A Case of Spinal Ependymoma Developed in the Extramedullary Location: A Case Report and Literature Review

Yasuhide MAKINO,1 Yoshifumi KAWANABE,1 Motoaki FUJIMOTO,1 Tsukasa SATO,1 and Minoru HOSHIMARU2

1The Department of Neurosurgery, Shizuoka General Hospital, Shizuoka, Shizuoka, Japan
2Shinaikai Spine Center, Katano Hospital, Katano, Osaka, Japan

Abstract

Intradural extramedullary (IDEM) ependymoma except for tumors originated from the filum terminale or conus medullaris is rare. The present study showed a case of IDEM ependymoma. A 16-year-old boy was referred to our hospital with a complaint of right hypochondriac pain and motor weakness in his right leg. MRI revealed a solitary intradural tumor at Th5–8 level with syringomyelia at Th2–4 level. Microscopic total tumor resection was performed with right hemi-laminectomy of Th4–9. Histological diagnosis was ependymoma (WHO grade 2). Although his leg weakness was worsened transiently, he showed improvement in leg weakness being able to go up and down the stairs 1 month after the surgery. There was no tumor recurrence until now, 7 years after the surgery, without any adjunctive therapies. A total of 44 cases of IDEM ependymoma had been reported in the past literatures. They are thought to arise from ependymal cells which remained during the process of neural tube closure. Like intramedullary ependymomas, most of the IDEM ependymomas have clear border to surrounding tissue and often removed completely. However, a small number of recurrences and malignant transformations had been reported after complete resections despite benign histological features tumors. In the case of totally resected low grade IDEM ependymoma, it is thought to be reasonable to perform long-term periodical radiographic follow-up without postoperative adjunctive therapy.

Keywords: ependymoma, intradural extramedullary spinal cord neoplasms

Introduction

Ependymoma is the most common spinal intramedullary tumor in adults and arises from ependymal cells at the central canal of spinal cord. Except for the tumors that occurred in the filum terminale or the conus medullaris, spinal ependymoma rarely develops as an intradural extramedullary (IDEM) tumor. IDEM ependymoma had been described only in some case reports; therefore, there is no enough knowledge on its clinical characteristics.

We reported a case of IDEM ependymoma surgically treated in our hospital with a review of the past literatures.

Case Presentation

A 16-year-old boy was referred to our hospital from an orthopedic clinic with a complaint of right hypochondriac pain and motor weakness in his right leg. He had no specific past medical history. Three years before, he had recognized asymptomatic muscle atrophy of the right leg, and he came to disable to run 10 months before. Right hypochondriac pain appeared 2 months before. His neurological symptoms at the first time visit are described as follows:

1) Muscle weakness in his right lower limb valued as MMT 4/5 in each.
2) Sensory disturbance in body trunk and lower limbs on both sides with niveau at Th6 dermatome.
3) Abnormal exaggeration of patellar tendon reflex and achilles tendon reflex on both sides.
4) No vesico-rectal disturbance.

MRI of thoracic spine revealed a solitary intradural tumor at Th5–8 level that showed iso-intensity in T1-weighted image and hyper-intensity in T2-weighted image compared with the spinal cord, and was slightly enhanced with Gd-DTPA (Fig. 1A–1C). In the axial section, the lesion occupied most of the thecal sac compressing the spinal cord unilaterally to the left side indicating that the tumor had extra-medullary location. Demarcation between the lesion and the spinal cord was clear. The compressed spinal cord was deformed in crescent shape (Fig. 1D and 1E), and at Th5 level the ventral part of the deformed spinal cord was involved into the tumor (D; arrow). (F–H) T2-weighted images of postoperative MRI (sagittal scan (F) and axial scans (G and H)). The tumor was completely resected, and compression of the spinal cord was improved with some residual deformity. (I and J) Microscopic view of the stained tissue specimens (hematoxylin & eosin). They showed perivascular pseudo-rosettes, which is a typical characteristic of ependymoma. (K and L) Immunohistochemical analysis of the specimens (GFAP (K) and MIB-1 (L)). GFAP-positive cells were observed especially in perivascular region (K). MIB-1 positive cells were exceptional (L).
Extramedullary Spinal Ependymoma

of intramedullary tumor (Fig. 1D). A syringomyelia was found cranial to the lesion at Th2–4 level (Fig. 1A). With these findings, this tumor was supposed to have natures of both intramedullary and extramedullary locations. The most possible diagnosis was ependymoma with extramedullary extension, and the differential diagnoses were subependymoma, neurinoma, and meningioma.

