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Schwannoma of Foot and Ankle: Seven Case Reports and Literature Review

XINGPEI HAO[1], DAVID LEVINE[1], JOON YIM[1], CHENFENG QI[2], LEE FIRESTONE[1], IAN BEISER[1], ENZO LEONE[1], KIRK WOELFFER[1] and GENE MIRKIN[1]

[1]*Foot and Ankle Specialists of the Mid-Atlantic, LLC., Rockville, MD, U.S.A.;*
[2]*Laboratory of Immunogenetics, National Institute of Allergy and Infectious Diseases, National Institute of Health, Rockville, MD, U.S.A.*

Abstract. *Background: Schwannoma is most often grown on the trunk, upper and lower extremities, and head and neck, but rarely on the foot. This study aimed to reveal clinical presentations, histopathology and treatment options for schwannoma of the foot. Materials and Methods: Seven schwannomas out of 174 soft-tissue tumors on the foot and ankle were retrieved from our Institute in a 3-year period, and 42 schwannomas on the foot and ankle in the literature in a 30-year period were reviewed. Results: The incidence of schwannoma of foot was found to be 4.0%. The patient age ranged from 8 to 84 years, with a mean of 47.4 years. More than 80% of tumors were located on the ankle, heel and plantar aspect. Overall, 77.6% of patients complained about a painful mass. Magnetic resonance imaging revealed a well-circumscribed, round or ovoid mass with iso-intensity signal compared with surrounding neuromuscular tissues on T1-weighted images and hyper-intensity signal on T2. Forty-eight out of 49 patients were treated with surgical excision or enucleation without recurrence in follow-up from 2 months to 4 years. Histologically, schwannoma was composed of hypercellular Antoni A zone with palisaded spindle cells with strong immunostaining for S-100 and hypocellular Antoni B zone with vascularization in myxoid stroma. Conclusion: Schwannoma of the foot and ankle is a rare, painful, indurated tumor. Magnetic resonance imaging reveals the location, size, texture and relationships with surrounding neuromuscular structures. Surgical excision is the primary treatment option with excellent outcome.*

Correspondence to: Dr. Xingpei Hao. 1600 Gude Drive, Suite 205, Rockville, MD 20852, U.S.A. Tel: +1 3014174372, Fax: +1 3019337137, e-mail: xhao@footandankle-usa.com; Dr. Gene Mirkin 10901 Connecticut Avenue, Suite 200, Kensington, MD 20895 U.S.A. Tel: +1 3019492000, Fax: +1 3019492002, e-mail: gmirkin@footandankle-usa.com

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Schwannoma, also called neurilemoma, derived from Schwann cells in the peripheral nerves, is a solid, slow-growing tumor. It was first reported by Verocay in 1910 (1), and was named 'schwannoma' by Masson in 1932 (2). Schwannoma accounts for about 5% benign tumors as revealed by an analysis of 18,677 benign soft-tissue tumors by Kransdorf (3) and others (4). It frequently occurs in the trunk, flexor side of upper and lower extremities, head and neck (3, 5, 6), especially in the eighth cranial vestibular nerves (7-9), but is uncommon on the foot and ankle (10-12). Toepfer *et al*. observed 11 (10.5%) neurinomas, including both schwannoma and neurofibroma, out of 104 benign soft-tissue tumors of the foot and ankle at a university tumor institute between 1997 and 2015 (13). Kehoe *et al*. recorded 12 out of 104 (11.5%) peripheral nerve tumors on the foot in a 32-year period (7), and Carvajal *et al*. reported eight out of 87 (9.2%) schwannomas were located on the foot in a 16-year period observation (14). In 1969, Das Gupta *et al*. analyzed 303 schwannomas with none of them being on the foot (5), whereas in 1998 with Chaudhuri, they reported four out of 104 schwannomas to be found on the foot (15). Odom *et al*. reviewed 557 schwannomas and noted 19 (2.93%) involving the foot (16). Most published results were reports of single case or small case series. Here, we report seven cases of schwannoma on the foot and ankle from our Institute in a 3-year period, and further review 42 cases in the literature from 1988 to date in a 30-year period, with the aim of describing its clinical manifestations, diagnosis, differential diagnosis and treatment options.

