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Structural Origin and Surgical Complications of Peripheral Schwannomas

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Abstract. *Background/Aim: In this study, we investigated the locations and surgical complications of schwannomas. Patients and Methods: Data of 130 patients with schwannomas were retrospectively reviewed. Pre- and post-operative neurological symptoms, tumor locations, and nerves of origin (sensory, motor, or mixed) were reviewed. Results: Before surgery, 69 patients had Tinel-like signs, 56 patients had pain, 32 patients had numbness, four patients had motor deficits. After surgery, 20 patients had developed a new neurological deficit; 11 patients had motor deficits, ten patients had sensory deficits, and one patient had both motor and sensory deficits. Most schwannomas occurred in mixed nerves, including the median nerve in 17 patients and tibial nerve in 13 patients. Conclusion: The most common site of schwannoma was the median nerve. Although the nerve of origin of the schwannoma could be identified in only 26.0% of cases, the data suggest that schwannomas occur in both sensory and motor nerves.*

Schwannomas, also known as neurilemmomas, are benign peripheral nerve sheath tumors originating from Schwann cells (1-5). Schwannomas usually occur in the third to fifth decades of life, with no racial and gender differences (3, 6). Common schwannomas are solitary (95%) (7). However, some studies reported multiple tumors in the extremities and referred to those as schwannomatosis (8). Schwannomas located in the upper extremity account for 12.0-19.0% of cases, and in the lower extremity for 13.5-17.5% (9). In the upper extremity, schwannomas are mostly located on the volar surface (2, 10-12). Schwannomas constitute 8.0% of all soft tissue tumors (9, 13).

The diagnosis of schwannoma arising within the nerve trunk of the upper or lower extremity is usually straightforward (14). Asymptomatic slow-growing masses and Tinel-like signs are useful for diagnosis. Magnetic resonance imaging (MRI) is particularly helpful for diagnosis (6, 15-17). Schwannomas contain varying proportions of two distinct patterns of cellular architecture in tumors, known as Antoni-A and Antoni-B. The Antoni-A component is a fibrillary, intensely polar, elongated-appearing tissue type. The Antoni-B is a distinct loose microcystic tissue adjacent to the Antoni-A regions (2, 18, 19). By immunohistochemistry, schwannomas typically show diffuse, strong expression of S100 protein (15, 20, 21). Folpe and Gown have stated that immunostaining for the S100 protein consistently identifies schwannomas and that it serves as an important diagnostic tool due to the strength of its expression (22). The tumor is well enveloped by a capsule consisting of perineurium from the nerve of origin. The remaining nerve fascicles are spread over the capsule of the tumor. This structure suggests that schwannomas can be removed without damaging the underlying nerve fascicles (23, 24). However, post-operative complications of schwannomas have been reported at 1.5-80.0%, with neurological deficits as one of the major complications (14, 25-29).

Correlation studies between locations and post-operative complications of schwannomas help predict the possibility of surgical complications in each schwannoma site. However, there are only a few reports about the schwannomas' nerve of origin because of the difficulty in identifying the difference between motor and sensory nerve fascicles. The schwannomas' nerve of origin, locations, and surgical complications are essential information for the

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Key Words: Schwannoma, neurological deficit, distribution, sensory nerve, motor nerve, complication.

operative indications and prevention of post-operative complications. In this study, the nerve of origin and surgical complications of schwannomas were investigated by reviewing clinical and surgical records.

Patients and Methods

Patients. This retrospective study included 130 patients with solitary schwannomas who underwent surgical excision between 2005 and 2018 in our hospital. The patients' mean age was 52.3 years (range=13-84 years). The mean period between symptom onset and surgery was 31.8 months (range=0-240 months). All tumors were histologically confirmed as schwannomas. Data were obtained from both clinical and operative records with radiological and histopathological features. The interval months between symptoms onset and surgery were calculated. This study excluded cases of multiple schwannomatosis and plexiform schwannoma. The schwannomas excised by non-orthopaedic surgeons (such as spine neurosurgeons) were also excluded.

