




Retrospective Analysis of 20 Patients Affected by Schwannomas in the Upper and Lower Limbs*

Análise retrospectiva de 20 pacientes acometidos por schwannoma nos membros superior e inferior

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Abstract

Objective To analyze the epidemiological profile and evolution of 20 patients diagnosed with upper- and lower-limb schwannomas.

Methods A group of patients was defined for a retrospective evaluation comprising the period between February 2002 and June 2018, in which we studied and evaluated 20 medical records of patients undergoing surgery due to schwannoma; the diagnosis was confirmed by an anatomopathological examination.

Results Male and female patients were equally affected. The average age was 50.85 years, ranging from 12 to 77 years. There was a predominance of the upper limb and of the flexor face. The most affected nerve was the ulnar nerve. In total, 6 (30%) patients had transient postoperative complications. No cases of tumor recurrence were identified.

Conclusion Schwannoma is a rare and difficult-to-diagnose lesion. It should always be considered as a hypothesis when facing a soft-tissue tumor affecting the limbs. The Tinel sign should be regarded, given its higher correlation with complications. The patients should be informed of the possible postoperative complications, which are frequent but usually transient.

Keywords

- ▶ neoplasia
- ▶ peripheral nerves
- ▶ neurilemmoma

Resumo

Objetivo Analisar o perfil epidemiológico e a evolução de 20 pacientes diagnosticados com schwannoma nos membros superiores e inferiores.

Métodos Definiu-se um grupo de pacientes para avaliação retrospectiva, compreendendo o período entre fevereiro de 2002 e junho de 2018, no qual foram estudados e avaliados 20 prontuários de pacientes submetidos a procedimento cirúrgico devido a schwannoma; a confirmação diagnóstica foi feita pelo exame anatomopatológico.

* Study conducted at the Department of Orthopedics and Traumatology, Irmandade da Santa Casa de Misericórdia de Marília, Marília, SP, Brazil.

Palavras-chave

- ▶ neoplasias
- ▶ nervos periféricos
- ▶ neurilemoma

Resultados Tanto os pacientes do gênero masculino quanto do feminino foram igualmente acometidos, e a média de idade foi de 50,85 anos, variando de 12 a 77 anos. Houve predomínio do membro superior e da face flexora. O nervo mais acometido foi o ulnar, e 6 (30%) pacientes apresentaram complicações pós-operatórias transitórias. Não foi identificado nenhum caso de recidiva tumoral.

Conclusão O schwannoma é uma lesão rara e de difícil diagnóstico. Deve sempre ser considerada como hipótese quando se estiver diante de um tumor de partes moles acometendo os membros. O sinal de Tinel deve ser levado em consideração por conta de sua maior correlação com as complicações. Os pacientes devem ser informados quanto às possíveis complicações pós-operatórias, que são frequentes, mas, geralmente, transitórias.

Introduction

Schwannoma, also called neurilemmoma, was first described by Verocay in 1908.¹ It originates from Schwann cells and, although rare, is the most common benign tumor of the peripheral nerve sheath, comprising 5% of all soft-tissue tumors. It usually presents as a solitary tumor, although cases of multiple tumors have been described in the literature. It is most common between 30 and 60 years of age, with no preference regarding gender or ethnicity. They most commonly occur on the head and neck, followed by the trunk, and then the upper and lower limbs.²⁻⁸ The upper limb is affected in up to 19% of the cases, while the lower limb is affected in up to 17.5%.¹ There is a predominance of the flexor face, due to the higher concentration of nerve fibers in this region, with preference for the mixed nerves.^{6,8,9} The most affected nerves are the ulnar and median nerves in the upper limbs, and the fibular and posterior tibial nerves in the lower limbs.^{1,10-12}

Although the etiology is not yet fully understood, there is some evidence for chromosomal abnormalities as the main cause, especially regarding chromosome 22.^{13,14}

Its clinical presentation is that of an oval mass of firm consistency, eccentric to the nerve, usually smaller than 3 cm in diameter, well encapsulated, slow growing and with a non-infiltrative pattern, smooth surface and yellowish-gray or whitish-gray coloration. It may persist as a painless edema for years before other symptoms such as pain, paresthesia, hypoesthesia, and motor deficit arise due to the compression of adjacent structures and the absence distensibility of the local tissue.^{3,8,13,15,16}

