Granular cell tumor involving the axillary nerve: an unusual occurrence

Case report

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✓Granular cell tumors (GCTs) are benign lesions that, paradoxically, despite originating from the Schwann cell, are most commonly seen in nonneuronal tissue including the skin, subcutaneous tissue, and tongue. Their presence in the brachial plexus is quite rare, but their involvement of peripheral nerves is exceptional. The authors report on a case of GCT involving the axillary nerve in a 54-year-old woman who underwent complete resection of the lesion. To the author's knowledge, this case marks the first report of a GCT involving the axillary nerve. Aspects pertaining to the radiographic and histopathological features as well as the surgical management of this lesion are discussed.

KEY WORDS • axillary nerve • granular cell • peripheral nerve tumor

GRANULAR cell tumors are relatively common extra-neural lesions, the majority of which are regarded as benign neoplasms. They occur most frequently in the skin, subcutaneous tissue, tongue, and other nonneuronal tissue, although the tumor appears to be of Schwann cell origin on the basis of morphological and immunohistochemical assessments.^{5,17} Their presence in the brachial plexus and peripheral nerves is an extremely rare occurrence, and to our knowledge, this case marks the first reported instance of a GCT involving the axillary nerve.

Case Report

History and Examination. In January 2006, this 54-year-old right-handed woman with a history of recurrent right-sided breast cancer, who had previously been treated with lumpectomy and axillary node dissection 9 years earlier and bilateral mastectomies with TRAM reconstruction 1 month earlier, presented with a 2-month history of severe right upper-extremity pain. She described the pain as searing and burning in quality and localized to the right lateral upper arm. The pain was more severe at night and frequently awakened her from sleep. Her neurological examination revealed diminished pinprick sensation over her deltoid, but no paresis was present. She was able to abduct her arm and shoulder with normal strength, and no muscle atrophy was noted. A magnetic resonance image of the brachial plexus revealed a 2.6 × 1.8 × 3-cm soft tissue mass located pos-

terior to the proximal humeral diaphysis, between the long head of the triceps muscle and the deltoid muscle, and adjacent to the posterior humeral circumflex vessels and axillary nerve (Fig. 1). The soft tissue mass demonstrated low signal intensity on T1-weighted images and high signal intensity on T2-weighted images and exhibited robust homogeneous postcontrast enhancement with no evidence of the involvement of adjacent structures. Given the presence of this mass in light of the patient's history of breast cancer, resection was planned for definitive tissue diagnosis and removal of the mass.

Operation. In a posterior right arm approach, a skin incision was made lateral to the deltoid and was extended upward, just inferior to the spine of the scapula. The fascia was then opened, the deltoid was reflected anteriorly, and the teres (major and minor) and triceps muscles were all identified. A large, white sclerotic mass measuring approximately 3 × 3 cm was noted encircling the axillary nerve. This mass appeared well circumscribed and appeared to displace the anterior branch of the axillary nerve medially, whereas it infiltrated the posterior branch of the nerve supplying the teres minor and lateral superficial cutaneous nerves. After identifying the proximal and distal aspects of the axillary nerve, the tumor was meticulously dissected away from the proximal anterior portion of the axillary nerve and was eventually successfully shelled from the nerve. Utilizing intraoperative electrophysiological stimulation, the proximal motor branches innervating the teres minor muscle and the deltoid muscles were both confirmed to be functional.

We then directed our attention to the posterior branch of

Abbreviations used in this paper: GCT = granular cell tumor; TRAM = transverse rectus abdominus flaps.

FIG. 1. Fat-saturated magnetic resonance images of the brachial plexus before (A and B) and after (C and D) Gd infusion, demonstrating the enhancing soft tissue mass located posterior to the proximal humeral diaphysis and between the long head of the triceps and the deltoid muscles.

the axillary nerve, where a small motor branch to the deltoid muscle and the lateral superficial nerve appeared to be encased by tumor. Because of this extensive involvement, neurolysis of these two branches was performed, and the tumor was successfully resected. We contemplated grafting to the larger cutaneous nerve innervating the lateral portion of the arm to maximize sensation to this area but believed that a graft in this region, which would only potentially offer sensation to the lateral portion of the arm, was not worth the guaranteed risk of numbness in the foot where the donor nerve graft would be harvested. Therefore, we deferred nerve grafting, and in this scenario the wound was closed in a standard fashion.

Pathological Studies. A firm brown nodule with an irregular outer surface and no evidence of necrosis or hemorrhage was noted. Histological analysis demonstrated a cellular neoplasm composed of bland monotonous cells with abundant granular eosinophilic cytoplasm and centrally located pyknotic nucleoli with inconspicuous nucleoli and a lack of necrosis or mitoses (Fig. 2). The tumor cells were negative for carcinoembryonic antigen, myelin basic protein, and calretinin but stained positive for S100 protein with numerous lysozymes identified in the cytoplasm; the diagnosis was consistent with a GCT of the axillary nerve.

