



Original article

Benign tumors affecting the median nerve. Case series report of diagnostic and surgical strategies[☆]



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ABSTRACT

Objective: The aim of this study was to describe the strategies adopted in this institution to diagnose and treat patients with benign tumors affecting the median nerve.

Methods: A retrospective chart review study of all patients operated on between 2010 and 2015. Histology, symptoms, complementary exams, surgical techniques performed, and demographic characteristics were analyzed.

Results: Fifty-four patients were included in the study. There were three neurofibromas, six schwannomas, 15 lipofibromatous hamartomas, three hemangiomas, 12 lipomas, one benign fibrohistiocytoma, and 14 synovial cysts. Complete tumoral resection was performed in 32 cases, partial resection in five, segmented nerve resection in one, nerve decompression in eight, and amputation for macrodactyly in eight.

Conclusions: The most important recommendations on treating benign tumors of the median nerve are related to the clinical symptoms, tumoral growth, and tumoral nature. The surgical approach resulted in good function for 60% of the patients. However, lipofibromatous hamartomas, hemangiomas, and neurofibromas were associated with preoperative functional deficit. It may be inferred that the diagnosis and treatment of these tumors should be performed earlier.

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Tumores benignos que afetam o nervo mediano. Relato das estratégias cirúrgicas e diagnósticas na série de casos

RESUMO

Objetivo: O objetivo deste estudo foi descrever as estratégias adotadas nesta instituição para o diagnóstico e tratamento de pacientes com tumores benignos que afetam o nervo mediano.

Métodos: Um estudo de revisão retrospectivo foi realizado com todos os pacientes operados entre 2010 e 2015. Foram analisados histologia, sintomas, exames complementares, técnicas cirúrgicas realizadas e características demográficas.

Palavras-chave:

Nervo mediano

Neoplasias do sistema nervoso periférico

Neoplasmas de partes moles

[☆] Study conducted at Rede Sarah de Hospitais de Reabilitação, Brasília, DF, Brasil.

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Resultados: O estudo incluiu 54 pacientes. Observou-se três casos de neurofibromas, seis schwannomas, 15 hamartomas lipofibromatosos, três hemangiomas, 12 lipomas, um fibrohistiocitoma benigno e 14 cistos sinoviais. Em 33 casos, foi feita ressecção tumoral completa; em cinco, ressecção parcial; em um, ressecção segmentar de nervo; em oito, descompressão de nervo; e em oito, amputação de macrodactilia.

Conclusões: As recomendações mais importantes no que diz respeito ao tratamento de tumores benignos do nervo mediano estão relacionadas aos sintomas clínicos, crescimento tumoral e natureza tumoral. A abordagem cirúrgica levou a bons resultados funcionais em 60% dos pacientes. No entanto, hamartomas lipofibromatosos, hemangiomas e neurofibromas foram associados ao déficit funcional pré-operatório. Pode-se inferir que o diagnóstico e o tratamento destes tumores devem ser realizados de forma precoce.

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Introduction

Most tumors affecting the median nerve are benign. They can originate in the peripheral neural sheath, or be intraneural or extrinsic. The latter can affect the nerve by compressing it, dislocating its structure, and disturbing its vascular flow. Deciding how to approach median nerve tumors is a complex process that involves knowledge about neurologic clinical exam, neurophysiological tests, nerve microanatomy, image diagnostic exams, and microsurgery.

Peripheral nerve tumors are uncommon lesions, generally benign, with slow growth, and few symptoms. The median nerve can be affected by tumors originating in: the neural sheath, schwannoma, and neurofibroma; intraneural lesions, lipoma, hemangioma, or hamartomas; and extrinsic compression by lipomas or cysts.¹

The peripheral nerve is a complex structure regulated by the interaction between the neurons and Schwann cells. When the axon is injured, there is usually a myelin disorganization. Seddon² and Sunderland³ published studies about the structural bases, histologic classification, and neural mechanisms of regeneration. For traumatic injuries, the neural regeneration process follows the Wallerian degeneration, which starts 24–36 h after the trauma. The pathophysiology of nerve injuries related to tumors differs from trauma in that it is characterized by slow growth and fewer symptoms, which is usually related to paresthesia, sensitive alterations, and median nerve entrapment syndrome.^{1,4-8}

