A 56-year-old Woman with a Right Arm Mass

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History and Physical Examination

A 56-year-old woman was admitted for a 5-year history of a painless right arm mass. The patient denied any recent enlargement. However, over the previous 2 years, the patient complained of gradually increasing numbness at the thumb, index finger, and middle finger of the ipsilateral arm. There was no history of trauma. Medical and family history was unremarkable.

Physical examination revealed a soft, oval, deep palpable mass on the medial side of her right arm with a maximum diameter of 4 cm (Fig. 1). Passive and active range of motion of the right elbow and hand were unaffected. Neurologic examination was normal. Routine laboratory analysis

including complete blood cell count, serum chemistries, erythrocyte sedimentation rate, and C-reactive protein were within normal limits.

We performed plain radiography (Fig. 2), ultrasonography (Fig. 3), and MRI (Fig. 4).

Based on the history, physical examination, laboratory tests, and imaging studies, what is the differential diagnosis?

Imaging Interpretation

A frontal radiograph of the right upper arm showed a cluster of rounded calcifications in the soft tissues along the medial aspect of the mid humerus. No underlying osseous abnormality was noted (Fig. 2).

Ultrasonography of the right arm showed a well-defined oval mass with heterogeneous internal echogenicity. The mass was closely related to the median nerve. Doppler examination revealed a moderate degree of vascularity within the lesion (Fig. 3).

MRI showed a fusiform lesion with well-circumscribed borders along the posteromedial aspect of the biceps. The lesion was intermuscular and centered along the expected course of the median nerve. The normal median nerve could not be identified as a distinct structure at this level. The lesion was heterogeneous and slightly hypointense to muscle on T1-weighted images (Fig. 4A–B) and heterogeneously hyperintense on T2-weighted images. On postcontrast T1-weighted images (Fig. 4C–D), the mass enhanced in fairly uniform fashion.

Differential Diagnosis

Hemangioma
Schwannoma

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Each author certifies that his or her institution has approved the reporting of this case and that all investigations were conducted in conformity with ethical principles of research.

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Fig. 1 A 56-year-old woman presented with a soft, oval, deep palpable mass on the medial side of her right arm with a maximum diameter of 4 cm.

Fig. 2 An anteroposterior plain radiograph of the right humerus shows round calcifications on the medial side of the right middle arm.

Glomus tumor and angioleiomyoma

Intraneural benign tumors (eg, intraneural lipoma, lipofibromatous hamartoma, hemangioma, and ganglion cysts)

Intraneural malignant tumors (eg, synovial sarcoma)

Fig. 3 Ultrasonography of the right arm shows a 40- × 21-mm well-defined oval mass with heterogeneous internal echogenicity and moderate vascularity. The mass is closely related to the median nerve (arrow) that shows flattening, distortion of architecture, and altered echogenicity.

We performed a CT-guided core biopsy of the lesion (Fig. 5).

An MR angiogram (Fig. 6A) was performed followed by a conventional angiogram for the purposes of embolization (Fig. 6B). Both studies showed the lesion was well vascularized. The arterial supply appeared to originate from the brachial artery and venous drainage was through small branches of the brachial and basilic veins. Small defects in the contrast column were thought to correlate with the phleboliths identified on the other imaging studies.

Through a medial approach to the right arm, the median nerve was exposed at the distal and proximal arm. Surgical exploration of the middle arm revealed a dark-red fusiform tumor that distended the trunk of the median nerve (Fig. 7A). After verifying the integrity of the median nerve, the tumor was resected through intraneural microdissection (Fig. 7B).

Based on the history, physical examination, laboratory tests, imaging studies, and histologic picture, what is the diagnosis and how should this lesion be treated?

