Primary Orbital Melanoma Associated With an Occult Episceral Nevus

Melanomas arising in the orbit can present diagnostic and management challenges to the physician. The pathogenesis of primary orbital melanomas is a matter of some debate. Primary melanomas arising in the orbit are rare, accounting for less than 1% of primary orbital tumors\(^1\) and about 2% of extenterations.\(^2\) Most orbital melanomas arise from the uveal tract, conjunctiva, eyelids, or sinuses, and, infrequently, as metastases from distant primary sites.\(^3\) Approximately 90% of primary orbital melanomas arise from melanocytes found in congenital ocular melanocytosis (including blue nevus and cellular blue nevus), orbital melanocytosis, or oculodermal melanocytosis (nevus of Ota).\(^4,5\) The presence of melanocytes has also been reported in the optic nerve sheath, orbital fat, extraocular muscles, and orbital periosteum, which theoretically may provide cells of origin for primary orbital melanomas.\(^5\)

Orbital biopsy may be required to diagnose orbital melanoma when no clinical evidence of melanocytosis of the pericocular tissues or uveal tract is present. Even with an orbital biopsy, the histopathologic diagnosis can often be difficult, especially if the tumor is amelanotic.\(^6\) We describe a 36-year-old woman who developed a primary orbital melanoma that apparently arose from a previously unreported focus of melanocytes, an occult nevus on the posterior sclera.

Report of a Case. A 36-year-old woman was evaluated for right exophthalmos. The right eye had become increasingly prominent over several years, without pain, diplopia, or change in vision. No history of trauma or systemic medical problems was reported. Magnetic resonance imaging (Figure 1) and computed tomography (Figure 2).
revealed a well-circumscribed intracanal mass in the superior medial quadrant of the right orbit, in apposition to the posterior surface of the globe. Orbital ultrasonography demonstrated irregular low internal reflectivity (Figure 3).

An examination revealed a visual acuity of 20/25 OU. The pupils were equally reactive to light. Movements of the right inferior oblique and medial rectus muscles were restricted with a small right hypertropia and exotropia. The right eye was 4 mm more prominent than the left, with moderate resistance to retraction. Eversion of the upper eyelids revealed a pink nodule in the superior conjunctival recess above the right eye (Figure 4). Results of an intraocular examination were unremarkable, and there was no evidence of unusual periorbital or facial pigmentation.

The patient underwent exploration of the superior right orbit through a conjunctival incision above the globe. A biopsy was performed on a clinically nonpigmented mass that was firmly adherent to the posterosuperior surface of the right eye. Frozen sections performed at the time of surgery were interpreted as “small blue cell tumor.” Permanent histologic sections revealed a highly cellular proliferation of small, oval- to spindle-shaped cells with moderate nuclear pleomorphism and small nucleoli, arranged as nests and diffuse sheets (Figure 5C). The mitotic cell count was low, with 1 mitosis per 100 high-power fields. Immunoperoxidase stains were strongly positive for the melanoma cell markers MART1 (melanoma antigen recognized by T cells) and NSE (neuron-specific enolase) antibodies, and the tumor also stained positive for HMB45 and S100 protein. The tumor cells did not stain for cytokeratin, LCA (leukocyte common antigen), chromogranin, synaptophysin, GFAP (glial fibrillary acidic protein), EMA (epithelial membrane antigen), desmin, muscle actin, smooth muscle actin, or Myo D-1. Electron microscopic examination confirmed melanocytic differentiation of the tumor. It revealed tightly packed cells with oval- to round-shaped nuclei with clumped chromatin and occasional nucleoli. Occasional cells contained membrane-bound structures with features of stage III and IV melanosomes and intertwining cytoplasmic processes suggestive of Schwann cell differentiation. The diagnosis of malignant melanoma was confirmed by independent reviewers at 3 different institutions. This lesion fits into a spectrum of previously reported primary melanocytic tumors of the orbit and central nervous system, as it shares many histologic features with meningeal melanocytomas.7

Figure 3. Orbital ultrasonography of the right orbit. A, Horizontal B-scan through visual axis, from the 3- to the 9-o’clock positions. The tumor (arrow) surrounds the optic nerve (asterisk). B, An A-scan through the tumor reveals irregular low internal reflectivity.