Sensitivity and motor tests, electrophysiological studies, computed tomography, magnetic resonance imaging, and ultrasound images are useful during preoperative evaluation to define the tumoral nature and location, nerve function, malignancy characteristics, size, necrosis, invasion, and surrounding tissues aspects. Tumors originating in the neural sheath can be confirmed by microscopy and immunohistochemistry (i.e., S-100 and Leu-7 stains).^{1,6,7}

The most common benign tumors of the neural sheath are the schwannomas (also known as neurilemmomas) and neurofibromas. Other tumors that can affect the median nerve are: giant cell tumors, lipomas, mixomas, hemangiomas, lipofibromatous hamartomas, hemangioblastomas, and meningiomas. Those tumors can jeopardize the nerve

with their intraneural growth or extrinsic compression, causing symptoms that are similar to those of carpal tunnel syndrome. Schwannomas are rarely associated with any clinical syndromes, and they can be solitary or plexiform. Neurofibromas are less common, are not encapsulated, can have malignant degeneration, and be associated with neurofibromatosis.

Tumors of the median nerve can occur at any age, however, incidence rates are highest between the third and sixth decades of life, except for hemangiomas and lipofibromatous hamartomas (which usually occur in childhood).

This case series report adds knowledge about the strategies used to handle with benign tumors affecting the median nerve. This information is important for diagnosis, surgical approach, as well as to minimize recurrences and decreased functionality.

Materials and methods

This study is a case series description of patients treated for benign tumors affecting the median nerve. It includes data from the charts of all patients operated on between 2010 and 2015 at our institution. Inclusion criteria included diagnosis of benign tumors that affect the median nerve (i.e., those originating at the peripheral sheath, as well as intraneural and extrinsic tumors). Malignant and traumatic tumors were excluded.

The research project was approved by an independent ethical committee, respecting the institutions guidelines and the international agreements for scientific experiments with human tissues, including the Declaration of Helsinki (1964) and their following recommendations of Fortaleza/Brazil (2013). All patients signed a consent term allowing the institution to use their health records for scientific purposes.

Clinical evaluation and diagnostic procedures included the Louisiana State University Medical Center Grading System for Motor and Sensory Function,⁶ the Semmes-Weinstein monofilament test, electroneuromyography (ENMG), Magnetic Resonance Imaging (MRI), ultrasonography imaging (USG), and histopathological studies.

Surgical treatment was indicated if the patient showed clinical symptoms such as pain, paresthesia, tumoral growth,

and carpal tunnel syndrome (CTS). The surgical techniques were performed according to the Kline⁴ principles, which consider tumoral characteristics and location. All patients underwent brachial plexus block or general anesthesia, had a tourniquet wrapped around the arm. Wide open surgical approaches were performed and the median nerve was inspected by magnification with loupes or microscope. When the lesion was distal or under the carpal tunnel, it was fully released until the ante-brachial fascia. Intraneural dissection was used to encapsulate intraneural tumors. With microsurgery instruments, the tumor capsule was opened and the neuro fascicles were individualized using a Penfield dissector, cottonoids, and neurosurgical aspirator. In some cases, a nerve stimulator was used for transoperative evaluation of the fascicles potential action. The fascicles that had their signs corrupted by the tumors were removed.

Results

The database identified 220 charts of patients with benign tumors in the superior limbs. According the inclusion criteria, 54 charts of patients that had a benign tumor affecting the median nerve were identified. These included: 15 (28%) lipofibromatous hamartomas associated with macrodactylia, 14 (26%) sinovial cysts, 12 (22%) lipoma, 9 (16.5%) intraneural lesions (3 neurofibromas and 6 schwannomas), 3 (5.5%) hemangioma, and 1 (2%) benign fibrohistiocytoma. Approximately 80% of the patients were female, with average age of 30 years (range: 10 months to 66 years). The anterior aspect of the limb was affected in all cases. There was a case of a benign fibrohistiocytoma, in which the lesion expanded to the dorsal aspect of the hand. The follow-up time ranged from six months to 10 years, with an average of three years.