Informed consent was obtained by the opt-out method, and this study protocol was approved by the Medical Ethics Committee of Kanazawa University (IRB number: 2019-011).

Definition of tumor location and origin. Locations such as the brachial plexus, retroperitoneum, and pelvic cavity were categorized into the "trunk;" *e.g.* a retroperitoneal tumor in the femoral nerve is categorized as originating from the trunk. In this study, subcutaneous schwannomas were classified as originating from pure sensory nerves, whereas intramuscular schwannomas were classified as pure motor nerves. A mixed nerve was defined as a nerve with both motor and sensory nerves (30). The superficial branch of the radial nerve, digital nerves, and the sural nerve were categorized as pure sensory nerves (31). The anterior and posterior interosseous nerves were categorized as pure motor nerves. The superficial branch of the radial nerve and posterior interosseous nerve were recognized separately from the radial nerve. The anterior interosseous nerve was also identified separately from the median nerve. The pre-operative MRI and surgical records identified the involved nerves.

Surgical procedures. A pneumatic tourniquet was applied as applicable (26). The skin incision was centered over the tumor and extended along the involved nerve (Figure 1A-C). The tumor was exposed, and the proximal and distal extent of the affected nerve were identified. After the exposure of the tumor capsule, normal nerve bundles over the tumor capsule were detected using a nerve stimulator. A longitudinal incision was then carefully made in the epineurium to avoid the normal nerve bundle. Once the shiny surface of the tumor was exposed, a small sample of the tumor was obtained and sent to the Department of Pathology. The histopathological diagnosis was confirmed during the operation. Gentle dissection (along with the capsule and epineurium) and enucleation were performed (Figure 1D).

Post-operative complications. Pre-operative and post-operative complications were obtained from the medical records. The presence of a Tinel-like sign (shooting paresthesia in the distribution of the involved nerve) upon percussion of the tumor (32), spontaneous pain, and sensory or motor deficits within the distribution of the parent nerve were recorded.

Table I. *Locations, size, and interval months of 130 schwannomas*.

	Affected nerve	N	Size (cm^3)	Interval months
Upper extremity (n=52)	Ulnar N	7	17.0	27
	Median N	17	8.1	18.5
	Radial N	10	3.8	48.8
	Digital N	5	0.9	41.9
	Others	13	10.9	34.4
Lower extremity (n=42)	Sciatic N	7	74.6	74.1
	Femoral N	4	15.5	31
	Tibial N	16	14.9	38.5
	Peroneal N	4	3.8	8.3
	Others	11	7.6	39.9
Trunk (n=36)	Brachial plexus	9	7.5	36.3
	Spinal root	13	46.7	22.2
	Others	14	75.9	50.9
		130	23.8	35.1

Interval months refers to the duration of symptoms from the onset up until surgery.

Results

This retrospective study included 130 patients with solitary schwannoma. There were 62 male and 68 female patients, with a mean age of 52.3 years (range=13-84 years). The mean period from onset to surgery was 35.1 months. The mean follow-up period was 12.1 months. A single nerve was affected in 130 patients. The mean tumor volume was 23.8±63.4 cm^3.

Locations of schwannomas. Schwannomas were located in the upper extremities in 52 patients (40.0%), in the lower extremities in 42 patients (32.3%), and in the trunk in 36 patients (27.7%). The locations of schwannomas arising from major nerves and the size of resected tumors are presented in Table I. In the upper and lower extremity, the most common affected nerve was the median nerve and the tibial nerve, respectively. The interval months refer to the duration of symptoms from the onset up until surgery. The longest interval months among affected nerves was seen in the sciatic nerve. Eighty-seven lesions (66.9%) involved a mixed nerve, 19 lesions (14.6%) involved a pure sensory nerve, and 15 lesions (11.5%) involved a pure motor nerve. In mixed and pure sensory nerves, the most common nerve origin was the median nerve and digital nerve, respectively. Schwannomas also occurred in spinal roots including the cervical nerve root, lumbar nerve root and sacral nerve root, but there were no schwannomas that originated from the thoracic nerve roots. A summary of the schwannomas' nerve of origin from major peripheral nerves is presented in Table II.

