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Article

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Spinal schwannomatosis of the cauda equina in the absence of neurofibromatosis: case report and treatment strategies

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Abstract: Schwannomatosis is a rare tumor syndrome characterized by the presence of multiple benign non-vestibular, non-intradermal schwannomas and by the absence of neurofibromatosis type 1 or 2 syndromes. Multiple schwannomas are clinically and genetically distinct from neurofibromatosis, and the main treatment in case of symptomatic lesions is represented by surgical resection. In case of asymptomatic lesions, the indicated treatment is neuroimaging follow-up (MRI). We are presenting the case of a patient with three schwannomas of the cauda equina, as well as the treatment strategy in the case of this rare pathology.
Key words: spinal schwannomatosis, multiple schwannomas, treatment

Introduction

Schwannomatosis is a syndrome characterized by the existence of multiple schwannomas at the level of the spinal cord, cranial or peripheral nerves, but without the presence of vestibular schwannomas, ependymomas, meningiomas, or astrocytomas, which are encountered in neurofibromatosis type 2 (NF2) (15, 22, 25, 27, 28). Nonetheless, infrequently, the existence of meningiomas or ependymomas has been reported within schwannomatosis (3, 9).

Schwannomatosis was reported for the first time in 1973, as neurofibromatosis type 3 (18), and even though some researchers considered it to be an incomplete form, or a subcategory of NF2 (7), the subsequent genetic and molecular studies have shown that schwannomatosis is a separate genetic and clinical syndrome (13, 20, 24). Schwannomatosis represents 3-5% of the patients with schwannomas (11, 23, 24).

Short case report

We are presenting the case of a 59 year old female patient who was hospitalized for the

first time in 2011, at "Prof. Dr. N. Oblu" Clinical Emergency Hospital of Iași, for long standing low back pain and bilateral sciatica with insidious onset 10 months previously, as well as paraparesis with insidious onset 5 months previously. The imaging explorations carried out in 2011 revealed three lumbar spinal schwannomas located at the level of the cauda equina (Figure 1). Moreover, the head and spine MRI did not detect the existence of other schwannomas. Surgery was performed with the complete resection of the symptomatic schwannoma (the bigger schwannoma) (Figure 2). The subsequent anatomopathological examination was of schwannoma with Antoni A and B regions (Figure 3), and the postoperative evolution was favourable, without neurological deficits or residual radicular pain. Even though the patient did not have clinical symptoms, she was monitored every year through spine MRI neuroimaging, which did not identify significant increases in the volume of the tumors. In 2016, the patient was admitted again in our neurosurgery unit for the occurrence of an important long standing low back pain and left side sciatica about 6 months before. The lumbar spine MRI performed (2016) revealed the increased size of one of the two tumors, in comparison with the previous imaging explorations (2011) (Figure 4). Both tumors were resected (Figure 5), and the postoperative evolution was favourable. Moreover, the anatomopathologic diagnosis of the two tumors was of schwannoma with Antoni A and B areas.

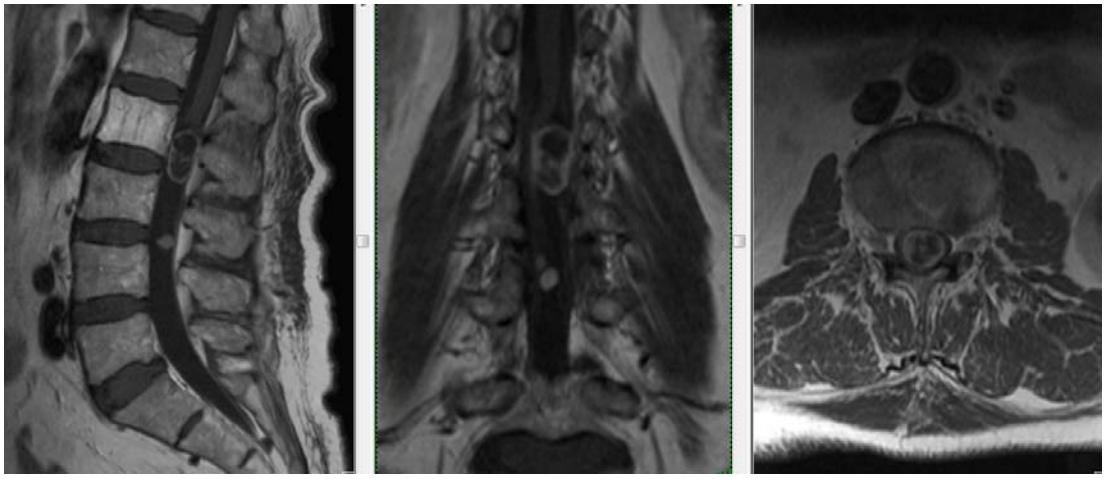

Figure 1 - T1-weighted (sagittal, coronal and axial) gadolinium-enhanced MRI images (2011) in which the 3 schwannomas of the cauda equina can be noticed