Patients and Methods

All tumors on the foot and ankle were retrospectively analyzed from Foot and Ankle Specialists of Mid-Atlantic (FASMA) in a 3-year period from Sept 1st 2015 to Aug 30th, 2018. FASMA comprises 63 podiatrists located in Washington DC, Maryland, Virginia, North Carolina and Pennsylvania who treat various foot and ankle conditions. All pathology slides of schwannomas were reviewed with confirmation of the original diagnoses (XPH). Clinicopathological

Table I. *Clinicopathological characteristics of study patients with schwannoma on the foot and ankle.*

Case	Age, years	Gender	Site	Clinical presentation	Histological features	Treatment	Recurrence
1	52	Male	Right medial ankle	A mass associated with paresthesias for 1 year. Ultrasound: An anechoic, oval shaped mass, 4 cm. MRI: A mass with iso-intensity signal relative to surrounding muscles on T1 and hyperintensity signal on T2-weighted images (Figure 1).	Typical schwannoma S-100$^+$	Surgical enucleation from tibial nerve	None (14 months)
2	66	Male	Right medial plantar heel	A painful nodular mass for 2 months. Tender with direct palpation. MRI: A 0.38 cm nodule of increased signal intensity on T2-weighted images in the subdermal region	Typical schwannoma S-100$^+$; αSMA$^-$ (Figure 2)	Surgical excision	None (12 months)
3	25	Female	Left 3rd interdigital space	Discolored, painful neoplasm for 3 months, 0.5 cm	Compound melanocytic nevus (CMN) with underlying schwannoma S-100+ and HMB-45+ for both neval cells of CMN and the spindle cells of schwannoma. αSMA$^-$ for both components	Opted for observation after biopsy	None (12 months) Lost to follow-up thereafter
4	75	Female	Right plantar	A soft tissue mass for decades, much tender with weight bearing for several years. Ultrasound: A well-defined hypoechoic mass, 2.5 cm	Typical schwanoma S-100$^+$, αSMA$^-$	Surgical excision	None (38 months)
5	71	Male	Right 2nd interdigital space	A painful mass for months. MRI: A moderately enhancing circumscribed bilobed soft tissue mass, 3.2×2.2×1.5 cm	Ancient type schwannoma with atypical nuclei S-100$^+$; αSMA$^-$, CD34-	Surgical excision	None (36 months)
6	36	Male	Left dorsal to the 4th and 5th metatarsals	A painful mass for 2 months, 1.2×1.5 cm	Typical schwannoma S-100$^+$; αSMA$^-$, CD34$^-$	Surgical excision	None (28 months)
7	34	Female	Left posterior ankle	A firm, tender, ganglion cyst-like mass for 2 years, 1 cm	Typical schwannoma S100$^+$; αSMA$^-$	Surgical excision	None (12 months)

IHC: Immunohistochemistry; αSMA: alpha smooth muscle actin; CD: cluster of differentiation; MRI: magnetic resonance imaging. Typical schwannoma is histologically composed of hypercellular Antoni A with elongated spindle or ovoid Schwann cells forming bundles and hypocellular Antoni B with fewer spindle or ovoid cells admixed with vascular vessels within the loose matrix with myxoid changes.

features were retrieved from FASMA's database, analyzed by one observer (XPH) and were further confirmed by the referring podiatrists.

Results

Clinicopathological characteristics of schwannoma of foot and ankle. In total, seven schwannomas out of 174 benign soft-tissue tumors were diagnosed in the foot and ankle areas in a 3-year period. The incidence of schwannoma of the foot and ankle was 4.0%. The clinicopathological characteristics of seven schwannomas are shown in Table I.

English literature of 42 schwannomas involving the foot and ankle from 1988 for a 30-year period were reviewed (Table II). Only cases with clear age, gender, size, site, MRI, histology report, treatment, follow-up *etc*. were included for further analysis. Other reports without detailed clinical information were not included. This brought the number to a total of 49 patients including the current seven cases, making this the most detailed analysis of schwannomas involving the foot and ankle. The clinicopathological features were analyzed based on these 49 cases.

Clinically, most of the patients (38/49, 77.6%) complained of painful mass on the foot or ankle with or without weakness or paresthesia. Three patients exhibited tarsal tunnel syndrome due to involvement of the tibial nerve in the tarsal tunnel. The duration from the symptom onset to surgery ranged from 2 months to 48 years, with a mean and median of 7.3 and 3 years, respectively. Both males and females were equally affected (males to females: 1:1). The

Table II. *Review of clinicopathological features of patients with schwannoma on the foot and ankle reported in literature.*

