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

Hidetaka ARISHIMA,1 Ryuhei KITAI,1 Toshiaki KODERA,1 Shinsuke YAMADA,1 and Ken-ichiro KIKUTA1

1Department of Neurosurgery, University of Fukui, Yoshida-gun, Fukui

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) 1,2,3) Histologically, neurofibromas are composed of neoplastic Schwann cells, fibroblasts, and perineurial cells (perineurial-like cells),2,4,5) which in a small number of cases, make it difficult to determine the differential diagnosis from schwannomas.2,6,7) An intramedullary spinal neurofibroma is very rare,8,9) 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 T1- and T2-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...
Intramedullary Neurofibroma in the Thoracic Spinal Cord

was intramedullary. 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). 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 intramedullary 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

Intramedullary spinal neurofibromas are very rare. In the large Mayo Clinic series reported by Rasmussen et al., no intramedullary lesion was present among 163 cases of spinal neurofibromas. Tonnis et al. reported only one intramedullary case among 82 cases of spinal neurofibromas. Nittner also found one intramedullary case among their 78 cases of spinal neurofibromas. We searched the titles of papers including “intramedullary neurofibromas” using PubMed, and to the best of our knowledge, there are only 6 case reports of intramedullary neurofibromas (Table 1). There are no cases in thoracic spinal cord.

It seems to be difficult to identify the exact numbers of intramedullary spinal neurofibromas previously reported from an extensive review of the literature because intramedullary neurofibromas might be confused with intramedullary schwannomas (neurinoma or neurilemoma), neuromas, and intramedullary aberrant nerve fibers. Neurofibromas are composed of a mixture of cell types including Schwann cells, perineurial-like cells, and fibroblasts. 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; however, occasionally, S-100 protein might not reliably distinguish these tumors, namely, the immunohistochemical reaction for S-100 protein is positive in both tumors. Usually, the immunoreactivity of S-100

Neurol Med Chir (Tokyo) 54, September, 2014
protein is higher in schwannomas than neurofibromas.\textsuperscript{2,6,26} In our case, tumor cells were partially positive for S-100, which suggested that the tumor might be a neurofibroma rather than a schwannoma.

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) | 50/F    | Tetraparesia                    | C2–4        | MRI                      | None       | HE                      |
| 2.       | Oka et al. (1992)      | 62/F    | Paresthesia of hands and feet   | C3–4        | CT, MRI                  | None       | HE, Bodian              |
| 3.       | Sharma V and Newton (1990) | 20/M  | Weakness in upper limbs         | C7          | Myelogram, CT            | None       | HE                      |
| 4.       | Gelabert González et al. (1985) | 29/F  | Paresthesia of hands            | C2–4        | Myelogram, CT            | None       | HE                      |
| 5.       | Sharma R et al. (1984) | 27/M    | Weakness in upper and lower limbs | C5–6        | Myelogram                | None       | HE                      |
| 6.       | Young et al. (1983)    | 33/F    | Paresthesia and weakness in legs | Conus medullaris | Myelogram             | None       | HE                      |
| 7.       | Present case           | 52/M    | Parapresia, 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.
Recently, the usefulness of immunohistochemical staining for CD34 has been reported to differentiate neurofibromas from schwannomas. CD34 was first identified as a marker of hematopoietic progenitor cells, and it is also a marker of nerve sheath cells. 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. 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. Limited numbers of EMA-positive cells also can be seen as residual perineurium in neurofibromas.

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; (b) intramedullary perivascular nerve bundles in the spinal cord; (c) aberrant intramedullary nerve fibers; (d) posterior roots near the root entry zone and development of tumors in the pia mater; and (e) transformation of pial cells of neuroectodermal origin into Schwann cells. 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 though the website for JNS members.

