Rev esp cir ortop traumatol. 2011;**55(3)**:220-223

Revista Española de Cirugía Ortopédica y Traumatología

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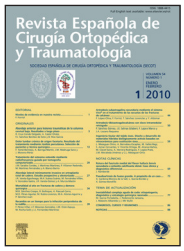

CLINICAL NOTE

Multiple bilateral schwannomatosis: presentation of a case

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Received November 28, 2010; accepted February 14, 2011

KEYWORDS
Multiple schwannomatosis;
Neurilemmoma;
Neurofibromatosis;
Tumour;
Hand

Abstract Multiple schwannomatosis is a rare disease characterised by masses of soft consistency affecting the nerve sheaf. It is important make a differential diagnosis with other soft tissue tumours, such as ganglia. We present a rare case, not described in literature reviewed by us, of a man with bilateral multiple schwannomatosis affecting both upper limbs, with a very florid clinical appearance and frequent recurrences. It is important to carry out periodic reviews of these patients to rule out new recurrences. Up until now, there have been no reported cases of malignant transformation.

PALABRAS CLAVE
Schwannomatosis múltiple;
Neurilemoma;
Neurofibromatosis;
Tumor;
Mano

Schwannomatosis múltiple bilateral: a propósito de un caso

Resumen La schwannomatosis múltiple es una rara entidad caracterizada por la aparición de tumoraciones de consistencia blanda afectando a la cubierta nerviosa. Es importante realizar el diagnóstico diferencial con otras tumoraciones de partes blandas como los gangliones. Presentamos el caso de un varón con schwannomas múltiples bilaterales a nivel de ambos miembros superiores, con una clínica muy florida y frecuentes recidivas, no descrito en la literatura revisada por nosotros. Es importante realizar un seguimiento periódico de estos pacientes para descartar nuevas recidivas tumorales. No se han descrito casos de transformación maligna hasta la fecha.

Introduction

Schwannoma, also known as neurilemmoma, is the most common benign tumour disease affecting peripheral nerves. They are lesions that originate in the Schwann cells producing a slow-growing tumour, which is eccentric, encapsulated with a well-defined covering of the nerve. They are usually diagnosed in people in their thirties to sixties and usually appear on their own without any other associated pathology; however, sometimes a patient can have many schwannomas located in the peripheral nervous system, including cranial nerves, brachial and lumbosacral plexus or major peripheral nerves.[1,2]

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Schwannomatosis shares many characteristics with neurofibromatosis, and has been considered as a type of this disease. The definitive schwannomatosis diagnosis is carried out after confirming the presence of two or more histologically demonstrated schwannomas and after dismissing any other type 1 neurofibromatosis symptoms (NF-1) (*cafe au lait* spots, freckles, Lisch nodules, optic glioma, pseudoarthrosis of tibia, affected relatives, etc.) or appearance of vestibular tumours in individuals over 18 years old, which is a characteristic feature of type 2 (NF-2) neurofibromatosis.

The majority of diagnosed schwannomatosis affect the head or torso (45%), with those located in the upper limbs being less frequently documented in literature (3%-19%).[5] When presenting on the upper limbs, they appear more often in the flexor surface of the forearm or hand, and in practically all cases affect only one limb. Bilateral appearance of schwannomas in the same patient is very rare, hardly described in literature until now. Between 2.4%-5% of all patients who require surgical removal of a schwannoma will present a schwannomatosis, which means that their appearance as an isolated tumour is more frequent.[3] Its prevalence is considered similar to NF-2, about 1 in every 40,000 births.

The clinical presentation consists of a slow-growing tumour that frequently ends up being painful, with this being a characteristic feature. They usually show a positive Tinel sign and allow transverse direction movement to the anatomical situation of the involved nerve. Affected individuals can present paresthesias and the appearance of an established neurological deficit is rare.

Differential diagnosis can be difficult, which means that there is incorrect diagnosis in up to 75%80%of cases. It is most often confused with ganglia, due to its cystic consistency.[5] The use of an MRI may be useful to delimit the lesion, confirm the presence of other associated tumours and plan surger; however, it is inefficient in differentiating it from other pathologies such as neurofibroma or nerve sheath tumour,[7] meaning that a pathological study is necessary to confirm the condition. Schwannomas are usually hypointense or isointense on T1-weighted scans, and hyperintense on T2-weighted.

There is controversy as to whether a genetic molecular study of patients and their lesions is required to obtain a correct diagnosis, but we will talk about this in the discussion section.

Clinical case

We present the case of a 67-year-old male with no clinical or family history of interest, who reports having had a slow-growing tumour removed in the volar region of his right hand when he was 14 years old (from which we have no histological record). Since then, the patient has had another 6 operations, in which he has had a total of 43 tumoral lesions removed in both upper limbs, with histological diagnosis being compatible with neurilemmomas or schwannomas in all cases.