Author (Ref), year	Age, years	Gender	Site	Clinical presentation	Histological feature	Treatment	Recurrence
Zuckerman *et al*. (23), 1988	73	M	Left medial and plantar	An asymptomatic mass for 40 years, increased pain for 2 months, 2.5×2.5 cm	Typical	Surgical excision from medial plantar nerve	None (30 months)
Buenger *et al*. (20), 1993	53	M	Left dorsal foot and ankle	Several painful, slowly growing nodules for 30 years after sustaining several injuries to the involved extremity, 0.5-2.5 cm	Typical	Surgical excision	N/A
Ikushima *et al*. (24), 1999	8	M	Left medial and plantar	Asymptomatic, soft, immobile, non-tender mass, 6×4 cm	Plexiform schwannoma with almost uniform cellular Antoni A	Surgical excision	None (24 months)
Ritte and Elston (25), 2001	19	M	Left dorsum	A solitary, pediculated, fleshy nodule for 1 year, 1 cm	Typical	Surgical excision	None (2 months)
Torossian *et al*. (18), 2001	30	M	Right heel	Incompletely excised small schwannoma 10 years earlier. Slow-growing mass with difficult walking for two year, 7.5×5.5×5 cm, ulcerated, irregular, ovoid, solid, well circumscribed	Typical	Surgical excision and reconstruction with a medial plantar flap	None (8 months)
Odom *et al*. (16), 2001	74	F	Left heel	A painful mass for 5 years. MRI: A 1.5 cm in diameter, round, circumscribed mass involving the medial plantar nerve	Typical	Surgical excision	None (18 months)
Still (26), 2001	55	F	Left foot bottom	A slowly enlarging painful mass for 2 years. MRI: An oval shaped mass associated with medial plantar nerve, 3.8×2.0 cm	Typical	Surgical enucleation	None (19 months)
Marui *et al*. (27), 2004	84	F	Right heel	A painful mass for 10 years. MRI: A soft-tissue mass within the medial plantar nerve. 1.8×1×1 cm	Typical	Surgical excision	None (15 months)
	53	M	Right heel	Painful nodule for 8 years. MRI: A soft tissue tumor associated with the first branch of the lateral plantar nerve, 1×0.9×1 cm	Typical S-100$^+$	Surgical enucleation	None (16 months)
Mangrulkar *et al*. (17), 2007	37	M	Left foot	A painful, multinodular, firm mass for years. MRI: A 14×5×8 cm soft tissue mass involving posterior tibial nerve, medial and lateral plantar nerves	Typical	Surgical excision. Surgical excision again due to recurrence at 9 months	Recurrence at 9 months, none after resection at 24-month follow-up
Ioannou *et al*. (28), 2009	29	M	Right ankle	A slowly growing mass with mild pain and paresthesia for 6 months. MRI: A multinodular, inhomogeneous lesion, 6×4×2.8 cm	Plexiform schwannoma S-100$^+$, actin$^-$, desmin$^-$	Surgical excision from posterior tibial nerve	None (28 months)
Kwok *et al*. (29), 2009	42	M	Left medial heel	Left medial heel pain radiating to the lateral sole for 6 months, Tinel$^+$. Ultrasonography and MRI: A neurogenic tumor inside the tarsal tunnel, 1-cm	Typical	Surgical excision from the first branch of the lateral plantar nerve.	None (14 months)
Mendeszoon *et al*. (30), 2009	56	F	Left foot	Left foot pain and swelling for 3 years. MRI: A large cystic lesion, 8×2.8×3.1 cm	Typical	Surgical excision	None (5 months)
Jacobson *et al*. (21), 2011	65	M	Left plantarlateral aspect of forefoot	A large, soft, nontender, partially pedunculated soft tissue mass for 48 years following minor trauma. 10.1×6.8×3.5 cm	Plexiform schwannoma S-100$^+$	Surgical excision	None (28 months)
Carvajal *et al*. (14), 2011	33	M	N/A	Left painful mass, 2 cm, paresthesias	Typical	Surgical excision	N/A
	45	F	N/A	Left painful mass, 2 cm Tinel+	Schwannoma associated with neurofibro-matosis-1	Surgical excision	Recurrence