Pre-operative and post-operative complications. Pre-operatively, 91 patients (70.0%) had palpable masses, 69 patients (53.1%) had Tinel-like signs, 56 patients (43.1%) had pain, 32 patients

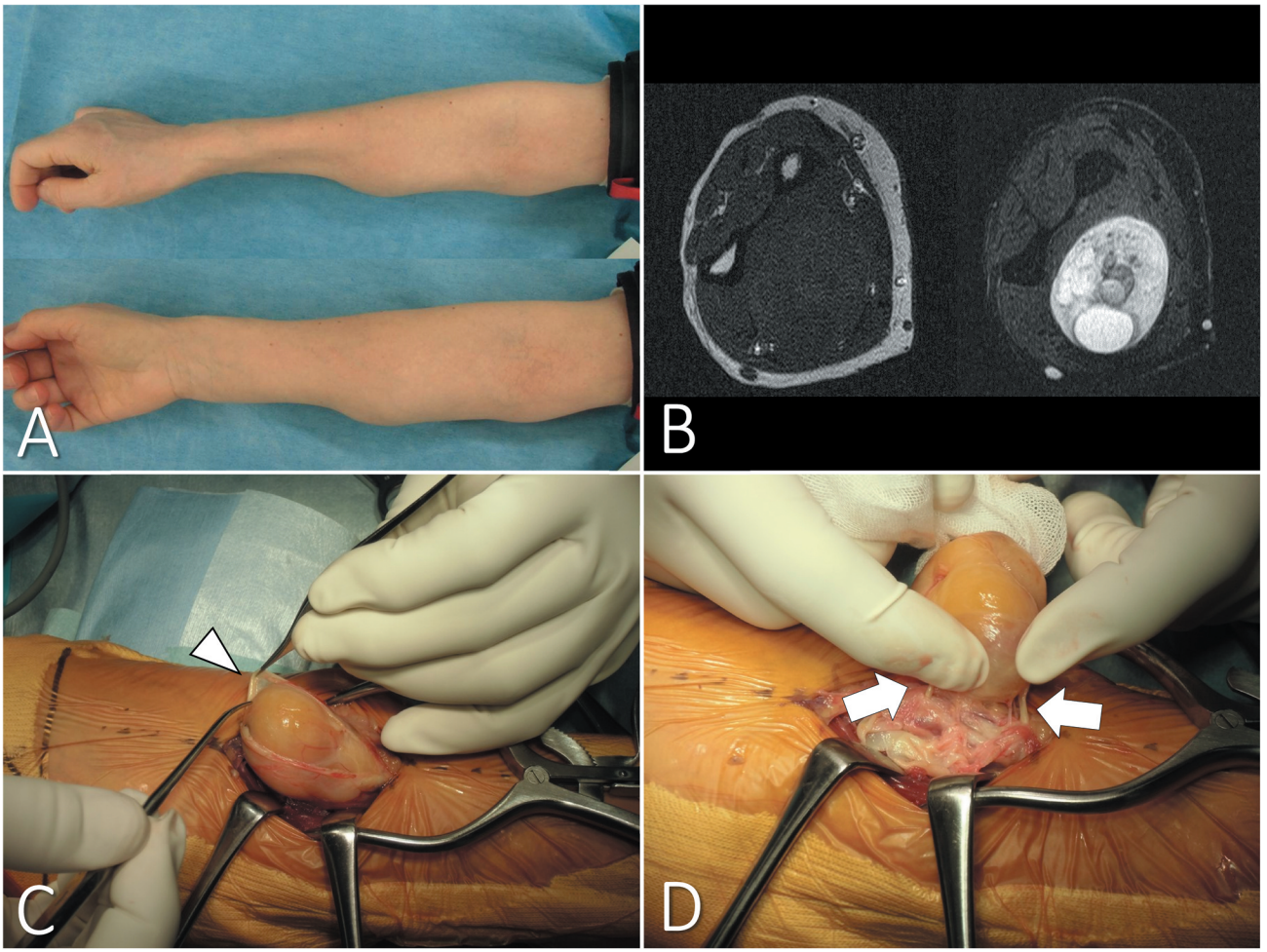

Figure 1. *Clinical findings of schwannoma and surgical procedure. (A) A 66-year-old female with a mass on the right forearm. (B) MRI revealed a tumor in the forearm (left: T1 weighted image, right: T2 weighed image with fat suppression). (C, D) Open biopsy diagnosis was schwannoma, enucleation after the confirmation of nerve fibers by the neurostimulator. Arrowhead; capsule. Arrow; nerve fibers.*

(24.6%) had numbness, four patients (3.1%) had motor deficits, and no patient had sensory deficits (Table III). Post-operatively, 37 patients (28.5%) had numbness, 11 patients (8.5%) had motor deficits, and 10 patients (7.7%) had sensory deficits. A palpable mass was common in the upper and lower extremities, but numbness was more common in the spinal roots. In median nerve and tibial nerve, Tinel-like sign appeared in 13 patients (76.5%) and 13 patients (81.3%), respectively. There was no motor deficit prior to surgery of schwannomas of the nerve roots. The details of pre-operative and post-operative symptoms in each group are shown in Tables IV-VI. No tumor recurrence was observed during the follow-up period.

Discussion