Histology Interpretation

Macroscopically, the resected tumor had a dark-red circumscribed fibroelastic appearance and measured $3.7 \times 2.8 \times 2$ cm (Fig. 7A). Histologic examination showed a proliferative vascular lesion composed of thin-walled vascular channels in a focally hyalinized stroma with areas of hemorrhage. The vascular channels were lined by endothelial cells without nuclear atypia or mitotic figures (Fig. 5A). CD34 immunoperoxidase stain confirmed the vascular nature of the lesion (Fig. 5B). Immunohistochemical stains for

Fig. 4A–D MR images show a fusiform lesion with well-circumscribed borders at the postero-medial aspect of the biceps, along the expected course of the median nerve. The lesion is heterogeneous and isointense or slightly hypointense to muscle on (A) T1-weighted axial and (B) T1-weighted sagittal images. On postcontrast (C) T1-weighted axial and (D) T1-weighted sagittal images, the mass enhances in fairly uniform fashion.

pankeratin, protein S-100, and smooth muscle actin were negative. There was papillary endothelial hyperplasia as an exuberant response to organizing thrombus. Foreign body giant cell reaction was present surrounding the embolism material (Fig. 5C).

Diagnosis

Intraneural hemangioma of the median nerve.

Discussion

Differential diagnosis of intraneural hemangiomas from other soft tissue tumors is challenging. Schwannoma, glomus tumor and angioleiomyoma, intraneural benign tumors (eg, intraneural lipoma, lipofibromatous hamartoma, and ganglion cysts), intraneural malignant tumors (eg, synovial

sarcoma), and posttraumatic hematoma may be included in the list of differential diagnosis of intraneural hemangioma [3, 16, 23, 34, 36, 41].

Schwannoma is an encapsulated nerve sheath tumor consisting of two components: a highly ordered cellular component (Antoni A area) and a loose myxoid component (Antoni B area). The presence of encapsulation, the two types of Antoni areas, and the uniformly intense immunostaining for S-100 protein is typical for schwannoma [41]. Glomus tumor and angioleiomyoma are usually hypervascular homogeneous solid masses with sharp margins [16, 36].

Intraneural lipomas are usually painless or cause only minimal discomfort. Involved nerves have included the median nerve, the sciatic nerve, or the brachial plexus [3]. Symptoms of compressive neuropathy secondary to an intraneural lipoma have been reported in most cases. MRI of intraneural lipomas shows signal characteristics consistent with those of normal adipose tissue, including

Fig. 5A–C (A) Histologic sections of the biopsy specimen show a proliferative vascular lesion composed of thin-walled vascular channels in a focally hyalinized stroma with areas of hemorrhage. The vascular channels are lined by endothelial cells without nuclear atypia (Stain, hematoxylin and eosin; original magnification, $\times 400$). (B) CD34 immunoperoxidase stain highlights the vascular nature of the lesion (Original magnification, $\times 100$). (C) The thrombosed cavernous lesion developed papillary endothelial hyperplasia as an exuberant response to organizing thrombus. Embolism material was surrounded by foreign body giant cell reaction (Stain, hematoxylin and eosin; original magnification, $\times 100$).

Fig. 6A–B (A) MR and (B) conventional angiograms show a well-vascularized lesion with discrete margins. The arterial supply appears to originate from the brachial artery and venous drainage is through small branches of the brachial and basilic veins. Small defects in the contrast column correlate with the phleboliths identified on the other imaging studies.

homogeneous high signal intensity on T1- and T2-weighted sequences, with suppression of the hyperintense signal on fat suppression sequences. The lesion's close relationship

to and possible splaying of the nerve fascicles of the involved nerve may be noted. However, histologic examination shows well-differentiated adipose cells in a delicate

Fig. 7A–B (A) Surgical exploration of the middle arm revealed a dark-red fusiform tumor that distended the trunk of the median nerve. (B) The perineurium was incised, and the tumor was resected through intraneural microdissection.

fibrous stroma; intracapsular nerve fascicles should not be seen [3, 5].