Table II. *Continued*

Table II. *Continued*

Author (Ref), year	Age, years	Gender	Site	Clinical presentation	Histological feature	Treatment	Recurrence
	37	F	N/A	Left painful mass, 2.3 cm Tinel+	Typical	Surgical excision	N/A
	67	F	N/A	Right painful mass, 2.5 cm, Tinel+	Typical	Surgical excision	N/A
Li *et al*. (31), 2011	19	F	Left plantar aspect	Progressive pain for 18 months. MRI: Three nodules, 0.5×0.5×0.8 cm, 0.7×1.0×1.2 cm, 1.0×1.1×1.5 cm	Plexiform schwannoma	Surgical excision from plantar digital nerve	None (30 months)
Milnes and Pavier (32), 2012	73	F	Left ankle	An exquisitely painful, solid and immobile mass for 8 years. Tinel+. Tarsal tunnel syndrome. MRI: A solid mass, 3 cm	Typical	Surgical enucleation from tibial nerve	None (6 months)
Schweitzer *et al*. (33), 2013	65	F	Left posteromedial ankle	Painful masses for 5 years. MRI: Five, well-defined, fusiform-shaped masses 0.5 to 2 cm	Typical	Surgical excision	None (12 months)
	63	M	Right ankle	An asymptomatic "lump" for 30 years, increased pain for 3 months. MRI: 3 separate masses, 0.8 to 2.8 cm	Typical S-100$^+$	Surgical enucleation	None (12 months)
Kellner *et al*. (34), 2014	N/A	N/A	Left ankle	A painful mass for 3 years, 2 cm, Tinel+. MRI: A well-circumscribed, enhancing lesion in the region of the tarsal tunnel	Typical	Surgical resection from tibial nerve	N/A
	N/A	N/A	Left medial ankle	A mass for 4 years, 2 cm. MRI: A well-circumscribed, noninvasive mass located on the calcaneal branch of the posterior tibial nerve	Typical	Surgical excision	N/A
	N/A	N/A	Left heel	A mobile mass for 20 years, 1.5 cm	Typical	Surgical excision	N/A
Kallini and Khachemoune (35), 2014	25	M	Left lateral heel	A painless, flesh-colored, soft, indurated nodule with mild hyperpigmentation for at least 1 year, 3×3 cm	Typical	Surgical excision	N/A
Hallahan *et al*. (36), 2014	54	F	Left ankle	A firm and palpable mass for 10 years, tarsal tunnel syndrome. MRI: A mass, 3.4×3.0×3.0 cm	Typical S-100$^+$	Surgical excision	None (9 months)
Mohammed *et al*. (37), 2014	38	F	Right heel	A painful, firm, immobile mass for 30 years, increased size 1 year ago. MRI: A serpiginous, lobulated mass, 2.1×1.5×2.3 cm	Plexiform schwannoma S-100$^+$	Surgical excision	None (10 months)
	11	M	Right plantar	A painful mass for 1 year. MRI: A multilobulated mass in the plantar soft tissues of the forefoot, 3.9×3.2×2.4 cm	Plexiform schwannoma S-100$^+$	Surgical excision	None (36 months)
Judd *et al*. (22), 2014	51	M	Right medial ankle	A soft-tissue mass for 2 years after injury of ankle. MRI: A lobular cystic lesion, 2.5×2.8×1.5 cm	Typical S-100$^+$	Surgical excision from small branches of the posterior tibial nerve	N/A
Nishio *et al*. (38), 2015	32	F	Right ankle	A slowly growing, painful mass for 5 years. MRI: Multiple nodular lesions with heterogeneous high signal intensity on T2-weighted sequences, 0.2 to 3 cm	Plexiform schwannoma	Surgical intracapsular enucleation	N/A
Min *et al*. (39), 2015	38	M	Left middle plantar	Persistent, pin-prick painful soft-tissue mass for 5 years, Tinel+. MRI: Two fusiform masses along the medial plantar nerve, 3.2×2.3×2.2 cm, 1×0.9×0.8 cm	Typical	Surgical excision	None (2 months)
Albert *et al*. (40), 2017	26	F	Heel	Lower extremity calf tenderness, pain, and progressive weakness. Ultrasonography: A hypoechoic soft tissue mass, 3 cm MRI: A soft-tissue mass along the course of the sural nerve	Typical	Surgical excision	N/A
	22	M	Heel	Tenderness and palpable mass on the lateral aspect of the heel inferior.	Typical	Surgical excision	N/A

Table II. *Continued*

Table II. *Continued*

Author (Ref), year	Age, years	Gender	Site	Clinical presentation	Histological feature	Treatment	Recurrence
				Ultrasonography: A hypoechoic solid soft tissue nodular mass, 1.1 cm×0.6 cm. MRI: A peripherally enhancing soft-tissue mass along the course of the sural nerve			
	66	F	Ankle	A painful mass at the level of tarsal tunnel, Tinel+. MRI: A solid, polylobulated mass within the subcutaneous fat, 1.9 cm	Typical	Surgical excision	N/A
Muratori *et al*. (41), 2017	65	F	Right medial and plantar	Painful swelling for 5 years. MRI: A soft-tissue mass, 12×8×5 cm	Typical S-100$^+$	Surgical excision	None (9 months)
Merritt *et al*. (42), 2019	56	M	Left plantar	Progressive, painful mass for 5 years. MRI: A well-circumscribed, subcutaneous mass, 0.8×0.6×0.5 cm	Typical S-100$^+$	Surgical excision	None (2 months)
Angelini *et al*. (43), 2019	57	F	Right plantar forefoot	An oval-shaped nodule with pain and paresthesia for 1 year, 1×1.5 cm	Typical	Surgical excision	None (3 months)
	45	M	Right plantar midfoot	Right foot pain and swelling 1st MRI: Synovial angiomatosis. Symptoms returned after 6 months surgical excision. 2nd MRI: tumor-like tissue in the plantar region of the foot suspected for local recurrence	1st Surgical excision: Synovial angiomatosis 2nd Surgical excision: Typical schwannoma	Surgical excision	N/A
	58	F	Left foot	Left foot pain for 4 years. MRI: A mass arising from the sural nerve near the lateral malleolus	Typical	Surgical excision	N/A
	35	F	Right medial ankle	A slowly growing, poorly mobile, painful mass for 2 years, Tinel+. MRI: A fusiform lesion along the course of the medial plantar nerve	Typical	Surgical enucleation	None (48 months)
Daniel *et al*. (44), 2019	61	M	Left heel	A sharp painful mass for 7 years, progressively worse. Tinel+. MRI: A hyperintense mass arising from tibial nerve, 2.2 cm	Typical S-100+	Surgical excision	None (12 months)