The observed symptoms were: pain, changes in sensitivity, palpable tumoral growth, and carpal tunnel syndrome. CTS was primarily observed in extrinsic tumors affecting nerve function. Fig. 1 shows a lipoma inside the carpal tunnel, causing median compression syndrome. ENMG showed severe

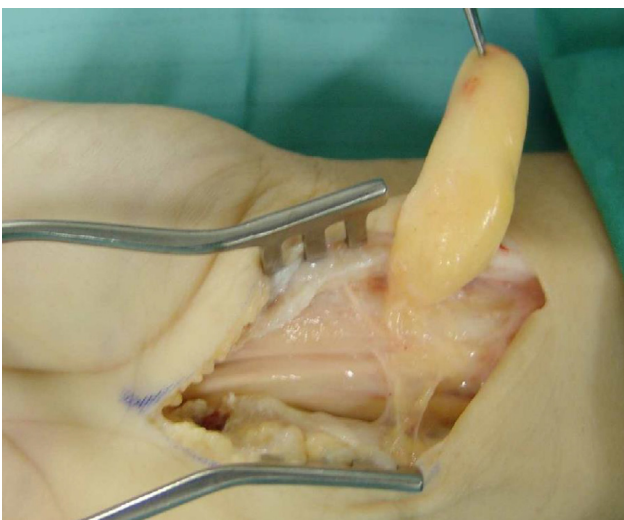


Fig. 1 – Photograph showing a lipoma inside the carpal tunnel, which caused median compression syndrome.

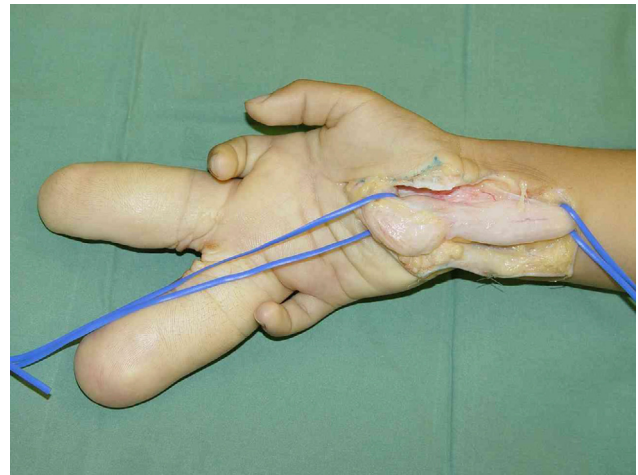


Fig. 2 – Intraoperative photograph showing the carpal tunnel released within the median nerve affected by a lipofibromatous hamartoma, associated with macrodactyly.

impairment in 83% of lipofibromatous hamartoma and in 73% of lipomas inside the carpal tunnel and wrist.

Lipofibromatous hamartoma is a condition that usually affects female children and young women. Symptoms include carpal tunnel syndrome, and it is associated with macrodactylia of one or two fingers. There were 4 male and 11 female cases. Four were adults (average of 33 years, standard deviation of ± 7) and 11 were children (average of 34 months, standard deviation of ± 36). Surgical exploration showed fusiform nerve expansion with the fibrofatty infiltrate. Carpal tunnel release was performed in 10 cases and giant finger amputation was necessary in 8 cases. Fig. 2 shows the carpal tunnel released with the lipofibromatous hamartoma, associated with macrodactyly.

For all tumors, surgical procedures were defined according clinical evaluation, exams, and intraoperative findings. It was possible to resect all extrinsic tumors; however it was only possible to partially resect the neurofibromas and hemangiomas. Complete microsurgery intraneural resection of the schwannomas was achieved. Neural decompression and digital amputation was necessary for the lipofibromatous hamartomas occurred. Fig. 3 is an example of the hemangioma along the median nerve.

The schwannoma was the most common benign tumor originating in the neural sheath that we found. They had average size of 2 cm, and were primarily located in the hand and wrist, with only one case located in the forearm (sized 6 cm). Histopathological study confirmed the presence of a limited tumor that was fusiform and consistent with Schwann cells. Immunohistochemical analysis with S-100 and Leu-7 stain confirmed the diagnosis. Electronic microscopy demonstrated ultra-structural findings of Schwann cells immersed in an extracellular matrix of collagen fibers. The treatment consisted on microsurgical resection and complete enucleation of the schwannoma occurred in five cases, as shown in Fig. 4. It was necessary to cut the fascicle with the tumor in only one case. Regardless of it, there were no cases of functional sequel or need for neural reconstruction.

