Primary Orbital Melanoma Associated With an Occult Episcleral 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 and about 2% of extenterations. Most orbital melanomas arise from the uveal tract, conjunctiva, eyelids, or sinuses, and, infrequently, as metastases from distant primary sites. Approximately 90% of primary orbital melanomas arise from melanocytes found in congenital uveal melanocytosis (including blue nevus and cellular blue nevus), orbital melanocytosis, or oculodermal melanocytosis (nevus of Ota). The presence of melanocytes has also been reported in the optic nerve sheath, orbital fat, extraocular muscles, and orbital peristeum, which theoretically may provide cells of origin for primary orbital melanomas.

Orbital biopsy may be required to diagnose orbital melanoma when no clinical evidence of melanocytosis of the periocular tissues or uveal tract is present. Even with an orbital biopsy, the histopathologic diagnosis can often be difficult, especially if the tumor is amelanotic. 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 intraconal 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 retropulsion. 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 periorcular 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 5 C). 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 otolaryngological 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 spindled 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 spindled 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
nerves, and have been found in most
believed to be derived from neural crest
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.10 Relatively low-grade tumors, such as the
two described here, may be managed fairly conservatively, without
the need for total exenteration.9 Mixed cell type and high mitotic
count,8 neither of which were found in this patient, were proposed as
negative prognostic indicators.

Melanomas are believed to arise
from cells derived from neuroecto-
dermal origin. In the orbit, these pre-
cursor cells are normally found in the uvea and the conjunctiva, but other
orbital tissues may harbor neuro-
ectodermal cells capable of trans-
formation into melanoma.1 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.1,5 It is
difficult to definitively classify the nevus identified in this case be-
cause of its small size, but the histologic features are different from
blue nevus or nevus of Ota. The histologic features of the nevus cells re-
semble those of type A nevomela-
nocytes of dermal common acquired or congenital nevi. Therefore, it may
represent an episceral analog of dermal common acquired or con-
genital nevus. The nevus was inti-
mately associated with the mela-
noma, and it is reasonable to
speculate that the melanoma arose
from this nevus. However, defini-
tive 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,8 this is the
first case suggested to be associated
with an occult nevus of non–blue ne-
vus type.

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**Undifferentiated Sinonasal Carcinoma With Nasolacrimal Duct Obstruction**

Sinosonal undifferentiated carcino-
ma (SNUC) is an uncommon ma-
lignancy of the nasal and paranasal
sinuses. First recognized by Frierson
et al1 in 1986 as a distinct clini-
cal and pathologic entity, it was re-
cently classified as a large cell
subtype of poorly differentiated neu-
roendocrine carcinoma by Mills.2

Common initial symptoms include
nasal obstruction, epistaxis, and
facial pain.3 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.4 We report a case of
SNUC in a patient with recurrent
dacryocystitis and epiphora.

Report of a Case. A 71-year-old Chi-
inese 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 re-
markable for recurrent dacryocys-
titis with tearing and discharge. The
problem had been waxing and wan-
ing for 1 year. There was no nasal
bleeding or congestion. Her symp-
toms were resolved with oral anti-
biotics 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 lac-
rimal drainage obstruction. Inci-
sion and drainage were offered for
infection control and specimen cul-
ture, 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 re-
vealed no intranasal mass. Endona-
sal dacryocystorrhinostomy was per-
formed, and the osteotomy was
created by bone punch. No lesions
were found in the lacrimal sac. To
minimize postoperative fibrinosis, 0.4
mg/mL of mitomycin C was applied
around the osteotomy for 5 min-
utes. A silicone tube was inserted,
linking the sac to the nasal cavity.

Two weeks after the opera-
tion, extensive granulation tissue
was found in the right nasal cavity
and immediately removed. The pa-
tient was instructed to clean the na-
sal cavity daily with isotonic so-
Dium chloride solution. Nine weeks
after the operation, a 2 × 1-cm mass
was noticed at the medial canthal
area (Figure 1). The dacryocysto-
rhinostomy site was blocked. Com-

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**Unlabeled**: This is a text-only excerpt and does not include the full article content. The full article can be found in the published journal. The text excerpt is focused on unrequited orbital melanomas and provides an overview of the clinical characteristics, management, and potential outcomes associated with these neoplasms. The authors review various case studies and discuss the importance of histopathologic evidence in guiding treatment decisions. The text also highlights the rarity of primary orbital melanoma and the challenges in establishing definitive prognosis indicators. The authors emphasize the need for further research and clinical guidelines to improve patient outcomes in this niche field of ophthalmology and oncology. The accompanying figures, tables, and references are crucial for a comprehensive understanding of the subject matter.