion with multiple biopsies taken of adjacent bulbar and palpebral conjunctiva is indicated. If adjacent areas are positive for pagetoid spread, exenteration may be necessary. If regional lymph node invasion is suspected, the patient may require a radical neck dissection by an otolaryngologist. Primary radiotherapy is considered inadequate because of early tumour recurrence.

SGC may be highly malignant and can carry a high mortality. Metastatic spread may be by hematologic or lymphatic spread. Distant metastatic spread is associated with a 50–67% five-year mortality.6

Intraocular Eye Cancers

Intraocular cancers may take many forms, from solid masses to diffuse vitreal infiltrates. Solid infiltrating tumours include uveal melanoma, choroidal hemangiomas, choroidal osteomas and metastatic spread from other primary cancers. The most common metastasis to the eye comes from breast and lung, with gastrointestinal adenocarcinoma, renal cell carcinoma, prostate and carcinoid occurring less frequently. Diffuse vitreal infiltrates may include primary ocular lymphoma and leukemia (Figure 4). Most patients who develop metastatic disease to their eye have a known primary malignancy, although it is estimated that 25% of patients who are found to have metastatic carcinoma in the eye develop that condition as the initial manifestation of their cancer. The cumulative lifetime incidence of clinically detected metastatic intraocular tumours is approximately 1 in 1,000 to 1 in 400.7

Uveal melanoma is the most common primary intraocular cancer in adults. It has a predilection for Caucasians, and has an annual incidence of six per million after the age of 30 years, increasing to 50 new cases per million after 70 years. The average age of detection is 55–60 years of age.8 Uveal melanoma, though sharing the same root name as skin melanoma, acts in a different manner. Uveal melanoma arises as a primary acquired malignant neoplasm of uveal melanocytes. It may affect the posterior aspect of the eye (called a choroidal melanoma), the ciliary body or the anterior aspect of the eye (iris melanoma).
Iris melanomas may be seen on the surface of the iris with the naked eye (Figure 5). They have a tendency to be darkly pigmented with zones of high vascularity. The larger the lesion, the greater the concern for potential malignancy. However, it is generally accepted that melanomas confined to the iris tend to have substantially less malignant potential than ciliary body or choroidal melanomas. Benign iris nevi have a similar appearance to an iris melanoma; therefore, careful examinations with clinical photomicrographs including high frequency ultrasound are used to monitor patients. Many suspected iris melanomas may be observed without intervention unless the lesion demonstrates significant enlargement over a short period of time. Treatment options for a growing iris melanoma consist of direct surgical excision by iridectomy or iridocyclectomy, plaque radiotherapy or eye removal. Due to the low risk of malignancy, a systemic baseline exam typically is not warranted for lesions that will be observed. However, if a lesion demonstrates growth, a systemic evaluation including liver enzyme levels should be performed.

Many choroidal and ciliary body melanomas are discovered by routine ophthalmologic exam, although patients commonly present with visual disturbances. Visual complaints include flashes and floaters, blurred or distorted vision, loss of peripheral vision or frank vision loss. Typically painless, choroidal melanomas are dome- or mushroom-shaped subretinal lesions which may be associated with substantial exudative fluid, causing an exudative retinal detachment. They may be melanotic or amelanotic in colour, and are unilateral (Figure 6).

The differential diagnosis of choroidal melanoma includes choroidal nevus, metastatic carcinoma, subretinal hematoma, nodular posterior scleritis, choroidal osteoma or ocular melanocytoma. The differential is narrowed by clinical intuition guided by ancillary tests, including B- and A-scan ultrasonography and fluorescein angiography. Microcirculatory patterns of these tumours are strongly associated with biological behaviour of the tumour, and research efforts are currently focused on the understanding of those characteristics which may predict tumour growth and metastatic spread. Those characteristics associated with tumour growth include surface orange pigment, subretinal fluid, tumour size and vascularity. Because survival is nearly 100% for small tumours, many small suspected choroidal melanomas may be observed for a period of time to document a pattern of growth. If a pattern of growth is documented which raises the suspicion of a neoplastic process, several treatment options are available.

The traditional treatment of choroidal melanoma was eye removal, but today more conservative treatments are available depending upon the size of the tumour. Enucleation is indicated for tumours that cause the eye to be blind or painful, are > 10mm in apical height or invade the optic nerve. Patients may elect for tumour removal for personal reasons. An ocular prosthesis can provide very satisfactory cosmesis and comfort, and most patients have little difficulty adjusting to monocular vision.

Today, conservative treatment for ocular melanoma includes radiotherapy in the form of brachytherapy or external beam/charged particle radiotherapy. Recently, the Collaborative Ocular Melanoma Study (COMS), the largest multicentre, prospective, randomized study for the treatment of ocular melanoma, concluded that there is no difference in survival benefit between eye enucleation and I-125 plaque brachytherapy. The overall five-year survival in both treatment groups was 82%, and the five-year rates of death in cases with histopathologically confirmed melanoma metastasis were 11% and 9% following enucleation and brachytherapy, respectively. The side effects of I-125 plaque brachytherapy include cataract formation, radiation retinopathy, neovascular glaucoma and optic neuropathy. The COMS study group has reported significant vision reduction of approximately 50% in patients treated with I-125 brachytherapy at three years. The degree of visual loss is dependent upon tumour location and amount of radiation.
delivered to the ocular structures. A history of diabetes, associated retinal detachment, thicker tumours, tumours close to or beneath the fovea or tumours that were not dome-shaped were most likely to predict poor visual outcomes. Following treatment, systemic evaluation including liver function test and CXR needs to be monitored for the patient’s lifetime.

New treatment modalities, including diode laser therapy, microsurgical resection, hyperthermia, photodynamic therapy, cryotherapy, chemotherapy and multi-modal therapy, may have a future role in patient management.

**Orbital Disease**

The geriatric population is susceptible to other disease processes that may have ocular consequences. The age-specific incidence of a primary orbital tumour is approximately two per million until the sixth decade of life, increasing to four per million in those older than 60 years, which further increases to 10 per million in those older than 80 years. In a retrospective case series by Demirci et al., the most common diagnoses among their study population were malignant lymphoma (24%), idiopathic orbital inflammation (10%) and cavernous hemangioma (8%) (Figure 7). Of the orbital lesions, 63% were found to be malignant in nature, most commonly metastatic from breast, prostate and lung. The most common clinical presentation included an orbital mass, eye protrusion and pain.

**Conclusion**

Overall, ocular cancer is a relatively rare event, yet life threatening conditions may present as benign visual disturbances or in a relatively painless and benign fashion. A high index of suspicion and prompt referral to an eye cancer centre may not only ease a practitioner’s anxiety, but also may allow for

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*Figure 6: Choroidal Melanoma.* (A) Note the highly pigmented nature of this lesion lying beneath the macula. Visual acuity was severely affected in this individual. (B) demonstrates an I-125 plaque positioned on the scleral surface to treat a ciliary body melanoma.

*Figure 7: Orbital Lymphoma.* Note the invasive superotemporal mass in the left orbit displacing the globe inferiorly and medially on axial (A) and coronal (B) MRI images.
prompt intervention in a life threatening process. With future collaborative efforts, we look forward to not only lower mortality, but also improved quality of life for our patients.

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