In this study, the median nerve was the most common site of schwannoma, followed by the tibial nerve, radial nerve, brachial plexus, sciatic nerve, ulnar nerve, femoral nerve, digital nerve, peroneal nerve, and superficial branch of the radial nerve. Some authors have also reported that the median nerve is most frequently involved (33, 34). In pure sensory nerves, digital nerves were the most common site, followed by the superficial branch of radial nerve, radial nerve, saphenous nerve, *etc*. In pure motor nerves, the obturator nerve, branch of radial nerve, posterior interosseous nerve, and the branch of the tibial nerve are common sites. Schwannomas were distributed throughout the body, including the trunk, upper arm, forearm, palm, digit, thigh, lower leg, and plantar area. In cases of schwannoma originating from peroneal nerves, median nerves and ulnar nerves, the interval (in months) between the surgery and onset of symptoms was relatively shorter than that in other cases. Ozdemir *et al*. reported 14 cases of Schwannomas in the hand and wrist, which were located in the median nerve in 10 patients and ulnar nerve in four patients, and the mean interval between

Table II. *Peripheral schwannomas grouped by the nerve of origin.*

Mixed nerve (n=87)		Pure sensory nerve (n=19)		Pure motor nerve (n=15)	
Median N	17	Digital N	5	Obturator N	2
Tibial N	13	Superficial branch of radial N	4	Branch of radial N	2
Brachial plexus	9	Radial N	3	Posterior interosseous N	2
Sciatic N	8	Saphenous N	2	Branch of tibial N	2
Ulnar N	7	Supraclavicular N	1	Axillary N	1
Femoral N	6	Greater occipital N	1	Anterior interosseous N	1
Radial N	5	Medial cutaneous N of calf	1	Branch of femoral N	1
Peroneal N	4	Tibial N	1	Superior gluteal N	1
Others	18	Lateral plantar N	1	Inferior gluteal N	1
				Others	2