In 1969, aged 33 years old, the patient underwent his second operation. At that time, 11 nodules located on his arms and forearms were removed, with one of them located in the right carpal canal, which caused clinical median nerve compression. He underwent further interventions in 1971, 1974 and 1985, with a total of 28 new tumours being removed from his fingers, volar and dorsal surfaces of both hands and forearms. The upper right limb always had more, and once again 3 were located in the right carpal canal. In the postoperative of this last intervention, a hypoesthesia in the median nerve area of the right hand was reported, together with an associated loss of strength. After three months of intensive rehabilitation, the patient completely recovered his grip strength, although he still had a slight lack of sensitivity in the first and second finger.

The last intervention up till now was undertaken in 2007, when 4 new tumours located in the upper left limb were removed (fig. 1).

The patient always referred to clinical symptoms consistent with slow-growing tumours located in both upper limbs, on the forearm, wrist and hand, predominantly on the volar surface. He also reported occasional pain defined as burning and distal paresthesias in the affected area.

The anatomical pathology for the last 5 recorded interventions documents a relatively homogeneous greyish-brown cut surface, with cystic areas but very few haemorrhagic areas. They present an expansive and compressed growth on the origin nerve and are clearly circumscribed by a thin fibrous capsule. The tumours are formed by an abundant spindle cell component, with little clear cytoplasm; they present basophilic nuclei, which are elongated with a palisade arrangement (Verocay bodies). This coincides with the diagnosis of schwannomas in every case. Similarly, immunohistochemical staining showed that the majority of cells reacted positively to the S-100 marker (fig. 1). No genetic study was carried out on any of the operation samples during any of the interventions.

Currently, nearly three years after the last surgery, the patient presents multiple tumours in his right upper limb, which now affect practically all the volar surface of the hand, as can be seen in the MRI images (fig. 2) and he finds himself awaiting a new operation.. During all these years of follow-up, the patient has not presented the rest of the clinical NF-1 or NF-2 characteristics.

Discussion

Schwannomas form part of the differential diagnosis for painful subcutaneous tumours with soft tissue consistency together with other entities such as ganglions, leiomyomas and lipomas.[5] Excisional biopsy is needed to clarify the definitive aetiology.

Neurofibromatoses are a group of hereditary transmitted diseases that affect the bone, central and peripheral nervous system, soft tissue and skin. Up to 8 different types of neurofibromatosis have been described, with 3 being those currently accepted: type 1 (NF-1) or von Recklinghausen disease; type 2 (NF-2) or central; and type 5 or segmental neurofibromatosis.[3] Schwannomatosis has been defined in the last few years as a pathology different from NF-2, with a partial expression characterised by the appearance of