F: Female; M: male; MRI: magnetic resonance imaging; N/A: not available. Typical schwannoma means, histologically, spindle cells arranged in palisading patterns in Antoni A zone and hypocellular regions in Antoni B zone.

patients' ages ranged from 8 to 84 years, with a mean and median of 47.4 and 51.5 years, respectively. The tumor size ranged from 0.38 cm to 14 cm in diameter, with an average of 3.3 cm and a median of 2.5 cm. The tumor locations of 46 patients were retrieved, with 28 (60.9%) being located on the left side. The tumors were mainly localized on the ankle (14/46, 30.3%), plantar aspect (14/46, 30.3%) and heel (9/46, 19.6%). Three tumors were found in the dorsal web of the interdigital spaces, one on the dorsum of the foot. Sub-anatomical locations on the foot were not specified in five patients. Out of the 49 patients, 29 were pre-surgically examined by magnetic resonance imaging (MRI). Typical MRI of schwannoma showed a well-circumscribed, round or oval mass with isointense or reduced signal intensity relative to surrounding skeletal muscle on T1-weighted images and significantly increased homogeneous or heterogeneous signal intensity on T2-weighted images (Figure 1). Fascicular sign (fascicular bundles in neurogenic tumors), target sign (centrally decreased with peripherally increased signal intensity) and split-fat sign (a rim of fat surrounding the tumor), reflecting different proportions of stromal tissues and tumor components (4), were described. Forty-eight out of 49 patients were selected to undergo surgical excision or enucleation, whereas one patient from our series opted for observation after biopsy due to the small size. No recurrences were reported, with a period of follow-up from 2 months to four years.

Grossly, schwannomas were usually round, ovoid, well-circumscribed, solid masses. The cut surface was often gray to yellow, solid, glistening and well-encapsulated. Degenerative changes including cystic formation and hemorrhage were observed in some cases. Histopathologically,

