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ORIGINAL ARTICLE

Management of benign nerve sheath tumors of the brachial plexus: relevant diagnostic and surgical features. About a series of 17 patients (19 tumors) and review of the literature

Annie Dubuisson[1] · Gilles Reuter[1] · Bruno Kaschten[1] · Didier Martin[1] · Tudor Racaru[1] · Maximilien Steinmetz[1] · François Gérardy[1]

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Abstract
Brachial plexus (BP) tumors are rare, potentially difficult-to-manage lesions. The method is retrospective chart analysis. Among the 17 patients, four had neurofibromatosis and one schwannomatosis (NF+). The latter has bilateral BP tumors that remain stable on MRI at a 6.5 year follow-up. Another NF+patient has bilateral non-operable BP plexiform neurofibromas. The complaints of the 15 operated patients were radiated pain, a mass, local pain, paresthesia, a neurological deficit ($n=15$, 12, 7, 10, 7). On MRI, the tumors appeared as nodular or ovoid large masses. Four operated tumors were proximal, reaching the foramen. The FDG-PET scan ($n=4$) always showed tumor hypermetabolism. A preoperative percutaneous biopsy was done in three patients before neurosurgical consultation; one of them developed neurogenic pain and a sensory deficit following two percutaneous biopsies for a misinterpreted cervical lymphadenopathy. Surgery was performed using a supra-, infra-, supra-+infra-clavicular or posterior subscapular approach ($n=8$, 3, 3, 1). Intraoperative electrophysiology was used in all patients. Complete or gross total resection was achieved in 14 patients. Two patients had fascicle reconstruction with grafts. Pathology revealed 13 schwannomas and two neurofibromas. Neurogenic pain transiently developed or worsened after surgery in five patients. At last follow-up, a mild deficit remained in four patients (preexisting in three). No recurrence had occurred. We conclude that a thorough examination of any patient with a cervical or axillary mass is crucial to avoid misinterpretation as a lymphadenopathy. MRI is the best imaging modality. Most BP benign tumors can be completely and safely resected through the use of microsurgical techniques and intraoperative electrophysiology.

Keywords Brachial plexus · Nerve sheath tumor · Schwannoma · Neurofibromatosis

Introduction

Brachial plexus (BP) benign nerve sheath tumors (NST) are rare, potentially difficult-to-manage lesions. Misinterpretation as a ganglion—which is not rare—should be avoided thanks to clinical examination and MRI. Preoperative biopsy, which is indicated if malignancy is suspected, is otherwise risky and not necessary. Surgical resection is not a risk-free procedure. Indeed, BP benign NST often cause no or minimal neurological deficit despite a very large volume, whereas dissection of the tumor from the nerve fascicles can be tough, especially in neurofibromatosis (NF). Other potential difficulties concern the optimal management of non-symptomatic tumors, of multiple NF-associated tumors as well as suspected malignancy. We here report a series of 17 patients with 19 BP benign NST and discuss several points of management in light of the published series—including three large series of more than 100 patients. We provide an illustrative case of a BP NST misinterpreted as a ganglion with subsequent risky management.

Patients and methods

We retrospectively analyzed the charts of 17 consecutive patients suffering from uni- or bilateral benign BP NST. The patients were seen in consultation by the different authors in a period extending from July1995 to May 2020. Two

✉ Annie Dubuisson
a.dubuisson@chu.ulg.ac.be

[1] Department of Neurosurgery, CHU Liege, Liège, Belgium

patients were not operated on, while surgical resection was performed by the first author in the remaining 15 patients.

Results

There were ten women and seven men. The mean age was 44.4 years (26–64). Five patients suffered from neurofibromatosis ($n=4$) or schwannomatosis ($n=1$); 11 of the 19 tumors were on the right side.

Two non-operated patients had bilateral BP tumors: a 50-year-old NF + patient with massive non-operable BP (and lumbar plexus) plexiform neurofibromas who progressed to dumbbell-shaped tumors, leading to spinal cord compression and severe tetraparesia; and a 46-year-old schwannomatosis + patient operated on for symptomatic retroperitoneal S2, intraspinal L3, median nerve and intraspinal C6 schwannomas and being followed for bilateral non-symptomatic BP tumors stable on MRI at a 6.5 year follow-up (Fig. 1).

The presenting complaints of the 15 operated patients were a radiculopathy ($n=15$), a palpable mass ($n=12$), local pain ($n=7$), and paresthesia ($n=10$). A usually mild neurological deficit was present in seven patients (motor: three, sensory: three, sympathetic: one). The mean duration of symptoms before diagnosis was 18.8 months.