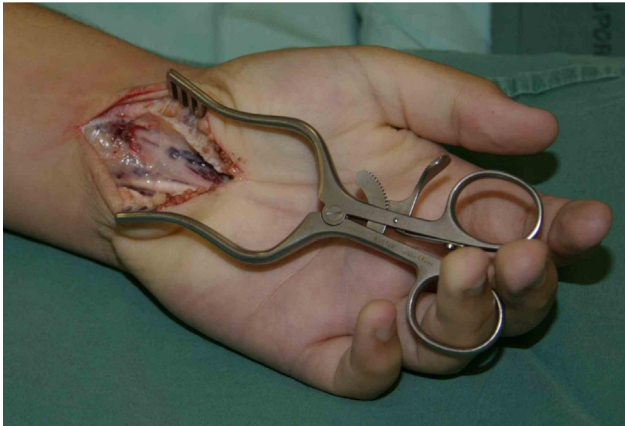


Fig. 3 – Intraoperative photograph of a hemangioma along the median nerve.

The neurofibromas presented as more symptomatic, with ENMG alterations and greater tumoral growth. Some cases were associated with type 2 neurofibromatosis, with changes in chromosome 17, and large tumoral volumes. In those cases we performed a biopsy before resecting the neural segment affected by the tumor. MRI was not always helpful for distinguishing between malign and benign tumors, thus biopsy was necessary for some cases. Fig. 5 shows a case in which it was not possible to completely resect the tumor because the lesion limits were unclear and thus neural reconstruction was not performed. There were no cases of malignant degeneration.

Sinovial cysts and lipomas were found to affect the median nerve by extrinsic compression. Three lipomas permeated

the neural fibers, however it was possible to completely remove these tumors without causing functional damage. The lipoma's width ranged from 0.5 to 4 cm. Fig. 6 shows the larger lipoma in the distal forearm.

According to functional evaluation at 3 year follow-up, surgical treatment resulted in 32 (60%) cases that were considered satisfactory (i.e., no functional sequel or deficit).

Table 1 shows all surgical procedures performed for each tumor and the results obtained. It highlights that each histological types required different surgical strategies and had different outcomes. Table 2 compares symptoms and ENMG for each tumor type. It highlights that the lipofibromatous hamartomas were associated with more clinical and electrophysiological alterations. However, the sinovial cysts had fewer ENMG alterations.

Discussion

Nerve tumors are uncommon,⁹ however this study was able to identify 54 cases of benign tumors that affected the median nerve and underwent operation between 2010 and 2015.

Carpal tunnel syndrome (CTS) is the most common peripheral entrapment neuropathy. It affects about 2.7% of the population (5.8% of women). In spite of this high prevalence rate, the pathogenesis is unclear and its cause has not yet been identified. Some conditions known to be associated with carpal tunnel syndrome are: diabetes, hypothyroidism, pregnancy rheumatoid arthritis, synovitis, wrist trauma, working with vibrating tools, and tumors. Dailiana et al.¹⁰ described a series of 32 hands that underwent operation for CTS caused by tumors, over 1100 carpal tunnel releases. Nakamichi and

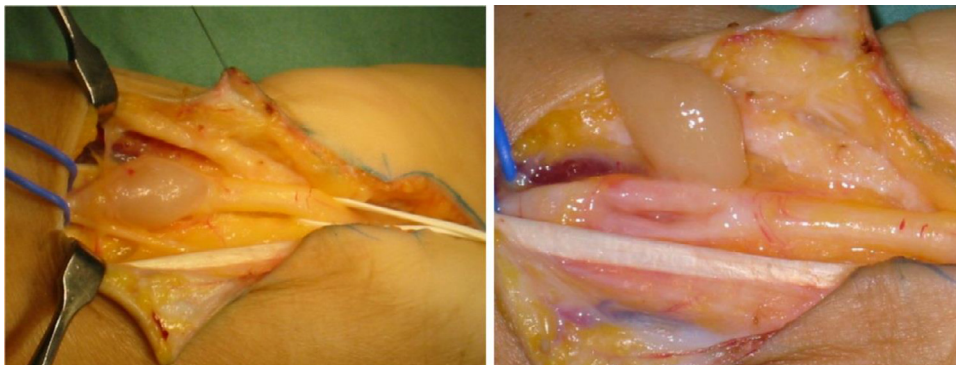


Fig. 4 – Intraoperative aspect of the median nerve schwannoma, in the left, and the tumor after fascicular dissection.

