Intraneural synovial sarcoma of the median nerve

Angelo B. Lipira,[1] Rahul Kasukurthi,[1] Wilson Z. Ray,[2] Mark E. Pruzansky,[3] Susan E. Mackinnon[1]

[1]Division of Plastic and Reconstructive Surgery and
[2]Department of Neurosurgery, Washington University School of Medicine, Saint Louis, MO, USA;

[3]Department of Orthopedic Surgery, Mount Sinai School of Medicine, New York, NY, USA

Abstract

Synovial sarcomas are soft-tissue malignancies with a poor prognosis and propensity for distant metastases. Although originally believed to arise from the synovium, these tumors have been found to occur anywhere in the body. We report a rare case of synovial sarcoma arising from the median nerve. To our knowledge, this is the twelfth reported case of intraneural synovial sarcoma, and only the fourth arising from the median nerve. Because the diagnosis may not be apparent until after pathological examination of the surgical specimen, synovial sarcoma should be kept in mind when dealing with what may seem like a benign nerve tumor.

Introduction

Synovial sarcomas are aggressive soft-tissue malignancies with a propensity for distant metastases, and can occur anywhere in the body.[1,2] They account for approximately 5-10% of soft tissue sarcomas, with about 800 cases per year in the United States. Overall, prognosis is poor, with only a 50-60% five-year survival rate despite radical surgical resection, local irradiation, and a fairly high response rate to chemotherapy.[3] Although they have been reported in patients of all ages, synovial sarcomas commonly occur in adolescents and young adults, with a reported male predominance.[3,4]

Although originally believed to arise from the synovium because of their frequent periarticular location, synovial sarcomas can occur virtually anywhere in the body, with less than 5% being microscopically continuous with the synovium.[4] They are now thought to arise from primitive undifferentiated mesenchymal cells.[5] While the majority of synovial sarcomas occur in skeletal muscle and supporting connective tissues of the extremities, most often in the leg,[6] they have also been reported in a variety of other anatomical locations including the head, neck, mediastinum, heart, esophagus, pleura, small intestine, and lung.[5]

We report here an extremely rare case of synovial sarcoma arising from the median nerve. To our knowledge, this is the twelfth reported case of intraneural synovial sarcoma, and only the fourth arising from the median nerve.

Case Report

A 66-year-old, right-hand dominant woman, with no significant past medical history, presented with pain in her right hand for one month. The pain was sharp, worse at night, and localized to her thenar eminence. She also complained of diminished sensation of her radial three digits, and recently she had been dropping objects. She had noted a mass on the volar aspect of her right wrist for the past 25 years, which had gradually diminished in size.

On examination, an approximately 2×3 cm, moderately tender mass was noted on the medial-volar aspect of the patient's right wrist. Tinel's sign was positive over the carpal tunnel, and atrophy of the thenar muscles was present. The neurovascular examination was otherwise within normal limits.

Electrodiagnostic tests, including electromyography and a nerve conduction study of the median nerve, were within normal limits. Magnetic resonance imaging showed a 2.7×1.95×1.35 cm, ovoid, lobular, heterogenous mass arising from the median nerve and nerve sheath. On T1-weighting, the mass was slightly brighter than skeletal muscle with punctate lower-signal foci. On T2-weighting, geographic foci of intermediate intensity were seen centrally with a brighter signal peripherally. The radiologist's impression, which was shared by the surgeon, was of a probable neurofibroma or schwannoma. With this in mind, marginal resection of the mass was undertaken with preservation of nerve fascicles where possible. The mass was found to be associated intimately with the nerve. Most of the nerve was seen to be intact at the end of the procedure.

Histopathology showed a 2×0.2×0.2 cm, gray-tan, firm mass. A typical spindle-cell morphology was seen with hematoxylin-and-eosin staining (Figure 1). Immunohistochemically the tumor stained diffusely positive for vimentin and cytokeratins AE1/AE3, CK7, CK18, and CK19, as well as bcl-2. There was also patchy positive staining for EMA and CD99. Stains for smooth muscle actin, desmin, CD31, CD34, and S-100 were negative. The histopathological and immunohistochemical assessments are consistent with a diagnosis of a monophasic intraneural synovial sarcoma. Fluorescent *in situ* hybridization resulted in 30% of cells showing heterozygous rearrangement of the SYT locus on 18q11.2; this type of SYT rearrangement is characteristic of synovial sarcoma (see Discussion).

