carcinosarcoma may occur in children and metastasize regionally as well.

Hayyam Kiratli, MD
Hulya Gökmen Soysal, MD
Suleyman Demir, MD
Ankara, Turkey

The authors have no relevant financial interest in this article.

Corresponding author: Hayyam Kiratli, MD, Ophthalmology, Hacettepe Hastanesi Goz ABD, Syihhiye 06100, Ankara, Turkey (e-mail: hhkiratli@hacettepe.edu.tr).


Aggressive Primary Orbital Melanoma in a Young White Man With No Predisposing Ocular Features

Primary orbital melanoma is an exceedingly rare tumor1 that probably develops from congenital rests of neural crest cells in the orbit.2 It represents less than 1% of primary orbital neoplasms and usually occurs in the presence of clinical or histological evidence of ocular melanosis or blue nevus syndrome.2 Although orbital melanoma in general carries a poor prognosis, our case was unusual for its extremely aggressive clinical course that resulted in the death of the patient 6 months after presentation.

Report of a Case. A 40-year-old white man was first seen by us in July 1998 with a painless 3-mm proptosis of the left eye of 6 months’ duration. There was no clinical evidence of ocular melanosis or blue nevus syndrome. A computed tomographic scan of the orbits revealed a well-defined intraconal mass that was discrete from the optic nerve and the horizontal rectus muscles (Figure 1). In the following 6 weeks, the proptosis enlarged, progressing from 3 mm to 8 mm. There was associated conjunctival exposure with ulceration, marked global restriction of movement, and transient visual obscurations. Optic nerve function was preserved, with Snellen visual acuity retained at 6/5, normal color vision, and intact pupillary reactions. A lateral orbitotomy with excision biopsy was performed in September 1998. A large pigmented mass was removed, histological analysis of which showed the lesion to be an orbital melanoma. A cilioretinal artery occlusion occurred postoperatively, reducing the left visual acuity to light perception.

Histologically, it is not possible to differentiate a primary from a metastatic orbital melanoma; therefore, we performed a thorough systemic evaluation for a primary source. Detailed clinical examination augmented with liver function tests; liver ultrasonography; computed tomographic imaging of the brain, chest, and abdomen; and a bone scan showed no evidence of systemic melanoma. Ocular B-scan ultrasonography, performed to look for an intraocular primary tumor, suggested a possible small anterior ciliary body lesion with a collagen-stud appearance and measuring 1.4 mm.

Five weeks after the excision biopsy, there was an alarmingly rapid recurrence of the left proptosis (Figure 2 and Figure 3). Magnetic resonance imaging revealed local tumor regrowth occupying the inferior aspect of the left orbit and extending superiorly as far as the superior rectus muscle. There was no evidence of spread beyond the orbit. A left exenteration with preservation of the eyelids was carried out in November 1998. Postoperative radiotherapy, to be followed by chemotherapy and adjunctive interferon...
treatment, was planned. However, 3 days before the commencement of radiation treatment, a firm swelling was noted at the lateral aspect of the left orbit. Results of fine-needle aspiration biopsy confirmed the presence of malignant melanoma cells, indicating that surgical clearance had not been achieved.

The patient’s clinical course rapidly deteriorated, with massive and disfiguring growth of the melanoma within the exenteration cavity. Magnetic resonance images showed that the extensive melanoma deposit was causing huge soft tissue expansion, with extension into the paranasal sinuses and left temporal fossa and destruction of the anterior aspect of the sphenoid wing (Figure 4). In December 1998, there was evidence of metastatic disease with distant dissemination to the anterior chest wall and the liver. Treatment with subcutaneous interferon alfa-2a, 20 mIU given on alternate days, failed to alter the course of the disease, and the patient died 2 weeks later.

Histopathological Findings. Excision Biopsy. A dark irregular mass measuring 23 mm × 32 mm was excised. Sections showed a partly necrotic, partly pigmented mass consisting of spindle cells (Figure 5). There were frequent mitoses, considerable nuclear pleomorphism, and large numbers of small microvessels, indicating a vascular tumor. The pigment, which was patchy, was negative for iron (Perls test). The tumor cells stained positively for NKIC3 antibody, S100 protein, and melanoma-associated antigen (HMB45), indicating their melanocytic nature.

Exenteration Specimen. The exenteration specimen (Figure 6) showed extensive infiltration of the orbital fibrofatty tissue by a high-grade malignant melanoma. The tumor was now formed from clusters of medium to large epithelioid cells (Figure 7), but with a staining pattern similar to that of the excision biopsy. There was a high mitotic rate (more than 50 mitoses per 10 × 40 objective fields) and geographic areas of necrosis. There was no evidence of congenital melanosis oculi. Biopsy specimens taken from the margins of excision showed that the skin from the left lateral eyelid and inferior orbital rim was clear, but residual tumor was found at the inferior orbital rim adjacent to the left infraorbital nerve and at the left orbital apex. Ten-micrometer histological sections were made of the entire globe (with every 10th section...
submitted for staining and examination) and demonstrated no pathological evidence of an intraocular or ciliary-body melanoma as was suggested on ultrasonography.

We found no histological evidence of any predisposing disease, either in the form of blue nevi or ocular melanosis in the excision biopsy or exenteration specimen. The overall conclusion was, therefore, of a highly aggressive malignant melanoma that, in the absence of an intraocular or systemic primary tumor, appeared to have arisen de novo within the orbit.

