response. This concept would be supported by the finding of numerous lipid-laden keratocytes throughout the cornea and not necessarily adjacent to vessels, pointing to a primary disturbance of this cell population rather than a simple inflammatory response. An ultrastructural study of a more conventional case of lipid keratopathy also demonstrated intracellular and extracellular lipid droplets and pyknotic keratocytes but revealed much fewer lipid-laden keratocytes.

Although the precise nature and pathogenesis of the corneal disease in our patient remain speculation, our case together with other case reports previously published in the literature (under different names) strongly supports the concept of an independent disease process. Data to corroborate our theory would be the bilaterality, the lack of previous inflammatory episodes, the normal appearance of the conjunctiva, fairly normal blood lipids, and massive involvement of the whole cornea. Should simple neovascularization be the trigger of such a lipid keratopathy, one would expect to see many more patients with this problem. Perhaps one could, even under the aspect of its hypothetical nature, apply the name idiopathic lipid corneal dystrophy to such a disorder and thereby stimulate more publications of otherwise neglected cases where further molecular studies of the families might shed more light on this disease.

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Giant Cell Angiofibroma of the Ocular Adnexae

Giant cell angiofibroma (GCA) is a rare tumor. It was originally described by Dei Tos et al as an orbital tumor. These tumors are characterized by a patternless proliferation of spindle cells, multinucleated giant cells, and pseudovascular spaces. The stroma is collagenized or myxoid. Tumor cells stain positively for CD34 and vimentin. The morphologic appearance is similar to that of solitary fibrous tumor (SFT) and
giant cell fibroblastoma (GCF). In fact, Guillou et al² have advocated that GCA is likely a giant cell-rich variant of SFT.

In this article, a case of GCA of the conjunctiva is described. The clinicopathologic features of this tumor are reviewed.

**Report of a Case.** A 24-year-old man had a 12-month history of an inferior conjunctival lesion of the right eye. The lesion was painless and had not changed in size, color, or texture. Fullness of the right lower eyelid region was present (Figure 1A). The lesion was palpable subcutaneously along the medial portion of the right lower eyelid. The discrete lesion arose from the inferior fornix and had a lobular surface with prominent vascularity (Figure 1B).

The patient underwent excisional biopsy of the conjunctival lesion.

**Results.** Gross examination disclosed a solid, firm, tan and red, lobular mass measuring $13 \times 14 \times 6$ mm. Light microscopy examination revealed a circumscribed, cellular mass with a partial fibrous pseudocapsule. A predominant proliferation of spindle cells with round-to-oval, bland nuclei with pseudoinclusions was present, although some cells were noted to have slightly larger, irregular nuclei with visible nucleoli (Figure 2A and B). Numerous capillary-sized blood vessels were present (Figure 2A), and “angiectoid,” pseudovascular spaces were present in areas (Figure 2C). Several growth patterns were present. The majority of the tumor was patternless, but myxoid areas were identified. Distinct bundles of more wavy spindle cells with a fibrillary background reminiscent of neural tissue were present (Figure 2D). Mitotic figures were present at a rate of 2 per high-power field. The extracellular matrix comprised a fibrillary eosinophilic material and keloidal bundles of collagen. Reticulin stain demonstrated numerous fibers in the extracellular matrix but not surrounding each individual cell (Figure 3).

Immunohistochemical analysis revealed strong positivity with CD34 (cytoplasmic and membranous pattern), vimentin, and Bcl-2 (Figure 4). Factor XIIIa demonstrated the presence of a small population of dendritic cells within the tumor. It is unclear whether these cells represent a type of tumor differentiation or are a reactive population of dendritic cells, although tumor giant cells are factor-XIIIa negative (Figure 4B). The tumor cells were negative for epithelial membrane antigen and myogenin. Although rare cells stained positively for CD68, the giant cells were CD68 negative. Focal areas within the wavy bundles demonstrated S100 positivity (Figure 4C). Although these areas also demonstrated positivity with focal desmin and smooth muscle–specific actin, they were negative with myogenin. These areas were also focally CD34 positive and appeared to be arising from the tumor rather than normal tissue encompassed within the tumor. All of the immunohistochemical stains were compared with appropriate positive and negative controls.