Microscopic tumor resection was performed with right hemi-laminectomy of Th4–9 (Fig. 2A). The extramedullary tumor was observed directly without myelotomy (Fig. 2B). The tumor was covered with the pia mater without any adhesion to the dura nor any connection to the nerve roots. Because dissection plane with the spinal cord was quite clear, microscopic total resection of tumor was achieved (Fig. 2C). The postoperative MRI showed total removal of the tumor and shrinkage of the syrinx (Fig. 1F–1H). Histological diagnosis was ependymoma (WHO grade 2) (Fig. 1I–1L). Immediately after the surgery, his leg weakness was worsened up to 2/5 in MMT evaluation on the right side and 4/5 on the left. Hypesthesia in his both legs was left unchanged. One month after the surgery, he showed improvement in leg weakness being able to go up and down the stairs by himself, and the leg hypesthesia also improved to be left only on the right side. Because the tumor was diagnosed as WHO grade 2 ependymoma and completely resected, we did not perform any adjunctive therapy. The periodical MRI scan has been performed, and there was no tumor recurrence until now, 7 years after the surgery.

Review of the Literatures

The case reports on IDEM ependymoma except for the lesion in the filum terminale and the conus medullaris were searched, and 44 cases in 41 articles were found finally. Characteristics of all 45 cases (including the present case) are summarized in Table 1. There were more women than men (19 men and 26 women), and tumor location was mainly in thoracic level; two tumors were in cranio-cervical junction, six in cervical, 23 in thoracic, four tumors lay from cervical to thoracic level, and 10 cases showed multiple lesions. Patients showed pain most frequently, and paraparesis, paresthesia, and/or sensory loss were other main symptoms. Except for the cases of multiple lesions, in preoperative axial MRI images which were presented in 32 cases, the number of ventral lesions was almost equal to that of dorsal lesions (ventral: 10 and dorsal: 13), and six tumors located laterally and three were dumbbell-shaped tumors (Fig. 3).

The major approach to expose dura mater was laminectomy, and cranietomy was performed or combined with it in three cranio-cervical junction tumors. In two of three cases of dumbbell-shaped ependymoma, additional technique to laminectomies was performed and they were described as an extended laminectomy or a spinosectomy. A less invasive technique, hemilaminectomy was selected in three cases, including the present case, and complete resection of tumor was achieved in each case. These three cases were two tumors located in dorsal-lateral of spinal canal and a tumor in lateral (the present case). In one case of thoracic...
In 35 cases, operative findings on relationship between the tumor and surrounding structures were described. Seven tumors had intramedullary component. In 28 cases without intramedullary component, 16 tumors had adhesion or connection with surrounding structures as follows: there were connecting tissues with spinal cord in four cases and nerve root in two respectively; nerve root was involved in tumor in two, and attachment to pia was seen in nine. In 32 cases in which preoperative MRI axial images were available, operative findings were obtained in 26 cases (Fig. 3). None of the lateral type and dumbbell-type tumors was separated from spinal cord or root, but there was no significance about the frequency of adhesion between these two types and other location types (dorsal-medial, dorsal-lateral, ventral-medial, and ventral-lateral type) by Fisher’s exact study using JMP Pro version 15.1.0 software (SAS Institute, Cary, NC, USA).

In many cases surgeon could specify the clear border of tumor using operative microscope. In 10 cases total resection of the tumor was not achieved. The reasons for tumor residuum in these 10 cases were as follows: four cases with intramedullary portion, four cases with multiple lesion or dissemination, one case with giant cystic lesion, and one case in which the tumor had firm adhesions with both spinal cord and nerve roots.

