Melanotic Schwannoma of the Cervical Spine Progressing With Pulmonary Metastasis: Case Report

Mário Henrique Girão Faria,1 Ricardo Henrique Dória-Netto,1 Gustavo Jun Osugue,1 Luciano de Souza Queiroz,2 and Feres Eduardo CHADDAD-Neto1

1Department of Neurosurgery, Hospital Municipal Dr. Mário Gatti, Campinas SP, Brazil; 2Department of Pathologic Anatomy, Faculdade de Ciências Médicas, Universidade Estadual de Campinas (FCM-UNICAMP), Campinas SP, Brazil

Abstract
Melanotic schwannoma (MS) is an unusual variant of nerve sheath neoplasm. Only 10% of these tumors will undergo malignant degeneration, with exceedingly rare reported metastasis. We present a 32-year-old woman with a 6-month history of cervical pain and left arm progressive weakness. Neurological examination showed a left upper limb radicular pain, with pyramidal syndrome at C5 level. The magnetic resonance imaging (MRI) study highlighted an intradural extramedullary heterogeneous mass along the spinal cord at the C4–C5 level, slightly hyperintense with T1 and hypointense with T2-weighted sequences, invading the left neural foramen. The patient underwent C3–C5 laminectomy with total resection of a black tumor. In the postoperative period, a patent deficit of shoulder abstraction ensued related to the nervous section. Microscopically, compactly fascicles of spindle-shaped cells with pleomorphic and hypercromatic nuclei, as well as some mitotic figures were seen. Immunohistochemical stains for S-100, Human Melanoma Black-45 (HMB-45), and vimentin were positive, with Ki-67 labelling index (LI) of 15% compatible with MS. Six months after radiotherapy she presents local recurrence and lung metastatic dissemination of the MS. She underwent left pulmonary segmentectomy, followed by chemotherapy and radiosurgery. The patient developed a febrile neutropenia and worsening of general status, and died after 3 months due to respiratory complications. MS are rare tumors with potential for local recurrence and distal metastasis. Complete surgical resection remains as the treatment of choice, once the uncommon cases with malignant progression shows low response to chemo and radiotherapy.

Key words: cervical neoplasm, melanotic schwannoma, metastasis, nerve sheath tumor, spine

Introduction
Melanotic neoplasm of the central nervous system (CNS) are rare, and most frequently they are metastatic.13,16) It is important to differentiate primary melanin-containing lesions of the CNS from metastatic melanomas, because these last tumors require a specific therapeutic approach. Other pigmented lesions include neoplasms that may undergo melanization, such as schwannoma, medulloloblastoma, and glioma, as well as melanocytic neuroectodermal tumors of infancy.11,12,20)

Melanotic schwannoma (MS) is an unusual variant of nerve sheath neoplasm composed of cells having the ultrastructure and immunophenotype of Schwann cells but containing melanosomes in varying stages of matura-

Received May 23, 2012; Accepted August 17, 2012
at an earlier age may be more likely to have Carney’s syndrome.\textsuperscript{11,19}"

MSs are more typically intracranial, but they also occur within the spinal canal. When they develop within spine, the tumors most often arise in the lombo-sacral region (47.2%) followed by thoracic (30.5%) and cervical (22.2%) levels, and may be intramedullary.\textsuperscript{12} The behavior of these tumors is typically benign, but 10% of MS will undergo malignant degeneration. Metastasis and meningeal seeding have been reported but are exceeding rare.\textsuperscript{17} Killeen et al. found a recurrence rate of 24% and a disease-related mortality of 16%, with complete surgical excision being the most common initial treatment.\textsuperscript{9}