Figure 4. A, Clinical appearance at the time of initial examination of a 36-year-old woman with primary orbital melanoma behind the right eye. B, A pink lesion over the superior medial quadrant of the right eye with overlying conjunctival injection is noted clinically.
Serial indirect ophthalmoscopy and ultrasonography revealed no evidence of an intraocular tumor. Extensive systemic workup, including chest radiography, abdominal imaging, liver function tests, bone scans, and thorough medical, dermatologic, and otolaryngologic evaluations, disclosed no evidence of systemic malignancy.

The patient underwent subtotal exenteration of the right orbit, including removal of the tumor and the eye but with preservation of the eyelids. Grossly, the tumor was present as a 1.8 × 1.6 × 1.0-cm, well-circumscribed solid mass on the posterior aspect of the eye, abutting but not invading the sclera, and surrounding the optic nerve (Figure 5). Microscopic examination revealed highly cellular spindle and epithelioid proliferation of predominantly amelanotic cells. In some areas, the cells were associated with pigment synthesis and were arranged in fascicles. There were 4 to 5 mitoses per 40 high-power fields. A ciliary nerve was present in the sclera, surrounded by tumor cells, but no communication with the choroid was identified. Extensive examination of multiple sections revealed a small focus of amelanotic melanocytic nevus cells in the posterior episcleral tissue (Figure 5).

The nevus was composed of round to oval epithelioid cells without cytoplasmic pigmentation and with bland nuclei and inconspicuous nucleoli reminiscent of the type A melanocytic nevus cells present in cutaneous common or congenital nevi. There was no evidence of pigmented spindle or dendritic cells characteristic of nevus of Ota or blue nevus. It was impossible to determine histologically if the melanoma arose from or in conjunction with the nevus. However, close association between the nevus and melanoma suggests that the nevus may be a precursor lesion. Because the tumor microscopically extended to the surgical margins, the patient underwent removal of additional orbital tissue 1 month later, at which time no tumor was found in any of the surgical specimens. The patient subsequently received a full treatment cycle of radiotherapy to the right orbit and has had no evidence of local recurrence or metastasis for 2 years.

Comment. Primary orbital melanomas may exhibit exophthalmos, distorted vision, or diplopia, and their onset may be rapid or insidious. Although slow growth is usually associated with a benign lesion, this case shows that an orbital melanoma may enlarge painlessly over several years.

Primary orbital melanomas have been reported to occur in all races, with an older age at onset in the setting of ocular or oculodermal melanocytosis (50-70 years) compared with the setting of a cellular blue nevus (6-27 years). The demographics for primary orbital melanoma are similar to those for uveal melanoma.

The rarity of primary orbital melanomas leads to low clinical suspicion in the differential diagnosis of orbital tumors. Intraoperative diagnosis may be difficult, especially in amelanotic tumors, as they are often mistaken for other more common lesions. Classically, orbital melanomas are often dark, circumscribed masses with a pseudocapsule. In many instances, frozen-section diagnosis will indicate a small blue cell tumor with a broad histologic differential diagnosis, which, in addition to melanoma, includes lymphoma, carcinoma, embryonal rhabdomyoma, and neuroendocrine tumors. Permanent