Histological diagnoses of the 45 tumors were 29 ependymoma (WHO grade 2), nine anaplastic ependymoma (WHO grade 3), five myxopapillary ependymoma, and two tanycytic ependymoma. Postsurgical treatment was performed in 13 cases that included six anaplastic ependymoma, six grade 2 ependymoma (three multiple lesions and three not completely resected), and one multiple myxopapillary ependymoma. On another view, in seven grade 2 ependymoma which was reported with residuum after surgery, five received adjuvant therapy. Conventional radiotherapy was performed in 11 cases and proton emission therapy in one. Chemotherapy with carboplatin was performed in one case, and chemoradiotherapy with temozolomide or carboplatin was selected in one case in each. In 29 grade 2 ependymoma cases, 23 cases did not receive postsurgical treatment, and six cases received postsurgical treatments because of the tumor residue. In nine anaplastic ependymoma cases, three cases were observed without postsurgical treatment, and six cases received postsurgical treatment whether the tumor removals showed total resection. In five myxopapillary ependymomas, all of which showed

| Number of cases | 45 |
|-----------------|----|
| Total number    |    |
| Sex             |    |
| Male : Female   | 19:26 |
| Age             |    |
| 10–19           | 3  |
| 20–39           | 18 |
| 40–59           | 18 |
| 60–             | 6  |
| Level           |    |
| Cranio-cervical junction | 2 |
| Cervical spine  | 6  |
| Cervical-thoracic spine | 4 |
| Thoracic spine  | 23 |
| Multiple        | 10 |
| Location (showed in axial plane) |    |
| Dorsal (and medial or lateral) | 13 (4 or 9) |
| Ventral (and medial or lateral) | 10 (6 or 4) |
| Lateral         | 9  |
| No detail (multiple or no axial image) | 13 |
| Diagnosis       |    |
| Myxopapillary ependymoma (WHO grade 1) | 5 |
| Ependymoma (WHO grade 2) | 29 |
| Tanycytic ependymoma (WHO grade 2) | 2 |
| Anaplastic ependymoma (WHO grade 3) | 9 |
| The site of adhesion or pia attachment (wrote in the records of surgeries) |    |
| Cord            | 12 |
| Root            | 3  |
| Cord and root   | 1  |
| No attachment   | 12 |
| Intramedullary  | 7  |
| No detail       | 10 |
| Initial symptom |    |
| Pain            | 35 |
| Sensory loss    | 27 |
| Paresthesia     | 20 |
| Paraparesis sensory loss | 18 |
| Bladder and rectal disorder | 13 |
| Gait disturbance| 8  |
| Monoparesis     | 5  |
| Upper limb weakness | 7 |

IDEM: intradural extramedullary.
multiple lesions, one case received radiotherapy and the others were observed. Two tanycytic ependymomas were completely resected and the patients were observed without postsurgical treatment.

There were nine cases of recurrence. In four cases, malignant transformations from grade 2 to grade 3 lesions were observed. In other five recurrent cases, histological diagnoses were grade 2 ependymoma in two, and anaplastic ependymoma in three, and recurrence pattern was recorded as two intracranial metastases, two dissemination, and one drop metastasis. The intervals between initial surgery and recurrence were 6 months to 2 years.

**Discussion**

Ependymoma is thought to arise from ependymal cell. In the spinal cord, ependymal cells are mainly...
arrayed at the central canal, but during the process of neural tube closure, some ependymal cells are supposed to remain and to become the origin of IDEM ependymoma. In the present case, the spinal ependymoma was located extramedullary compressing the spinal cord unilaterally. This peculiar location implied the presence of heterotopic ependymal cells apart from the central canal as origins of tumor. In the review of IDEM ependymomas described by Das et al., they classified all 54 reported cases into four types, and showed “pure IDEM ependymoma” was the most common type (32 cases). Like their report, our literature review revealed that almost all IDEM ependymoma had no connection with spinal cord, nerve root, or dura mater, and the present case was also thought to be “pure IDEM ependymoma.”