**Case Report**

A 32-year-old woman had a 6-month history of cervical pain and left arm progressive weakness. On admission, neurological examination showed a left upper limb radicular pain, with pyramidal syndrome and paresthetic area at C5 level. The magnetic resonance imaging (MRI) study highlighted an intradural extramedullary heterogeneous mass along the spinal cord at the C4–C5 level, slightly hyperintense with T\textsubscript{2} and isointense with T\textsubscript{1}-weighted sequences, invading the left C5 neural foramen (Fig. 1). The patient underwent C3–C5 laminectomy with total resection of a black encapsulated tumor measuring 37 × 30 × 16 mm (Fig. 2). In the postoperative period, a patent deficit of left shoulder abduction and paresthesia persist related to the nervous section. The search for clinical signs of melanoma, neurofibromatosis, or Carney’s syndrome was negative. Microscopically, compact fascicles of epithelioid and spindle-shaped cells with pleomorphic and hypercromatic nuclei and dark brown intracellular pigment as well as some mitotic figures were seen. Several foci of necrosis and macrophage with large brown cytoplasmic granule were also visible. Immunohistochemical stains for S-100, Human Melanoma Black-45 (HMB-45) and vimentin were positive, with Ki-67 labelling index (LI) of 15%, compatible with MS (Fig. 3). She was submitted to external radiotherapy (40 Gy) and remains clinically stable. Six months later, she presents worsening of cervical pain and dyspnoea, with evidence of local recurrence.

**Fig. 1** A: MRI study with sagittal T\textsubscript{2}-weighted sequence disclosing a hypointense heterogeneous intradural C4–C5 mass, disrupting the medulla. B: axial T\textsubscript{2} proton density (PD)-weighted sequence showing a slightly hyperintense. C: Axial FLAIR isointense extramedullary neoplasm extension for the left C5 root without bone destruction, presenting an hourglass shape directed toward the paravertebral area. FLAIR: fluid attenuated inversion recovery, MRI: magnetic resonance imaging.

**Fig. 2** Surgical view of C3–C5 laminectomy followed by durotomy, revealing (A) intradural extramedullary mass, with (B) black multilobulated appearance that extended to C5 foramen, as confirmed after (C) the total removal of tumor.

Neurol Med Chir (Tokyo) 53, October, 2013
and multiple pulmonary nodules (Fig. 4). She was started on multiagent chemotherapy (dicarbazine, cisplatin, and interferon) and submitted to cervical stereotactic radiosurgery (800 cGy). The patient also underwent left pulmonary segmentectomy, which confirmed the metastatic dissemination of the MS. She evolved with progressive deterioration of general status and pleural effusion, being diagnosed a febrile neutropenia. The patient died after 3 months due to respiratory/infectious complications.

**Discussion**

Primary pigmented tumors of the nervous system are rare. MS generally arise from the roots of spinal nerves, or occasionally from soft tissues. A number of cases were reported in the bone, sympathetic chain, cerebellar, heart, liver, choroids, and skin. Intramedullary, these tumors seems to appear more frequently in the lombo-sacral region and less commonly in the cervical spine. Moreover, most previously reported cases behaved in a clinically benign fashion.2,3,8,12)

MS presents a 1.1:1 male-female ratio, age at diagnosis varying from 10 to 84 years, with the highest frequency of occurrence in the fourth decade. Patients who develop tumors at an earlier age (third decade) may be more likely to have Carney’s syndrome which is associated up to 50% of cases of these lesions.15) For this, it is necessary to search for clinicopathologic components of Carney’s complex.18) The patient described herein had no evidence of genetic syndromes, including neurofibromatosis, consisting probably in an example of a sporadic case of MS.11)

In these neoplasms, the common radiological features include a hyperintense signal on the T1-weighted images related to the considerable amount of melanin, whereas ordinary schwannomas give isosignals on T1-weighted images. The MRI study reveals early erosion of the intervertebral foramen with an “hourglass” extension and isointense to slightly hyperintense signal in the T2-weighted images. However, their signal characteristics vary, and areas of T1 and T2 prolongation may be seen.
On post contrast images, the enhancement pattern of the lesions also varies.2,16)

The histological findings of the present case are similar to those sporadic MS reported previously, consisting of spindle cells packed in interlacing fascicles. Mitoses, cellular atypia, increased cellularity, and infiltrating ill-defined borders are described as signs of malignancy in nerve-sheath tumors.5,19) The differential diagnosis between MS and other pigmented lesions can be difficult, including primary or metastatic melanoma, a diagnosis with obvious prognostic and therapeutic relevance. In addition, these tumors may histologically closely resemble leptomeningeal melanocytomas and cellular blue nevi.1,5,12)

Several theories for the etiology of MS have been proposed, including the melanomatous transformation of neoplastic Schwann cells, phagocytosis of melanin by Schwann cells, and the simultaneous presence of two distinct neoplastic populations of proliferating melanocytes and Schwann cells.14) However, it is actually accepted that Schwann cells, melanoblasts, and melanocytes are of neuroectodermal origin and also that melanocytes appear to migrate with Schwann cells.13) So, we hypothesize that some genetic alterations in a common precursor may trigger the tumorigenic process, making these proliferating cells with schwannian phenotype to synthesize melanin, leading finally to the development of MS.