Under microscopy, two types of tissue can be distinguished: Antoni-A and Antoni-B. The first is characterized by spindle cells with indistinct boundaries, and deformed or wavy nuclei, arranged in leaves or bundles, and mitoses are sparse. There are palisade arrangements and anucleated areas between them, which characterize the Verocay bodies. The second type is less cellular and without distinctive architectural features; its matrix has sparse collagen, numerous blood vessels, and a mixture of spindle and oval cells. Inflammatory-cell foci, including histiocytes, may be present, and some contain hemosiderin. There usually is a predominance of a

histological type in each lesion. Degeneration is common due to vessel-wall hyalinization, hemorrhage and fibrin deposition, with consequent cyst formation, matrix fibrosis and focal calcification. The Schwann cell nucleus becomes hyperchromatic and multilobulated, and the tumor presents a grayish-yellow color in these cases.^{1,3,16-18}

Upon physical examination, the mass is painful at pressure and movable on the transverse axis, but not longitudinally to the limb; tumor percussion induces painful paresthesia in the nerve area, like a positive Tinel sign.^{3,15}

Among the complementary exams, ultrasound and magnetic resonance imaging can be used to assist in the diagnosis. The latter is the preferred imaging exam. Immunohistochemical tests, which show immunopositivity for the S-100 and Leu-7 proteins, can also be used. However, the diagnostic confirmation is only made through the anatomopathological examination.^{1,14,16,17,19}

The differential diagnoses include ganglion, tenosynovitis, neurofibroma, lipoma, xanthoma, myxoma, hemangioma, and giant-cell tumor of the tendon sheath.^{4,7,19,20}

The treatment of choice is early surgical excision by the intra- or extracapsular techniques, and it aims to remove the tumor and preserve nerve function. Surgery is indicated in symptomatic cases, and there still is no consensus on which technique is the best.^{1,3,6,7} Although it has a good prognosis, postoperative temporary sensory and/or motor disorders, such as hypoesthesia and paresthesia, are widely reported in the literature. These disorders are due to nerve dissection or retraction and do not significantly interfere with the daily activities.^{2,6,19}

The aim of the present paper is to analyze the epidemiological profile and the evolution of 20 patients diagnosed with schwannoma between 2002 and 2018.

Materials and Methods

A group of patients was defined for a retrospective evaluation, comprising the period between February 2002 and June 2018, and 20 medical records of patients undergoing surgery due to schwannoma were studied and evaluated.

The inclusion criteria were upper- and lower-limb tumor surgeries performed at the Orthopedics Service of

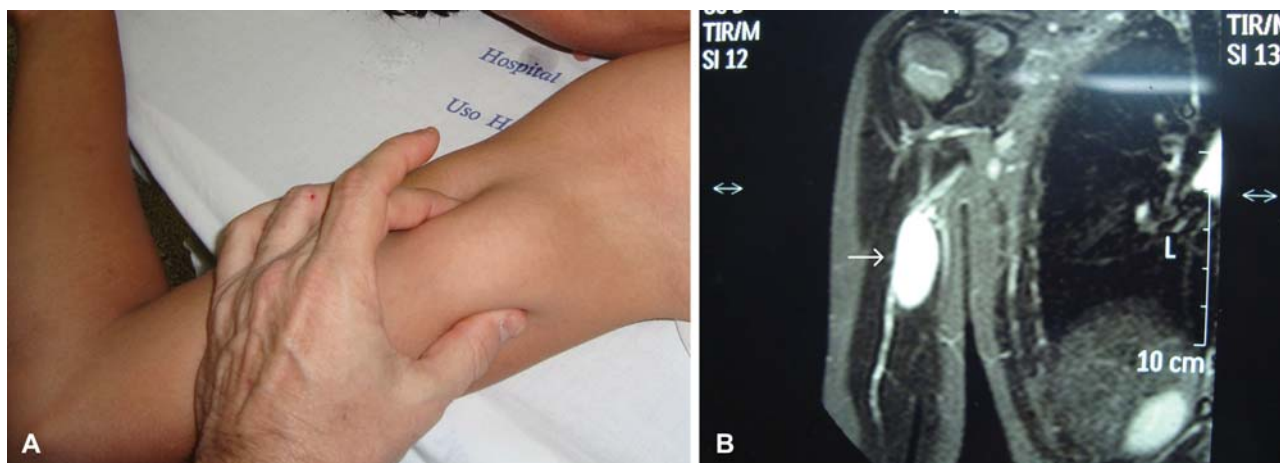


Fig. 1 Preoperative photographs of patient number 5, affected by schwannoma in the right arm. (A) Top view of the right arm with tumors in the medial region highlighted by palpation. (B) Photograph of the magnetic resonance imaging scan of the right upper limb with the arrow indicating the schwannoma in the medial cutaneous nerve of arm.