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Figure 5. A, Gross exenteration specimen, sagittal section. B, Histopathologic section of specimen (original magnification ×20). The tumor is a solid mass on the posterior aspect of the eye, surrounding the optic nerve. C, Melanoma biopsy specimen (original magnification ×200). D, The transition zone shows melanoma cells arising from an amelanotic spindle cell melanocytic nevus of the posterior sclera (original magnification ×100). E, High magnification (original magnification ×200) shows nevus cells. F, High magnification (original magnification ×200) shows melanoma. S indicates sclera; N, nevus; and M, melanoma.
histologic sections and immunohistochemical studies using markers of melanocytic differentiation, such as S100, MART1 (melanin A), NSE, HMB45, and tyrosinase or microphthalmia transcription factor are necessary to establish the final diagnosis. Identification of melanosomes on electron microscopy may prove helpful. The potential for local invasion or metastasis varies widely, and strict prognostic indicators for orbital melanoma have not been established. Histopathologic evidence of aggressive behavior may be instrumental in guiding therapy. Owing to the small number of reported cases of primary orbital melanoma, the best management has not been clearly established. Relatively low-grade tumors, such as the one described here, may be managed fairly conservatively, without the need for total exenteration. 

Mixed cell type and high mitotic count, neither of which were found in this patient, were proposed as negative prognostic indicators. Melanomas are believed to arise from cells derived from neuroectodermal origin. In the orbit, these precursor cells are normally found in the uvea and the conjunctiva, but other orbital tissues may harbor neuroectodermal cells capable of transformation into melanoma. Blue nevi and cellular blue nevi are also believed to be derived from neural crest cells migrating with developing nerves, and have been found in most primary orbital melanomas. It is difficult to definitively classify the nevus identified in this case because of its small size, but the histologic features are different from blue nevus or nevus of Ota. The histologic features of the nevus cells resemble those of type A nevomelanocytes of dermal common acquired or congenital nevi. Therefore, it may represent an episcleral analog of dermal common acquired or congenital nevi. It may be necessary to place the melanoma arose from this nevus. However, definitive proof that the nevus is indeed a precursor lesion is lacking. To our knowledge, of the approximately 50 cases of primary orbital melanoma reported in the literature, this is the first case suggested to be associated with an occult nevus of non–blue nevus type.

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Undifferentiated Sinonasal Carcinoma With Nasolacrimal Duct Obstruction

Sinosal undifferentiated carcinoma (SNUC) is an uncommon malignancy of the nasal and paranasal sinuses. First recognized by Frierson et al in 1986 as a distinct clinical and pathologic entity, it was recently classified as a large cell subtype of poorly differentiated neuroendocrine carcinoma by Mills.

Common initial symptoms include nasal obstruction, epistaxis, and facial pain. Late-stage SNUC may exhibit an orbital mass, causing proptosis, diplopia, and visual loss. Orbital invasion occurs in 59% of nasal and paranasal malignant tumors, occasionally demonstrating dental symptoms. We report a case of SNUC in a patient with recurrent dacryocystitis and epiphora.

Report of a Case. A 71-year-old Chinese woman was first seen in April 1999. Her chief complaints were sudden onset of swelling and pain over the right medial canthal area for 1 week. Her medical history was remarkable for recurrent dacryocystitis with tearing and discharge. The problem had been waxing and waning for 1 year. There was no nasal bleeding or congestion. Her symptoms were resolved with oral antibiotics each time. An examination revealed a tender swelling at the right medial canthal region. There was no regurgitation from the punctum on massaging. The clinical diagnosis was dacryocystitis secondary to lacrimal drainage obstruction. Incision and drainage were offered for infection control and specimen culture, but she preferred treatment with antibiotics. Within 1 week, the inflammation subsided. Plain x-ray films of the skull and sinuses were unremarkable. A distal block was confirmed during syringing and probing of the lower canaliculus.

An endoscopic examination revealed no intranasal mass. Endonasal dacryocystorhinostomy was performed, and the osteotomy was created by bone punch. No lesions were found in the lacrimal sac. To minimize postoperative fibrosis, 0.4 mg/mL of mitomycin C was applied around the osteotomy for 5 minutes. A silicone tube was inserted, linking the sac to the nasal cavity.

Two weeks after the operation, extensive granulation tissue was found in the right nasal cavity and immediately removed. The patient was instructed to clean the nasal cavity daily with isotonic saline solution. Nine weeks after the operation, a 2 × 1-cm mass was noticed at the medial canthal area (Figure 1). The dacryocystorhinostomy site was blocked. Com-