Given the diagnosis of the malignant neoplasm, a radical resection of the lesion with reconstruction was performed six weeks later. An extensor indicis proprius opponensplasty was performed in order to return some thumb function lost from the median nerve palsy. The median nerve was identified inside the carpal tunnel and followed proximally into the forearm, and approximately 8 cm of it was removed and sent for margin analysis. All frozen and permanent sections taken from the tumor bed were reported to be free of synovial sarcoma. In addition, microsurgical nerve transfers using the ulnar digital nerve of the ring finger, the radial digital nerve of the little finger to the index finger proper digital nerve, and the palmar sensory nerve to the thumb, respectively, were sutured with 9-0 nylon. At the six-month follow-up, the patient was status post-radiotherapy, and had approximately 20% range of motion of her digits owing to scarring and edema. She had no sensation in the reinnervated digits.

Discussion

Intraneural synovial sarcomas are extremely rare, with our case being one of only a handful reported in the literature.[7-16] Previously, three intraneural synovial sarcomas have been reported arising from the median nerve, along with one apiece from the radial, common digit-

Correspondence: Susan E. Mackinnon, Washington University School of Medicine, 660 S. Euclid Ave., Campus Box 8057, St. Louis, MO 63110, USA.
E-mail: mackinnon@wudosis.wustl.edu

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Table 1. Reported cases of intraneural synovial sarcoma.

Author (Year)	Age (yrs)	Sex	Nerve	Histology	EMA	VIM	KRT, CK	S-100 protein	CD99	Cytogenetics	Surgery
Cugola and Pisa (1985)[14]	16	F	radial	biphasic	+	+	+	+		-	ER
Rinehart *et al.* (1989)[15]	23	F	median	monophasic						-	ER
O'Connell *et al.* (1996)[7]	16	F	common digital	biphasic	+	+	+	-		-	ER
Tacconi *et al.* (1996)[12]	44	F	brachial plexus	monophasic	+	+	+	±		-	TR
Spielmann *et al.* (1997)[11]	43	M	posterior tibialis	monophasic	+	+	+	-	+	SYT-SSX	A
Chesser *et al.* (1999)[8]	16	ND	median	biphasic		+	+			-	TR
Zenmyo *et al.* (2001)[16]	58	F	S1 root	monophasic	+	+	+	+		SYT-SSX1	TR
Lestou *et al.* (2002)[10]	54	M	peroneal	monophasic	+	+	+	+	+	SYT-SSX2	TR
Chu *et al.* (2004)[9]	46	F	facial	biphasic	+	+	+	-	-	SYT-SSX	ER
	11	F	C7 root	monophasic	-	+	-	-	+	SYT-SSX	TR
Uehara *et al.* (2008)[13]	33	F	median	monophasic	+	±	+	+		SYT-SSX1	TR
Current study	66	F	median	monophasic	+	+	+	-	+	-	TR

EMA, epithelial membrane antigen; VIM, vimectin; KRT, keratin; CK, cytokeratin; ER, extended resection; TR, total resection; A, amputation. Modified with permission from Uehara, *et al.* (2008).[13]

al, posterior tibialis, peroneal, and facial nerves and one from each of the S1 root, C7 root, and brachial plexus (Table 1).

Three separate histopathological patterns of synovial sarcoma are recognized. The most commonly reported overall is the biphasic type, consisting of distinct epithelial cells in gland-like arrangements along with fibroblast-like spindle cell components in varying proportions. Monophasic tumors, such as the one in our case, morphologically consist of spindle cells only and were difficult to distinguish from other soft tissue and nerve tumors before the introduction of immunostaining for epithelial membrane antigen (EMA), vimentin, S-100, and cytokeratins CK7, CK19, and CD99.[4] The epithelial components of monophasic synovial sarcomas only become evident when stained for EMA and cytokeratins, although these are not specific for synovial sarcoma. A third histopathological pattern of synovial sarcomas, the poorly differentiated subtype, is also recognized.[5] While poorly differentiated tumors are associated with a worse prognosis, the prognostic value of monophasic versus biphasic tumors is still debated.[11,17-19] Although biphasic morphology is most frequently reported overall, eight of the twelve reported intraneural synovial sarcomas have had monophasic histopathology. Of those reported to arise from the median nerve, three of the four have been monophasic, with one biphasic.