Immunostaining analyses are important, but not always useful in sorting out this differential diagnosis. All these lesions generally express S-100, which can be explained by their common neural crest origin. Melanocytic differentiation can be expressed by HMB-45 and Melan-A positivity, which recognizes melanosomal components in tumor cells.21) Although stains for components of the basement membrane can be useful in discriminating tumors with schwannian differentiation from tumors with melanocytic differentiation, overlap in staining patterns has been noted.7)

Surgery is universally accepted as the best form of treatment. Radical surgical excision with wide range margins and without regional lymph-nodes dissection remains the technique of choice, as lymph-node involvement is extremely rare. Incomplete tumor removal is associated with recurrence risk. As for other sarcomas, the role of postoperative radiation therapy and/or chemotherapy is not yet well defined.5,5,11) In recent studies, postoperative radiation therapy is also recommended to reduce the possibility of local recurrence. Chemotherapy has been advocated for patients with unresectable recurrent tumor or distant metastases. The role in survival of adjuvant therapies has yet to be defined.13,16)

Advanced age seems to be a factor of poor prognosis in sporadic forms; indeed, metastatic recurrence occurs among populations aged less than 40 years. No other prognosis factors such immunohistochesmal stains or efficiency of chemotherapy or radiotherapy protocols has been reported in the literature.9,17)

Thereafter, the multiple pulmonary lesions diagnosed on patient’s clinical course showed exactly the same histological configuration as the initial cervical lesions, including the pigmented macroscopic appearance and the immunohistochemical findings, reinforcing the causal and temporal relationship between these lesions. Though this type of tumor may arise from peripheral nerves located within the bronchial wall, primary endobronchial schwannomas are extremely rare, with incidence estimated in 0.2% of all lung tumors, presenting usually as a single nodule or mass.11,21)

Thus, the current case presented an unusual malignant progression, with pulmonary metastasis. Multiple MS of the nerve sheath and/or heterotypic sites are possible and have been commonly thought to be synchronous or metachronous tumors of different origins rather than metastatic foci.12,19) Moreover, as in some previous reports, the complete macroscopic removal of the main lesion does not guarantee recovery which would be free of local recurrence and future metastasis.2,5,11,16)

**Conclusion**

MS is a rare neoplasm composed of Schwann cells capable of melanogenesis, which may be encountered by spine surgeons involving cervical nerve trunks. These tumors are usually benign, but they may become aggressive and metastasize. Total excision with tumor-free margins and a long-term follow-up is recommended, including the screening for Carney’s syndrome especially in young patients.

**Conflicts of Interest Disclosure**

None declared.

**References**

1) Ditz C, Brunswig K, Meyer C, Reusche E, Nowak G, Tronnier V: Intracranial melanotic schwannoma: a case report of recurrence with extra- and intradural manifestation two decades after initial diagnosis and treatment. *Cent Eur Neurosurg* 72: 211–214, 2011

2) El Benna N, Ouachtou K, Mahroug N, Abdelouafi A, Karkouri M: [Melanocytic cervical schwannoma]. *J Neuroradiol* 36: 114–115, 2009 (French)

3) Er U, Kazanci A, Eyriparmak T, Yigitkanli K, Senveli E: Melanotic schwannoma. *J Clin Neurosci* 14: 676–678, 2007

4) Hodson JJ: An intra-osseous tumour combination of biological importance—invasion of a melanotic schwannoma by an adamantinoma. *J Pathol Bacteriol* 82: 257–266, 1961

5) Hoover JM, Bledsoe JM, Giannini C, Krauss WE: Intramedul lary melanotic schwannoma. *Rare Tumors* 4: e3, 2012