The designation lipofibromatous hamartoma was coined by Johnson and Bonfiglio [15] to describe a diffuse lipofibromatous infiltration of a nerve. The median and digital nerves are almost exclusively affected, although involvement of other nerves has also been reported [3, 11]. The origin and pathogenesis of lipofibromatous hamartomas are unknown. Some authors have suggested repetitive micro-trauma may cause a reactive fibrofatty cell proliferation [33]. Most patients present in adolescence or early adulthood; in most the mass has been present for several years before the onset of symptoms. The most common symptom is a compressive neuropathy of the median nerve at the carpal tunnel or digital enlargement attributable to fibrofatty infiltration of perineural soft tissue in lipofibromatous hamartomas that involve the digital nerves. In approximately $\frac{1}{3}$ of cases, the bone and soft tissues of the digit are diffusely enlarged, causing true macrodactyly (macro-dystrophia lipomatosa) [3, 11]. Pathognomonic MRI findings of lipofibromatous hamartoma consist of serpiginous T1- and T2-weighted low-intensity structures

containing and surrounded by fat (hyperintense on T1- and hypointense on T2-weighted fat suppression sequences), giving the lesion a spaghetti-like appearance on sagittal images and a coaxial cable-like appearance on coronal images [21]. Calcifications or enhancement after intravenous administration of gadolinium have not been documented [3].

Intraneural synovial sarcomas are extremely rare in the main nerve trunks of the upper limb [4, 7, 26, 32]. They were originally thought to originate from synovial membrane; however, less than 5% are microscopically in continuity with the synovium [9]. Ichinose et al. [13] first postulated a neural origin of synovial sarcomas from a single sample showing nonmyelinated nerve fibers. Synovial sarcomas frequently present as painless, slow-growing masses [9]. They may occur at any age but are more prevalent in young adults, and the extremities are the commonest site. In the upper limb, they can be confused clinically with a ganglion [4, 10].

Posttraumatic hematoma may also be included in the differential diagnosis of intraneural hemangioma. It is associated with well-defined borders, peripheral enhancement, and low signal intensity at T2-weighted imaging owing to methemoglobin deposits [16, 36]. However, in our patient, given the history of a 5-year course, this was not a likely diagnosis.

Benign vascular proliferations of the soft tissue are separated into two major groups, hemangiomas and vascular malformations. Hemangiomas are the most frequently encountered vascular soft tissue anomalies, accounting for approximately 7% of all benign soft tissue tumors. They do not involute and remain present throughout life but have limited growth potential. Vascular malformations are composed of dysplastic vessels, are present at birth, and enlarge proportional to growth. They do not regress spontaneously [38]. Most hemangiomas are superficial lesions that have a predilection for the head and neck. However, they may also involve deep soft tissue structures, such as the liver, the skeletal muscles, the synovial lining, and the peripheral nerves, as in our patient. Hemangiomas of the deep soft tissue are uncommon and more frequently present a diagnostic dilemma. Intramuscular hemangioma is probably the most common form of hemangioma of deep soft tissue, accounting for approximately 0.8% of all benign vascular tumors. It is most frequently located at the muscles of the lower extremities, especially the muscles of the thigh. Differential diagnosis of intramuscular hemangioma should include angiosarcoma, liposarcoma, and angiomatosis. Treatment of intramuscular hemangioma is aimed at complete excision; prior embolization can be used to facilitate surgical excision [38, 41]. Synovial hemangioma is rare and almost always involves the knee, especially the suprapatellar pouch. These lesions can show

extraarticular involvement and cause pressure erosions of adjacent bone. Treatment of synovial hemangioma consists of simple extirpation of the lesion. Diffuse synovial hemangiomas that are more difficult to eradicate surgically can be treated with small doses of radiation [38, 41].