Table III. *Pre-operative and post-operative complications and findings.*

	Pre-operative					Post-operative			
Type of nerve	Mass	Motor deficit	Sensory deficit	Pain	Numbness	Tinel-like sign	Motor deficit	Sensory deficit	Numbness
Nerve in upper Ext. (%)	47 (79.7)	1 (1.7)	0 (0)	24 (40.7)	14 (23.7)	37 (62.7)	5 (8.5)	4 (6.8)	13 (22.0)
Nerve in lower Ext. (%)	30 (63.8)	2 (4.3)	0 (0)	26 (55.3)	10 (21.3)	25 (53.2)	2 (4.3)	4 (8.5)	7 (14.9)
Spinal root (%)	5 (38.7)	0 (0)	0 (0)	2 (15.4)	6 (41.2)	3 (23.1)	3 (23.1)	1 (7.7)	2 (15.4)
Unknown (%)	9 (81.8)	1 (9.1)	0 (0)	4 (44.4)	2 (22.2)	4 (44.4)	1 (11.1)	1 (11.1)	0 (0)
Total (%)	91 (70.0)	4 (3.1)	0 (0)	56 (43.1)	32 (24.6)	69 (53.1)	11 (8.5)	10 (7.7)	37 (28.5)

Ext.: Extremity.

Table IV. *Nerves (upper extremity) and complications.*

		Pre-operative					Post-operative			
Type of nerve		Mass	Motor deficit	Sensory deficit	Pain	Numbness	Tinel-like sign	Motor deficit	Sensory deficit	Numbness
The nerve of the upper extremity (n=59)										
Brachial plexus	9	5			4	3	6	2		2
Axillary N	2	1					1			
Supraclavicular N	1	1								
Median N	17	16			8	2	13		2	6
Radial N	10	8			6	4	5	1	1	1
Ulnar N	7	6			3	1	4	1		2
AIN	1				1					
PIN	2	1	1			1	1			
SB of radial N	4	4				2	3			
MCN	1	1					1	1		
Digital N	5	4			2	1	3		1	2
Total (%)	59 (100)	47/59 (79.7)	1/59 (1.7)	0/59 (0)	24/59 (40.7)	14/59 (23.7)	37/59 (62.7)	5/59 (8.5)	4/59 (6.8)	13/59 (22.0)

AIN: Anterior Interosseous nerve; PIN: posterior interosseous nerve; SB: superficial branch; MCN: musculocutaneous nerve.

Table V. *Nerves (lower extremity) and complications*.

Type of nerve		Pre-operative					Post-operative			
		Mass	Motor deficit	Sensory deficit	Pain	Numbness	Tinel-like sign	Motor deficit	Sensory deficit	Numbness
The nerve of the lower extremity (n=47)										
Sciatic N	8	5			4	2	4			
Superior gluteal N	1									
Inferior gluteal N	1	1								
Femoral N	7	5	1		3	2	2	1	2	3
Obturator N	5	2	1		1				1	1
Tibial N	16	12			10	2	13		1	1
Peroneal N	4	3			4	3	3	1		1
Saphenous N	2	1			1		1			
MCN of calf	1				1		1			
Lateral plantar N	2	1			2	1	1			1
Total	47	30/47	2/47	0/47	26/47	10/47	25/47	2/47	4/47	7/47
(%)	(100)	(63.8)	(4.3)	(0)	(55.3)	(21.3)	(53.2)	(4.3)	(8.5)	(14.9)

MCN: Medial cutaneous nerve.

Table VI. *Nerves (spinal root and unknown) and complications*.

Type of nerve		Pre-operative					Post-operative			
		Mass	Motor deficit	Sensory deficit	Pain	Numbness	Tinel-like sign	Motor deficit	Sensory deficit	Numbness
Spinal root (n=13)										
GON (C2)	1	1							1	
CNR (C4, 5, 8)	5	4			1	2	3	1		1
LNR (L2-5)	5				1	3		2		1
SNR (S1, 2)	2					1				
Total	13	5/13	0/13	0/13	2/13	6/13	3/13	3/13	1/13	2/13
(%)	(100)	(38.7)	(0)	(0)	(15.4)	(41.2)	(23.1)	(23.1)	(7.7)	(15.4)
Unknown (n=11)	11	9/11	1/11	0/11	4/11	2/11	4/11	1/11	1/11	0/11
(%)	(100)	(81.8)	(9.1)	(0)	(44.4)	(22.2)	(44.4)	(11.1)	(11.1)	(0)

GON: Greater occipital nerve; CNR: cervical nerve root; LNR: lumbar nerve root; SNR: sacral nerve root.

