logic and immunohistochemical findings, the diagnosis of a perineuroma with atypical histological features in the bulbar conjunctiva was made. After the resection, the patient was lost to follow-up.

Comment. Although perineurial cell proliferation may be suspected histologically with routine hematoxylin-eosin staining, a definite identification needs the demonstration of perineurial cell features using immunohistochemical studies. The morphologic criteria include spindle cells with curvy or wavy thin nuclei and thin, elongated cytoplasmic processes, arranged in lamellae, and a storiform growth pattern forming loose whorls and bundles. By immunohistochemistry, perineurial cells stain positive for EMA, GLUT-1, and Claudin-1; may stain positive for protein gene product 9.5 and CD34; and stain negative for S-100 protein, CD57, and neurofilaments.6

Perineuriomas are benign soft-tissue neoplasms, but atypical and malignant examples have been reported.1,3,4 According to Hornick and Fletcher,1 cases with atypical plasmacytoid cytologic results that show abrupt transition from typical cytomorphicologic findings and storiform architecture to markedly hypercellular areas with a fascicular growth pattern and diffuse infiltration of adjacent skeletal muscle have been classified as atypical perineurioma or perineural sarcoma.6-8 The origin of these rare tumors is unknown. However, topographic analysis from our case and those in the literature provides evidence that most anterior scleral nerve sheath tumors arise from intrascleral nerve loops.

Evidence That Anterior Episcleral Nerve Sheath Tumors Arise From the Axenfeld Nerve Loop

The occurrence of solitary episcleral neurofibroma has been described previously in 3 case reports1-3; episcleral schwannomas have been reported 4 times.3-8 The origin of these rare tumors is unknown. However, topographic analysis from our case and those in the literature provides evidence that most anterior scleral nerve sheath tumors arise from intrascleral nerve loops.

Report of Cases. A 45-year-old woman had a mildly tender, white nodule of a few weeks’ duration that was adherent to the sclera, measuring 3.5 × 3.5 mm in surface dimension and located approximately 4 mm from the limbus in the inferotemporal quadrant. Neither prior eye operations nor traumatic injury occurred in this region. Microscopic examination of histologic sections revealed a spindle cell tumor with features of a nerve sheath tumor (Figure). The tumor did appear encapsulated.

Culled from the literature of episcleral nerve sheath tumors are summarized in the Table. Under the assumption that benign nerve sheath tumors enlarge in a symmetric fashion, the distance of the tumor from the limbus (d) was calculated from the photograph by the following equation: d = (d/photograph)(11.7)/11.7, where c indicates the mean corneal diameter in millimeters measured in the photograph and 11.7 represents the corneal diameter in millimeters.10

The key characteristics of episcleral peripheral nerve sheath tumors are shown in the Table. The mean age of
Table. Characteristics of Episcleral Nerve Sheath Tumors

<table>
<thead>
<tr>
<th>Case No./Sex/Age, y</th>
<th>Source</th>
<th>Histopathologic Diagnosis</th>
<th>Location</th>
<th>Size, mm</th>
<th>Distance From Limbus, mm</th>
<th>Systemic Neurofibromatosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M/78</td>
<td>Kumar et al., 2005</td>
<td>Neurofibroma</td>
<td>Superotemporal</td>
<td>4 × 3</td>
<td>3</td>
<td>No</td>
</tr>
<tr>
<td>2/M/36</td>
<td>Ang et al., 1998-1999</td>
<td>Neurofibroma</td>
<td>Inferotemporal</td>
<td>10 × 5</td>
<td>4</td>
<td>No</td>
</tr>
<tr>
<td>3/F/22</td>
<td>Perry, 1982</td>
<td>Neurofibroma</td>
<td>Inferior</td>
<td>6 × 8</td>
<td>4</td>
<td>No</td>
</tr>
<tr>
<td>4/F/45</td>
<td>Current case</td>
<td>Neurofibroma</td>
<td>Inferotemporal</td>
<td>3.5 × 3.5</td>
<td>4</td>
<td>Yes, developed bilateral acoustic neuromas 4 y later</td>
</tr>
<tr>
<td>5/F/713</td>
<td>Graham et al., 1989</td>
<td>Schwannoma</td>
<td>Superotemporal</td>
<td>19 × 7 × 7</td>
<td>4</td>
<td>No</td>
</tr>
<tr>
<td>6/M/14</td>
<td>McLaughlin et al., 2007</td>
<td>Schwannoma (review of photographs shows presence of Verocay bodies)</td>
<td>Superonasal</td>
<td>Not described</td>
<td>4</td>
<td>No</td>
</tr>
<tr>
<td>7/F/34</td>
<td>Quintana and Lee, 1976</td>
<td>Schwannoma</td>
<td>Posterior near emissary channels</td>
<td>2</td>
<td>Not applicable</td>
<td>Yes</td>
</tr>
<tr>
<td>8/F/76</td>
<td>Kyrieleis, 1927</td>
<td>Schwannoma</td>
<td>Nasal, posterior</td>
<td>25 × 23 × 22</td>
<td>Not applicable</td>
<td>No</td>
</tr>
</tbody>
</table>

aStandardized measurement (see "Report of Cases").