6) Horvath A, Bossis I, Giatzakis C, Levine E, Weinberg F,
Meoli e, Robinson-White a, Siegel J, Soni P, Groussin L, Matyakhina L, Verma S, Remmers E, Nesterova M, Carney JA, Bertherat J, Stratakis CA: Large deletions of the PRKAR1A gene in Carney complex. Clin Cancer Res 14: 388–395, 2008

7) Huang HY, Park N, Erlandson RA, Antonescu CR: Immuno-histochemical and ultrastructural comparative study of external lamina structure in 31 cases of cellular, classical, and melanotic schwannomas. Appl Immunohistochem Mol Morphol 12: 50–58, 2004

8) Kaehler KC, Russo PA, Katenkamp D, Kreusch T, Neuber K, Schwarz T, Hauschild A: Melanocytic schwannoma of the cutaneous and subcutaneous tissues: three cases and a review of the literature. Melanoma Res 18: 438–442, 2008

9) Killeen RM, Davy CL, Bauserman SC: Melanocytic schwanna. Cancer 62: 174–183, 1988

10) Kusters-Vandevelde HV, van Engen-van Grunsven IA, Kusters B, van Dijk MR, Groenen PJ, Wesseling P, Blokx WA: Improved discrimination of melanotic schwannoma from melanocytic lesions by combined morphological and GNAQ mutational analysis. Acta Neuropathol 120: 755–764, 2010

11) Marton E, Feletti A, Orvieto E, Longatti P: Dumbbell-shaped C-2 psammomatous melanotic malignant schwannoma. Case report and review of the literature. J Neurosurg Spine 6: 591–599, 2007

12) Peltier J, Page C, Toussaint P, Bruniau A, Desenclos C, Le Gars D: Melanocytic schwannomas. Report of three cases. Neurochirurgie 51: 183–189, 2005

13) Rodriguez FJ, Folpe AL, Giannini C, Perry A: Pathology of peripheral nerve sheath tumors: diagnostic overview and update on selected diagnostic problems. Acta Neuropathol 123: 295–319, 2012

14) Sauka-Spengler T, Bronner-Fraser M: A gene regulatory network orchestrates neural crest formation. Nat Rev Mol Cell Biol 9: 557–568, 2008

15) Shields LB, Glassman SD, Raque GH, Shields CB: Malignant psammomatous melanotic schwannoma of the spine: a component of Carney complex. Surg Neurol Int 2: 136, 2011

16) Smith AB, Rushing EJ, Smirniotopoulos JG: Pigmented lesions of the central nervous system: radiologic-pathologic correlation. Radiographics 29: 1503–1524, 2009

17) Vallat-Decouvelaere AV, Wassel M, Lot G, Catala M, Moussalam M, Caruel N, Mikol J: Spinal melanotic schwannoma: a tumour with poor prognosis. Histopathology 35: 558–566, 1999

18) Vezzosi D, Vignaux O, Dupin N, Bertherat J: Carney complex: clinical and genetic 2010 update. Ann Endocrinol 71: 486–493, 2010

19) Welling LC, Guirado VM, Tessari M, Felix AR, Zanelatto C, Figueiredo EG, Taricco MA, Teixeira MJ: Spinal melanotic schwannomas. Arq Neuropsiquiatr 70: 156–157, 2012

20) Yeh I, Argenyi Z, Vemula SS, Furmanczyk PS, Bouffard D, McCalmont TH: Plexiform melanocytic schwannoma: a mimic of melanoma. J Cutan Pathol 39: 521–525, 2012

21) Zhang HY, Yang GH, Chen HJ, Wei B, Ke Q, Guo H, Ye L, Bu H, Yang K, Zhang YH: Clinicopathological, immunohistochemical, and ultrastructural study of 13 cases of melanotic schwannoma. Chin Med J 118: 1451–1461, 2005

Address reprint requests to: Mário Henrique Girão Faria, MD, PhD, Avenida das Amoreiras, 407 AP 42, Parque Itália, CEP 13036-225, Campinas, SP, Brazil.

e-mail: mariofaria@doctor.com