

MEDICAL CERTIFICATION OF PILOTS WITH UVEAL MELANOMA

CASE REPORT, BY TIM D. DUFFY, DO, MOH

Uveal tract (iris, ciliary body, or choroid) melanoma is the most common primary intraocular malignancy in adults. The incidence in the United States is approximately 4.3 new cases per million people, which is comparable to international rates of 5.3 to 10.9. This article presents a case report of an airman who presented to a physician with visual complaints. Included is a review of the disease process, treatment, and aeromedical concerns.

History

A 36-YEAR-OLD WHITE MALE presented to an ophthalmologist in 2007 due to decreased visual acuity of his right eye. On examination, his right eye vision was 20/30 and otherwise normal except for a membrane suggestive of histoplasmosis. He underwent yearly Avastin (bevacizumab) injections for three years and had no further problems until 2013, when he returned with left eye symptoms. The left eye exam was normal, but a slit lamp examination of the right eye discovered an anterior pigmented mass with a convoluted surface pressing anteriorly on the iris and posteriorly on the lens. This mass did not transilluminate, and there were pigmentary changes in the macula.

He was sent to a specialist who repeated the dilated fundus exam. An ultrasound showed a mass with a lesion height of 3.27 mm. A fine needle aspiration (FNA) of the mass was performed, and a gene expression assay for uveal melanoma using a new RT-PCR assay indicated a Class 1A ciliary body melanoma. This Class 1 molecular signature is associated with a low risk of near-term clinical metastasis. Ninety-eight percent of patients with a Class 1A tissue diagnosis are cancer-free at 5 years with external plaque radiation treatment (1). During the subsequent workup, the patient underwent a CT of the chest, abdomen, and pelvis. No metastatic lesions were discovered. Post-radiation, the patient's vision was 20/40 on the right and 20/20 in the left. The specialist released him to observation and subsequent 6-month evaluations.

This applicant presents to your office for a third-class student pilot certificate, having flown 3.7 hours with a flight instructor at the local airport.

Aeromedical Issues

The ultimate aeromedical concern for melanoma is the risk of in-flight incapacitation. The clinical issue of aeromedical concern is recurrence and the clinical effects of metastasis. Numerous studies have attempted to explore the relationship between sunlight exposure and the risk of uveal melanoma, which to date, yield a weak association. Other associations include Caucasian race, fair skin that tans easily, and light-colored eyes. The cancer is more commonly diagnosed in males in their 60s and is not considered an inherited disease, even though there are sporadic reports of family clusters. Whether some environmental exposure triggers the development of uveal melanoma remains an open question. Sunlight is the strongest environmental factor, since it has been established in melanoma of the skin. Unlike cutaneous melanoma, uveal melanoma rates have not increased over time and do not vary by latitude.

Whether or not altitude exposures to airmen are contributing risk factors is yet to be determined (2).

Our student pilot candidate is an atypical case, since he is 43 years old, Caucasian, has brown eyes, and does not tan easily. There is no family history of melanoma. The aeromedical concern for melanoma for him is potential incapacitation associated with metastasis.

Role of the AME

According to the *Guide for Aviation Medical Examiners*, if this is a first-time application for an applicant with a history of melanoma, the examiner must defer to the Aerospace Medical Certification Division (AMCD) or Regional Flight Surgeon for the initial determination:

Examiners may re-issue an airman medical certificate under the provisions of an Authorization, if the applicant provides the following: An Authorization granted by the FAA; and a current status report performed within 90 days that must include all the required follow-up items and studies as listed in the Authorization letter and that confirms absence of recurrent disease. The Examiner must defer to the AMCD or Regional Flight Surgeon if: There has been any recurrence of the cancer, or any new treatment is initiated. A Special Issuance or AASI is required for any metastatic melanoma regardless of Breslow level. A Special Issuance or AASI is required for any melanoma which exhibits Breslow Level > .75 mm with or without metastasis. A melanoma that exhibits a Breslow Level < .75 mm which has no evidence of metastasis may be regular issued (3).

Role of the FAA

The FAA will send a "cancer letter" requesting the following documentation: a current detailed report from the treating physician, operative and pathology reports, complete laboratory studies, and any other testing the physician performed. Based on the type of cancer, other reports may be requested. Uveal melanoma is an aggressive cancer that metastasizes in up to half of patients. It spreads preferentially to the liver, and metastatic disease is almost always fatal. Currently there are no effective therapies for advanced metastatic disease, so the most promising strategy for determining suitability for flight would be staging and prognosis. Until recently, the gold standard for staging uveal melanoma was chromosome 3 testing for monosomy (3). Within the last two years, a new gene expression profile (GEP) was developed based upon a 15-gene, qPCR-based assay of a FNA of the mass. This assay, known as DecisionDx-UM, is a proprietary assay highly accurate for predicting which patients will develop metastatic disease. The assay molecular signature is divided into Class 1A, 1B, or 2, with respective 5-year metastasis-free rates of 98%, 79%, and 28%, respectively.

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Using the FAA's 1% rule as a guideline and this new prognostic assay, it was determined that this airman poses a low risk for sudden incapacitation. Aviation safety is the FAA's primary goal, and issuing a Special Issuance (SI) for this individual poses low risk to the airman or others.

Outcome

The applicant was subsequently evaluated by an ophthalmologist with expertise in uveal melanoma. An ultrasound showed a tumor height of 3.27 mm. A FNA and subsequent GEP assay staged him as Class 1A. He underwent plaque radiotherapy and was risk stratified to have less than a 2% 5-year risk of metastasis. The FAA requested a copy of the ultrasounds, copies of the radiation treatment records, and current Humphrey visual field graphs. Since uveal melanomas behave differently than cutaneous melanomas, the FAA's decision was to certify and follow without brain MRIs. The airman received a student pilot third class-certificate and a SI for uveal melanoma.

References

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ETIOLOGY OF UVEAL MELANOMA

Uveal melanoma can arise from either the anterior (iris) or posterior (ciliary body or choroid) uveal tract. Anterior lesions have a better prognosis because they tend to be small, slow growing, and can be visually detected. Posterior lesions tend to be detected only upon slit lamp exams and have a more malignant histologic appearance. A choroidal nevus may be mistaken for a melanoma, or it may develop into a malignant melanoma. The USAF School of Aerospace Medicine reviewed the eye exams of more than 5,000 aviators over a period of 14 years; 2.2% of aviators were noted to have one or more choroidal nevi. These lesions were found not to affect the aviators' visual performance, but following these lesions at regular intervals by an ophthalmologist was recommended.

In a large, retrospective, single-center series of 2,514 consecutive patients with choroidal nevi, the progression rates to melanoma at 5, 10, and 15 years was 8.6%, 12.8%, and 17.3%, respectively (4). The 5-year mortality rate associated with metastasis from posterior lesions was 30%, compared to the 3% rate of anterior lesions.

There are many treatment options available for uveal melanoma. These include: enucleation, plaque radiotherapy, proton beam radiotherapy, and transpupillary thermotherapy. Each treatment has potential aeromedical concerns. Enucleation results in monocular vision, and radiotherapy has a 5-year, 50% risk of radiation retinopathy. Cutaneous melanoma metastasizes to the brain, while uveal melanoma spreads to the liver. For this reason, the risks of sudden incapacitation with uveal melanoma are less (5).