On MRI, the tumors appeared as a nodular or more often ovoid mass, hypo- or iso-intense on T1-weighted sequences, enhanced by contrast injection either homogeneously or at the periphery; three tumors were partly cystic (Fig. 1). The mean longest dimension was 39.8 mm (20–68). The tumors were supraclavicular in eight patients;four tumors were proximal, extending to or into the foramen.

FDG-PET scan was obtained in three NF + patients, showing moderate hypermetabolism in all patients including the schwannomatosis + patient being followed for bilateral BP tumors. PET scan was performed in a fourth 26-year old patient with a huge tumor diagnosed during early pregnancy (Fig. 2). PET scan which was done after child delivery to document the optimal timing of surgery demonstrated hypermetabolism.

A preoperative percutaneous biopsy was done in three female patients before neurosurgical consultation: the first patient had suffered from a breast cancer in the past, so that biopsy under CT scan guidance was planned by the oncologist; the second patient consulted a senologist for a retropectoral mass and obtained breast X-rays and biopsy under US guidance. The third patient underwent a US-guided and a second CT scan-guided biopsy for a suspected huge adenopathy on a cervical spine CT scan; she developed neurogenic pain and increased sensory deficit (Fig. 3).

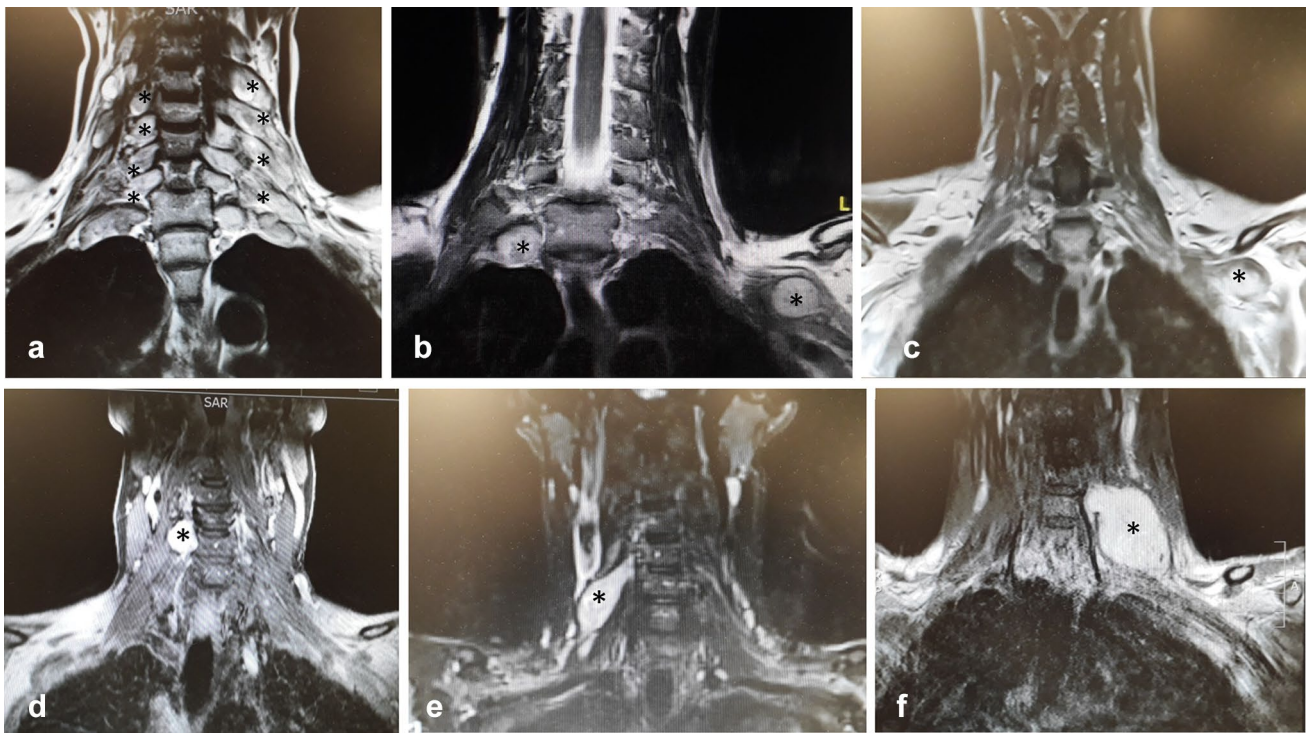

Fig. 1 Enhanced T1-weighted Magnetic Resonance Imaging sequences in coronal views showing the typical appearance of BP benign nerve sheath tumors (NST = *). **a** bilateral neurofibromatosis-associated plexiform neurofibromas; **b** bilateral schwannomatosis-associated nodular NST; **c–f** non-NF-associated NST in the infraclavicular (**c**) or supraclavicular (**d–f**) regions appearing as nodular or ovoid large masses occasionally extending to (**e**) or into (**f**) the foramen