Postoperative Course. At the patient's 2-month postresection visit, she reported incomplete improvement of the paresthesias in the lateral upper portion of her arm but no subjective neurological weakness. Closer evaluation of individual muscle groups did in fact reveal trace weakness in the deltoid. The patient also demonstrated some limitation in the range of motion in her shoulder, which we ascribed to the mastectomies and the TRAM performed 3 months earlier. At 14 months after the tumor resection, she described herself as having no functional limitations whatsoever and resolution of the arm paresthesia.

FIG. 2. A: Photomicrograph of representative tumor section demonstrating characteristic bland monotonous cells with abundant granular eosinophilic cytoplasm, small centrally located nuclei, and inconspicuous nucleoli. No mitoses or necrosis was identified. B: Photomicrograph revealing strong, diffuse cytoplasmic staining for S100 protein. C: Photomicrograph displaying strong, diffuse cytoplasmic staining for lysozyme antigen. H & E (A), S100 protein (B), and lysozyme antigen (C). Original magnification $\times 20$ (B and C) and $\times 40$ (A).

Discussion

Granular cell tumors are exceedingly rare peripheral nerve tumors. Although these tumors have been demonstrated to have a neural origin, they rarely arise in peripheral nerve trunks. In Kim and colleagues' 30-year review detailing the treatment of 543 peripheral nerve tumors, only two GCTs were reported, both of which involved the brachial plexus and not the peripheral nerve trunks.^{8,9} A review of the literature from the last 10 years has revealed reports of only three GCTs involving the ulnar nerve and one involving the sural nerve.^{3,4,18} It remains to be elucidated why these lesions do not involve the peripheral nerves more frequently, which would be surmised from their neural origin.

Most GCTs occur in the skin or subcutaneous tissue of middle-aged adults with a slight female predominance, although the overall age range is wide. Virtually any anatomical site can be affected, but the trunk and tongue are the most common locations. Lesions in the breast, biliary tree, and larynx have been reported.¹⁵ Up to 10% of patients with GCTs have multiple lesions, which are more common in African-Americans.⁶ In most cases the tumor is slow growing, rarely causes tenderness, and usually measures less than 3 cm in its maximum dimension. The local recurrence rate in benign lesions is less than 5% and usually reflects incomplete excision.

Granular cell tumors seldom present a diagnostic problem histologically. Although granular cells can be encountered in schwannoma or neurofibroma, the differing basic nature of these tumors is readily apparent. Some lesions must be distinguished from rhabdomyoma, histiocytoid carcinoma (for example, from the breast), or infrequently a reactive lesion complicating previous trauma or inflammation.¹⁶ Rare variants of GCT include gingival GCT in newborn infants,¹¹ primitive polypoid GCT,¹² and malignant GCT.^{6,7,10}

Most benign GCTs present as solitary masses, most frequently involving the upper extremities and exhibiting symptoms caused by neural compression rather than primary involvement of the nerve.^{3,4,18} Treatment for these lesions entails wide local excision with tumor-free surgical margins, which usually prevents recurrence in cases of benign and extraneural tumors. Because GCTs can occasionally infiltrate the nerve, however, complete extirpation may not be feasible.² Almost invariably, there is some degree of microscopic infiltration of the nerve fascicles by the tumor cells even if the tumor can be dissected and shelled from the nerve. Therefore, a wide surgical exposure is utilized so that the proximal and distal anatomy relative to the tumor are clearly visualized. Safe microsurgical removal of the mass can then be attempted by skeletonizing the mass from the involved nerve. If the involved peripheral nerve is completely infiltrated by tumor, however, a segmental resection with nerve reconstruction should be considered.

Malignant GCTs account for no more than 2 to 3% of all GCTs.^{1,10} They seem to occur mainly in the deep soft tissues of adults and are often associated with an underlying malignancy. Most often they directly extend or metastasize to a nerve and can secondarily involve the nerve and insinuate themselves into the epineurium, perineurium, and eventually the individual nerve fascicles themselves. Among the approximately 30 cases reported in the literature, more than 50% have had a metastasizing fatal course. Because of their rate of growth and degree of invasion, nerve preservation

is not feasible, and these lesions are treated with segmental resection and nerve reconstruction. Criteria for their recognition are hard to define, given that some cases have appeared remarkably bland and monomorphic histologically.^{13,14} Nonetheless, any unusually large lesion with infiltrative margins, prominent nucleoli, and conspicuous mitoses should be regarded with suspicion.

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