our institution in the predefined period, which showed diagnostic confirmation of schwannoma by anatomopathological examination.

The patients were assigned a chronological number based on the date of the surgical treatment.

To assist in the diagnostic elucidation, magnetic resonance and/or ultrasound were performed. Subsequently, the diagnostic hypothesis was confirmed by the results of the anatomopathological examination.

The treatment of choice was complete tumor excision. All procedures were performed using the microsurgical technique, that is, the equipment was used to enlarge the surgical field, such as magnifying glasses with magnification of at least four times and/or surgical microscope. In addition, the instruments used were delicate and specific for peripheral-nerve surgery.

Based on the information provided by the magnetic resonance and/or ultrasound examinations, the access route was always planned considering the region of the tumor,

focusing on it (► **Figure 1**). When we reach the deepest planes, we always begin nerve dissection proximally and distally to the tumor, where the nerve is “normal.” Next, we isolate the nerve with the aid of fine Penrose drains (► **Figures 2, 3 and 4**), and we begin the effective tumor resection by the intra- or extracapsular techniques. The cleavage plane between the neural fibers unaffected by schwannoma may be used. In this surgical procedure, it is often necessary to assess the nerve circumferentially during tumor excision. The surgery aims to completely remove the tumor and preserve nerve function.

The patients were evaluated using a protocol previously prepared by the authors. Based on the data from the medical records, we collected information regarding age, tumor location, region, side, face and nerve affected, preoperative signs and symptoms – such as pain, mobility, Tinel sign, change in sensitivity and weakness – date of surgery, post-operative complications, anatomopathological description and presence or absence of relapses.

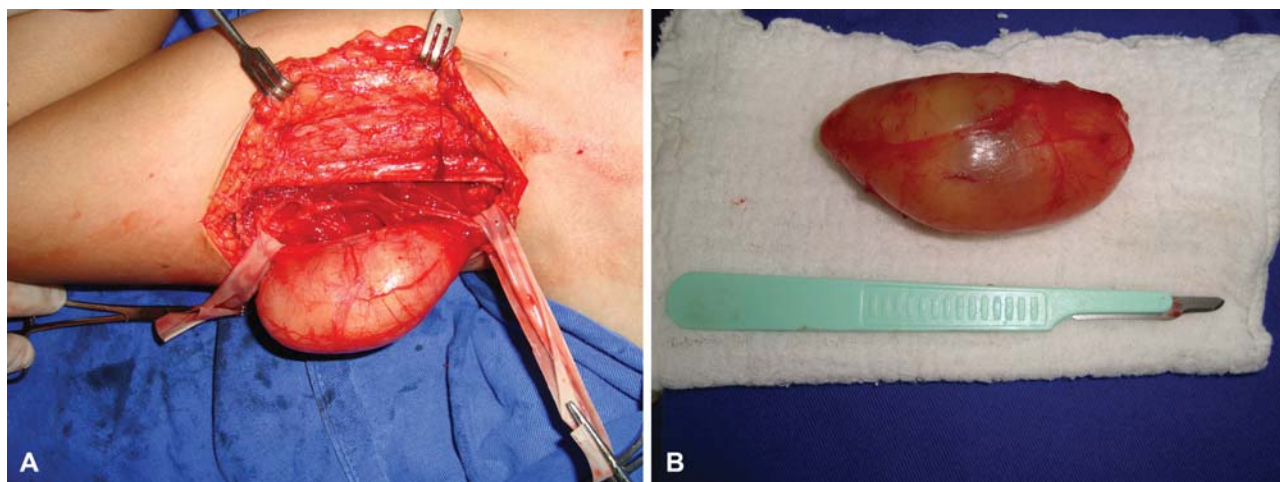


Fig. 2 Perioperative photographs during and after right-arm medial-tumor dissection (patient number 5). (A) Penrose drains are used to isolate the nerve, enabling the integrity of the vascular-nervous structures to be maintained during surgery. (B) Tumor specimen after excision, presenting as a large oval grayish-yellow mass; beside it, a scalpel for the comparison of dimensions.

