

CASE REPORT

Invasive intramedullary melanotic schwannoma: case report and review of the literature

Xing Cheng^{1,2} · Jiagang Liu¹ · Jun Le³ · Siqing Huang¹ · Haifeng chen¹ · Chao You¹

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Abstract

Purpose Melanotic schwannoma (MS) is rare, accounting for less than 1% of primary peripheral nerve sheath tumors, and most often occurs in the paraspinal nerve roots. Intramedullary MS is exceedingly rare, and to the best of our knowledge, only nine cases have been reported in literature.

Methods and Results We present a 47-year-old male, who underwent excision of thoracic intraspinal space-occupying lesion 6 years ago, as the 10th known case to date of intradural intramedullary MS that had a more invasive growth pattern than those reported before, and we review the diagnosis, clinicopathologic features, treatment and prognosis of intramedullary MS.

Conclusions Intramedullary MS' behavior is unpredictable and can have an aggressive clinical course such as recurrence and metastasis.

Keywords Intramedullary · Melanotic · Invasive · Schwannoma

Introduction

Melanotic schwannoma (MS) is a rare tumor, accounting for less than 1% of primary peripheral nerve sheath tumors, that was first identified in 1932 by Millar, who described it as “malignant melanotic tumor of the ganglion cells arising from the thoracic sympathetic ganglion” [1, 2]. Since then, literatures on the topic were mainly restricted to single case reports or small case series, including <200 cases most often occurred in the paraspinal nerve roots [3]. Intramedullary MS is even more rare, and only nine cases have been reported in literature [4–12]. We present the 10th known case to date of a patient with a more invasive intradural intramedullary MS than those reported before, and to the best of our knowledge, this is the second reported patient to be of Asian ethnicity [4].

Case report

Presentation and history

The patient was a 47-year-old male with back pain, zosteresthesia below papillary level, and left-leg weakness that progressively got worse over a period of fourteen months. The pain was particularly worse when lying down and turning over. No any other neurological symptoms were complained, such as lower limbs numbness, hemianesthesia, and bladder or anal sphincter dysfunction.

Physical examination

His examination demonstrated mild (grade 3 strength) weakness and hypermyotonia of the left leg, together with hyperactivity of tendon reflexes, ankle clonus and presence of Babinski sign. Temperature and pain sensation

Jiagang Liu contributed equally to this work, and is the co-first author of this article.

✉ Chao You
cx.steven@163.com

¹ Department of Neurosurgery, West China Hospital, Sichuan University, No.37, Guoxue Alley, Chengdu 610041, Sichuan, People's Republic of China

² Department of Neurosurgery, Chongqing Cancer Hospital, Chongqing, People's Republic of China

³ Department of Neurosurgery, Yingtan People's Hospital, Yingtan, Jiangxi, People's Republic of China

was reduced below the T4 level bilaterally. The neurological examination of his right leg, upper limbs and cranial nerves was negative and also, no pigmentation of skin was found.

Radiography and initial diagnosis

A magnetic resonance imaging (MRI) scan of the thoracic spine revealed an enhancing, oval-shaped, space-occupying mass with a $1.8 \times 2.1 \times 4.4$ cm diameter at the level of T4-T5 (Fig. 1a–c). There was spinal cord edema and syringomyelia above and below the mass evidenced by T2 hyperintensity. Significantly, We initially considered that the patient's clinical diagnosis might be a schwannoma or meningioma.

Surgery

The patient underwent T4–T6 laminectomies in order to a better exposing and protecting the spinal cord. The dural sac swelled and the dura mater thinned posteriorly where the lesion presented intradurally. The dura mater was opened longitudinally in the midline exposing a huge, dark brown intramedullary lesion reminiscent of a melanoma. The lesion invaded the spinal cord extensively, accompanying with an intensive adhesion and indistinct border. Microsurgical resection was carefully performed, however, some small tumor spots were residual due to unable separating from the spinal cord (Fig. 1d, e).

