Neuroblastic tumors can be classified as neuroblastoma, ganglioneuroblastoma (GNB), or ganglioneuroma. Ganglioneuroblastomas consist of small, round, immature neuroblast cells and matured ganglion cells. They are most commonly found in the mediastinum and retroperitoneum; intraspinal GNBs are extremely rare. There are only 5 cases of intraspinal GNB reported in the English literature. The authors report a case of GNB of the filum terminale. The duration of follow-up after the initial treatment is longer than in any other published reports.

Methods. A 36-year-old woman underwent resection of an intradural extramedullary tumor at L1–2 in 1993. Pathological diagnosis was GNB. After surgery, her symptoms resolved and she recovered to a normal condition. In 2009, when she was 53 years old, she presented to the hospital with paralysis of both legs. Magnetic resonance imaging suggested recurrence of spinal tumor. She underwent subtotal resection of the tumors, followed by 4 weeks of radiation therapy.

Results. Neurological symptoms improved, and, after radiation therapy, the patient was able to walk with a crutch. Histological investigation of the excised tumor indicated that it was a nodular type GNB, which was consistent with the diagnosis from the time of the initial surgery in 1993. Follow-up MRI studies showed no growth of residual tumors in the 3 years following the surgery.

Conclusions. The authors present a rare case of spinal GNB. The duration of follow-up after the initial surgery in 1993 represents the longest description of clinical course after treatment for spinal GNB.

Key Words • ganglioneuroblastoma • spine • filum terminale • surgery • radiotherapy • oncology

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Case Report

Initial History and Examination. This 36-year-old woman experienced mild pain on bilateral buttocks to posterior thighs and visited another outpatient clinic in the summer of 1992. She was initially treated with non-steroidal analgesics, but the pain gradually increased. Then, she presented to the hospital with severe pain at the end of that year. Neurological examination revealed reduced sensation in bilateral L2–5 dermatomes. There was no urinary disturbance and the lower-limb muscle power and reflexes were normal. Admission MRI studies revealed a mass in the spinal canal at L1–2 with a longitudinal length of 30 mm. The tumor exhibited isointensity on T1-weighted MRI, high intensity on T2-weighted MRI, and enhanced equally with Gd. The tumor was round with a clear margin.

First Operation. The patient underwent tumor resection followed by T12–L2 laminectomy early in 1993. Pink tumor was exposed after durotomy from L-1 to L-2. The artery and vein feeding the tumor communicated with the artery of Adamkiewicz. The tumor was not attached to the conus medullaris or caudal nerves, but was directly attached to the filum terminale. The artery and vein feeding the tumor were occluded. The tumor was removed completely. After surgery, her symptoms resolved and she recovered to a normal condition.

Case Report

Abbreviation used in this paper: GNB = ganglioneuroblastoma.
Ganglioneuroblastoma of filum terminale

connected with the filum terminale. The tumor was first disconnected from the feeding artery and vein. Then the filum terminale was amputated proximal to the attachment and the tumor was completely removed with the capsule intact.

First Postoperative Course. Histopathological examination of the excised tumors showed that the majority of the lesion was ganglioneuroma and consisted of large ganglion cells, but there was a transition to the dense growth of immature small neuroblastoma cells with a stroma-rich background (Fig. 1). Based on the report from the pathology department, the histopathological diagnosis was GNB. Postoperatively, pain and sensory function recovered to normal. Adjuvant radiotherapy after the surgery was not performed. Postoperative T1-weighted MRI of the lumbar spine performed 6 months after the surgery demonstrated no residual tumor (Fig. 2). The patient was followed for 5 years after the surgery and did not exhibit any progression of symptoms, and did not return to the hospital.

Tumor Recurrence. In January 2009, when the patient was 53 years old, she began to have low-back and bilateral buttock pain. Although the symptoms gradually increased, their intensity was tolerable for her, so she did not see the doctor at that time. However, one day in August, she suddenly experienced numbness, pain, and lassitude in her right leg that occurred after straining on defecation. She presented to the hospital with difficulty in walking and urination. Neurological examination revealed reduced sensation, reduced muscle strength (manual muscle testing score of 3/5 in the right leg below the inguinal region), and loss of tendon reflex in both lower extremities. Admission MRI studies revealed multiple tumors in the spinal canal between L-2 and L-4. The tumors exhibited low intensity on T1-weighted MRI, a mosaic pattern in T2-weighted MRI, and enhanced equally with Gd (Fig. 3). Admission CT scans revealed calcification in the spinal canal at the same level as the mass.

