

# A Large Intramedullary Neurofibroma in the Thoracic Spinal Cord: Case Report

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## Abstract

Neurofibromas are occasionally present in spinal roots; however, an intramedullary neurofibroma is especially rare. Although a few cases of intramedullary neurofibromas in cervical spinal cord have been reported, to the best of our knowledge, there are no reports of intramedullary neurofibromas in thoracic spinal cord, and moreover, no reports have clearly reported immunohistochemical findings. We report a rare case of a large intramedullary neurofibroma in the thoracic spinal cord and show immunohistochemical examination of the tumor. A 52-year-old man presented with a 2-year history of progressive gait disturbance. Neurological examinations demonstrated complete motor and sensory deficit of his legs. Magnetic resonance imaging of the thoracic spine demonstrated an intramedullary enhancing mass within the spinal cord between T4 and T5 levels. The patient underwent T3–T6 laminectomy surgery. The dura mater was opened to reveal fusiform dilatation of the spinal cord and a midline myelotomy was performed. An intramedullary mass was revealed and could be resected totally. Histopathological examination revealed that the tumor cells exhibited spindle-shaped and wavy nuclei with abundant collagen, which resembled schwannoma or fibrous meningioma. By immunohistochemical examination, some tumor cells were positive for S-100 proteins; however, most tumor cells were strongly positive for CD34. From these pathological findings and immunohistochemical reactions, we diagnosed the intramedullary tumor as a neurofibroma.

Key words: CD34, intramedullary neurofibroma, S-100 proteins, spinal cord

## Introduction

Neurofibromas typically present most commonly as a cutaneous nodule, less often in a peripheral nerve, occasionally in spinal roots, and multiple neurofibromas are typically associated with neurofibromatosis (NF) 1.<sup>1–3)</sup> Histologically, neurofibromas are composed of neoplastic Schwann cells, fibroblasts, and perineurial cells (perineurial-like cells),<sup>2,4,5)</sup> which in a small number of cases, make it difficult to determine the differential diagnosis from schwannomas.<sup>2,6,7)</sup> An intramedullary spinal neurofibroma is very rare,<sup>8–16)</sup> and to the best of our knowledge, there are no reports of intramedullary neurofibromas in thoracic spinal cord, and moreover, no reports have clearly shown immunohistochemical findings. This report presents a large intramedullary neurofibroma of the thoracic spinal cord and we particularly show the histopathological findings

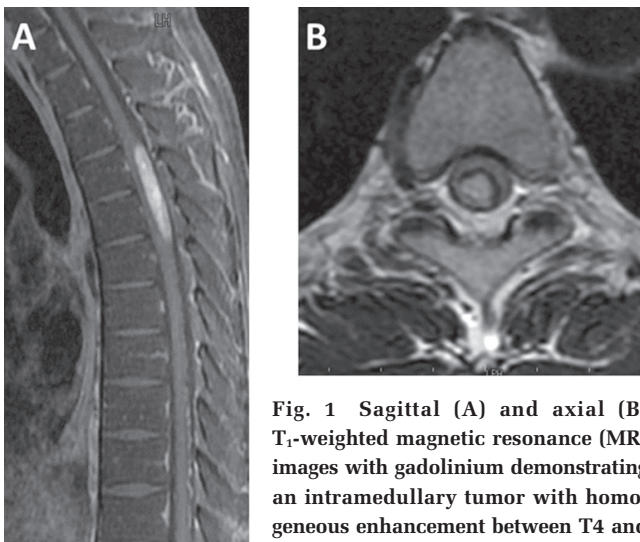
of the tumor, especially immunohistochemical findings of S-100 protein and CD34.