Pathology

Pathological analysis with hematoxylin and eosin staining was performed and demonstrated a heavily pigmented spindle cells arranged in fascicular or swirling pattern with notable vascular tissue, which indicated a melanotic schwannoma (Fig. 1f, g). Immunohistochemistry was positive for diffuse Human Melanoma Black-45 (HMB-45, not shown), melan-A, Ki-67 (about 10%, not shown), and S-100. In addition, transmission electron microscopy demonstrated the presence of melanosomes existed in the cytoplasm of tumor cells and continuous basal lamina in tumor cells (Fig. 1h–k). Thus, the final diagnosis of the patient was identified as intramedullary melanotic schwannoma (MS).

Post-operative course and follow-up

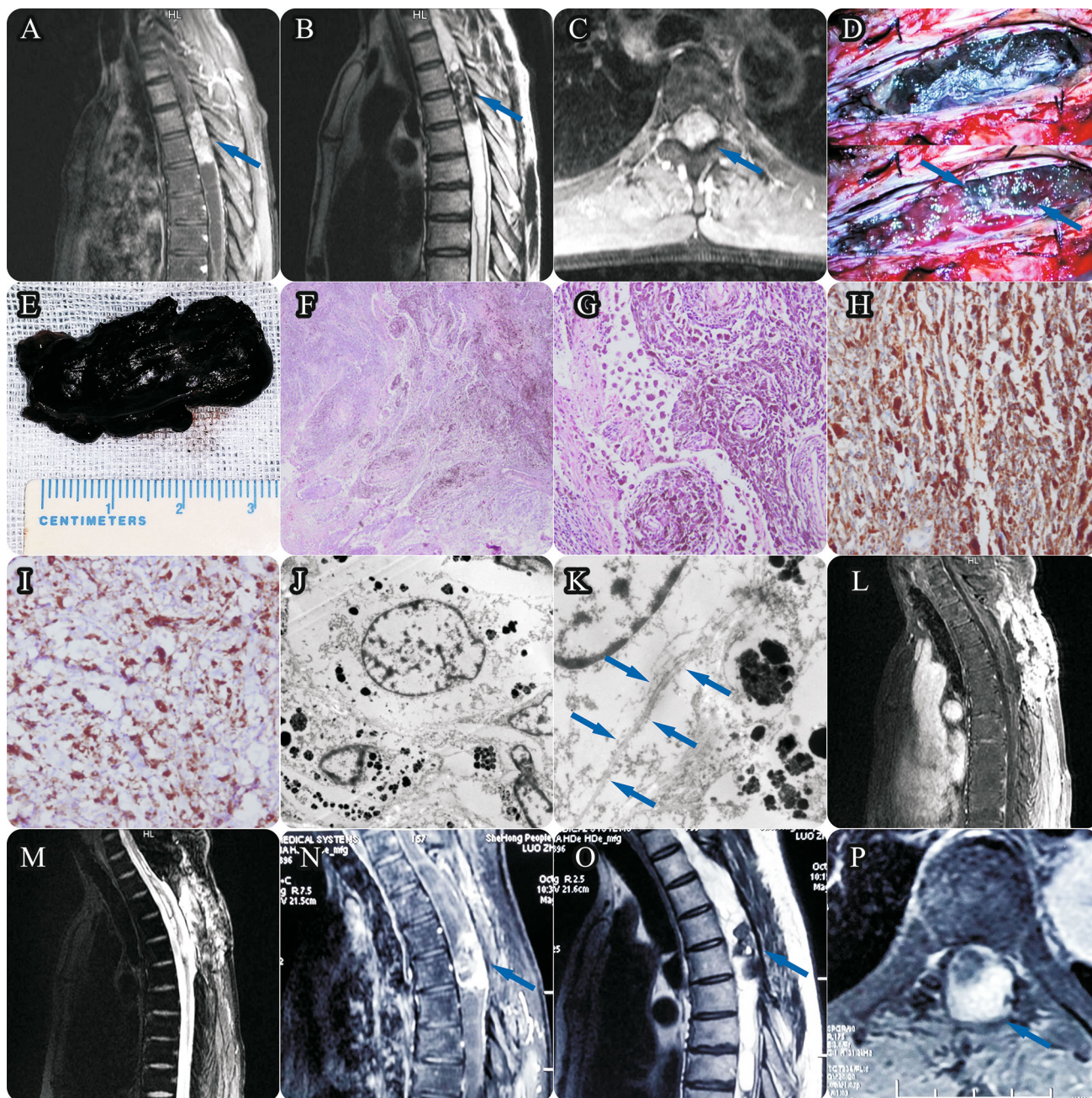
Immediately after surgery, the patient had worse muscle strength in lower limbs together with dysesthesias bilaterally. Physical examination demonstrated grade 1 on the left and grade 0 on the right, however, there was no urination disorder or defecation dysfunction. Delightingly, his strength and sensation improved over the following weeks, and the patient was