Second Operation. Emergency surgery was performed to remove the tumors. Following the laminectomy of L-3 and L-4, and the removal of scar tissue at L-1 and L-2 that had been created by the primary surgery
in 1993, the dura mater was exposed between L-1 and L-4. The tumor was removed with the aid of a Cavitron ultrasonic surgical aspirator. A total of 8 pieces of tumor were excised. The longest approximate diameter of the tumors was 20–30 mm in 3 pieces, 10–20 mm in 4, and less than 10 mm in 1. However, almost all of the tumors tightly adhered to the cauda equina and arachnoid, and were hemorrhagic; therefore the surgery was limited to subtotal removal.

Second Postoperative Course. Paralysis improved immediately after surgery, but had deteriorated by 3 days postsurgery. Postoperative MRI revealed a hematoma at the surgical site and a residual tumor. These were suspected to be the cause of the neurological deterioration, and we performed an evacuation of hematoma and residual tumor resection. However, again due to the strong adhesion of the tumor with the cauda equina, total resection was not completed. The MRI studies obtained 2 weeks after this surgery revealed several small residual tumors. The patient underwent radiation therapy to the surgical site, with a dose of 43 Gy over 4 weeks. Postoperatively, screening CT scans for chest to abdomen and MRI for brain and whole spine revealed no additional metastasis or other primary sources. Neurological symptoms gradually improved and, at the end of the radiation therapy, the patient was able to urinate without a catheter and walk with a crutch.

Histopathological examination of the excised tumors in H & E–stained sections showed identical findings with the 1993 diagnosis of GNB (Fig. 4). Immunological staining demonstrated that the neuroblastoma cells were positive for neuron-specific enolase and synaptophysin. The MIB-1 index was 5%–10%. We classified the tumor as nodular GNB (composite schwannian stroma-rich/stroma-dominant and stroma-poor) based on the International Neuroblastoma Pathology Classification system. Based on these observations, the tumor was considered to be a recurrence of GNB.

At the latest follow-up visit 3 years after the second...
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surgery, the patient was able to walk with two crutches and urinate without a catheter. The MRI studies showed no growth of residual tumors compared with the images obtained immediately after the surgery (Fig. 5).

Discussion

Approximately 10% of all neuroblastic tumors are GNB. The adrenal medulla is the most common site for GNB tumors, followed by the mediastinum and the temporal lobe. The development of GNB tumors in the spinal region is extremely rare, and we could find only 5 reported cases (Table 1). Three patients were male and 2 were female, and their ages ranged from 16 to 42 years. The GNB tumors were located in the thoracolumbar region in 3 cases, the thoracic spinal cord in 1 case, and across the holocord extending from C-3 to the conus medullaris in 1 case. The case reported here was that of a 36-year-old woman, and the tumor developed at the filum terminale. The characteristics of this small group of patients with spinal GNB therefore indicate that lesion location is heterogeneous. Ganglioneuroblastomas commonly develop in childhood, and the incidence in adults more than 20 years of age is reported to be only 4%. Because all 5 cases of spinal cord GNB reported to date are in patients aged older than 16 years, the age at onset for patients with spinal GNB may be older than for those with GNB located in other areas.

The standard treatment for GNB is resection. In all but 1 of the 5 previously reported cases of spinal GNB the patients underwent resection, and the tumors were described as having no defined interface with the cord. Myelotomy was performed to remove the tumors in 2 intramedullary cases, and surgery was completed with subtotal resection of the tumors in the other 2 cases. In our case, total resection was performed in the initial surgery in 1993 and was accomplished by removing the tumor with the filum terminale. However, there was recurrence after a period of 16 years. Although the recurrence could be due to the natural history of the GNB itself, there was a possibility of some residual tumor despite the description of the gross-total resection.