**Comment.** Giant cell angiofibroma was first described in 1995 as a “distinctive orbital tumor in adults.”¹ It is rarely described in the ophthalmic literature, and it most commonly occurs in the ocular adnexae. Dei Tos et al¹ identified GCA in 7 cases involving the orbit. Six patients were men. The age range was from 23 to 73 years. Although predominantly and first described in the orbit, extraorbital locations such as the eyelids, conjunctiva, and nasolacrimal duct have been described.³⁻⁵ Since the original article,¹ other orbital and periorbital cases have been described.⁵⁻⁶ In 1 article,⁶ a patient had nasal obstructive symptoms. Giant cell angiofibroma of the nasolacrimal duct and lacrimal sac was found. A dacryocystectomy and...
medial maxillectomy were performed. Giant cell angiofibroma has also been described in the retroauricular region, submandibular region,7 scapular region,7 back,8 axillary and groin regions,9 parotid gland,9 scalp, neck, mediastinum,10 retroperitoneum, and vulva.9 Two cases of GCA in the buccal mucosa have been described as well.11,12

Giant cell angiofibroma is usually a soft, painless mass. In orbital cases, proptosis and eyelid swelling are the most common symptoms.1-3,5 The extraorbital cases are usually long-standing, painless masses as well.2,9

Giant cell angiofibroma has usually been described as an isolated mass; however, 1 case of GCA of the eyelids associated with tuberous sclerosis has been described.4 In the case report, a 30-year-old man had edematous, pedunculated, painless eyelid lesions. He had undergone excision of the lesions twice in the past. Although tuberous sclerosis is associated with adenoma sebaceum, which are angiofibromas, this was a unique association of GCA with tuberous sclerosis. A cutaneous case of GCA has also been described in a patient with dermatofibrosarcoma protuberans.13 This patient had a polypoid mass of the right thigh.

Immunohistochemical staining reveals strong reactivity of GCA for CD34 and vimentin. The CD34 antigen is a glycoprotein found in precursor myelocytic cells, and it is a common antigen found in soft tissue tumors and vascular endothelial cells. Giant cell angiofibroma typically does not stain with markers of muscular, neural, or epithelial differentiation. One patient with parotid GCA had patchy staining for S100 and glial fibrillary acid protein.9 Ultrastructural analysis showed external lamina in these areas, suggesting Schwannian differentiation.

Giant cell angiofibroma is characterized by a relatively uniform, patternless, richly vascularized proliferation of spindle cells that may have occasional myxoid areas. Angiectoid, or pseudovascular, areas and hyalinization of tumor blood vessels are noted. Multinucleated giant cells may have a floret pattern. Giant cell angiofibroma typically has a low mitotic rate (≤2 per 10 high-power fields).

Figure 2. A, Low-power photomicrograph of the tumor demonstrating numerous capillary-sized blood vessels on the left side of the photograph, several tumor giant cells in the center, and more loosely arranged tumor cells on the right side corresponding to the angiectoid, or pseudovascular, spaces (hematoxylin-eosin, original magnification ×50). B, Higher magnification of tumor, illustrating nuclear details and nuclear pleomorphism. Nuclear pseudoinclusions are present in some cells (arrow). A few tumor giant cells are present (arrowheads) (hematoxylin-eosin, original magnification ×200). C, Angiectoid spaces containing occasional red blood cells but lacking an endothelial lining are found within the tumor (asterisks) (hematoxylin-eosin, original magnification ×100). D, Focal areas containing wavy bundles resembling neural tissue can be seen within the tumor (hematoxylin-eosin, original magnification ×50).
The differential diagnosis of GCA includes SFT, GCF, fibrous histiocytoma, and other spindle cell tumors. Although there is overlap among the various spindle cell tumors, the 2 tumors histologically most similar to GCA are SFT and GCF. Solitary fibrous tumor, occurring predominantly in the pleura, has been described in the orbit as well. Patternless spindle cell proliferation and vascularization are present. Dense keloidal bundles of collagen are typically present. Immunohistochemical staining shows strong staining for vimentin and CD34. Giant cell fibroblastoma is an uncommon benign soft tissue tumor that most commonly occurs in early childhood. It has a local recurrence rate of approximately 50%. Histopathologic examination reveals a biphasic pattern of solid and angiectoid areas. Multinucleated giant cells are present in GCF. Giant cell fibroblastoma, as compared with GCA, has infiltrative margins. To our knowledge, there have been no described cases of GCF in the orbit.