Comment. Primary orbital melanoma is a rare condition that is histopathologically similar to uveal melanoma.2 It is primarily seen in white adults who seek care most commonly for painless proptosis and has an average age at onset of 42 years.2 Predisposing ocular features are present in most cases. In the series by Tel ludat,2 47.5% of the patients had clinical evidence of some form of congenital melanosis. Intraorbital blue nevus was recognized histologically in 90%. The case presented herein is remarkable for the absence of both. Had there been any evidence of ocular melanosis, this patient would probably have proceeded, after orbital computed tomography, to excision biopsy sooner than actually occurred, as clinical suspicion would have been greater.

It is possible to miss small foci of pigmentation, both clinically and histologically, that may represent ocular, oculodermal, or orbital melanocytosis. Detailed inspection of the gross specimens of both the excision biopsy and the exenteration took place to look for minute areas of pigmentation that could have predisposed to the development of melanoma. This was augmented by a thorough intraoperative examination of the orbital periosteum, with multiple biopsy specimens taken from suspicious areas of grey, brown, or black pigmented areas, specifically at the orbital apex and the lateral orbital rim. No evidence of melanocytosis was found. We accept, however, as no autopsy was performed, that it is possible (although unlikely) that an isolated area of melanocytosis from which the melanoma could have arisen may have been overlooked.

B-scan ultrasonographic examination suggested that the orbital mass represented spread from an anterior ciliary primary melanoma, tumors that are known to behave more aggressively than more posteriorly located lesions.3 Histological examination confirmed that this was not the case. The B-scan had been performed the day after excision biopsy, suggesting that the “lesion” observed represented a postoperative artefact, as it would be unlikely that our method of histopathological sampling could have missed a lesion picked up on ultrasonography 5 weeks earlier and estimated to be at least 1.4 mm.

Although primary orbital melanoma carries a poor prognosis, with a 4.5-year mortality of 38%,2 our case represents a particularly aggressive lesion. The best approach to treatment of orbital melanoma is not scientifically known. In our case, an active multidisciplinary approach to tumor control was taken. Surgical excision and local radiotherapy to the orbit followed by chemotherapy and adjunctive interferon treatment was considered the combination most likely to achieve success. However,
the very active nature of tumor recurrence, following both the excision biopsy and exenteration, was surprizing, and the likelihood of radiotherapy or chemotherapy controlling such macroscopic disease was remote.1,4,6 Radical skull base surgery, which entails an intraoperative mortality rate of several percent, was considered. However, it was highly improbable that even this kind of surgery could have successfully eradicated the tumor, and the patient declined further intervention.

This unusual case report of a rare but life-threatening condition illustrates that primary orbital melanoma should be considered in cases of rapidly progressing proptosis in young white patients, even where no predisposing ocular disease is present.

Yvonne M. Delaney, FRCOphth
Susan Hague, FRCOphth
Brendan McDonald, FRCPath
Oxford, England

Corresponding author: Susan Hague, FRCOphth, Radcliffe Infirmary, Oxford Eye Hospital, Woodstock Road, Oxford OX2 6HE, England (e-mail: y.delaney@virgin.net).


Is Coxsackievirus the Cause of Unilateral Acute Idiopathic Maculopathy?

Unilateral acute idiopathic maculopathy (UAIM) is an inflammatory process involving the outer retina and retinal pigment epithelium (RPE) of the macula. It is typically associated with a serous neurosensory detachment and is sometimes associated with papillitis, subretinal exudation, intraretinal hemorrhages, and/or vitreous cells.1,2 Patients report a loss of central vision followed by a remarkable spontaneous recovery over a period of several weeks. This entity frequently affects young, healthy individuals and is often associated with a prodromal flulike illness. We describe 2 patients who developed ocular findings consistent with UAIM shortly after developing classic signs and symptoms of hand-foot-and-mouth disease. We believe that coxsackievirus, which causes hand-foot-and-mouth disease, may also cause UAIM.

Report of Cases. Case 1. A 30-year-old woman had a 5-day history of decreased vision in her left eye. Hand-foot-and-mouth disease had spread through her child’s daycare center that same week. The patient had a sore throat and small erythematous papules on the palms of her hands and the soles of her feet.

Visual acuity was 20/20 OD and 20/200 OS. Findings from an anterior segment examination were unremarkable in both eyes; intraocular pressure was normal in both eyes. Results of a fundus examination were unremarkable in the right eye. Ophthalmoscopic examination of the left eye revealed a yellow lesion bisecting the fovea at the level of the outer retina, RPE, and choroid. There was no evidence of vitreous cells, subretinal fluid, or papillitis. Some motting of the RPE was present (Figure 1A). Fluorescein angiography of the left eye revealed early irregular hyperfluorescence and late staining (Figure 1B).

The patient was observed without intervention and 3 weeks later her visual acuity improved to 20/20 OS. The RPE and choroid had lost their yellow appearance with the development of a bull’s-eye flat pigmented scar (Figure 2). Coxsackievirus titers drawn 3 weeks after the onset of symptoms showed that the level of coxsackievirus A16 antibody was elevated at 1:8 (reference range, <1:8), which may be indicative of a past or recent infection. The level of coxsackievirus B6 antibody titer was also elevated at 1:16 (reference range, <1:8).

Case 2. A 38-year-old white man developed signs and symptoms characteristic of hand-foot-and-mouth disease including a fever, sore throat, and erythematous papules on the palms of his hands.

Figure 1. Case 1. A, Lesion bisects the fovea and shows some thickening and early pigment mottling. B, Fluorescein angiogram shows staining and leakage of the lesion.