There is no established evidence regarding the effectiveness of chemotherapy or radiotherapy in the survival of patients with GNB or neuroblastic tumor; however there are some reports indicating that survival might not be influenced by chemotherapy or radiation. One previous patient with spinal GNB received chemotherapy and was living independently at 1-year follow up. In contrast, a patient with spinal GNB who underwent resection without chemotherapy or radiotherapy died 5 months after surgery. The other 2 previously reported cases of spinal GNB were treated by resection alone and were alive at the time of the report, but this was within 1 year of surgery. Our patient received no adjuvant therapy at the time of primary surgery in 1993, and she received radiotherapy after the second surgery in 2009. The duration of follow-up from the initial surgery in 1993 represents the longest description of clinical course available for spinal GNB.

The histological description of the tumor is an important factor for prognosis. According to the International Neuroblastoma Pathology Classification system, neuroblastoma can be classified into 4 different categories: neuroblastoma, ganglioneuroma, intermixed GNB, and nodular GNB. The current case was diagnosed as nodular GNB. The prognosis of the nodular subtype of GNB is poor, with a reported 5-year overall survival rate of 68%. Nevertheless, Umehara et al. classified the nodular components of GNB in the favorable or the unfavorable subset.

Fig. 5. Sagittal T1-weighted MRI study obtained 3 years after the 2009 surgery demonstrating no residual tumors.
based on the evaluation of these components by applying histopathological criteria including patient age, grade of neuroblastic differentiation, and mitosis-karyorrhexis index. The survival rate in the favorable subset was 95%, and those authors concluded that the nodular components of the GNB were not always aggressive. The histological grade of the tumor from the 2009 surgery in the current case was intermediate, with an MIB-1 index of 5%–10%, and the patient was alive 19 years after the initial surgery. Therefore, the subtype of GNB in this case can be considered of favorable histology and a good prognosis can be expected, but careful follow-up is mandatory to monitor metastasis and re-recurrence.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Okudera. Acquisition of data: Okudera. Analysis and interpretation of data: Okudera. Drafting the article: Okudera. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Okudera. Statistical analysis: Miyakoshi, Hongo, Kasukawa, Ishikawa, Shimada. Study supervision: Miyakoshi, Sugawara, Hongo, Kasukawa, Ishikawa, Shimada. Administrative/technical/material support: Miyakoshi, Sugawara, Hongo, Kasukawa, Ishikawa, Shimada. Statistical analysis: Miyakoshi, Hongo, Kasukawa, Ishikawa, Shimada. Administrative/technical/material support: Miyakoshi, Sugawara, Hongo, Kasukawa, Ishikawa, Shimada. Study supervision: Miyakoshi, Sugawara, Hongo, Kasukawa, Ishikawa, Shimada. Reviewing the submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Okudera. Accepted April 22, 2014.

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**TABLE 1: Summary of reported cases of GNB of filum terminale**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Age (yrs), Sex</th>
<th>Levels</th>
<th>Treatment</th>
<th>Follow-Up</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miele et al., 2011</td>
<td>23, M</td>
<td>C3–conus</td>
<td>resection + chemo</td>
<td>1 yr</td>
<td>NED</td>
</tr>
<tr>
<td>Raina et al., 1993</td>
<td>21, M</td>
<td>T10–L4</td>
<td>chemo</td>
<td>2 yrs</td>
<td>AWD</td>
</tr>
<tr>
<td>Sibilla et al., 1995</td>
<td>42, M</td>
<td>T5–8</td>
<td>resection</td>
<td>3 mos</td>
<td>AWD</td>
</tr>
<tr>
<td>Singh et al., 2010</td>
<td>16, F</td>
<td>T-12</td>
<td>resection</td>
<td>5 mos</td>
<td>DOD</td>
</tr>
<tr>
<td>Tripathy et al., 2000</td>
<td>39, F</td>
<td>L-3</td>
<td>resection</td>
<td>6 mos</td>
<td>AWD</td>
</tr>
<tr>
<td>present study</td>
<td>36, F</td>
<td>L2–4</td>
<td>resection + RT</td>
<td>19 yrs</td>
<td>AWD</td>
</tr>
</tbody>
</table>

* AWD = alive with disease; chemo = chemotherapy; DOD = died of disease; NED = no evidence of disease; RT = radiotherapy.