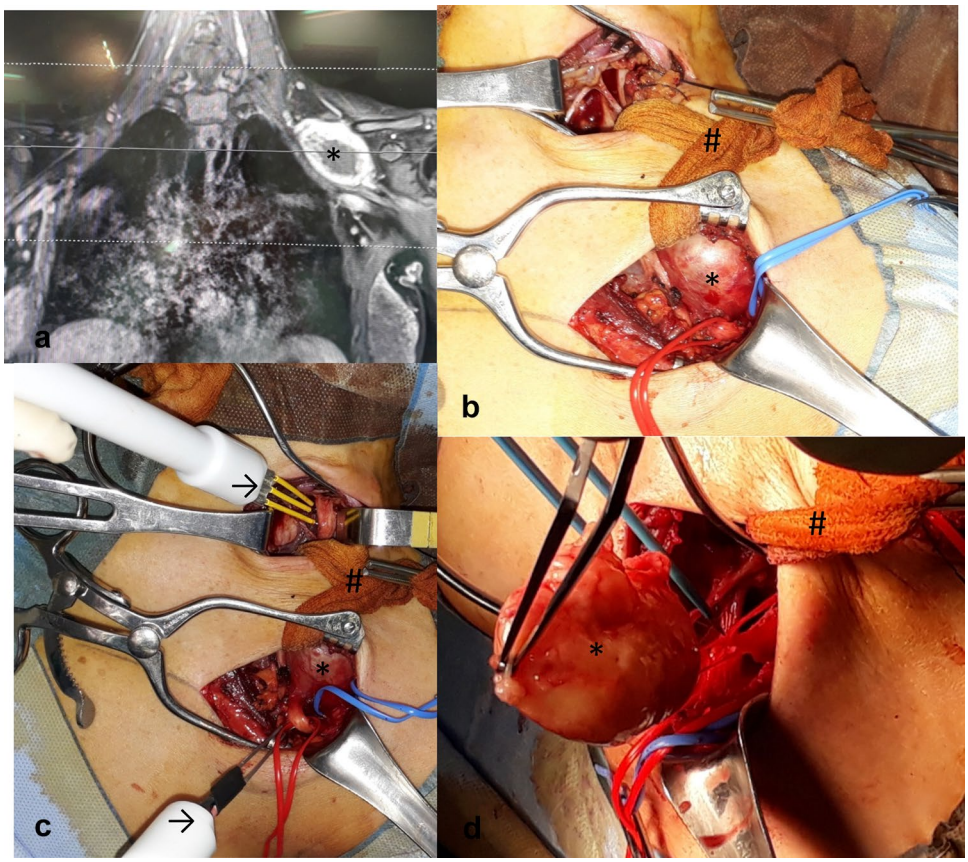

Fig. 2 Magnetic Resonance Imaging (**a**) and operative views (**b–d**) of a large BP schwannoma extending above and mostly below the clavicle in a 26-year-old neurologically intact patient. The tumor was moderately hypermetabolic on PET scan. A combined supra- and infra-clavicular approach is used (**b**). A sponge (#) is placed around the clavicle to lift it up and facilitate tumor dissection. Intraoperative electrophysiology allows the safe complete tumor (*) resection (**c**; → = stimulating and recording electrodes). At the end of the procedure, the lower pole of the tumor is dissected free of a non-functioning fascicle through the infra-clavicular incision (**d**)