References

1) Halliday AL, Sobel RA, Martuza RL: Benign spinal nerve sheath tumors: their occurrence sporadically and in neurofibromatosis types 1 and 2. J Neurosurg 74: 248–253, 1991
2) Scheithauer BW, Louis DN, Hunter S, Woodruff JM, Antonescu CR: Neurofibroma, in Louis DN, Ogaki H, Wiestler OD, Cavenee WK (eds): WHO classification of tumours of the central nervous system, ed 4. Lyon, IARC, WHO press, 2007, pp 156–157
3) Seppälä MT, Haltia MJ, Sankila RJ, Jääskeläinen JE, Heiskanen O: Long-term outcome after removal of spinal neurofibroma. J Neurosurg 82: 572–577, 1995
4) Hirose T, Sano T, Hizawa K: Ultrastructural localization of S-100 protein in neurofibroma. Acta Neuropathol 69: 103–110, 1986
5) Ushigome S, Takakuwa T, Hyuga M, Tadokoro M, Shinagawa T: Perineurial cell tumor and the significance of the perineurial cells in neurofibroma. Acta Pathol Jpn 36: 973–987, 1986
6) Fine SW, McClain SA, Li M: Immunohistochemical staining for calretinin is useful for differentiating schwannomas from neurofibromas. Am J Clin Pathol 122: 552–559, 2004
7) Naber U, Friedrich RE, Glatzel M, Mautner VF, Hagel C: Podoplanin and CD34 in peripheral nerve sheath tumours: focus on neurofibromatosis 1-associated atypical neurofibroma. J Neurooncol 103: 239–245, 2011
8) Gelbert M, Prieto A, Sobrío A, García-Pravos A, Bandin F, Bollard A, Calle J, García-Allut A: [Cervical intramedullary neurofibroma]. Rev Neurol 24: 836–837, 1996 (Spanish)
9) Gelbert González M, García Allut A, Conde Alonso C, Bollard Babala A, Martinez Rumbo R, Reyes Olivares F: Intramedullary spinal neurofibroma diagnosed with computed tomography: report of a case. Neurosurgery 16: 543–545, 1985
10) Nittner K: Spinal meningiomas, neurinomas, neurofibromas and hourglass tumors, in Vinken PJ, Bruyn GW (eds): Handbook of Clinical Neurology. New York, American Elsevier Publishing, vol 20, pt 2, pp 177–322
11) Oka H, Tachibana S, Yada K, Suwa T, Iida H, Mii K: Intramedullary neurofibroma in the cervical spinal cord; a case report. No Shinkei Geka 20: 599–603, 1992 (Japanese)
12) Rasmussen TB, Kernohan JW, Adson AW: Pathologic classification, with surgical consideration, of intraspinal tumors. Ann Surg 111: 513–530, 1940
13) Sharma R, Tandon SC, Mohanty S, Gupta S: Intramedullary neurofibroma of the cervical spinal cord: case report with review of the literature. Neurosurgery 15: 546–548, 1984
14) Sharma V, Newton G: Cervical intramedullary neurofibroma. J Korean Med Sci 5: 165–167, 1990
15) Tonnis W, Friedmann G, Nittner K: [Roentgenological diagnosis and differential diagnosis of intraspinal tumors with a reference to clinical symptomatology]. Fortschr Geb Rontgenstr Nuklearmed 88: 288–301, 1958 (German)
16) Young HA, Robb P, Hardy DG: Large intramedullary neurofibroma of the conus medullaris: case report. Neurosurgery 13: 48–51, 1983
17) Darvish BS, Balakrishnan V, Maitra R: Intramedullary ancient schwannoma of the cervical spinal cord: case report and review of literature. J Clin Neurosci 9: 321–323, 2002
18) Mason TH, Keigher HA: Intramedullary spinal neurilemoma: case report. J Neurosurg 29: 414–416, 1968
19) Vailati G, Occhiogrosso M, Troccoli V: Intramedullary thoracic schwannoma. Surg Neurol 11: 60–62, 1979
20) Wood WG, Rothman LM, Nussbaum BE: Intramedullary neurilemoma of the cervical spinal cord. Case report.

Neurol Med Chir (Tokyo) 54, September, 2014
21) Arishima H, Takeuchi H, Tsunetoshi K, Kodera T, Kitai R, Kikuta K: Intraoperative and pathological findings of intramedullary amputation neuroma associated with spinal ependymoma. Brain Tumor Pathol 30: 196–200, 2013

22) Johnson MW, Burger PC: Intramedullary amputation neuromas associated with spinal ependymomas. Am J Surg Pathol 33: 639–643, 2009

23) Sung JH, Mastri AR, Chen KT: Aberrant peripheral nerves and neuromas in normal and injured spinal cords. J Neuropathol Exp Neurol 40: 551–565, 1981

24) Hughes JT, Brownell B: Aberrant nerve fibres within the spinal cord. J Neurol Neurosurg Psychiatr 26: 528–534, 1963

25) Koeppen AH, Ordinario AT, Barron KD: Aberrant intramedullary peripheral nerve fibers. Arch Neurol 18: 567–573, 1968

26) Hirose T, Tani T, Shimada T, Ishizawa K, Shimada S, Sano T: Immunohistochemical demonstration of EMA/Glut1-positive perineurial cells and CD34-positive fibroblastic cells in peripheral nerve sheath tumors. Mod Pathol 16: 293–298, 2003

27) Paulus W, Scheithauer BW, Perry A: Mesenchymal, non-meningothelial tumours, in Louis DN, Ogaki H, Westler OD, Cavenee WK (eds): WHO classification of tumours of the central nervous system, ed 4. Lyon, IARC, WHO press, 2007, pp 173–177

28) 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 61: 34–43; discussion 44, 2004

29) Riggs HE, Clary WU: A case of intramedullary sheath cell tumor of the spinal cord; consideration of vascular nerves as a source of origin. J Neuropathol Exp Neurol 16: 332–336, 1957

30) Scott M, Bentz R: Intramedullary neurilemmoma (neurinoma) of the thoracic cord. A case report. J Neuropathol Exp Neurol 21: 194–200, 1962

31) Adelman LS, Aronson SM: Intramedullary nerve fiber and Schwann cell proliferation within the spinal cord (schwannosis). Neurology 22: 726–731, 1972

32) Russell DS, Rubinstein LJ: Pathology of Tumors of Nervous System, ed 3. London, Edward Arnold, 1971, pp 36–37

Address reprint requests to: Hidetaka Arishima, MD, Department of Neurosurgery, University of Fukui, 23-3, Matsuokashimoizuki, Elheiji-cho, Yoshida-gun, Fukui 910-1193, Japan. e-mail: ari@u-fukui.ac.jp