Intraneural hemangioma of peripheral nerves is rare [23, 34]. It is a benign lesion of mesodermic origin and of the melanoblastic type, arising from the proliferation of various types of blood vessels [2, 16, 30]. Intraneural hemangioma can arise within the nerve, in its sleeve, or around it; apparently, the tumor arises from the vasa nervorum. Involved nerves have included the trigeminal, ulnar, median, digital, posterior tibial, and peroneal nerves [16, 18, 24, 34, 41]. Solitary intraneural hemangiomas within the sheaths of a lumbar spinal nerve root [22] and a nerve root of the cauda equina have also been reported [25]. Among the 13 cases reported in the literature [2, 6, 16–18, 20, 23, 24, 29–31, 42], there is no characteristic anatomic distribution; the median nerve is most commonly affected (six cases), followed by the tibial (three cases), ulnar, digital, sciatic, and superficial peroneal nerves. Solitary intraneural hemangiomas, confined to one or more nerve roots of the cauda equina [22, 25] and the inferior trunk of the brachial plexus [3], have also been reported. All but one intraneural hemangioma occurred in children and young adults younger than 40 years; in all but two of the reported cases, the patients were women [3, 41]. The tumor may present as a palpable mass of variable size or as spontaneous localized pain; although numbness and muscle wasting may occur, motor or sensory deficits are rare [23, 42]. A few cases of carpal tunnel syndrome attributable to a hemangioma of the median nerve have been described as well [6, 37]. In our case, the patient presented with a painless, gradually increasing mass and numbness at the median nerve distribution.

Ultrasonography is useful and efficient in the exploration of musculoskeletal pathology, particularly in the extremities. It is cost-effective, widely available, and easy to perform, with high patient acceptability. In addition, it provides easy guidance for biopsy, and it may be useful for detecting suspected tumor recurrence in patients with implanted hardware in which artifact precludes other means of cross-sectional imaging [1, 14, 40]. Nevertheless, ultrasonography has not achieved a uniformly broad acceptance for evaluating the musculoskeletal system. Ultrasonography is operator dependent, which in select hands could be a useful adjunct imaging modality in some tumor clinics but is not a modality in routine use for musculoskeletal tumor staging or diagnosis, especially in complex anatomic sites [14]. In addition, many have found it difficult to distinguish benign from malignant solid tumors using sonographic and Doppler criteria [8, 12, 19, 28]. The sonographic characteristics of soft tissue tumors

are quite variable. A most common and serious interpretation is mistaking a tumor for a hematoma or muscle tear, even in the absence of any clearly documented history of trauma sufficient to cause a muscle injury and of any direct ultrasound signs of muscle tear [8]. In our study, ultrasonography was performed at the initial diagnostic evaluation of the patient and to assess the vascularity of the soft tissue mass. However, as in our case, more definitive information was gained by MRI.

MR features of intraneural hemangiomas include hyperintense signal on T1- and T2-weighted images with fat suppression sequences. Flow voids are usually apparent and feeding vessels may be seen; these lesions are also noted to enhance after intravenous administration of gadolinium. On angiography, an early and persistent tumoral blush is seen [3, 39]. As in our patient, feeding arteries and draining vessels and hemosiderin deposits or phleboliths on T2-weighted images are the most suggestive findings for hemangiomas [16].

Current treatment for intraneural hemangioma includes intraneural or intrafascicular microdissection with preservation of the continuity of the nerve [2, 3, 6, 23, 37]. Nerve grafting may be required if the tumor cannot be resected free of a motor nerve. It is more successful in children because of their capacity for regeneration. On the sensory branch of a nerve, resection followed by direct coaptation of the nerve ends without grafting is usually adequate [23, 29, 31, 42].

It is not always possible to excise intraneural lesions totally. Partial resection usually provides pain relief and alleviation of neuropathic symptoms for variable periods of time. However, unless resection is total, there is a risk of recurrence; in two of the 13 reported cases [29], incomplete resection resulted in the recurrence of symptoms within 3 years. Certain cases of multifocal localization with major functional loss have in the past required amputation [23, 29].

Although the use of radiotherapy has yielded some favorable results in treating hemangiomas at other anatomic sites [27, 35], its use in the treatment of intraneural hemangiomas has not been previously reported [3].

In our patient, the tumor was located within the median nerve in the arm and was diagnosed by histology. Intraneural marginal resection was performed. The contribution of preoperative embolization cannot be determined. The patient's recovery was uneventful; there were no postoperative complications or wound healing problems. Early postoperative examination showed no clinically detectable loss of sensation in the median nerve distribution of the ipsilateral hand. By 1 year after the operation, the numbness had resolved completely; the patient had no complaints related to the lesion. We observed no imaging findings suggesting residual or recurrent mass at the 1-year followup.