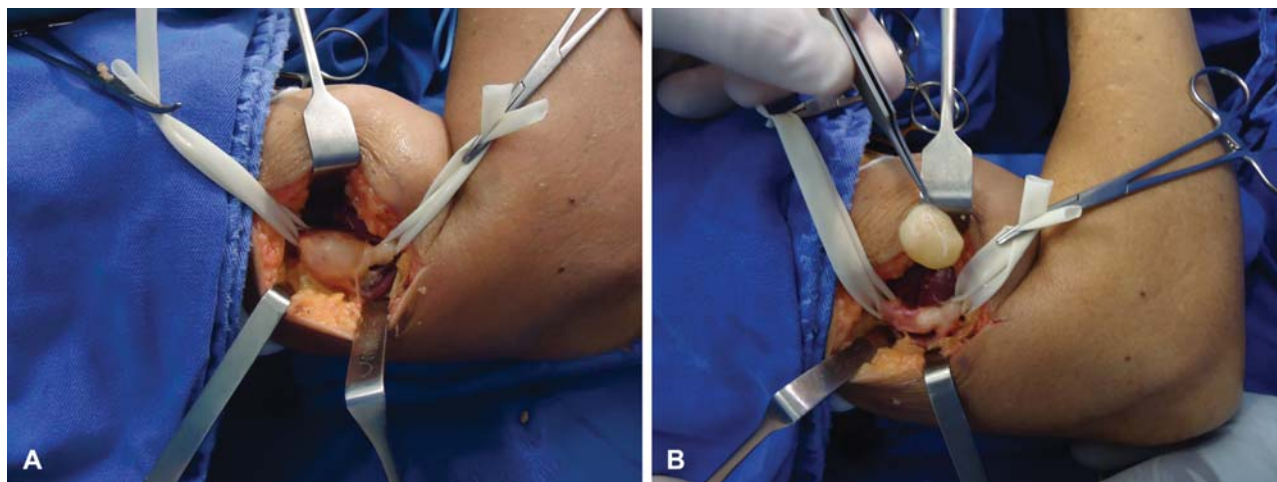


Fig. 3 Intraoperative lateral view photographs of right-arm schwannoma removal (patient number 9). (A) The use of Penrose drains to isolate the radial nerve, proximally and distally to the tumor, can be observed. (B) Nerve repair evidencing, externally, the tumor removed in its totality.