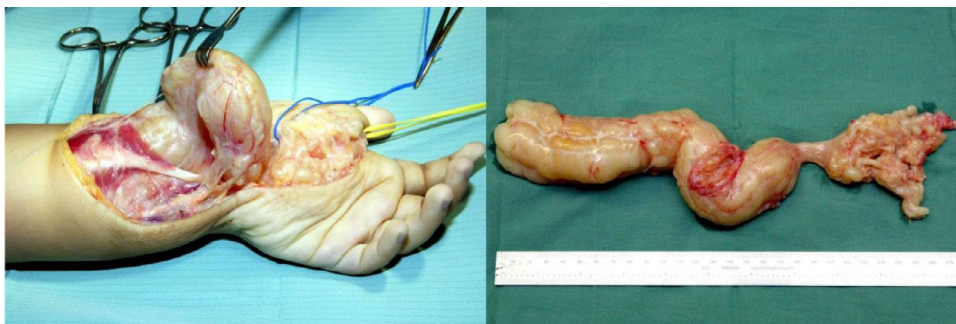


Fig. 5 – Intraoperative photograph of the median nerve neurofibroma and the tumor aspect after segmented resection.

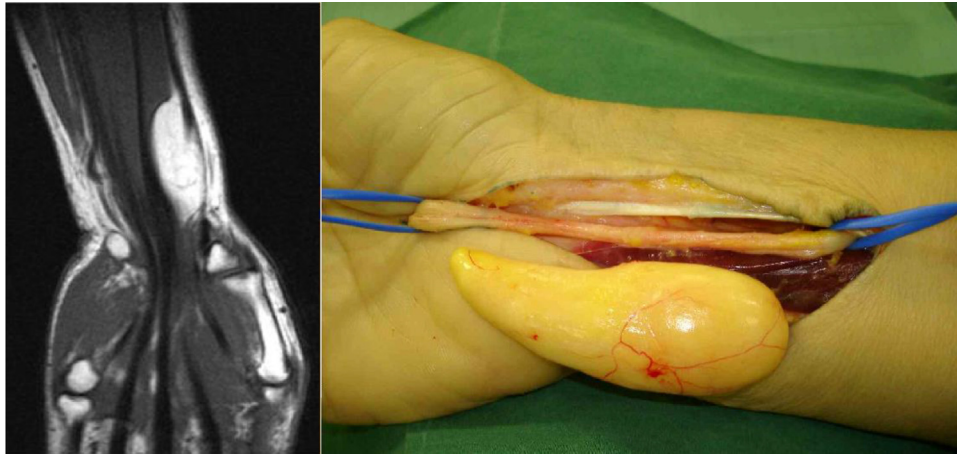


Fig. 6 – A large lipoma. MRI showing the expansive solid lesion in the flexor wrist compartment, compressing the median nerve (left). The intraoperative tumor aspect after dissection (right).

Table 1 – Surgical procedures performed for each tumor and the results obtained.

Tumors	Surgical procedures	Results
3 Neurofibromas	1 Segmented nerve resection 2 Partial tumor resection	Persistent area of anesthesia in the hand
6 Schwannomas	6 Complete tumoral resection by intraneural dissection	No functional deficit
15 Lipofibromatous hamartomas ^a	4 Carpal tunnel release and finger amputation 4 Carpal tunnel release 2 Carpal tunnel release and arciform pulley release 4 Finger amputation 1 Digital shortening	Improvement of function and ENMG findings ^b
3 Heman-giomas	2 Partial resection 1 Embolization	Persistent clinical symptoms
12 Lipoma	9 Tumoral resection 3 Intraneural dissection	No functional deficit
1 Benign fibro-histiocitoma	Tumoral resection. tumoral limits were imprecise and it expended to the wrist dorsum	Functional and pain improvement
14 Sinovial cysts	Tumoral resection and neural decompression	No functional deficit

^a In one case of macrodactyly, the extensor indicis proprius tendon of the giant amputated finger was transferred to the thumb opposition.

^b Severe electroneuromyography alterations were found preoperatively. The improvement depended of the time to diagnosis and nerve decompression.

Tachibana¹¹ found seven cases of space-occupying lesions causing CTS in a series of 128 patients. They highlighted that all cases were in a group of 20 patients with unilateral symptoms. We agree that the wrist imaging is recommend to exclude tumors when the CTS only affects one limb.