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References

1. Arya S, Nagarkatti DG, Dudhat SB, Nadkarni KS, Joshi MS, Shinde SR. Soft tissue sarcomas: ultrasonographic evaluation of local recurrences. *Clin Radiol*. 2000;55:193–197.
2. Bilge T, Kaya A, Alatli M, Bilge S, Alatli C. Hemangioma of the peroneal nerve: case report and review of the literature. *Neurosurgery*. 1989;25:649–652.
3. Châtillon CE, Guiot MC, Jacques L. Lipomatous, vascular, and chondromatous benign tumors of the peripheral nerves. *Neurosurg Focus*. 2007;22:E18.
4. Chesser TJ, Geraghty JM, Clarke AM. Intraneural synovial sarcoma of the median nerve. *J Hand Surg Br*. 1999;24:373–375.
5. Chiao HC, Marks KE, Bauer TW, Pflanze W. Intraneural lipoma of the sciatic nerve. *Clin Orthop Relat Res*. 1987;221:267–271.
6. Coessens B, De Mey A, Lacotte B, Vandenbroeck D. Carpal tunnel syndrome due to an haemangioma of the median nerve in a 12-year-old child. *Ann Chir Main Memb Super*. 1991;10:255–257.
7. Cugola L, Pisa R. Synovial sarcoma: with radial nerve involvement. *J Hand Surg Br*. 1985;10:243–244.
8. Doyle AJ, Miller MV, French JG. Ultrasound of soft-tissue masses: pitfalls in interpretation. *Australas Radiol*. 2000;44:275–280.
9. Fisher C. Synovial sarcoma. *Ann Diagn Pathol*. 1998;2:401–421.
10. Fleegler EJ. An approach to soft tissue sarcomas of the hand and upper limb. *J Hand Surg Br*. 1994;19:411–419.
11. Guthikonda M, Rengachary SS, Balko MG, van Loveren H. Lipofibromatous hamartoma of the median nerve: case report with magnetic resonance imaging correlation. *Neurosurgery*. 1994;35:127–131.
12. Hoglund M. Ultrasound diagnosis of soft-tissue tumours in the hand and forearm: a prospective study. *Acta Radiol*. 1997;38:508–513.
13. Ichinose H, Powell L, Hoerner HE, Derbes VJ, Byers JF. The potential histogenic relationship of the peripheral nerve to synovium. *Cancer Res*. 1979;39:4270–4273.
14. Ilaslan H, Sundaram M. Advances in musculoskeletal tumor imaging. *Orthop Clin North Am*. 2006;37:375–391.
15. Johnson RJ, Bonfiglio M. Lipomatous hamartoma of the median nerve. *J Bone Joint Surg Am*. 1969;51:984–990.
16. Kerimoglu U, Uzumcugil A, Yilmaz G, Ayvaz M, Leblebicioglu G, Altinok G. Intraneural hemangioma of digital nerve diagnosed with MR imaging. *Skeletal Radiol*. 2007;36:157–160.
17. Kojima T, Ide Y, Marumo E, Ishikawa E, Yamashita H. Haemangioma of median nerve causing carpal tunnel syndrome. *Hand*. 1976;8:62–65.
18. Kon M, Vuursteen P. An intraneural hemangioma of a digital nerve: case report. *J Hand Surg Am*. 1981;6:357–358.
19. Latifi HR, Siegel MJ. Color Doppler flow imaging of pediatric soft tissue masses. *J Ultrasound Med*. 1994;13:165–169.
20. Losli EJ. Intrinsic hemangiomas of the peripheral nerves, a report of two cases and a review of the literature. *AMA Arch Pathol*. 1952;53:226–232.
21. Marom EM, Helms CA. Fibrolipomatous hamartoma: pathognomonic on MR imaging. *Skeletal Radiol*. 1999;28:260–264.