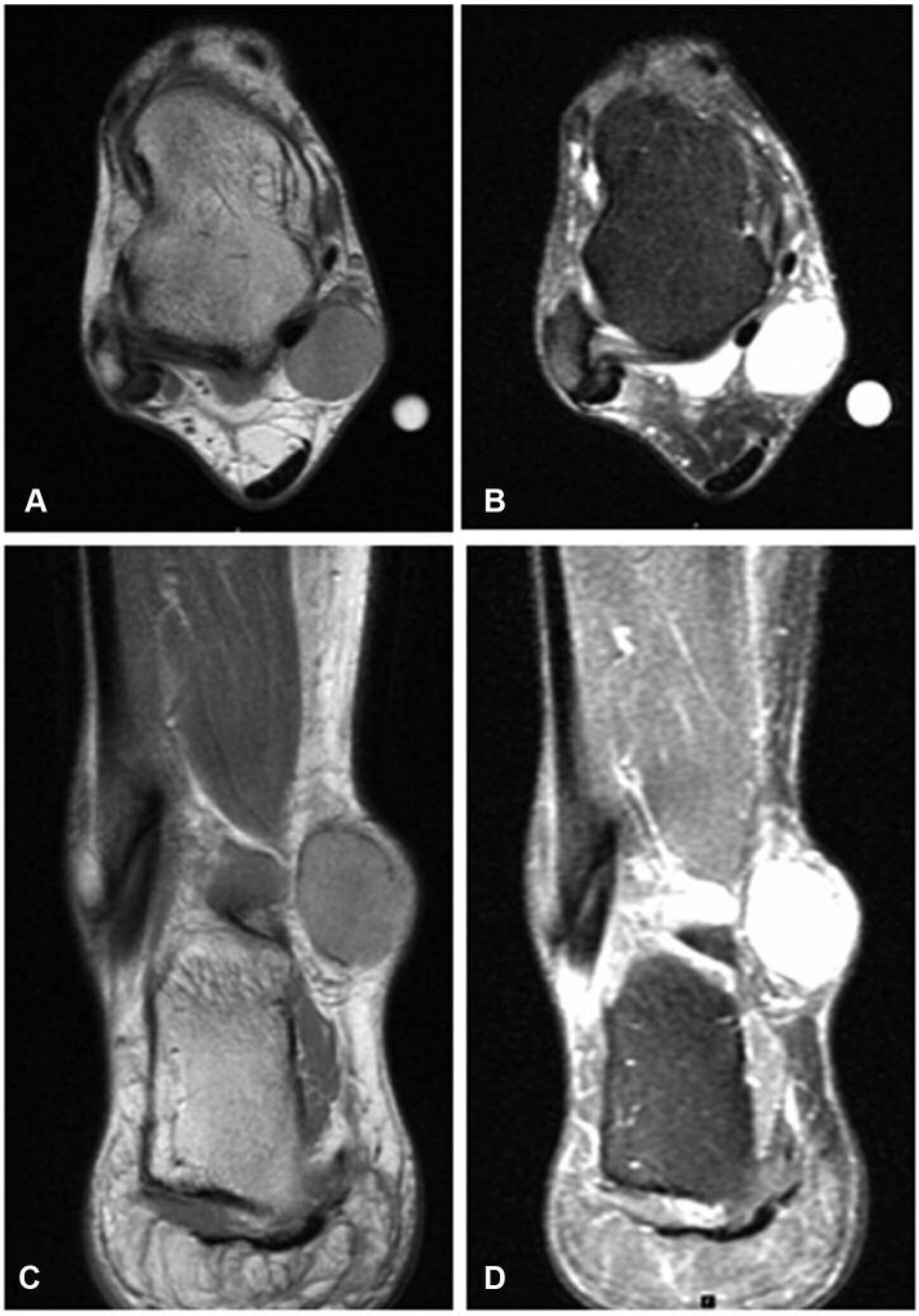

Figure 1. *Magnetic resonance imaging of patient 1 showing a well-circumscribed, solid mass along the posteromedial aspect of the right ankle with iso-intensity signal relative to surrounding muscles on T1-weighted images (A, coronal view; C, sagittal view) and hyperintensity signal on T2-weighted images (B: coronal view, D: sagittal view).*

the majority of schwannomas exhibited typical biphasic morphology, composed of hypercellular Antoni A and hypocellular Antoni B zones. Antoni A zone consisted of elongated spindle cells with indistinct borders palisaded together, forming a Verocay body, while Antoni B presented reduced cellularity in a myxoid matrix with increased vascularization (Figure 2). Other variants, including plexiform and ancient types, were reported. One variant of schwannoma with 'ancient' changes in our series showed atypical nuclei with increased size and chromatin density. Immunostain showed strong positive cytoplasmic staining for S-100 but negative staining for alpha smooth actin (αSMA) and CD34