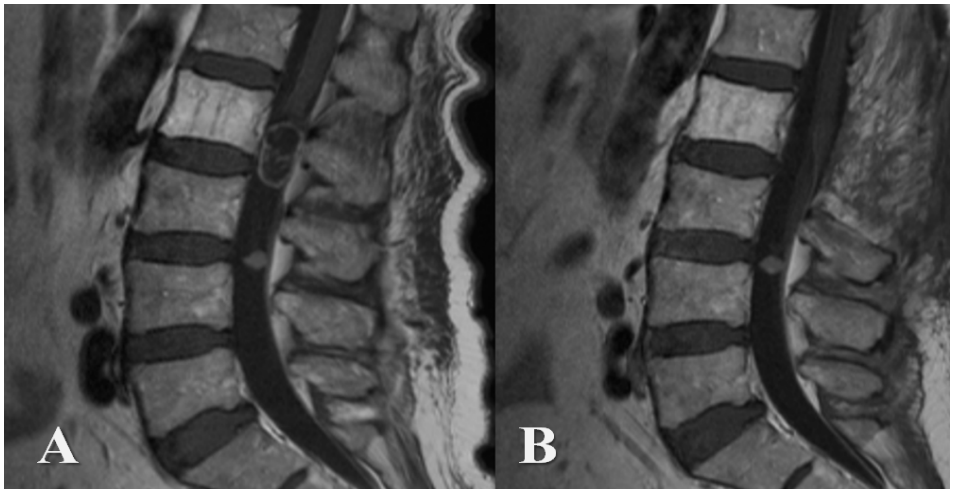

Figure 2 - Preoperative (A) and postoperative (B) gadolinium-enhanced MRI images (2011)

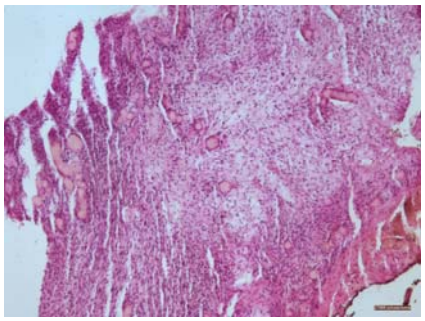

Figure 3 - The tumour had a biphasic feature as it was made up of hypercellular areas (Antoni A) composed of a haphazard arrangement of bland cells with spindled and oval nuclei, and myxoid hypocellular areas (Antoni B) with large irregularly spaced vessels (Hematoxylin-Eosin, x100

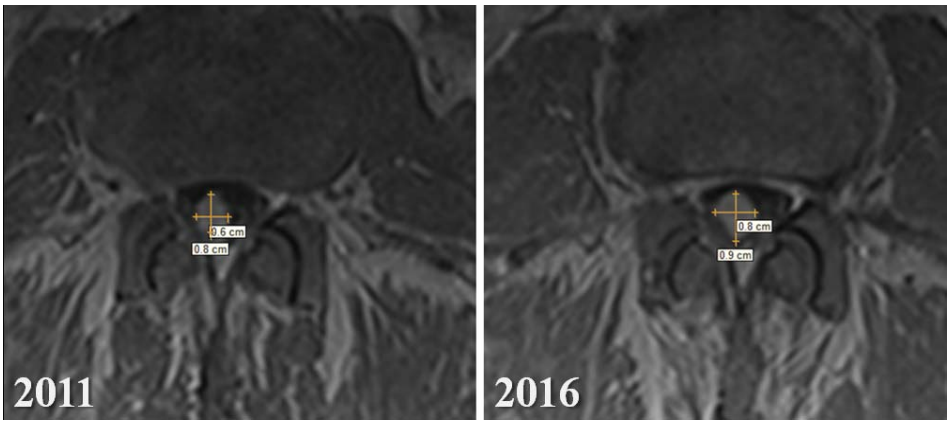

Figure 4 - T1-weighted (axial) gadolinium-enhanced MRI images (2011/2016) highlighting the increased size of one of the schwannomas