## Case Report

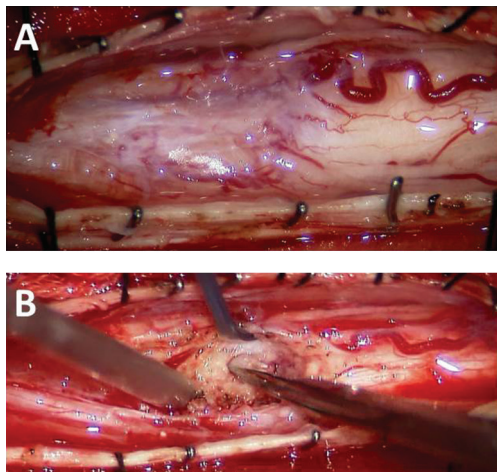
A 52-year-old man presenting with a 2-year history of progressive gait disturbance was referred to our hospital. He had neither a past history of NF1 nor any particular disease. Neurological examinations demonstrated complete motor and sensory deficit of his legs with bladder and bowel disturbance. Magnetic resonance (MR) imaging of the thoracic spine demonstrated the intramedullary lesion as a hyperintense mass on T<sub>1</sub>- and T<sub>2</sub>-weighted images between T4 and T5 levels. After gadolinium injection, homogeneous enhancement of the intramedullary lesion was visualized (Fig. 1A, B). Our preoperative diagnosis was ependymoma. The patient underwent surgery in the prone position. A T3–T6 laminectomy was performed to expose the lesion. Following dural opening, we found spinal cord swelling with a thick arachnoid membrane and thin pia mater (Fig. 2A). We confirmed that the tumor

was intraductal. A midline myelotomy was carried out and a grayish tumor immediately appeared (Fig. 2B). The tumor was sharply circumscribed and could be resected easily. During resection of the tumor, we found the posterior spinal root adhered to the dorsal part of tumor, and cut it. We performed total resection of the tumor with the proximal part of the posterior spinal root.

The grayish tumor had a firm consistency and homogeneous cut surface. Microscopically, in some parts of the tumor, tumor cells were composed of interlacing bundles of fibroblast-like cells with abundant collagen (Fig. 3A). These findings resembled a fibrous meningioma; however, neither whorl formation nor psammoma bodies could be seen. In other parts of the tumor, the tumor was characterized by high cellularity with spindle-shaped cells (Fig. 3B).



**Fig. 1** Sagittal (A) and axial (B) T<sub>1</sub>-weighted magnetic resonance (MR) images with gadolinium demonstrating an intraductal tumor with homogeneous enhancement between T4 and T5 level mimicking an ependymoma.



**Fig. 2** Intraoperative photographs. A: Intraoperative photograph after opening dura showing swollen spinal cord with thick arachnoid membrane. B: Intraoperative photograph after midline myelotomy showing an intraductal tumor.

These findings resembled a cellular schwannoma; however, no typical palisading could be seen. Neither mitosis nor necrotic foci were identified in the tumor. Immunohistochemical staining for S-100 protein showed that the tumor cells were partially positive; however, most of fibrous areas with fibroblast-like cells were negative (Fig. 3C). Immunohistochemical staining for CD34 showed that most of the tumor cells were diffusely positive and, especially, fibrous areas with fibroblast-like cells were strongly positive (Fig. 3D). Neurofilament staining showed a few axons in the tumor tissues (Fig. 3E). Most tumor cells were negative for epithelial membrane antigen (EMA) except only limited numbers of EMA-positive cells that was considered to be residual perineurium (Fig. 3F). The tumor cells were negative for glial fibrillary acid protein (GFAP). The Ki-67 labeling index was less than 0.1%. Based on these immunohistochemical findings, especially reactivity for S-100 protein, CD34, and neurofilament, the diagnosis of the intraductal tumor was neurofibroma, not schwannoma.