In our series, 14 sinovial cysts that were associated with symptoms of CTS were found. Those tumors are the most

common ones in the general population's wrists. The association of ganglions with CTS has been reported since 1952 by Brooks,¹² and was followed by the well-known series presented by Phalen (1966) as well as Hybbinette and Mannerfelt (1975) apud Harvery¹³ and Kerrigan et al.¹⁴ Although causality was not established, this tumor's presence in the volar wrist and the CTS symptoms relieve after their removal, strongly suggest a causal relationship. This line of thinking is countered by the findings of Jacobs and Govaers,¹⁵ which reported 71 cases of volar wrist ganglia in which only five patients had CTS. Four received no operations because the symptoms were considered not severe enough to justify surgical intervention. The patient that had the carpal tunnel released was also pregnant.

Among tumors originating in the neural sheath, the schwannoma was the most frequent and was found in six cases. This tumor is described as the most common type found in peripheral nerves. About 19% of schwannomas are found in the superior limbs where ENMG is normal.¹ In this study, the ENMG was normal in four of six cases. The image exams were important for evaluating the tumor location, size, and limit characteristics. In general, the schwannomas were isointenses as muscles or slightly hyperintenses in T1, but hyperintense in T2. They presented intense envode-nousus contrast impregnation and the smaller tumors were more homogenous. They were fusiform along the nerve, and, the bigger tumors, dislocated the fascicles to the lesion periphery.^{16,17}

The schwannoma characteristics generally differed from the neurofibromas, while their epineural growth turns them encapsulated. Otherwise, neurofibromas originate in the neural fascicles, are located centrally in relation to the nerve, and are rarely encapsulated, all of which are important for the surgical preoperative plan.^{9,18}

Three cases of neurofibromas were operated on. One was associated with type 2 neurofibromatosis, and it was necessary to remove a median nerve segment that was affected by the tumor. According to Kline and Hudson,⁴ nerve graft reconstruction does not provide satisfactory results after segment resection, even though it could reduce neuroma

Table 2 – Tumors and the presence of clinical symptoms or ENMG alterations.

Tumors	Number of cases	Positive clinical symptoms	Positive ENMG
Lipofibromatous hamartoma	15/28%	15	13
Sinovial cysts	14/26%	7	2
Lipoma	12/22%	9	8
Schwannoma	6/11%	1	2
Neurofibroma	3/5.5%	3	2
Hemangioma	3/5.5%	2	0
Benigns fibrohistiocitoma	1/2%	1	0

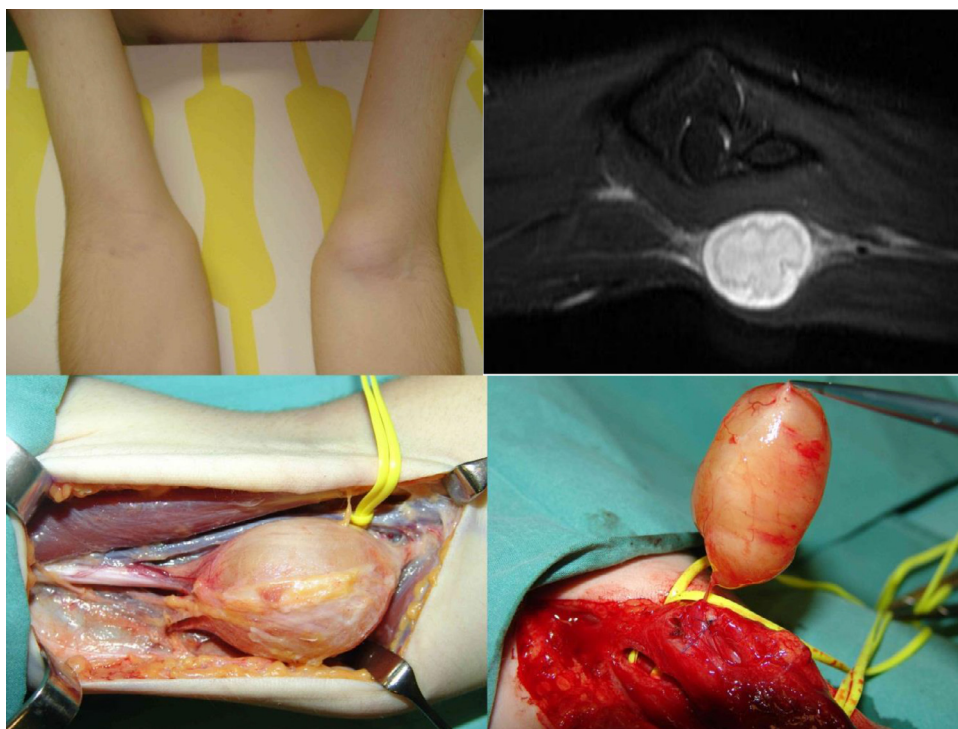


Fig. 7 – Photograph of the clinical characteristics, MRI, and intraoperative tumor dissection of a schwannoma in the proximal forearm.