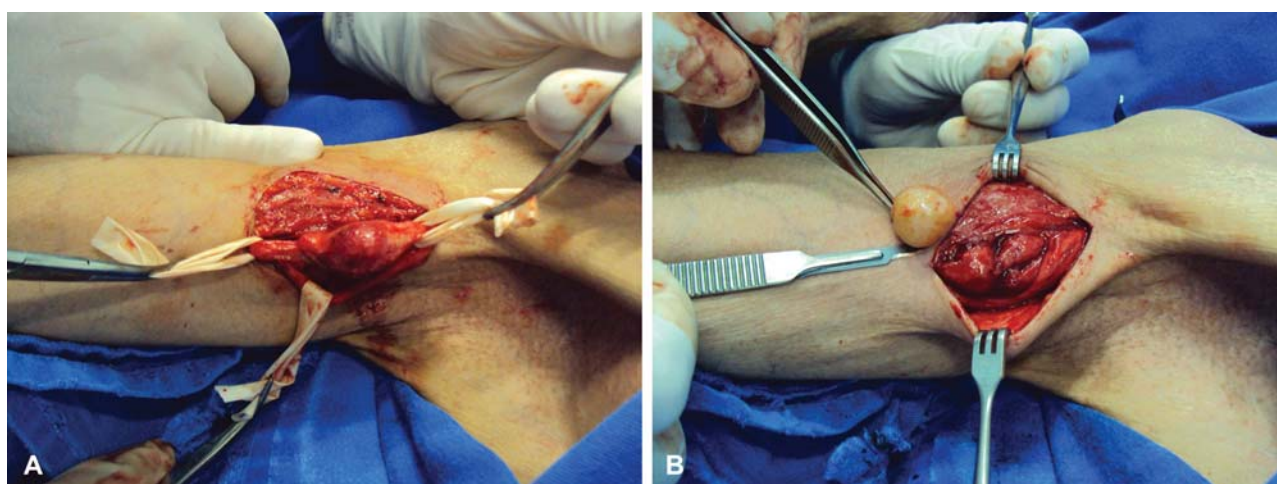


Fig. 4 Perioperative photographs showing dissection of the tumor in the right axillary region (patient number 7). (A) Isolation of the nerve with Penrose drains is evidenced, facilitating tumor exposure and enabling the thorough dissection of the tumor piece to avoid complications. (B) Bloody area of the tumor bed and, adjacent to it, a grayish-yellow tumoral part characteristic of schwannomas.

The present study was submitted for evaluation and approval by the Ethics in Research Committee of our institution.

Results

Regarding gender, 10 patients were female and 10 were male. The average age was 50.85 years, ranging from 12 to 77 years. Regarding ethnicity, all patients were white.

► **Table 1** shows data regarding patient number, sex, age and date of surgery.

► **Table 2** displays data on the number the patients, the preoperative signs and symptoms (pain, mobility, Tinel sign, change in sensitivity and weakness) and the postoperative complications.

The upper limb was affected in 14 cases (70%), and the lower limb, in 6 (30%). Regarding the anatomical region predominantly occupied by the tumor, there was involve-

ment of the volar face in 12 cases (60%), and of the dorsal face in 8 (40%).

Regarding the location of the tumor, six were in the hand, four, in the arm, three, in the forearm, one, in the armpit, three, in the thigh, one, in the leg, one, in the ankle, and one, in the foot. The left side was affected in 11 cases, while the right side, in 9. The ulnar nerve was the most affected, representing seven cases, followed by the radial and median nerves.

The arithmetic mean of the three tumor dimensions was calculated based on macroscopy, and a value of $3.31 \text{ cm} \times 2.12 \text{ cm} \times 1.68 \text{ cm}$ was found.

► **Table 3** shows data on the number the patients, the location, the face, the side, and the nerve affected by the tumor, as well as the dimensions of the tumors.

Regarding the postoperative complications, two patients had paresthesia, two had hypoesthesia, one had hyperesthesia, and one had hypoesthesia associated with paresthesia. No

Table 1 Patient number, gender, age and date of surgery of the patients

Patient number	Gender	Age	Date of Surgery
1	M	77	February-02
2	F	32	January-06
3	F	53	August-07
4	F	56	February-10
5	M	12	August-10
6	F	32	August-10
7	M	71	December-11
8	M	75	July-12
9	F	66	September-12
10	F	64	November-12
11	M	34	December-12
12	M	53	February-13
13	M	24	March-13
14	F	63	April-14
15	F	41	October-14
16	F	77	January-15
17	M	37	June-16
18	M	48	June-16
19	F	53	April-18
20	M	49	June-18

motor deficit was observed in any patient postoperatively. In total, 6 (30%) patients had postoperative complication. However, all of these complications were transient, and after six months none of the patients had any sensitivity changes.

There were no reports of functional or sensory loss of the previously-affected nerve regions during late postoperative reevaluations.

To date, no cases of tumor recurrence have been identified.

Discussion

Although rare, schwannoma is the most common benign tumor of the peripheral nerve sheath. It most commonly affects the head and neck, followed by the trunk, and then the upper and lower limbs.^{8,15,21}

It is more common on the flexor face of the limbs, and typically occurs in individuals between the fourth and sixth decades of life, with no tendency for gender or ethnicity. The most affected nerves are the ulnar and median nerves in the upper limbs, and the fibular and posterior tibial nerves in the lower limbs.^{8-12,16}

The classic schwannoma triad comprises the presence of mass, accompanied by a positive Tinel sign and mobility in the transverse axis of the limb. The clinical picture may also include pain, paresthesia, hypoesthesia and motor deficit.^{4,7,16}

Rabari et al.²² conducted a study in which they comment on the delayed diagnosis of schwannoma. Jonathan et al.⁴ explain that the absence of a specific clinical test, the variety of signs and symptoms, and the rarity of the lesion are possible factors that contribute to this greater difficulty and delayed diagnosis. In addition, it is a lesion that usually grows slowly and is usually painless for several years, leading to a delay in seeking care.^{2,20}

In the Anatomopathology Service of our institution, 20 cases of schwannoma were found, 14 of which were on the upper limb (70%), and 6, on the lower limb (30%). (► **Figure 5**).