Fig. 1 **a** Sagittal T1 MRI with contrast demonstrated a mass with obvious heterogeneous enhancement at the level of T4-T5 (*arrowhead*). **b** Sagittal T2 MRI demonstrated a space-occupying mass with heterogeneous intensity at the level of T4-T5 (*arrowhead*). Spinal cord edema and syringomyelia above and below the mass could be seen. **c** Axial T1 MRI with contrast demonstrated heterogeneous enhancement within the spinal cord (*arrowhead*). **d** Intra-operative photograph showed a huge, dark brown intramedullary lesion almost occupying the whole subdural space and photograph after subtotal tumor resection showed very thin spinal cord being squeezed by tumor and some small black spots (*arrowhead*) were still residual due to unable separating from the spinal cord. **e** The photograph of gross specimen cut off showed a huge black mass with a diameter approximately to $1.2 \times 1.8 \times 3.0$ cm. **f** HE $\times 40$ Pigmented spindle cells were arranged in fascicular or swirling pattern, with notable vascular tissue. **g** HE $\times 400$ Pigmented epithelioid cells were arranged in a sheet or a nest-like pattern with invasive growth and melanin pigments were presented in some cytoplasm. **h** HE $\times 400$ The nuclei and cytoplasm of tumor cells were positive for S-100. **i** HE $\times 400$ The cytoplasm of tumor cells were positive for Melan-A. **j** $\times 1200$ Transmission electron microscopy demonstrated the presence of melanosomes existed in the cytoplasm of tumor cells. **k** $\times 5000$ Continuous basal lamina (*arrowhead*) could be seen in tumor cells under electron microscopy (**d**). **l** Post-operative sagittal T1 MRI with contrast demonstrated no enhanced mass or nodule that was significantly. **m** Post-operative sagittal T2 MRI demonstrated syringomyelia also improved after tumor was removed. **n** Sagittal T1 MRI with contrast demonstrated a new mass with obvious heterogeneous enhancement at the previous surgical location (*arrowhead*). **o** Sagittal T2 MRI demonstrated a recurrent space-occupying mass with heterogeneous intensity (*arrowhead*) and spinal cord syringomyelia above and below the recurrence revealed to be even worse. **p** Axial T1 MRI with contrast demonstrated heterogeneous enhancement of the recurrent tumor within the spinal cord (*arrowhead*)

subsequently transferred to rehabilitation department. Three months later, muscle strength of the bilateral lower limbs of the patient recovered partially, presented with an American Spine Injury Association (ASIA) C examination below the involved cord level, but still can not walk. A post-operative magnetic resonance imaging (MRI) scan demonstrated no evidence for residual or recurrence, also, syringomyelia improved (Fig. 1l, m). One year after surgery, the patient was able to walk slowly and independently with a walker.

Since melanotic schwannoma (MS) was considered to be a low grade malignant tumor, and subtotal resection was performed together with no enhanced mass or nodule radiographically, oncologist did not recommend any adjuvant radiotherapy or chemotherapy. Close clinical follow-up and radiographic observation with semiannual MRI were recommended.

Six years post-operatively the patient suffered from back pain and weakness of lower limbs again, and that progressively got worse. Magnetic resonance imaging (MRI) was performed immediately and unfortunately, a new enhanced, space-occupying mass with an even bigger diameter at the previous surgical location was found (Fig. 1n–p), which indicated recurrence. Considering that



the recurrent tumor was larger in size, we recommend reoperation, however, the patient and his family refused. At present, the patient is still alive with paraplegia of both lower limbs, fecal and urine incontinence.

Literature review and analysis

Since Solomon et al. [5], had reported the first case of intramedullary Melanotic schwannoma (MS) in 1987, there were only nine cases had been reported in literature [4–12].