22. Mastronardi L, Guiducci A, Frondizi D, Carletti S, Spera C, Maira G. Intraneural capillary hemangioma of the cauda equina. *Eur Spine J*. 1997;278–280.
23. Mestdagh H, Lecomte-Houcke M, Reyford H. Intraneural haemangioma of the posterior tibial nerve. *J Bone Joint Surg Br*. 1990;72:323–324.
24. Nagay L, McCabe SJ, Wolff TW. Hemangioma of the digital nerve: a case report. *J Hand Surg Br*. 1990;15:487–488.
25. Nowak DA, Gumprecht H, Stolzle A, Lumenta CB. Intraneural growth of a capillary haemangioma of the cauda equina. *Acta Neurochir (Wien)*. 2000;142:463–468.
26. O'Connell JX, Browne WL, Gropper PT, Berean KW. Intraneural biphasic synovial sarcoma: an alternative “glandular” tumor of peripheral nerve. *Mod Pathol*. 1996;9:738–741.
27. Ogino I, Torikai K, Kobayashi S, Aida N, Hata M, Kigasawa H. Radiation therapy for life- or function-threatening infant hemangioma. *Radiology*. 2001;218:834–839.
28. Ozbek SS, Arkun R, Killi R, Memis A, Dagdeviren A, Sevinc E. Image-directed color Doppler ultrasonography in the evaluation of superficial solid tumors. *J Clin Ultrasound*. 1995;23:233–238.
29. Patel CB, Tsai TM, Kleinert HE. Hemangioma of the median nerve: a report of two cases. *J Hand Surg Am*. 1986;11:76–79.
30. Peled I, Iosipovich Z, Rouso M, Wexler MR. Hemangioma of the median nerve. *J Hand Surg Am*. 1980;5:363–365.
31. Prosser AJ, Burke FD. Hemangioma of the median nerve associated with Raynaud's phenomenon. *J Hand Surg Br*. 1987;12:227–228.
32. Rinehart GC, Mustoe TA, Weeks PM. Management of synovial sarcoma of the median nerve at the elbow. *Plast Reconstr Surg*. 1989;83:528–532.
33. Scheithauer BW, Woodruff JM, Erlandson RA. *Tumors of the Peripheral Nervous System. Atlas of Tumor Pathology*, 3rd Series, Fascicle 24. Washington, DC: Armed Forces Institute of Pathology; 1997.
34. Strickland JW, Steichen JB. Nerve tumors of the hand and forearm. *J Hand Surg Am*. 1977;2:285–291.
35. Suparna HC, Vadhiraja BM, Apsani RC, Seetharamaiah T, Fernandes DJ, Rao K, Vidyasagar K. Symptomatic vertebral hemangiomas: results of treatment with radiotherapy. *Indian J Radiol Imag*. 2006;16:37–40.
36. Theumann NH, Bittoun J, Goettmann S, Le Viet D, Chevrot A, Drape JL. Hemangiomas of the finger: MR imaging evaluation. *Radiology*. 2001;218:841–847.
37. Van Meir N, De Smet L. Carpal tunnel syndrome in children. *Acta Orthop Belg*. 2003;69:387–395.
38. Vilanova JC, Barceló J, Smirniotopoulos JG, Pérez-Andrés R, Villalón M, Miró J, Martín F, Capellades J, Ros PR. Hemangioma from head to toe: MR imaging with pathologic correlation. *Radiographics*. 2004;24:367–385.
39. Vilanova JC, Barceló J, Villalón M. MR and MR angiography characterization of soft tissue vascular malformations. *Curr Probl Diagn Radiol*. 2004;33:161–170.
40. Vincent LM. Ultrasound of soft tissue abnormalities of the extremities. *Radiol Clin North Am*. 1988;26:131–144.
41. Weiss SW, Goldblum JR. *Enzinger and Weiss's Soft Tissue Tumors*. 4th ed. St Louis, MO: CV Mosby; 2001.
42. Wood MB. Intraneural hemangioma: report of a case. *Plast Reconstr Surg*. 1980;65:74–76.