In the present study, there was a predominance of the upper limbs over the lower limbs, and of the flexor face over the extensor face. Females and males were equally affected. The mean age was 50.85 years, ranging from 12 to 77 years, with a tendency for the interval between the 4th and 6th decades of life. The ulnar nerve was the most affected, followed by the radial and median nerves. These data are in line with those of the literature.

Regarding the sample, all patients had palpable masses, 17 had pain on palpation, 17 had mobility in the transverse axis of the limb, 6 had a positive Tinel sign, 6 had a change in sensitivity, and 4 had debility.

To assist in the diagnostic elucidation of the tumor, ultrasound and magnetic resonance imaging may be performed. On magnetic resonance imaging, the tumor reveals itself as a well-defined, usually fusiform mass, closely related to the nerve, isointense on T1 and hyperintense on T2, and it may present the target signal.^{1,19} Ultrasonography shows the fascicular structure of the nerves. This enables the surgeon to define the site, the size and the relationship to adjacent structures, which helps identify the origin of the tumor and the affected nerve, in order to contribute to the surgical planning (choice of material, equipment and augmentation methods for microsurgery), as noted in the Materials and Methods section.² Although magnetic resonance imaging is the exam of choice, its high cost is its disadvantage. The ultrasound exam, although cheaper, is operator-dependent. However, the definitive diagnosis is only made by anatomopathological examination.^{1,15,16} The authors point out that because it is a rare tumor and is in a noble structure, where technical and surgical errors can lead to severe functional deficit, it is very important that professionals keep in mind this diagnosis to avoid poor surgical planning.

The recommended treatment is early surgical intervention, which, despite having a favorable prognosis, commonly presents temporary postoperative complications, such as sensory and/or motor disorders.^{6,7} Therefore, it is extremely important that the patients be informed of the risks to which they will be exposed during and after the surgical procedure.⁴ In our study, there were only sensory complications, comprising 30% of the sample. All of these complications were transient.

Gosk et al.¹⁰ and Ujigo et al.²³ comment in their studies on factors that may affect the course of the treatment and that may lead to a higher risk of postoperative complications. Such factors are positive Tinel sign, tumor size and location,

Table 2 Patient number, preoperative symptoms and signs (pain, mobility, Tinel sign, change in sensitivity, weakness) and postoperative complications

Patient number	Pain	Mobility	Tinel sign	Change in sensitivity	Weakness	Postoperative complications
1	+	+	+	-	+	Hypoesthesia
2	+	+	-	-	+	-
3	+	+	-	-	-	-
4	-	+	-	-	-	Paresthesia
5	+	+	-	-	-	-
6	+	-	-	+	-	-
7	+	+	-	-	-	-
8	+	+	-	+	-	Hypoesthesia
9	+	+	+	-	+	-
10	+	-	+	+	-	-
11	+	+	-	-	-	-
12	+	+	-	-	-	-
13	+	+	-	+	-	-
14	+	+	-	-	-	-
15	+	+	+	+	+	Paresthesia and hypoesthesia
16	+	+	-	-	-	Hyperesthesia
17	+	-	+	-	-	Paresthesia
18	-	+	-	-	-	-
19	-	+	-	-	-	-
20	+	+	+	+	-	-

Table 3 Patient number, location, face, side and nerve affected, as well as the size of the tumors