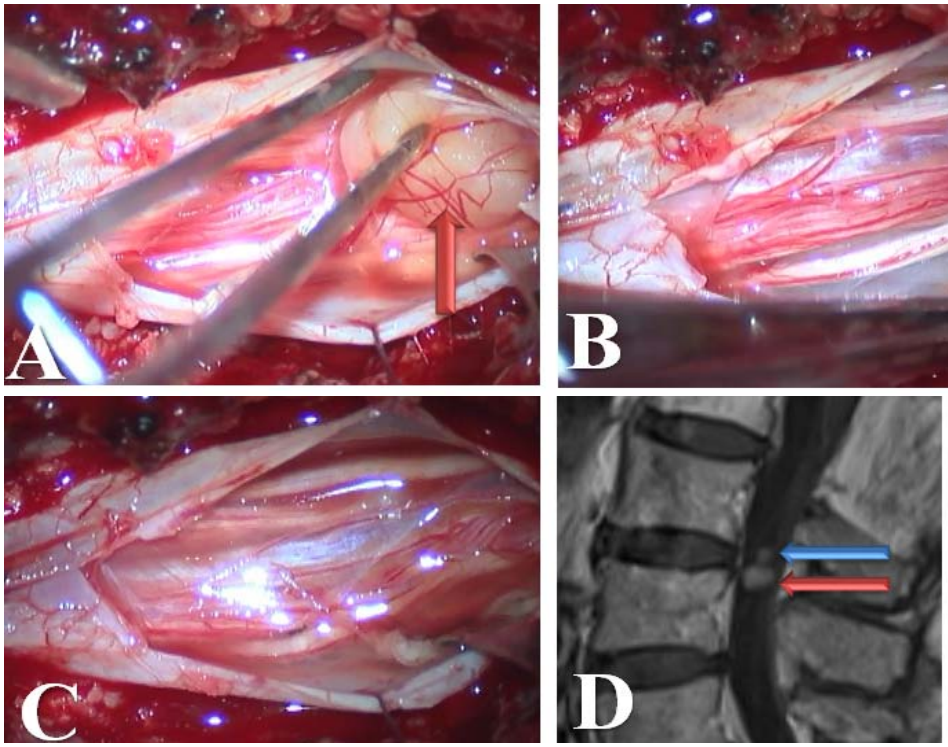

Figure 5 - Intraoperative appearance of the two schwannomas (A, B), postoperative appearance (C) and their correspondence in MRI neuroimaging (D) (the bigger schwannoma – red arrow, the smaller schwannoma – blue arrow)

Table I

MacCollin's diagnostic criteria for schwannomatosis (16)

DEFINITIVE SCHWANNOMATOSIS	POSSIBLE SCHWANNOMATOSIS
- age >30 years AND - two or more non-intradermal schwannomas, at least one with histologic confirmation AND no evidence of vestibular tumor of high-quality MRI scan AND no known constitutional NF2 mutation	- age <30 years AND - two or more non-intradermal schwannomas, at least one with a histologic confirmation AND no evidence of a vestibular tumor on a high-quality MRI scan AND no known constitutional NF2 mutation
OR	OR

- one pathologically confirmed non-vestibular schwannoma plus a first-degree relative who also meets the above criteria	- age >45 years AND two or more non-intradermal schwannomas, at least one with histologic confirmation AND no symptoms of 8th nerve dysfunction AND no known constitutional NF2 mutation
	OR
	- radiographic evidence of a non-vestibular schwannoma and a first degree relative also meeting the criteria for definite schwannomatosis

Discussion

Spinal schwannomas are benign tumors that develop from the schwann cells of the nerves and represent approximately one third of all benign primary spinal tumors (17). The majority of schwannomas are solitary lesions that can affect one or several nerves (5, 10), but they can also be multiple, suggesting the presence of syndromes, the most frequent of which is NF2.

Spinal schwannomas unassociated with neurofibromatosis was reported for the first time in 1993 by the American Daras M., at the Metropolitan Hospital from New York (5).

The schwannomatosis diagnosis is supported by the anatomopathological diagnosis which, apart from the Antoni A and Antoni B regions (26), also highlights other histological findings, such as: nerve oedema, intraneural growth pattern and myxoid stroma (21). Like in NF2, the schwannomas are growing slowly and do not turn into malignant lesions (2).

The genetics of schwannomatosis is complex and not yet fully understood (14), given that over 90% of the sporadic cases and 50% of the familial cases of schwannomatosis do not have an identified genetic mutation (19, 20). An associated germline mutation inactivating the SMARCB1 gene is encountered in only 40-50% of the familial forms, and in less than 10% in the sporadic cases (20). Moreover, the family history is present only in 15-25% of the cases (20).