In the first step of surgery, laminectomy was the most common technique to approach the dura mater and tumors, and extended technique was performed in some cases. However, some tumors which located laterally in spinal canal can be resected completely with hemilaminectomy. In preoperative imaging, it is difficult to distinguish IDEM ependymoma from meningoim or schwannoma. Sometimes it even shows dumbbell tumor pattern extending into paravertebral location. In many cases, IDEM ependymoma was encapsulated and has no attachment with dura mater or nerve root, unlike meningioma or schwannoma, and thus this tumor was often removed completely. But, based on the review of the present study, it is difficult to decide whether a tumor attaches spinal cord or nerve root if there is no finding of intramedullary tumors. In summary, many IDEM ependymoma can be resected completely, but it is essential to confirm the presence of attachment during surgery, and maximum safe resection should be considered in the case with tight adhesion to a spinal cord or a nerve root.

Because of the small number of cases, there is no standard postsurgical treatment for IDEM ependymoma. Many cases were only followed-up with serial imaging study. If postsurgical treatment was needed, many authors selected radiotherapy, and many cases had been observed without recurrence. On the other hand, even in the cases of grade 2 ependymoma which was removed totally, unpreferable courses such as malignant transformation or drop metastasis were sometimes reported. According to these facts, in the case of totally resected low grade IDEM ependymoma, it is thought to be reasonable to perform long-term periodical radiographic follow-up without postoperative adjunctive therapy.

Conclusion

We reported a rare case of IDEM ependymoma. It was totally resected without major deterioration of neurological functions, and there was no recurrence for more than 7 years after the surgery. Further follow-up was thought to be necessary.

Conflicts of Interest Disclosure

The authors have no conflicts of interest.

References

1) Wagle WA, Jaufman B, Mincy JE: Intramedullary ependymoma: MR-pathologic correlation. J Comput Assist Tomogr 12: 705–707, 1988
2) Katoh S, Ikata T, Inoue A, Takahashi M: Intramedullary ependymoma. A case report. Spine (Phila Pa 1976) 20: 2036–2038, 1995
3) Wolfia CE, Azzarelli B, Shah MV: Primary extramedullary ependymoma of the thoracic spine. J Neurosurg 87: 643, 1997
4) Payer M, Yonekawa Y, Imhof HG: Solitary thoracic intramedullary ependymoma: case report and review of the literature. Spine (Phila Pa 1976) 25: 1993–1995, 2000
5) Hentschel SJ, McCutcheon IE, Ginsberg L, Weinberg JS: Exophytic ependymomas of the spinal cord. Acta Neurochir (Wien) 146: 1047–1050, 2004
6) Schuurmans M, Vanneste JA, Verstegen MJ, van Furth WR: Spinal extramedullary anaplastic ependymoma with spinal and intracranial metastases. J Neurooncol 79: 57–59, 2006
7) Benzagmout M, Boujraf S, Oulali N, et al.: Intramedullary ependymoma: is there constantly a hormonal relationship? Surg Neurol 70: 536–538; discussion 538, 2008
8) Duffau H, Gazzaz M, Kujas M, Fohanno D: Primary intramedullary ependymoma: case report and review of the literature. Spine (Phila Pa 1976) 25: 1993–1995, 2000
9) Graça J, Gültasli N, D’Haene N, Brotch J, Salmon I, Balériaux D: Cystic extramedullary ependymoma. AJNR Am J Neuroradiol 27: 818–821, 2006
10) Schuurmans M, Vanneste JA, Verstegen MJ, van Furth WR: Spinal extramedullary anaplastic ependymoma with spinal and intracranial metastases. J Neurooncol 79: 57–59, 2006
11) Benzagmout M, Boujraf S, Oulali N, et al.: Intramedullary ependymoma: is there constantly a hormonal relationship? Surg Neurol 70: 536–538; discussion 538, 2008
12) Fasoli F, Minniti G, Serio N, et al.: Primary intramedullary ependymoma: imaging findings and review of the literature. A case report. Neuroradiol J 21: 239–243, 2008
13) De Bonis P, Montano N, Cioni B, et al.: Primary extramedullary extramedullary ependymoma of the thoracic...
Extradural Spinal Ependymoma