Table VII. *Pre-operative and post-operative complications of previous studies and this study*.

	Pre-operative complications				Post-operative new complications		
	Tinel-like sign	Paresthesia	Motor deficit	Sensory deficit	Paresthesia	Motor deficit	Sensory Deficit
Oberle, 1997 (38)	–	–	5/16 (31.3%)	4/16 (25.0%)	–	2/16 (12.5%)	6/16 (37.5%)
Knight, 2007 (14)	155/191 (81.0%)	9/191 (4.7%)	3/191 (1.6%)	–	–	–	–
Date, 2012 (26)	31/35 (88.6%)	–	0/35 (0%)	21/35 (60.0%)	–	–	–
Kim, 2012 (27)	22/30 (73.3%)	15/30 (50.0%)	0/30 (0%)	3/30 (10.0%)	2/30 (6.7%)	2/30 (6.7%)	2/30 (6.7%)
Siqueira, 2013 (37)	29/72 (40.3%)	16/72 (22.2%)	4/72 (5.6%)	9/72 (12.5%)	–	3/72 (4.2%)	7/72 (9.7%)
Ujigo, 2014 (36)	51/76 (67.1%)	–	4/76 (5.3%)	17/76 (22.4%)	–	–	–
Gosk, 2015 (35)	24/26 (92.3%)		7/26 (26.9%)	20/26 (76.9%)	1/26 (3.8%)	1/26 (3.8%)	–
Hirai, 2019 (39)	–	21/141 (14.9%)	6/141 (4.2%)	–	42/141 (29.8%)	8/141 (5.7%)	–
This study	69/130 (53.1%)	32/130 (24.6%)	4/130 (3.1%)	0/130 (0%)	37/130 (28.5%)	11/130 (8.5%)	10/130 (7.7%)

the onset of symptoms and excision was 25 months (34). This period was similar to the schwannoma involving the median nerve and ulnar nerve in this study. In contrast, the interval between the surgery and onset of symptoms is the longest in cases of schwannoma originating from sciatic nerves. The reason for this long interval of symptom manifestation of schwannomas of the sciatic nerve is due to the deep location of the tumor and difficulty in recognition. In this study, no schwannomas originated from the thoracic nerve roots.

The most common pre-operative symptom of schwannomas is a palpable mass, followed by positive Tinel-like signs, pain, and paresthesia (7, 12, 14, 27, 35-40). Previous reports showed that a Tinel-like sign was seen in 40.3-92.3% of pre-operative patients (14, 26, 27, 35-39) (Table VII), while motor and sensory deficits were seen in 0%-31.3% and 12.5-76.9%, respectively (14, 26, 27, 35-39). Abe *et al*. reported that 103 of the 131 tumors (78.6%) produced pre-operative neurological symptoms. Tinel-like sign was observed in 77 (58.8%), spontaneous pain in 32 (24.4%), tenderness in 58 (44.3%), and numbness in 38 cases (29.0%) (41). In spinal nerve roots, George *et al*. reported that motor deficit was observed in 83.3%, and sensory deficit in 59.5% at the time of diagnosis; but in this study, no patients had motor and sensory deficits before surgery (42). In human median nerves, Ikemoto *et al*. reported that nerve compression produces a localized axonal depolarization at the compression site, followed by hyperpolarization upon release of compression, as expected from the focal ischemia (43). In addition, Hofmeijer *et al*. reported that peripheral sensory axons are more vulnerable to ischemia than motor axons, with faster inexcitability during ischemia (44). For this reason, there is a possibility of some differences in pre-operative symptoms due to tumor compression.