Figure. Photomicrographs from sections of the anterior scleral tumor. A, The spindle cell tumor had a myxoid background with nuclei that are curved and tapered at the ends (hematoxylin-eosin, original magnification ×250). Inset, The drawing shows the size and distribution of the 6 episcleral nerve sheath tumors. The numbers refer to the percentage of Axenfeld nerve loops at the various positions as noted by Stevenson. B, Marked reactivity for S100 protein antibody in most of the cells (original magnification ×100). C, Antineurofilament antibody reacts with occasional axonal fibers in the tumor (original magnification ×400). D, An overview of the lesion shows fibrous tissue at the base but a lack of defined encapsulation (hematoxylin-eosin, original magnification ×20). Inset, Trichrome stain shows the infiltrative edge of the lesion (original magnification ×100).
the patients was 39.5 years. The mean distance from the limbus to the center of the tumor for anterior neurofibroma and schwannoma was 4 mm. The relative size and topographic location of the lesions are shown in the inset of part A of the Figure.

Comment. Episcleral neurofibromas and schwannomas likely arise from the long posterior ciliary nerves within the sclera. The ciliary nerves pierce the sclera near the optic nerve and pass anteriorly within the sclera and suprachoroidal space while branching to form a loose connection between the long and short posterior ciliary nerves, leading to 20 to 30 branches at the level of the ciliary body.11,12 The nerve loop of Axenfeld is an anastomotic interconnection of the long ciliary nerve that occasionally turns to enter the sclera before turning back again to continue anteriorly to the ciliary body.13 The loops occur in the area 2 to 4 mm posterior to the limbus, and no loops occur in the zones directly anterior to the medial and lateral rectus tendons.9

Anterior episcleral nerve sheath tumors have a topographic distribution similar to the Axenfeld nerve loop, permitting speculation of their relationship. The distances from the center of the tumor to the limbus narrowly ranged from 3 to 4 mm. None of these tumors occurred directly anterior to the horizontal rectus muscle tendons (Table). The anterior tumors were evenly distributed among the remaining quadrants as described for Axenfeld nerve loops. Two of 4 episcleral schwannomas occurred in the posterior sclera. If the distribution were random in the ciliary nerves, then some tumors would be expected to be found in the horizontal plane and at more variable distances from the limbus.

The apex of the loop can extend through the full thickness of the sclera and project above the scleral surface.13 Pain and tenderness have been noted when the nerve loops are located anteriorly. The sharp bend in the nerve and the ensuing stress perhaps facilitate the abnormal proliferation of nerve sheath cells and the formation of these tumors. The differential diagnosis for all of the reported episcleral nerve sheath tumors includes solitary circumferential melanocytoma and schwannoma. The nerve loops typically caused pain and tenderness when the tumor was entered or when the tumor was mobile. In some tumors, the patient reported tenderness overlying the neurofibroma or schwannoma.


Vitreal Seeding From Uveal Melanoma Detected by High-Resolution Spectral-Domain Optical Coherence Tomography

High-resolution spectral-domain optical coherence tomography (SD-OCT) is a new exciting technology for visualization of microstructural alterations in retinal diseases. We investigated the applicability of this noninvasive method to detect in vivo early vitreous seeding of a histologically proven choroidal melanoma with transretinal tumor extension (Knapp-Ronne melanoma).

Report of a Case. A 68-year-old man had blurred vision and inferior temporal visual field defect of the right eye for 4 months. His visual acuity was 20/30 OD and 20/20 OS. On funduscopy, a large pigmented choroidal mass with overlying hemorrhages was observed in the superonasal quadrant (Figure, A). Subretinal fluid around the tumor and inferior serous retinal detachment were present. Echography revealed a solid mass of 4.8-mm prominence, 11.2 × 10.6 mm² base, and low homogeneous reflectivity, with a more reflective apical cap, implying a uveal melanoma rupturing the Bruch membrane and covered by an apical hemorrhage (Figure, B). Ultrasound could neither exclude nor confirm tumor extension through the retina.

The patient was investigated using a commercially available SD-OCT (Spectralis HRA+OCT; Heidelberg Engineering, Heidelberg, Germany). Discrete, irregularly spheroidal bodies were present in the vitreous (Figure, C). The retina overlying the tumor showed thinning toward the tumor apex where the retina was completely obliterated and particles 20 to 30 µm in size could be detected in the immediately adjacent vitreous, suggesting transretinal seeding of the uveal melanoma (Figure, D). Without evidence of a primary or metastatic lesion elsewhere in the body, the tumor was classified as T2a N0 M0, according to the 2009 tumor, node, metastasis (TNM) classification system. Enucleation of the right eye was performed.

Macroscopically, the sectioned globe disclosed a 5-mm, 12-mm-wide, gray-white mass with a prominent brownish cap and dark pigmented foci (melanin) on the surface. The apex of the tumor extended through the full thickness of the sclera and projected above the scleral surface. The tumor involved the choroid and conjunctiva. The histologic findings of this tumor were those of a choroidal melanoma.