Now we present the 10th known one to date of intradural intramedullary MS. Where available, corresponding outcomes from 10 patients were summarized in Table 1. The average age of the 10 patients reviewed was 51.4 years and most ($n = 6$, 60%) were female. The majority of patients were diagnosed within thoracic segment ($n = 7$, 70%). Nine patients underwent microsurgical resection, one underwent fine needle aspiration. Most ($n = 8$, 80%) patients received gross total resection (GTR), whereas the present one received subtotal resection because of an invasive growth pattern. Only one patient received

Table 1 A literature review of 10 reported cases of intramedullary melanotic schwannoma, including the present report

No. literature index	Age (years)	Gender	Presentation	Duration of symptoms	Tumor localization	Treatment	Follow-up/outcome
1. Solomon et al. [5]	69	M	Right Bmwn-Sequard's syndrome	4 years	Caudal medulla-C3	GTR	No long term follow up data/ Sensory impairment deterioration after operation
2. Marchese et al. [6]	72	F	Quadriparesis	20 years	C4–C6	GTR	NA/partial neurological recovery
3. Sola-Pérez et al. [7]	63	F	Right cervical dorsal radicular pain	NA	C7–T1	Fine needle aspiration	NA/NA
4. Acciarri et al. [8]	44	F	Spastic quadriparesis	10 years	T2–T3	GTR	4 months/Partial neurological recovery
5. Santaguida et al. [9]	35	M	Right neck pain and right hemiparesis	10 months	C4–C6	GTR; RT and CT at recurrence	4 years/recurrence at 10–12 months, RT, CT, reoperation at 4 years, postoperative improvement
6. Mouchaty et al. [10]	56	F	Lower limbs were not improving correspondingly to her arms	>6 months	T12–L1	GTR	1 year/partial neurological recovery
7. Hoover et al. [11]	62	F	Radicular thighs pain, reduced strength and numbness in lower limbs, urinary urgency and incontinence	<6 months	T11	GTR	10 months/neurological recovery except sensory deficits
8. Pan SY, et al. 2014 [4]	23	F	Incomplete flaccid paraplegia with urinary incontinence	<6 months	T4–T5	GTR	3 years/near total neurological recovery except sensory deficits
9. Mohamed et al. [12]	43	M	Left-leg weakness	2 years	T9–T10	GTR	6 months/neurological recovery
10. Cheng et al. (present report)	47	M	Back pain, zonesthesia below papillary level, and left-leg weakness	14 months	T4–T5	Subtotal resection	6 years/recurrence, paraplegia, fecal and urine incontinence

M male, F female, NA not available, GTR gross total resection, RT radiotherapy, CT chemotherapy

radiotherapy and chemotherapy due to recurrence. Patients completed follow-up for 4–120 months, and 42.6 months on average, 80% of which had no recurrence.

Discussion

Melanotic schwannoma (MS) is a rare pathologic variant of schwannoma, characterized by comprising melanin-producing cells and ultrastructural features of schwann cells, accounting for less than 1% of primary peripheral nerve sheath tumors [13]. MS is subdivided microscopically into nonpsammomatous melanotic schwannoma (NPMS) and psammomatous melanotic schwannoma (PMS) depending on the presence of psammoma bodies [14]. MS can be sporadic or part of the Carney complex, a syndrome described by Carney, which consisting of myxomas (cardiac, cutaneous, and mammary), skin pigmentation, endocrine overactivity (Cushing's syndrome and acromegaly),

often accompanied with PMS [15]. However, it has not been associated with neurofibromatosis type 1 or 2 [9, 16]. Thus, it is necessary to search for clinicopathologic components of Carney complex. The present patient had no evidence of above clinical characteristics or family history, indicating probably a sporadic case. MS has been reported to present at a younger age than conventional schwannoma without gender predilection [11]. Most literatures have described MS as a histopathologically benign tumor, however, approximately 10–15% cases with malignant biological behaviour have been reported [9, 13, 14].

Although MS can occur in various tissues and organs (brain, stomach, bone, heart, bronchus, liver, pancreas, retroperitoneum, and parotid gland), the most common location is paraspinal nerve root and gastrointestinal tract [3, 17–19], and similar to conventional schwannoma, intramedullary MS is a vary rare entity. So far, only nine cases [4–12] of intramedullary MS have been reported and this is the 10th one to our knowledge describing this tumor.