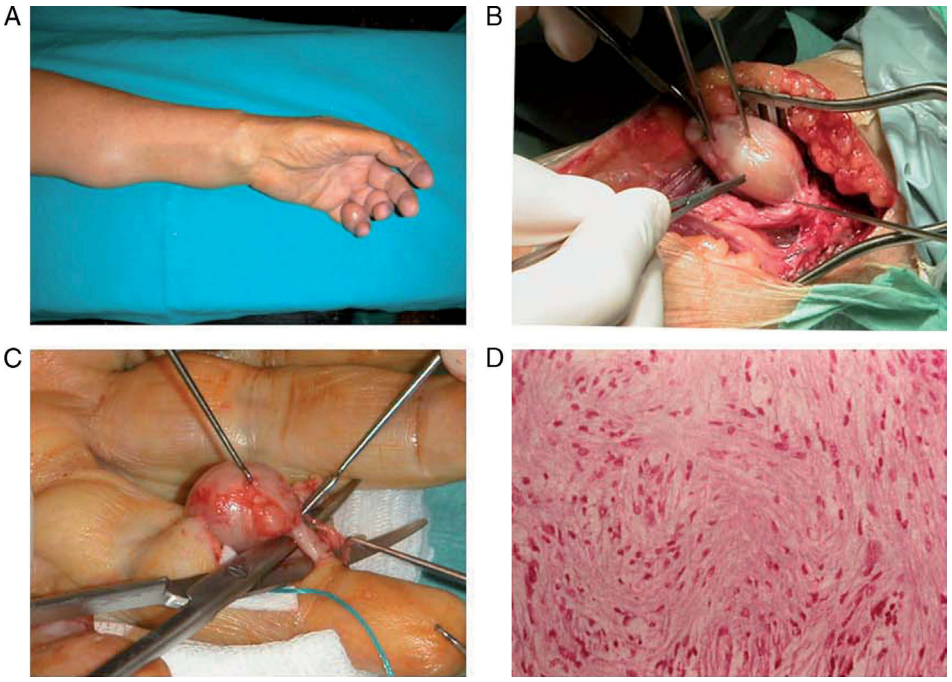

Figure 1 A. Pre-surgery image of the patient in 2007; we can see tumours on the antero-ulnar edge of forearm, volar wrist surface and little finger of the upper left limb. B. Intra-operative image; the tumour is seen adjacent to the ulnar nerve in his left forearm. C. Intra-operative image for the tumour removal of the radial digital nerve of the fourth finger. D. Histology. Spindle cell bundles arranged in a palisade arrangement (hematoxylin-eosin × 100).

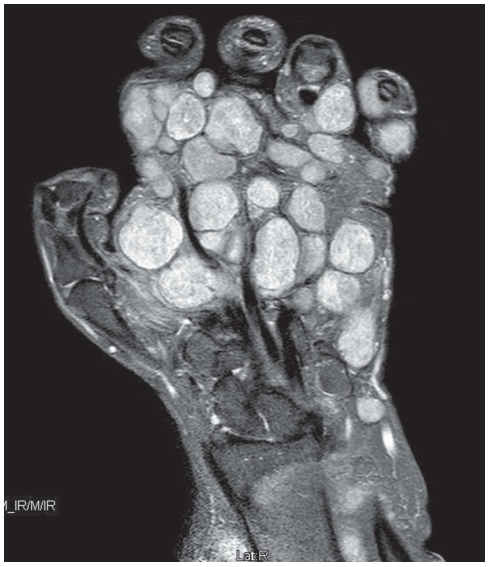

Figure 2 An enhanced MRI image, T2-weighted; there are multiple tumours on the volar surface of right forearm and hand.

tumours in the nerve sheaf, without the vestibular schwannomas that are diagnosed in NF-2.

In literature of the 90's, schwannomatosis and segmental neurofibromatosis have been indistinctly referred to as a pathology consistent with the appearance of multiple tumours limited to an anatomical area without crossing the mean line and without presenting the rest of the characteristic traits of NF-1 and NF-2.[3] Today they are considered different pathologies.

Schwannomatosis usually presents sporadically as in our patient, but family group presentation cases have been reported. Various genetic theories have been put forward over the years to explain this disease. A debate existed as to whether the appearance of multiple schwannomas without vestibular schwannoma evidence were a variant of NF-2, or if they were a different clinical entity. Honda[6] indicated that the molecular mechanism was due to a mutation of the NF-2 gene, which meant that this was an incomplete form of NF-2. Leverkus[7] carried out a molecular genetic analysis of the removed tumours in a patient, finding two different mutations in the NF-2 gene in two different schwannomas. Here he diagnosed schwannomatosis instead of segmental neurofibromatosis or a variant of NF-2. Later Murray[8] published the case of a patient with bilateral affectation of the upper limbs, accompanied by other medular lesions, where the genetic molecular analysis showed that this was due to a post-zygotic mutation in the NF2 gene that produced somatic mosaicism or segmental hyper-expression of it, which could be what our patient presented. Currently, we think that the disease could be due to a mutation of the SMARCB1/ INI1 gene on chromosome 22[9] in a different location from the NF-2 gene.

Approximately a third of patients with schwannomatosis present tumours that are confined to one limb, in a specific spinal segment or side of the body,[7] but we have found no clinical series in literature. The most commonly-cited cases describe affectation of the ulnar nerve in the upper limbs[7]

and of the sciatic nerve in the lower limbs[2]. In our case, schwannomas affected both upper extremities exclusively, similar to the case presented by Murray in 2006,[8] although here we also saw lesions in the torso, back and face.

We can choose observation or removal as treatment options. Surgical treatment is indicated when there are compressive symptoms that make the patient's life difficult. However, we must point out that there is a chance of neurological deficit during the intervention in 4% of cases, with a greater risk in interventions carried out after an incision biopsy or after a relapse, and in cases of multiple removals.[4] For this reason, to minimise neurological side effects, we recommend using micro-surgery techniques, using a team with experience in this field, and carrying out an intra-capsular removal of the tumour after a longitudinal incision on the epineurium and the capsule.[5]

Prognosis after removal is excellent, although there is a possibility of lesion recurrence or the appearance of new tumours, such as in the case we present. We have not found studies that describe possible tumour transformation in schwannomatosis patients in the references reviewed, although we have seen cases described where solitary schwannomas have become malignant.[10] We recommend performing a biopsy on those tumours that present a progressive increase in pain or other neurological signs.

Evidence level

Evidence level IV.

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