Patient number	Location	Face	Side	Nerve	Dimensions (cm)
1	Hand	Volar	Left	Ulnar	1.7 × 1.2 × 0.9
2	Forearm	Dorsal	Left	Posterior interosseous	1.4 × 0.9 × 0.9
3	Foot	Dorsal	Right	Lateral dorsal cutaneous branch of the sural nerve	3.6 × 1.9 × 1.5
4	Hand	Dorsal	Right	Ulnar	3.5 × 2.7 × 2.0
5	Arm	Volar	Right	Medial cutaneous nerve of arm	7.5 × 3.4 × 3.5
6	Ankle	Dorsal	Left	Posterior tibial	2.3 × 1.8 × 1.2
7	Armpit	Volar	Right	Musculocutaneous	1.5 × 1.5 × 1.5
8	Arm	Dorsal	Right	Radial	10.5 × 6.5 × 4.0
9	Arm	Dorsal	Right	Radial	2.0 × 1.5 × 1.0
10	Hand	Volar	Left	Median	0.9 × 0.7 × 0.7
11	Thigh	Dorsal	Right	Lateral femoral cutaneous	3.6 × 2.2 × 1.8
12	Leg	Volar	Left	Fibular	4.3 × 2.5 × 1.6
13	Forearm	Volar	Left	Ulnar	1.8 × 1.8 × 1.4
14	Thigh	Dorsal	Left	Saphenous	4.8 × 3.0 × 2.7
15	Arm	Volar	Left	Ulnar	2.5 × 1.8 × 1.6
16	Thigh	Volar	Left	Femoral	7.5 × 5.0 × 4.2
17	Hand	Volar	Right	Median	1.6 × 1.1 × 0.5
18	Hand	Volar	Right	Proper palmar digital branch of the ulnar nerve	1.3 × 0.4 × 0.6
19	Hand	Volar	Right	Ulnar	2.5 × 1.3 × 1.0
20	Forearm	Volar	Right	Ulnar	1.5 × 1.2 × 1.0

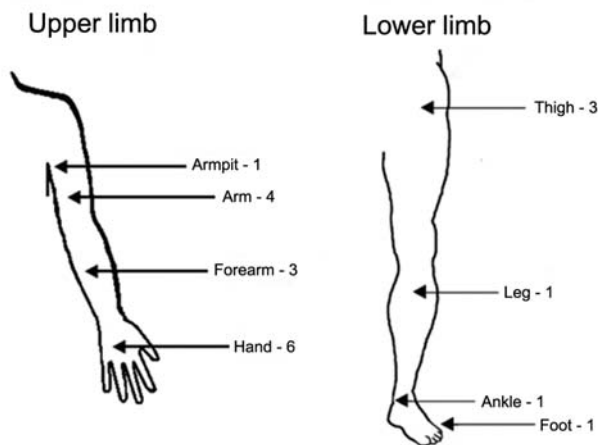


Fig. 5 Illustration of the upper and lower limbs showing the topographic distribution of the tumors found in the study.

histological characteristics, severity of symptoms manifested prior to the operation, tumor with a longer history, and inadequate surgical technique.

We consider that, among these factors, the presence of the Tinel sign should be highlighted, since it already demonstrates a local neurological alteration. In our series, 50% of the patients with positive Tinel sign had postoperative complications, while in patients who did not present it, the complication rate was of 21.4%. These data confirm the appreciation of the presence of the Tinel sign in the prognosis.

Schwannoma recurrence and malignancy are rare.^{6,8,15,16} In the present study, there were no cases of relapse. Regarding malignancy, we found a case in patient number 8, in whom a moderate nuclear-grade malignant schwannoma with a moderate mitotic index was found, with epithelioid areas, invasive from the subcutaneous and fibromuscular tissues to the periosteum, with tumor borders with an expansive pattern, and focal areas of stromal inflammation, necrosis and hemorrhage.

Because it is an Orthopedics Service, we chose to evaluate patients with schwannoma only in the upper and lower limbs. In addition, there are few case series studies on this topic in Brazil. Therefore, the authors decided to perform an analysis of the epidemiological profile, as well as of the natural evolution and intervention in this disease in our service, noting that complementary examinations should help to formulate the schwannoma hypothesis, which will require microsurgical material and a technique compatible with the nobility of the affected structure. Given the results, it can be considered that the data obtained agree with those described in the literature.

Conclusion

Schwannoma is a rare and difficult-to-diagnose lesion. It should always be considered as a hypothesis when facing a soft-tissue tumor affecting the limbs, especially when associated with the presence of transverse axis mobility and

neurological symptoms, among which the Tinel sign should be valued, considering its greater correlation with postoperative complications. The patients should be informed of the possible complications, which are frequent (~ 30%) but usually transient.

Conflict of Interests

The authors have none conflict of interests to declare.

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