The first clinical sign of patients who are suffering from schwannomatosis is pain on the tract of the implied nerve (8, 12, 16), unlike patients suffering from NF2, who seek medical care for the occurrence of neurological deficit, which is represented in 95% of the cases by hearing impairment (6). In our patient's case, the onset symptomatology was represented by long standing low back pain and bilateral sciatica, followed by the insidious onset of neurological deficit.

The age of onset of schwannomatosis is represented by the fourth decade (1, 11, 24),

unlike patients with NF2, who seek medical care at an earlier age (5).

Even though some criteria for diagnosing schwannomatosis have been proposed, they are currently unclear. In 1997, Jacoby et al. proposed as a criterion for schwannomatosis the presence of 2 or more schwannomas, in the absence of vestibular schwannomas, in patients over the age of 18 (13). Later on, in 2005, MacCollin et al. also enumerated several criteria: the presence of 2 or more non-intradermal schwannomas, over 30 years of age, the absence of MRI-detectible vestibular schwannomas, as well as the absence of constitutional mutations encountered in NF2 (Table 1) (16). The treatment indicated in schwannomatosis is the surgical removal in symptomatic cases (4) and follow-up in non-symptomatic cases. Moreover, in our patient's case, the biggest schwannoma which was actually symptomatic, was initially resected (Figure 1, Figure 2). For the other two smaller, non-symptomatic schwannomas (Figure 5), a conservative follow-up treatment was decided upon. Five years after the initial surgery, the patient was hospitalized for the occurrence of pain, due to the increased size of the second schwannoma. Thus, surgery with the complete resection of the two tumors was performed, having a favourable postoperative evolution.

Conclusions

In the case of multiple spinal schwannomas, head neuroimaging (MRI) and audiological testing must also be taken into consideration in order to exclude NF2. In spite of the similarities between NF2 and schwannomatosis, they are two distinctive entities, both genetically and clinically, which can pose diagnosis problems. The MacCollin criteria can be useful to differentiate between these two syndromes. In the case of patients with spinal schwannomatosis, we recommend surgical treatment in the case of symptomatic tumors, and conservative follow-up treatment in case nonsymptomatic tumors.

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References

1.Antinheimo J, Sankila R, Carpén O, Pukkala E, Sainio M, Jääskeläinen J. Population-based analysis of sporadic and type 2 neurofibromatosis-associated meningiomas and schwannomas. Neurology. 2000; 54:71-76.

2.Bhattacharyya AK, Perrin R, Guha A. Peripheral nerve tumors: management strategies and molecular insights. J Neurooncol. 2004; 69:335–349.

3.Boyd C, Smith MJ, Kluwe L, Balogh A, Maccollin M, Plotkin SR. Alterations in the SMARCB1 (INI1) tumor suppressor gene in familial schwannomatosis. Clin Genet. 2008; 74(4): 358-366.

4.Conti P, Pansini G, Mouchaty H, Capuano C, Conti R. Spinal neurinomas: retrospective analysis and long-term outcome of 179 consecutively operated cases and review of the literature. Surg Neurol. 2004; 61(1):34-43, discussion 44.

5.Daras M, Koppel BS, Heise CW, Mazzeo MJ, Poon TP, Duffy KR. Multiple spinal intradural schwannomas in the absence of von Recklinghausen's disease. Spine. 1993; 18(16): 2556-2559.

6.Evans DG, Huson SM, Donnai D, Neary W, Blair V, Newton V, Harris R. A clinical study of type 2 neurofibromatosis. Q J Med. 1992; 84:603-618.

7.Evans DG, Mason S, Huson SM, Ponder M, Harding AE, Strachan T. Spinal and cutaneous schwannomatosis is a variant form of type 2 neurofibromatosis: a clinical