Surgery was proposed to the 15 patients with symptomatic tumors. All procedures were performed by the first author. The different coauthors did participate, as well. Surgery was done using a supraclavicular ($n=8$), infraclavicular ($n=3$), supra- + infra-clavicular ($n=3$), or posterior subscapular approach ($n=1$). The tumors involved the C5/C6 roots and/or upper trunk ($n=6$), C7 root/middle trunk ($n=2$), C8/T1 roots and/or lower trunk ($n=3$), T1/T2 roots ($n=1$), posterior cord to radial nerve ($n=2$), and lateral cord ($n=1$). Tumor resection was helped using the Ultrasonic aspirator (CUSA) in two patients. Removal of the C5 transverse process was done in one patient to reach the intraforaminal portion of the tumor. Clavicle osteotomy was necessary in one patient with a tumor extending in the supra-, retro-, and infra-clavicular regions (sole case of subtotal resection). Intraoperative electrophysiological testing with nerve action potential recording was used in all patients (Fig. 2). This allowed the safe sacrifice of non-functional fascicle(s) in seven patients, while reconstruction with grafts—from the cervical plexus or sural nerve—of a sacrificed functional fascicle was performed in two patients. A small weakly functional fascicle was sacrificed without reconstruction in another patient. Tumor resection was total in 11 patients, gross total with coagulation of an intraforaminal residue in three patients, and subtotal in one patient.

Pathology revealed 13 schwannomas (three in cystic degeneration) and two neurofibromas (one nodular and one plexiform).

Our last operated patient had had two percutaneous biopsies before complete resection of the tumor, in May 2020 (Fig. 3). She was discharged following an uneventful early postoperative course; she subsequently developed heavy pain and swelling in the supraclavicular region, and was reoperated at postoperative day 7 for suspected hematoma; no hematoma was found; a marked fibroinflammatory reaction of the scalene musculature was visualized; the patient improved with antiinflammatory medication, analgesics, and physical therapy.

Four of the remaining 14 operated patients developed neurogenic pain during the early postoperative course, sometimes pronounced but which resolved within a few weeks; eight patients presented a new or aggravated neurological deficit. At last follow-up (mean 5.3 years, 2 months–17.5 years), there was no pain; all patients led a normal live; there was no recurrence; four patients presented a mild deficit which was preexisting in three.