27) Morselli C, Ruggeri AG, Pichieri A, Marotta N, Anzidei M, Dell’Inni R: Intradural extramedullary primary ependymoma of the craniocervical junction combined with C1 partial agenesis: case report and review of the literature. World Neurosurg 84: 2076.e1–2076.e6, 2015

28) Oral S, Tunturk A, Kucuk A, Menku A: Cervical hemilaminoplasty with miniplates in long segment intradural extramedullary ependymoma: case report and technical note. Turk Neurosurg 28: 158–163, 2018

29) Pomeraniec IJ, Dallapiazza RF, Sumner HM, Lopes MB, Shaffrey CI, Smith JS: Anaplastic extramedullary cervical ependymoma with leptomeningeal metastasis. J Clin Neurosci 22: 1871–1876, 2015

30) Severino M, Consales A, Doglio M, et al.: Intradural extramedullary ependymoma with leptomeningeal dissemination: the first case report in a child and literature review. World Neurosurg 84: 865.e13–865.e19, 2015

31) Toktaş ZO, Demir MK, Yapıcıer Ö., Akakın A, Yılmaz B, Konya D: Disseminated adult spinal extramedullary myxopapillary ependymoma. Spine J 15: e69–e70, 2015

32) Vats A, Randasi R, Zaveri G, Pandya S: Multicentric intradural extramedullary ependymoma: report of a rare case. J Cervicovertebr Junction Spine 6: 134–136, 2015

33) Chung CY, Koffie RM, Dewitt JC, Aronson JP: Thoracic exophytic ependymoma masquerading as a benign extra-axial tumor. J Clin Neurosci 33: 221–225, 2016

34) Maugeri R, Giugno A, Graziano F, Visocchi M, Giller C, Iacopino DG: Delayed chronic intracranial subdural hematoma complicating resection of a tanycytic thoracic ependymoma. Surg Neurol Int 7: S20–22, 2016

35) Chakravorty A, Frydenberg E, Shein TT, Ly J, Earls P, Steel T: Multifocal intradural extramedullary anaplastic ependymoma of the spine. J Spine Surg 3: 727–731, 2017

36) Honda A, Mizuya Y, Hirato J, Kiyohara H, Iizuka H: Multiple intradural-extramedullary spinal ependymomas including tumors with different histological features. Eur Spine J 26: 222–224, 2017

37) Evzikov GY, Konovalov NA, Bashlachev MG, et al.: Surgical treatment of intramedullary-extramedullary ependymomas. Two clinical cases and a literature review. Vopr Neurokhirurgii Im N N Burdenko 82: 48–55, 2018 (Russian)

38) Liao D, Zhang J, Chen H: Rare giant intradural extramedullary ependymoma. World Neurosurg 111: 139–141, 2018

39) Garg K, Sharma R, Dash C, Agrawal D, Sharma BS: Spinal intradural extramedullary ependymoma with intracranial metastasis and leptomeningeal spread: a case report and comprehensive review of literature. Neuro Ind 67: 1352–1357, 2019

40) Akhunbay-Fudge CY, Chakrabarty A, Derham C, Patel D: Thoracic intradural extramedullary ependymoma with anaplastic transformation: case report and discussion. World Neurosurg 134: 549–554, 2020

41) Das KK, Attrri G, Singh S, et al.: Intradural extramedullary nonconus nonfilum spinal ependymomas:
report of a rare variant and newer insights into their histogenesis with proposal of a classification scheme and a management algorithm based on a review of literature. World Neurosurg 134: 323–336, 2020

Corresponding author: Yoshifumi Kawanabe, MD, PhD
The Department of Neurosurgery, Shizuoka General Hospital, 4-27-1 Kitaandou, Aoi-Ku, Shizuoka, Shizuoka 420-8527, Japan.
e-mail: bwh5255725@yahoo.co.jp