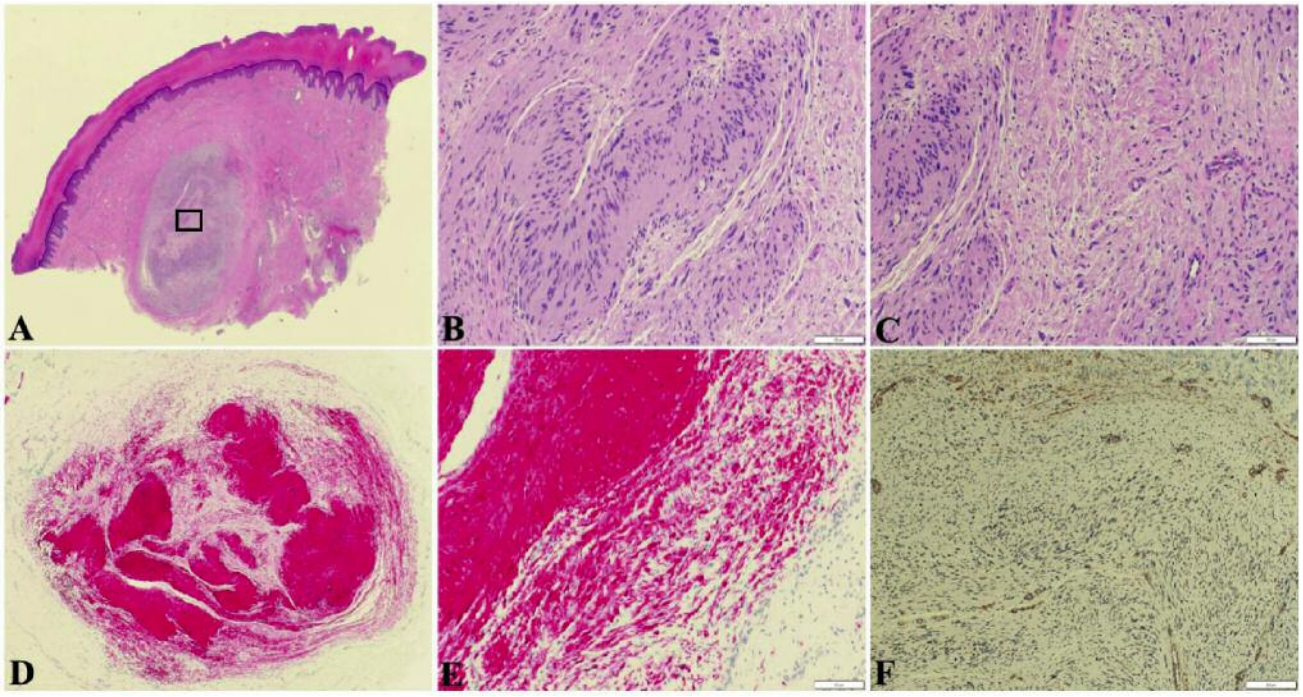

Figure 2. *Microphotographs of hematoxylin and eosin and immunostained schwannoma on the heel of patient 2. A: A full view of the slide showing a well-circumscribed subcutaneous mass with hypercellular and hypocellular regions (×2). Inset shows areas described in B and C. B: The Antoni A zone, characterized by spindle Schwann cells arranged in palisading pattern (Verocay body) (×200). C: The left third of the image shows the Verocay body in (A), while the right two-thirds shows Antoni B zone featuring hypocellularity in myxoid stroma (×200). D: Microphotograph showing strong S-100 immunoexpression in tumor whereas surrounding stromal tissues were negative (×5). E: Higher magnification of D showing S-100 cytoplasmic expression in spindle tumor cells where the encapsulated fibroblasts were negative (×200). F: Microphotograph of immunostaining showing negative alpha-smooth muscle actin expression in spindle tumor cells but strong positive expression in vascular smooth muscle cells among tumor cells and surrounding stromal tissues, which served as an internal positive control (×100).*

in spindle cells (Figure 2). One of our patients showed coexistence of compound melanocytic nevus with underlying schwannoma, both neval cells of the nevus and spindle cells of the schwannoma exhibited positive staining for both S-100 and HMB-45.

Discussion

We presented seven cases of schwannoma of foot and ankle with its clinical manifestation, histopathology and treatment. Schwannoma accounted for 4.0% among 174 benign soft-tissue tumors involving the foot and ankle diagnosed in a 3-year period at our Institute with 63 podiatrists. Ruggieri *et al*. reported that 14 schwannomas out of 189 benign soft-tissue tumors of the foot (7.5%) were diagnosed at the Rizzoli Institute in an 18-year period between 1990 and 2007 (12). These data further support the observation that schwannoma on the foot and ankle is rare.

Clinically, schwannoma on the foot and ankle usually presents as a painful, movable, well-defined mass; weakness and paresthesia can be observed when associated nerves are affected. The symptoms are mainly related to the tumor location, especially on the sites of weight bearing or easily compressed regions including the plantar aspect and inter-digital spaces. Tinel sign and tarsal tunnel syndrome can be elicited when the tibial nerve is evoked. Even though tumor can occur on any part of the foot, the most frequent locations were found to be the ankle, heel and plantar aspect of the foot (78.3%). Occurrences in interdigital spaces and on dorsum of foot were uncommon. Both males and females were found to be equally affected. Interestingly, 60.9% of tumors occurred on the left foot. The modalities of pre-surgical diagnosis include X-ray radiography, ultrasound and MRI. Radiography usually does not reveal remarkable changes unless calcification noticed inside tumor tissue or bone tissues are involved. Ultrasound examination of schwannoma usually exhibits a round or ovoid, solid, well-delineated, hypoechoic homogenous mass and is useful for distinguishing between cystic and solid lesions. MRI is the most valuable tool for evaluating schwannoma, not only for location, size and texture, but also for relationships with