Post-operative complications of schwannomas have been reported in 1.5-80.0% of cases (14, 25-27, 45-49). Previous reports have shown that motor and sensory deficits are 3.8-12.5% and 6.7-37.5 %, respectively (27, 35, 37-39) (Table VII). However, for mixed nerves, the neurologic deficit might not be necessarily caused by the tumor compressing the nerve from which it originated. Instead, it might be caused by the schwannoma growing from one type of nerve (*e.g*., sensory). However, it is affecting (or compressing) another type of nerve (*e.g*., motor), which causes the deficit. Therefore, it is difficult to investigate the nerve of origin of the schwannoma by pre-operative and post-operative neurological deficits. Nonetheless, it is valuable to investigate the origin of peripheral schwannomas by the tumor location and affected nerve. This study's data showed that the peripheral schwannomas could arise from both motor and sensory nerves.

This study identified intramuscular schwannomas classified as pure motor nerves. Kwon *et al*. reported that there was no pain or muscle weakness after excision of intramuscular schwannoma (50). In this study, all cases of superior gluteal nerve, inferior gluteal nerve, anterior interosseous nerve, and posterior interosseous nerve were classified as pure motor nerve. These patients also had no sensory deficit, motor deficit and numbness.

To prevent complications, knowledge about the nerve of origin of schwannomas is important. However, few reports have detailed the origin of schwannomas from the motor or sensory nerves, because the distinction of these fibers is difficult. Some reports described methods to identify motor and sensory fibers (51, 52). Karnovsky staining enables the identification of motor and sensory fibers (51). Raman spectroscopy enables the identification of motor and sensory fascicles in a peripheral nerve trunk (52). However, these methods are complex or require special equipment. Mioton *et al*. investigated motor and sensory nerve distribution in the brachial plexus of fresh cadavers using immunofluorescent staining, with choline acetyltransferase and neurofilament 200 (53). They reported that the median nerve exhibited the greatest number of motor axons (44.0%), while the ulnar nerve contained only 13% motor axons. The musculocutaneous (p=0.03), radial (p=0.01), and ulnar (p=0.0005) nerves exhibited significantly lower motor axon percentages. In spinal schwannomas, Gelpi *et al*. reported that 75.0% of schwannomas were located in the sensory dorsal roots (54). Although this study did not include spinal schwannomas, the results supported the occurrence of schwannomas in both sensory and motor nerves. Tang *et al*. reported eight schwannomas in upper extremities. One patient (12.5%) had involvement of the motor nerve, three patients (37.5%) had involvement of the sensory nerve, and four patients (50.0%) had involvement of the mixed nerve (30). Unfortunately, the study by Tang *et al*. did not show a categorizing method of schwannomas originating from the sensory, motor, and mixed nerves. In addition, this study demonstrated a categorizing protocol with a large number of patients.

This study has some limitations. First, this study did not include asymptomatic schwannomas. This selective bias may affect the results of tumor locations and frequency. Therefore, further investigation is required, such as a whole-body MRI in larger populations. Second, the surgical indication for schwannomas differs, not only among patients but also among surgeons. In this study, the surgery was performed by multiple physicians. Third, this study did not analyze the influence of pre-operative biopsy. Levi *et al*. reported that neurological deficits were significantly more frequently observed in patients who had undergone a pre-operative biopsy (12 of 29 patients) than in those who had not (10 of 58) and suggested that pre-operative needle biopsy causes neurological deficits (55). Therefore, further investigation is necessary in the future.

Conclusion

In this study, the most common site of schwannomas was the median nerve. Peripheral schwannomas can arise from both

motor and sensory nerves. However, further investigations such as immunohistochemistry, electron microscopy, and electrophysiological studies are needed.

Conflicts of Interest

The Authors declare they have no conflicts of interest in relation to this study.

Authors' Contributions

All Authors conceived the presented idea. HY and SM conducted the review of the literature. HY, SM and NY verified the method. All Authors discussed the results and contributed to the final manuscript.

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