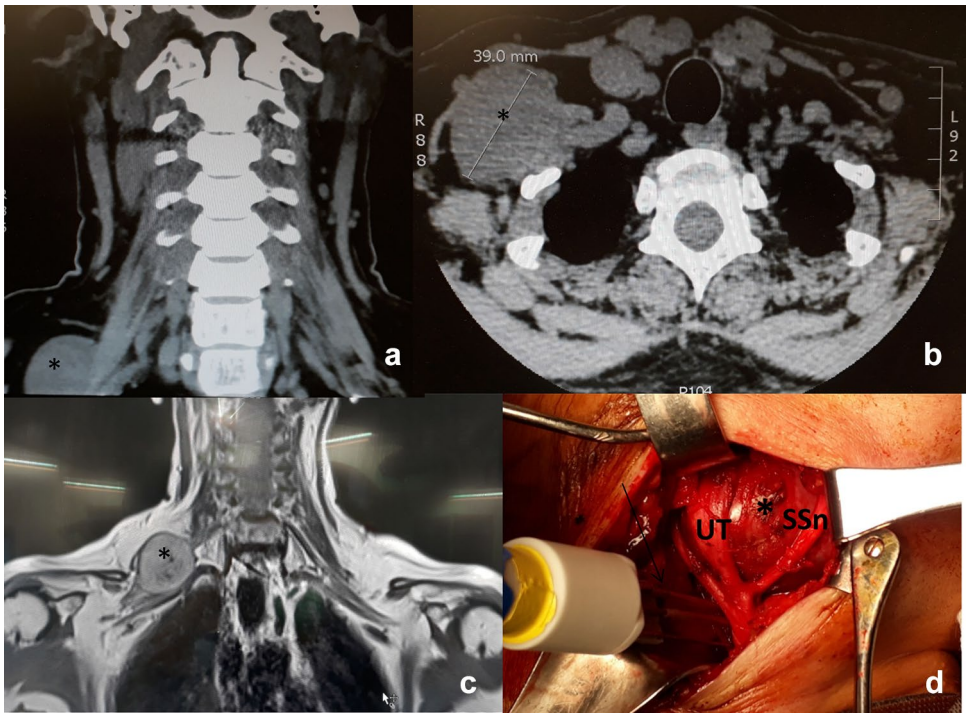

Fig. 3 Illustrative case of a BP tumor misinterpreted as a large adenopathy. This 49 y–o right-handed woman developed mild neurogenic symptoms in the right upper extremity and hand. The general practitioner, suspecting a carpal tunnel syndrome, prescribed an electroneuromyographic study which was negative. The EMG physician suggested imaging studies of the cervical spine. The CT scan in coronal (**a**) and axial (**b**) views showed no significant disc degenerative disease, but revealed a huge supraclavicular mass (*) diagnosed as lymphadenopathy. A first US-guided biopsy was non-contributive. The patient complained of heavy pain during the second, CT-scan guided biopsy. Histologic studies diagnosed a schwannoma. When the patient was seen in the Neurosurgical Clinics, she suffered from neurogenic pain and a sensory deficit in the C6 dermatoma. A Tinel sign was elicited on palpation of the mass. MRI (**c**) well visualized the BP tumor (*), arising from the C7 root-middle trunk. At surgery by a supraclavicular approach (**d**), the upper trunk (UT) and suprascapular nerve (SSn) were visualized being stretched at the periphery of the tumor (*); these nerve elements being perfectly functional when stimulated (→) were cautiously dissected from the tumor capsule. The tumor was completely resected with sacrifice of the posterior division of the middle trunk, following repeated electrophysiological testing. Postoperatively, the patient had triceps weakness which progressively regressed. At reoperation after 7 days for suspected hematoma, a marked inflammatory reaction of the scalene musculature was visualized. Proximal nociceptive pain and upper arm neurogenic pain gradually improved with medication and manual therapy

Discussion

The literature review from 2000 to 2020 contains multiple publications on brachial plexus (BP) tumors, arising from neurological [1–12], plastic [13], hand [14–16] surgeons, as well as ENT [17–23] surgeons. Indeed, many series report BP tumors included in cervical/head and neck nerve sheath tumors (NST) [17, 19–21, 23]. Several publications report the NST in all locations (extremities + cervical) [10, 24–26], while others concern both the benign and malignant BP NST [1, 4, 5, 7, 11, 14, 15].

Many articles focusing on BP NST concern small series—like ours—of 4–25 patients or case reports [1, 4, 6–9, 11–14, 16, 18, 22–30]. We found three large series of more than 100 BP tumors: the Kline's series was published in 2007 by Das et al. [2], about 144 BP tumors patients managed over a 30-year period (1969–1999); two other recent large series arise from India [3] and China [15] with, respectively, 115 and 131 benign BP tumors managed over a decade.

The long symptom duration of 18 months in our series is the same as in Desai's large series [3]. The clinical symptoms at presentation are in the three large series local pain, radiculopathy, paresthesia, and a mass [2, 3, 15]. Pain is usually mild-to-moderate; it can be present at rest in very large tumors. The majority of the patients are neurologically intact (87.8%) in Desai's series [3].

The tumor is usually first analyzed by US and/or CT scan done for a cervical lump or radiculopathy [30, 31]. The radiological work-up should then include MRI. The differential diagnosis of a cervical or axillary mass (lymphadenopathy, BP NST, …) involves a good clinical examination and a thorough work-up with MRI in all cases and PET scan in selected cases. Several case reports have been published about BP tumors misinterpreted as lymphadenopathy in the

supraclavicular or axillary regions, with potential subsequent risky management [22, 30, 32–34]. We have encountered one patient with an iatrogenic BP injury following resection by a general surgeon of a cervical "ganglion" worked-up by US and PET scan, which proved to be schwannoma on histology [35]. In the present series, one patient developed neurogenic pain following two different percutaneous biopsies for a presumed large supraclavicular ganglion seen on a CT scan. Histology revealed a schwannoma and the subsequent MRI perfectly showed the NST on the C7 root–middle trunk level. The typical MR appearance of a BP NST is that of an ovoid well-defined mass, occasionally partly cystic [27], enhanced by contrast. The predominant supraclavicular location is found in the large series of Desai (61.7%) [3] and Jia et al. (80.4%) [15].

FDG-PET scan has been rarely used in the three published large series of BP tumors. We found it useful for very large tumors developing in young patients and especially for neurofibromatosis-associated tumors. However, the FDG uptake can be high in benign NST [34, 36]. The Mayo Clinic team retrospectively analyzed the maximum standardized uptake value (SUV max) of 38 NST: it was below 4.3 in the 23 benign tumors and above 8.1 in the 20 malignant tumors; their cut-off level of 6.1 needs validation by others [36].