Although SFT and GCF closely resemble GCA, differences in clinical and histologic appearances exist among these soft tissue tumors. Giant cell fibroblastoma occurs in childhood; GCA has been described in adults. Recurrence of GCF is common and may progress to fibrosarcoma. Solitary fibrous tumor has a variable cellularity and prominent vasculature, sometimes described as a “staghorn” appearance. Solitary fibrous tumor, as compared with GCA, does not have multinucleated giant cells or pseudovascular spaces.

The differential diagnosis of GCA also includes other spindle cell neoplasms, such as pleomorphic hyalinizing angiectatic tumor, dermatofibrosarcoma protuberans, fibrous histiocytoma, and multinucleate cell angiohistocytoma and pleomorphic lipoma.

Although the follow-up periods of described GCA cases have been relatively short, GCA is considered a benign tumor. Local recurrence and persistent tumor have been described in 2 of the 5 patients with documented follow-up. One patient had local recurrence after a 6-month follow-up. A second patient had residual tumor. Thomas et al described no tumor recurrence in their 4 patients after a 25-month follow-up. Our patient has been free of recurrence for 8 months.

In summary, GCA is a recently described and rare mesenchymal tumor originally noted in the orbit. It has distinct clinical and histologic characteristics, occurs in adulthood, and has solid and pseudovascular spaces, spindle cells, collagenous stroma, multinucleated giant cells, and prominent vascularity. Intense staining for CD34 and vimentin are characteristic. In this case, we describe the additional finding of neuromuscular tumor differentiation. Giant cell angiofibroma has a benign clinical course. As more cases of GCA are being described, various ocular and extracocular locations are being recognized. More
studies need to be performed to better understand this unusual tumor.

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Figure 4. Immunohistochemical analysis. A, Strong positive staining with CD34 within the undifferentiated tumor cell cytoplasm and focal positivity within the neural-like bundles (original magnification ×50). B, Factor XIIIa highlights the presence of dendritic cells within the tumor, but tumor giant cells are negative (arrowheads) (original magnification ×50). C, Focal positive staining with S100 within the sheaths of the neuromuscular bundles (original magnification ×50). D, Desmin stain demonstrates strong positive staining of cells within the core of the neuromuscular bundles (original magnification ×100). E, Smooth muscle–specific actin demonstrates a similar staining pattern to that of desmin (original magnification ×50). F, Cytoplasmic pattern of staining with Bcl-2 in most tumor cells (original magnification ×100). All of the immunohistochemical staining was performed with the immunoperoxidase method, with diaminobenzidine as the chromogen and with hematoxylin counterstain.


Bilateral, Localized Orbital Neurofibromas and Charcot-Marie-Tooth Disease

Localized neurofibromas are rare in the orbit and, unlike plexiform neurofibromas, are not typically associated with von Recklinghausen neurofibromatosis. To our knowledge, bilaterality of such localized neurofibromas has been reported only once.1 We report a patient known to have Charcot-Marie-Tooth disease (CMTD) who developed multiple localized neurofibromas in both orbits.

Report of a Case. A 35-year-old man, known to have CMTD polyneuropathy since the age of 12 years, was referred to us because of the accidental finding of bilateral orbital tumors on magnetic resonance imaging of the brain. The brain imaging had been requested by a neurologist after the patient developed a right-sided trigeminal neuralgia.

On evaluation, bilateral exophthalmos was noted, and this was reported by the patient to be of longstanding duration (at least 5 years). Best-corrected visual acuity was 20/30 in either eye. Hertel exophthalmometry measurements were 23 mm in both eyes. There was mild limitation of supraduction in both eyes. Tonic pupils were noted. There were no enlarged corneal nerves and no iris Lisch nodules. Fundus examination showed mild pallor of both optic nerve heads. No café au lait spots were noted on physical examination. Extensive distal muscle atrophy was seen (Figure 1A). Family history was negative for neurofibromatosis.

Orbital computed tomography was performed and showed large masses filling the superior aspect of both orbits, displacing the globes inferiorly (Figure 1B). The bony orbital roof was expanded and thinned in some areas.

Figure 1. A, Right hand of patient showing extensive atrophy of the dorsal interossei muscles with flexion contracture of the fingers, which is characteristic of Charcot-Marie-Tooth disease. B, Computed tomographic scan of coronal cuts showing bilateral superior orbital tumors with thinning of the adjacent bone (top) and axial cuts showing 2 adjacent, interconnected tumors in each orbit (bottom).