formation. Sandberg et al.¹⁹ found that neurofibroma recurrence is uncommon. In spite of it we also did not observe recurrence, however we were worried that partial resection could imply on it. As it was said, sometimes complete neurofibroma removal is difficult because the lesion limits are not clear.

The literature describes low recurrence of nerve tumors (approximately 5%).⁵ After an average follow-up of three years, we did not observe any tumor recurrences in any of the 54 cases. Furthermore, functional deficits normally occur in 9% of schwannomas and 78% of neurofibromas; in our study, the surgical procedures performed did not increase functional losses to the patients. In the case where the nerve was segmentally removed, this procedure did not add any functional deficit because the nerve was not working before surgery.

Usually, tumors located in the proximal limb regions have the worst prognosis,²⁰ however we removed a schwannoma in the proximal third of the forearm and no function deficit occurred. Fig. 7 shows the case, and includes images

indicating the clinical characteristics, MRI, and intraoperative tumor dissection. In our study, the worst functioning was found in that cases that were treated later, where there was a long evolution of the disease and preoperative deficit.

For the MRI, benign tumors of the neural sheath presented a “target sign” on the T2 sequence, (e.g., a peripheral hyperintense signal with central hypointense) in 52% of cases. Histologically, this represents the peripheral myxomatous tissue and the central fibrocollagenous. Accordingly to the literature, schwannomas are composed of Schwann cells, with biphasic architecture (Antoni A and B patterns), nuclear palisading (Verocay bodies), fibrous capsule with displaced parent nerve, and degenerative changes (nuclear pleomorphism, hemosiderin deposition).^{18,20,21}

MRI is also helpful for lipofibromatous hamartoma diagnosis. The nerve seems to be like a “coaxial cable,” enlarged, with bundles interspersed evenly in the fat and the encased in epineural fibrous tissue. The nerve’s innate MRI signal is unchanged, but those characteristics are pathognomonic of these tumors.^{22,23}

Lipofibromatous hamartomas are considered rare tumors. They affect the median nerve in 66–80% of cases. Their pathophysiology is unknown but their histological characteristics are well described as a lipomatosis of the nerve. There are identified by fibro-fatty proliferation within nerve bundles, with disorganized overgrowth of the neural structures and no inflammation of the surrounding tissues.^{24,25} Although this tumor is rarely mentioned in the literature, the lipofibromatous hamartoma was the most common tumor in our small series. All were associated with macrodactyly. It is important to clarify that this study does not proposed to define the incidence of lipomatous hamartoma. As a case series, it is not possible to infer that the distribution found here reflects the prevalence in our region. It is likely that this anomalous occurrence happened because our hospital is a major reference center for limb deformities and reconstruction. As Ulrich et al.²⁶ suggested, for lipofibromatous hamartomas, we recommend the median nerve early prophylactic decompression in all sites it was potentially entrapped, and partially removal of the fibrofatty tissue. We do not think that whole tumor excision is a safe option for preserving sensory and motor function.

Hemangiomas of the median nerve are extremely rare, with only a few cases reported in the literature.^{27,28} They are described as painful masses that show signs and symptoms of nerve entrapment. We operated on three patients who had this tumor. Two of the tumors were partially removed and one was treated with embolization, because it was a large tumor involving the median nerve from the wrist to the palm. All three patients had lingering compression symptoms but no wrist pain. There is no established protocol to treat this condition, however conservative treatment tends to fail and complete tumor removal is the goal.²⁸

Conclusion

In conclusion, the most important factors to consider when treating benign tumors of the median nerve include clinical symptoms, tumoral growth, and the tumoral nature. Surgery resulted in good functioning for 60% of cases. However, lipofibromatous hamartomas, hemangiomas and neurofibromas were associated with preoperative functional deficit. We may infer that diagnosis and treatment of these types of tumors should be performed earlier.

Conflicts of interest

The authors declare no conflicts of interest.

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