and molecular study. J Neurol Neurosurg Psychiatry. 1997; 62:361-366.
8.Govind M, Radheyshyam M, Achal S, Ashok G. Intradural extramedullary spinal cord tumors: a retrospective study at tertiary referral hospital, Romanian Neurosurgery. 2016; XXX (1):106-112.
9.Hadfield KD, Newman WG, Bowers NL, Wallace A, Bolger C, Colley A, McCann E, Trump D, Prescott T, Evans DG. Molecular characterisation of SMARCB1 and NF2 in familial and sporadic schwannomatosis. J Med Genet. 2008; 45(6):332-339.
10.Halliday AL, Sobel RA, Martuza RL. Benign spinal nerve sheath tumours: their occurrence sporadically and in neurofibromatosis types 1 and 2. J Neurosurg. 1991; 74:248-253.
11.Huang JH, Simon SL, Nagpal S, Nelson PT, Zager EL. Management of patients with Schwannomatosis: report of six cases and review of literature. Surg Neurol. 2004; 62:353-361.
12.Iacob G. Spinal meningiomas. Personal experience and review of literature, Romanian Neurosurgery. 2014; XXI (2):146-160.
13.Jacoby LB, Jones D, Davis K et al (1997) Molecular analysis of NF2 tumour suppressor gene in Schwannomatosis. Am J Hum Genet 61:1293–1302.
14.Koontz NA, Wiens AL, Agarwal A, Hingtgen CM, Emerson RE, Mosier KM. Schwannomatosis: the overlooked neurofibromatosis? AJR Am J Roentgenol. 2013; 200: w646–w653.
15.MacCollin M, Woodfin W, Kronn D, Short MP. Schwannomatosis: a clinical and pathologic study. Neurology. 1996; 46:1072–1079.
16.MacCollin M, Chicocca EA, Evans DG Friedman JM, Horvitz R, Jaramillo D, Lev M, Mautner VF, Niimura M, Plotkin SR, Sang CN, Stemmer-Rachamimov A, Roach ES. Diagnostic criteria for schwannomatosis. Neurology. 2005; 64:1838-1845.
17.Mautner VF, Tatagiba M, Lindenau M, Funsterer C, Pulst SM, Baser ME, Kluwe L, Zanella FE. Spinal tumors in patients with neurofibromatosis type 2: MR imaging study of frequency, multiplicity, and variety. AJNR Am J Roentgenol. 1995; 165(4):951-955.
18.Nimura M. Neurofibromatosis. Rinsho Derma. 1973; 15:653-663.
19.Piotrowski A, Xie J, Liu YF, Poplawski AB, Gomes AR, Madanecki P, Fu C, Crowley MR, Crossman DK, Armstrong L, Babovic-Vuksanovic D, Bergner A, Blakeley JO, Blumenthal AL, Daniels MS, Feit H, Gardner K, Hurst S, Kobelka C, Lee C, Nagy R, Rauen KA, Slopis JM, Suwannarat P, Westman JA, Zanko A, Korf BR, Messiaen LM. Germline loss-of-function mutations in LZTR1 predispose to an inherited disorder of multiple schwannomas. Nat Genet. 2014; 46: 182-187.
20.Plotkin SR, Blakeley JO, Evans DG, Hanemann CO, Hulsebos TJM, Hunter-Schaedle K, Kalpana GV, Korf B, Messiaen L, Papi, L, Ratner N, Sherman LS, Smith MJ, Stemmer-Rachamimov AO, Vitter J, Giovannini M. Update from the 2011 International Schwannomatosis Workshop: from genetics to diagnostic criteria. Am J Med Genet A. 2013;161A:405-416.
21.Poliani PL, DeSantis S, Bettensky RA et al. Defining histologic criteria for the diagnosis of schwannomatosis, Aspen, CO, 2005.
22.Purcell SM, Dixon SL. Schwannomatosis. An unusual variant of neurofibromatosis or a distinct clinical entity. Arch Dermatol. 1989; 125: 390-393.
23.Radek M, Tomasik B, Wojdyn M, Snopkowska-Wiaderna D, Błaszczyk M, Radek A., Neurofibromatosis type 2 (NF 2) or schwannomatosis?--Case report study and diagnostic criteria. Neurol Neurochir Pol. 2016; 50(3):219-225.
24.Seppala MT, Saino MA, Haltia MJ, Kinnunen JJ, Setälä KH, Jääskeläinen JE.. Multiple schwannomas: Schwannomatosis or neurofibromatosis 2. J Neurosurg. 1998. 89:36-41.
25.Shin KH, Moon SH, Suh JS, Jahng JS. Multiple neurilemomas. A case report. Clin Orthop. 1998; 357: 171-175.
26.Wippold FJ 2nd, Lubner M, Perrin RJ, Lämmle M, Perry A. Neuropathology for the neuroradiologist: Antoni A and Antoni B tissue patterns. AJNR Am J Neuroradiol. 2007; 28(9):1633-1638.
27.Wolkenstein P, Benchikhi H, Zeller J, Wechsler J, Revuz J. Schwannomatosis: a clinical entity distinct from neurofibromatosis 2. Dermatology. 1997; 195: 228-231.
28.Yamamoto T, Maruyama S, Mizuno K. Schwannomatosis of sciatic nerve. Skeletal Radiol; 2001; 30: 109-113.