Cytogenetic testing is the most definitive way to establish the diagnosis of synovial sarcoma. A stereotyped gene translocation between chromosomes 18 and X t(x;18)(p11.2;q11.2) occurs in over 90% of synovial sarcomas.[4] This leads to fusion of one of two variants of the *SSX* gene with the *SYT* gene, resulting in either the SYT/SSX1 or SYT/SSX2 chimeric fusion proteins.[4,5] Nearly all biphasic tumors express SYT/SSX1, while monophasic tumors express SYT/SSX1 in approximately half of the cases and SYT/SSX2 in the remainder.[18] Patients with SYT/SSX2 expressing tumors have a significantly better prognosis when compared to those with SYT/SSX1 tumors in terms of rates of metastasis and overall survival.[18,20-22]

Other factors reported to be associated with poor prognosis include tumor size greater than 5 cm, areas of necrosis, bone or neurovascular invasion, poor differentiation, and high mitotic rate.[17,19,23] Although older age has also been associated with a poorer prognosis, more recent studies have been unable to reproduce this finding.[7]

Adequate surgical margins, radiation therapy, and adjunct chemotherapy have been reported to correlate with better prognosis.[2,24] However, despite advances in treatment, mortality rates of synovial sarcoma remain quite high with five-year survival rates around 50-60%.[2,3,25] Death most frequently results from distant metastases, most commonly to the lung.[5] While improved local control with radical surgical excision and irradiation has led to a substantial decrease in local recurrence, rates of distant metastatic disease remain high even with systemic chemotherapy.[17]

Synovial sarcoma is an aggressive tumor that can occur nearly anywhere in the body, including within peripheral nerves as illustrated in our case. Although extremely rare, the potential for a malignancy such as an intraneural synovial sarcoma was presented in the differential diagnosis to this patient. This is important since the diagnosis may not be apparent until after pathological examination of the surgical specimen, resulting in drastic alterations to the original treatment strategy and an altered impact on the patient. While the presence of a nerve tumor most commonly indicates a benign lesion, one must be cognizant of the potential for a life-threatening malignancy, and that the diagnosis will not be final until a pathological examination has been completed.

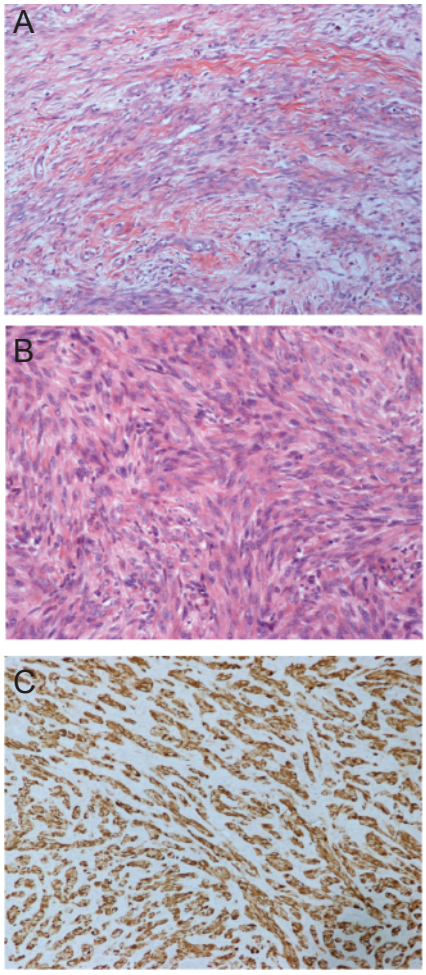

Figure 1. Hematoxylin-and-eosin staining shows atypical spindle-cell morphology associated with intraneural synovial sarcoma at 200X (A) and 400X (B) magnifications. (C) Immunohistochemical staining was diffusely positive for cytokeratins.

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