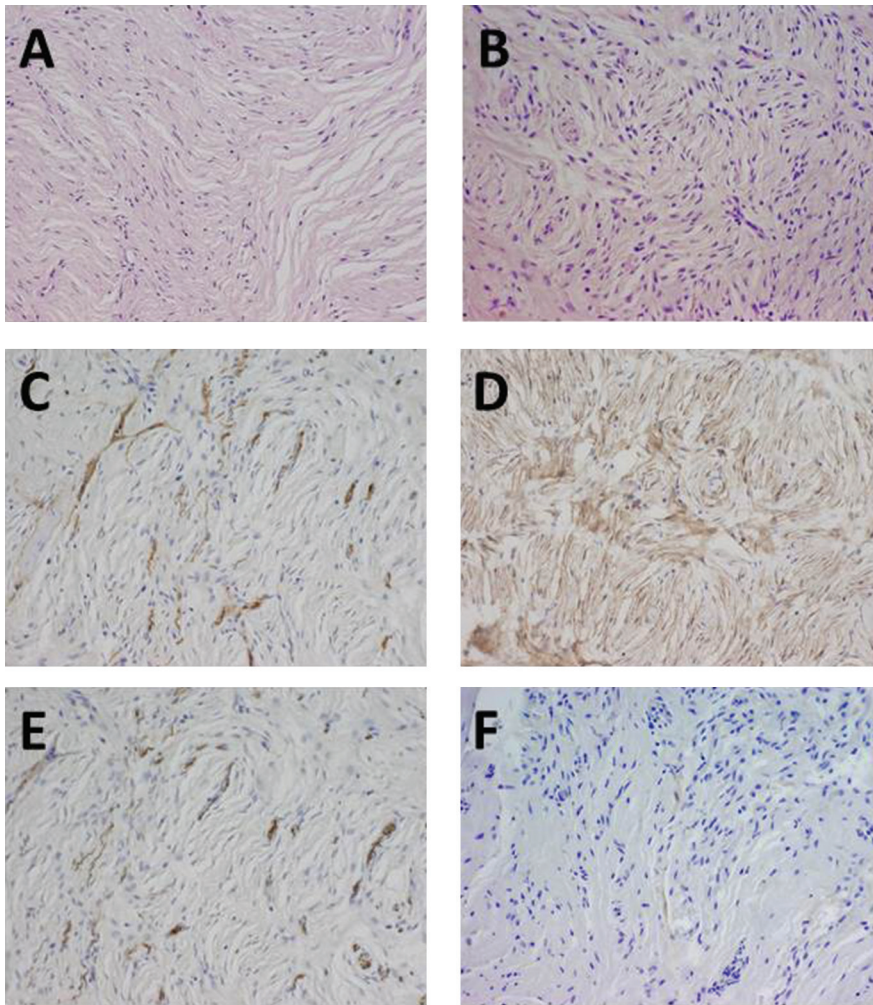
His postoperative course was uneventful, and his neurological deficits were unchanged after the operation. Postoperative MR imaging demonstrated no residual tumor.

## Discussion

Intraductal spinal neurofibromas are very rare. In the large Mayo Clinic series reported by Rasmussen et al., no intraductal lesion was present among 163 cases of spinal neurofibromas.<sup>12</sup> Tonnis et al. reported only one intraductal case among 82 cases of spinal neurofibromas.<sup>15</sup> Nittner also found one intraductal case among their 78 cases of spinal neurofibromas.<sup>10</sup> We searched the titles of papers including “intraductal neurofibromas” using PubMed, and to the best of our knowledge, there are only 6 case reports of intraductal neurofibromas (Table 1).<sup>8,9,11,13,14,16</sup> There are no cases in thoracic spinal cord.

It seems to be difficult to identify the exact numbers of intraductal spinal neurofibromas previously reported from an extensive review of the literature because intraductal neurofibromas might be confused with intraductal schwannomas (neurinoma or neurilemoma),<sup>17–20</sup> neuromas,<sup>21–23</sup> and intraductal aberrant nerve fibers.<sup>23–25</sup>

Neurofibromas are composed of a mixture of cell types including Schwann cells, perineurial-like cells, and fibroblasts.<sup>2,4,5</sup> To distinguish neurofibromas from schwannomas and neuromas, careful and precise pathological examinations should be performed. Immunohistochemical staining for S-100 protein has been used classically as a marker in the differential diagnosis of neurofibromas from schwannomas;<sup>2,4,5</sup> however, occasionally, S-100 protein might not reliably distinguish these tumors,<sup>2,6</sup> namely, the immunohistochemical reaction for S-100 protein is positive in both tumors. Usually, the immunoreactivity of S-100



**Fig. 3** Histological examination of an intramedullary tumor. **A:** Photomicrograph showing interlacing bundles of fibroblast-like cells with abundant collagen. HE stain, magnification  $\times 200$ . **B:** Photomicrograph showing high cellularity with spindle-shaped cells. HE stain, magnification  $\times 200$ . **C:** Immunohistochemical staining for S-100 protein showing that the tumor cells were partially positive; however most of fibrous areas with fibroblast-like cells were negative. Magnification  $\times 200$ . **D:** Immunohistochemical staining for CD34 showing that most tumor cells were diffusely positive. Magnification  $\times 200$ . **E:** Neurofilament staining showing a few axons in the tumor tissues. Magnification  $\times 200$ . **F:** Epithelial membrane antigen (EMA) staining showing that most tumor cells were negative except limited numbers of EMA positive cells. Magnification  $\times 200$ .