According to Desai [3] and Jia et al. [15], the preoperative biopsy or needle aspiration of a benign BP tumor is risky and of limited value; this proved true in the patient shown in the illustrative case, intact BP elements being stretched at the periphery of the tumor. Percutaneous or open biopsy should be obtained only if a malignant BP tumor is suspected. Malignancy should be suspected at BP as in other nerve locations in front of a rapidly growing, painful mass at rest and/or in case of a progressive neurological deficit [2, 15, 37]. Radiologically, a malignant tumor should be suspected if an expanding mass harbors irregular and infiltrative margins, necrotic and/or hemorrhagic areas, non-homogeneous contrast enhancement, and/or bone erosion.

Among our five patients with NF-associated tumors, three were operated on without any particular surgical difficulty nor postoperative deficit. On the other hand, one patient had massive bilateral plexiform BP tumors that were judged inoperable. The fifth patient, suffering from schwannomatosis, is being followed for bilateral asymptomatic BP tumors, that are moderately hypermetabolic on FDG-PET scan and remain stable on MRI at 6.5 years. Desai [3, 24] has addressed the watch and follow attitude in two publications. In his series of 146 BP tumors, 46 asymptomatic tumors were followed up, including 13 tumors over 3 cm [3]. In another recent publication about 442 NST of neck and extremities, 90 asymptomatic tumors were followed up; 15 patients eventually needed surgery, while 75 patients with stable tumors (13 over 3 cm) had further follow up [24]. According to Desai [3, 24], tumor size alone is never a criterion for surgery, which should be proposed for symptomatic tumors. We mostly agree with this attitude, especially for non-NF-associated tumors. The threshold toward surgery is more difficult to define for schwannomatosis or neurofibromatosis-associated tumors, given the 5–10% risk of malignant degeneration [38–40]. Surgical resection is indicated for symptomatic tumors but an aggressive, surgical attitude could be discussed in other contexts due to the fear of malignancy. Metabolic activity should be analyzed on FDG-PET scan for the non-symptomatic NF + tumors, to give supplementary arguments toward either a "watch and follow" or a surgical attitude. We have for 11 months participated in the new European registry of NST where cases are collected by the German neurosurgeon colleagues; one of the objectives is to define some guidelines in difficult cases.

Surgical resection is not a risk-free procedure [16]. Most patients being neurologically intact, the surgeon should do his/her best to minimize the neurological insult [25, 41]. A case report has been published in 2007 about the use of intraoperative nerve action potential recording during a BP tumor resection procedure [28]. Other authors including those of the three large series emphasize the importance of this intraoperative electrophysiological testing, with nerve action potential (NAP) or EMG recording [2, 3, 7, 8, 15, 18]. Desai [3] reports that while he does not ask for routine preoperative EMG, he finds it critical the use of intraoperative NAP recording. This proved useful in most of our patients, allowing the safe sacrifice of a non-functional fascicle in seven or leading to the reconstruction with grafts of a resected functional fascicle in two. We have seen several patients with iatrogenic nerve injury following NST resection with fascicle or complete nerve trunk sacrifice without electrophysiology and/or without any reconstruction [35].

Total resection was obtained in all schwannomas in Jia et al. [15] and Das et al. [2]'s series, in all solitary neurofibromas in Das et al. [2]'s series but only in two of 12 neurofibromas in Jia et al. [15]'s series. The difficulties of dissection of neurofibromas are reported by Desai [3], as well, because of tight adherence of the tumor capsule to the nerve fascicles. Like Desai (60.9%) [3] and Jia et al. (90.8%) [15], we found a predominance of schwannomas and, therefore, were able to reach complete resection in most patients.

In their large series, Desai [3] and Jia et al. [15] report that pain and paresthesia commonly develop in the early postoperative course, resolving within a few weeks in the vast majority of patients. All our BP-operated patients—from Thoracic Outlet Syndrome, trauma, NST—receive prophylactic gabapentin in the postoperative period, that is maintained for several weeks or months.

The optimal follow-up of operated patients is not well defined; Desai [3] advices a follow-up MRI at 3 months postoperative, then at 1 year intervals for at least 3 years, in all neurofibromas.

In conclusion, the management of a BP NST should be based on an accurate diagnosis with a good clinical examination, MRI in all cases, and PET scan in selected cases. The differential diagnosis needs to be done particularly from a cervical or axillary lymphadenopathy. A biopsy should be performed only if malignancy is suspected from clinical, metabolic, and radiological criteria. Surgery for symptomatic tumors is not a risk-free procedure. However, most BP benign tumors can be completely and safely resected by a surgeon who masters the complex BP anatomy, and will use both microsurgical techniques and intraoperative electrophysiology.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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