Table III. *Differential diagnosis of schwannoma from other tumor types.*

Tumor	Clinical presentation	Histology	Immunohistochemistry
Ganglion cyst	Fluid feeling on palpation, most on dorsal surfaces and transillumination, aspiration with yellow to clear viscous fluid	Cyst surrounded by dense fibrous tissues admixed with inflammatory cells, no synovial or epithelial lining	
Spindle cell lipoma	Soft solid mass in the skin and subcutaneous tissue	Well-encapsulated spindle adipose cells without atypia	$CD34^+$, $S\text{-}100^+$
Neurofibroma	Non-encapsulated, usually painless, often multiple lesions throughout the body, frequently seen in second and third decades	Mixed cell types including Schwann cells, perineurial-like cells, fibroblastic cells and entrapped axons. Uniphasic, rare palisading pattern. Variants including focal and diffuse cutaneous, plexiform, intraneural and pigmented neurofibroma	$S\text{-}100^+$, $SOX10^+$, $CD34^+$ (focal), factor $XIII^+$ (focal)
Solitary fibrous tumor	Usually occurring in older adults, slow-growing and painless mass with low rate of infiltration and metastasis	Relatively bland and uniform spindle cells within long, thin and parallel bands of collagen in a 'patternless' arrangement	$CD34^+$, $CD99^+$, $vimentin^+$, $desmin^-$, $S\text{-}100^-$, *NAB2–STAT6* fusion gene, strong nuclear STAT6 expression (45)
Fibroma	Usually occurring along the plantar medial arch within the central and/or medial band of the plantar fascia	Well encapsulated, spindled, oval or round cells in fascicles	Vimentin+, reticulin+, collagen I+, CD34–, α-SMA–
Leiomyoma	Usually located in the skin and subcutaneous tissue, frequently seen in early adulthood	Intersecting fascicles of benign smooth muscle bundles without mitosis	$\alpha\text{-SMA}^+$, $myosin^+$, $desmin^+$, $CD34^-$
Neuroma	Usually occurring in interdigital spaces, painful with activity but relieved with rest and massage, radiating to the adjacent toes	Wavy nerve bundles surrounded by dense fibrosis	$S100^+$

NAB2–STAT6: NGFI-A binding protein 2 gene and signal transducer and activator of transcription 6; α-SMA: alpha smooth muscle actin; CD: cluster of differentiation; SOX10: SRY-related HMG-box 10.

nerves and other surrounding anatomical structures. Typical MRI of schwannomas show isointense or reduced signal intensity relative to surrounding skeletal muscle on T1-weighted images and significantly increased signal intensity on T2-weighted images.

Surgical excision or enucleation is the primary treatment option, even though for a smaller tumor observation can be opted for. Extreme care needs to be taken to dissect the tumor from associated nerves in order to preserve or restore nerve functions to a maximal level. Recurrence is extremely rare (less than 1%) unless tumor tissue is incompletely excised (4, 17, 18).

Morphologically, schwannoma of the foot and ankle is similar to that at other sites of the body. It is composed of an Antoni A zone with hypercellularity with palisaded spindle cells arranged in short bundles or fascicles, and an Antoni B zone with hypocellularity with vascu-larization in myxoid matrix. Immunostaining for S-100 is positive, whereas that for αSMA and CD34 is negative, which is useful for diagnosis and differential diagnosis. One of our patients had coexistence of compound melanocytic nevus and underlying schwannoma. It is not clear if there is any etiological relationship between these two lesions.

Schwannoma on the foot and ankle needs to be differentiated from other lesions, including ganglion cyst, neuroma, spindle-cell lipoma, neurofibroma, solitary fibrous tumor, fibroma, leiomyoma. Careful clinical and histopathological evaluation with immunohistochemistry can lead to an accurate diagnosis (Table III).

Trauma, Carney's complex, and neurofibromatosis type 1 or 2 may be associated with the development of schwannoma (19). One of our patients related frequently hitting the inside of his ankle against his chair at work as the probable cause of his tumor. In total, four [one of our cases plus three others (20-22)] out of 49 patients (8.0%) reported minor trauma in the related areas before development of schwannoma. In one patient, schwannoma was associated with neurofibromatosis 1 (14), whereas no clinical presentation of neurofibromatosis for any of the other patients, suggesting that the majority of schwannomas involving the foot and ankle occur spontaneously.

In conclusion, schwannoma on the foot is a rare tumor. Both males and females are equally affected. It is histologically composed of palisaded spindle cells forming Antoni A and B zones. Ultrasound and MRI are good diagnostic tools for revealing tumor location, size, texture,

involved nerves and relationships with surrounding muscular structures. Surgical excision is the primary treatment option with recurrence being rare.

Financial Disclosure

None reported.

Conflicts of Interest

None reported.

Authors' Contributions

Xingpei Hao: Study conceptualization, data collection, analysis and interpretation, writing and revising the article. David Levine: Patient care, data collection, analysis and interpretation, article revision. Joon Yim: Diagnosis, data collection, analysis and interpretation, article revision. Chenfeng Qi: Diagnosis, data collection, analysis and interpretation, article revision. Lee Firestone: Patient care, data collection, analysis and interpretation, article revision. Ian Beiser: Patient care, data collection, analysis and interpretation, article revision. Enzo Leone: Patient care, data collection, analysis and interpretation, article revision. Kirk Woelffer: Patient care, data collection, analysis and interpretation, article revision. Gene Mirkin: Study conceptualization, patient care, data collection, analysis and interpretation, coordination, article revision.

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