**Table 1** Summary of cases of intramedullary neurofibroma

Case no.	Author (year)	Age/sex	Symptoms	Location	Radiological examination	NF1 or NF2	Pathological examination
1.	Gelabert et al. (1996) <sup>8)</sup>	50/F	Tetraparesia	C2–4	MRI	None	HE
2.	Oka et al. (1992) <sup>11)</sup>	62/F	Paresthesia of hands and feet	C3–4	CT, MRI	None	HE, Bodian
3.	Sharma V and Newton (1990) <sup>14)</sup>	20/M	Weakness in upper limbs	C7	Myelogram, CT	None	HE
4.	Gelabert González et al. (1985) <sup>9)</sup>	29/F	Paresthesia of hands	C2–4	Myelogram, CT	None	HE
5.	Sharma R et al. (1984) <sup>13)</sup>	27/M	Weakness in upper and lower limbs	C5–6	Myelogram	None	HE
6.	Young et al. (1983) <sup>16)</sup>	33/F	Paresthesia and weakness in legs	Conus medullaris	Myelogram	None	HE
7.	Present case	52/M	Paraparesia, bladder, and rectal disturbance	T4–5	MRI	None	HE, S-100, CD34

C: cervical, CT: computed tomography, F: female, HE: hematoxylin and eosin, M: male, MRI: magnetic resonance imaging, NF: neurofibromatosis, T: thoracic.

protein is higher in schwannomas than neurofibromas.<sup>2,6,26)</sup> In our case, tumor cells were partially positive for S-100,

which suggested that the tumor might be a neurofibroma rather than a schwannoma.



Recently, the usefulness of immunohistochemical staining for CD34 has been reported to differentiate neurofibromas from schwannomas.<sup>26)</sup> CD34 was first identified as a marker of hematopoietic progenitor cells, and it is also a marker of nerve sheath cells.<sup>7,26)</sup> The nature of CD34-positive cells is thought to correspond to that of endoneurial fibroblasts. Neurofibromas are strongly positive for CD34, unlike most schwannomas. In our case, CD34 was diffusely positive for most tumor cells, and was especially strongly positive for fibroblast-like cells. S-100 protein was demonstrated in some parts of tumor cells, and moreover, negative in fibrous areas with fibroblast-like cells. These findings suggested that the tumor was a neurofibroma. Solitary fibrous tumors (SFTs) also should be distinguished from neurofibromas. Although both tumors are positive for CD34, SFT are usually negative for S-100 protein.<sup>27)</sup> Immunohistochemical reactions for S-100 protein suggested this tumor was not a SFT. In addition, neurofibromas grow within and envelop the nerve of origin, and neurofilaments are seen as entrapped nerve remnants in tumors, which are not present in schwannomas and SFT.<sup>2)</sup> Limited numbers of EMA-positive cells also can be seen as residual perineurium in neurofibromas.<sup>2)</sup>

Various hypotheses have been suggested to explain the origin of intramedullary spinal neurofibromas as follows: (a) aberrant neural crest cells displaced into the spinal cord during embryonic development;<sup>19,28)</sup> (b) intramedullary perivascular nerve bundles in the spinal cord;<sup>29,30)</sup> (c) aberrant intramedullary nerve fibers;<sup>23,24,25,31)</sup> (d) posterior roots near the root entry zone and development of tumors in the pia mater;<sup>17,18,20)</sup> and (e) transformation of pial cells of neuroectodermal origin into Schwann cells.<sup>32)</sup> In the current case, the tumor was situated at a posterior site in the spinal cord in close proximity to the dorsal root entry zones. The tumor tightly adhered to the dorsal root. It seems likely that the tumor in our case arose from the dorsal root sheath zone and grew into the pia mater considering operative findings. Therefore this tumor might not be “pure” intramedullary neurofibroma in a sense.

### Conflicts of Interest Disclosure

The authors declare that they have no conflict of interest. All authors who are members of The Japan Neurosurgery Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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