Various explanations and hypotheses have been put forward to attempt explicating the tumor's unusual occurrence intramedullary. Hughes et al. [20]. argued that the occurrence was caused by displacing Schwann cells centrally during embryogenesis, and intramedullary spinal nerve fibers could occur infrequently. Ho et al. [21]. considered that perivascular bundles of peripheral nerves had the potential to displace Schwann cells intramedullary, which could normally occur. Acciarri et al. [8]. believed intramedullary MS was a neoplastic extension of Schwann cells through the insertion site of the dorsal root. However, MS tumor cells show microscopically the differentiation of the nerve sheath and the melanoma cells at the same time, which suggests that the tumor derives from neural crest. Thus, it is now generally considered that intramedullary MS may derive from disordered migration of undifferentiated pluripotent neural crest cells during neural tube closure, which may have the capacity to differentiate into both lineages [11, 12, 22, 23].

MRI has important diagnostic role in the intramedullary MS. Normally melanotic lesions will appear hyperintense on T1 weighted images and hypointense on T2 weighted images due to paramagnetism effect of melanin, and on post contrast would expect homogeneous enhancement [11, 12, 24]. However, MRI appearance varies as a result of different content and distribution of melanin, and only when the melanin content of tumor >10%, T1 weighted and T2 weighted images appear hyperintense and hypointense respectively. Hypointense on T2 weighted images is characteristic appearance of melanoma, but only occurs in about 25% of all cases and it may be heterogeneous in the presence of haemorrhage or maldistribution of melanin within the lesion, which is what most likely led to a radiographic misdiagnosis [11, 25]. In contrast, non-melanotic tumors such as standard schwannoma would typically demonstrate hypointense on T1 weighted images and hyperintense on T2 weighted images, and also be typically homogeneous enhancement, which would be useful for differential diagnosis.

As far as the treatment of intramedullary MS was concerned, complete microsurgical excision was considered as a curative, effective, and safe way by most of the previous reports [4–6, 8–12] and among these patients, most had no recurrence. To protect the spinal cord, We recommended using neurophysiologic monitoring routinely during resection. Usually, we monitored motor evoked potential (MEP) in 3–4 muscles (quadriceps femoris, biceps femoris, gastrocnemius and muscoli hippicus) and when the MEP of any of these muscles dropped lower than 50% or more, the resection would be suspended. If this occurred frequently, we might consider ending the resection. Our patient just underwent subtotal resection due to a more

invasive growth pattern with intensive adhesion and poor boundary, and suffered from local recurrence six years later. It just so happened that Santaguida C, et al. [9]. also reported a similar intramedullary MS case in 2004, who underwent rapid and multicentric recurrence after surgical excision. They pointed out that it was just because MS might derive from undifferentiated progenitor cells that had the capacity to differentiate into both Schwann and melanoma cells, if these primitive cells were either trapped or could migrate into intramedullary site during neural tube closure and then sequestered in an environment not conducive to either differentiated Schwann cells or melanocytes, intramedullary MS could result. Further more, some MS tumor cells might be prone to show more aggressive growth characteristics than the typical well differentiated Schwann cells occasionally.

Unless significant residue or recurrence, radiotherapy or chemotherapy were not recommended conventionally in most literatures [4, 8–12] when a gross total resection is possible, which was in line with our view, in spite of a subtotal resection in our patient. On the other hand, no evidence is available to support the efficacy of radiotherapy and chemotherapy due to lack of intramedullary MS cases. While we do not believe radiotherapy or chemotherapy is necessary or can effectively delay the recurrence even if a partial resection. Instead, we only recommend close MRI follow-up. In view of the above-mentioned facts, we recommend re-operation if recurrence occurs and semi-annual or annual MRI follow-up of patients with intramedullary MS which is our general procedure for spinal cord tumors following surgical resection. Unfortunately, our patient and his family refused further therapy for various reasons and we also lost the chance to know more.

Conclusions

Intramedullary melanotic schwannomas is exceedingly rare, and we present the 10th known case as well as the second of Asian ethnicity to date of a patient with a more invasive one than those reported before. These tumors' behavior is unpredictable and can have an aggressive clinical course such as recurrence and metastasis, in spite of malignant in only 10–15%. Microsurgical gross total resection is a curative, effective, and safe way that should be the goal of neurosurgical treatment since patients may benefit.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest. The authors alone are responsible for the content and writing of this article.

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