Presacral ganglioneuromas

Report of five cases and review of the literature

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Ganglioneuromas are rare, benign, slow-growing tumors belonging to the neuroblastoma group. The authors describe the presentation and treatment of five consecutive patients who presented with presacral ganglioneuromas; these cases represent the largest series to date. A review of the literature is also performed.

KEY WORDS • ganglioneuroma • pelvis • retroperitoneum • sacrum

Case Reports

All five patients underwent resection of the tumor between 1998 and 2002; the procedures were performed by one surgeon (M.B.). Four patients presented with symptomatic pain (Table 1). No patient suffered neurological deficits or significant medical comorbidities. The diameter of the tumors ranged from 5 to 12 cm. Imaging studies revealed that the lesion extended from the sacral foramen into the presacral area. Two young women (age 19 and 21 years, respectively) were thought to have uterine fibroid tumors based on initial CT findings. In one patient surgical exploration was performed before the diagnosis of ganglioneuroma was made. Prior to tumor resection, FNAB sampling was conducted in three patients (Cases 2, 4, and 5). In the patient in Case 5 the preliminary diagnosis was chondroid tumor, whereas in those in Cases 2 and 4 the diagnosis was schwannoma. In no case was a diagnosis of ganglioneuroma established preoperatively.

Tumors located in the midline, low in the pelvis (Cases 3–5), were exposed via an anterior intraperitoneal approach (midline incision and laparotomy). In patients with tumors located higher and laterally in the pelvis (Cases 1 and 2) an anterolateral retroperitoneal approach was undertaken to reach the presacral region. Intraoperatively, a nerve stimulator was used to identify the nerves of the lumbosacral plexus. The tumor was debulked intralesionally to reduce its mass and to make manipulation of its capsule and identification of functional nerve roots easier. After the tumor volume was reduced, the surgeon attempted to dissect the capsule off the surrounding tissues. This was readily accomplished when the tumor was in the midline (Cases 4 and 5) but difficult when more laterally located because of dense adherence to the lumbosacral plexus (Cases 1–3). In these cases, the tumor capsule was left in place to prevent the potential neurological dysfunction due to an aggressive capsular resection from functional nerve roots. The patients in Cases 2 and 5 with significant intraforaminal tumor required subsequent resection via a posterior sacral laminectomy because radiculopathy persisted after the first surgery. In both cases the tumor was completely resected and symptoms resolved.

Ganglioneuromas are typically avascular, as evidenced by the small amount of blood loss (100–500 ml) in our first three cases; however, in the patient in Case 4, the tumor was markedly hypervascular and this resulted in a 7500-ml blood loss, subtotal resection, and subsequent lower-extremity pain most likely due to manipulation of the lumbosacral plexus. Based on this experience we perform angiography and embolization in all patients with potential neurogenic pelvic tumors, although no subsequent hypervascular tumors have been identified. Alternatively, with the low risk of neurogenic tumors being hypervascular, one could embolize only those tumors found to be hypervascular on initial intraoperative exploration.
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Illustrative Case

Case 2

Presentation and Examination. This 28-year-old healthy woman presented with a 2-month history of low-back pain. She exhibited no deficits on physical examination, but MR imaging of the lumbosacral spine revealed a large lesion in the presacral space arising from the left S2–3 foramen (Fig. 1). The results of axial CT scanning–guided FNAB were suspicious for a low-grade chondroid lesion. Prior to excision of the lesion, the patient underwent colonoscopy to ensure the absence of bowel involvement.

Operation. A midline incision and transperitoneal exposure were performed. The small bowel, uterus, left fallopian tube, and left ovary were retracted to expose the tumor in the deep left pelvis lateral to the rectum. The course of the left ureter was seen to be normal, along the left pelvic side wall, anterior and lateral to the mass. The distal sigmoid and rectum and their mesenteries were elevated out of the retroperitoneum away from the left pelvic wall. The hypogastric nerves and vessels were identified and preserved. The sciatic nerve was seen to course lateral to the tumor. The left sacral sympathetic chain was observed to be a fine network of threadlike fibers draped over and forming part of the tumor capsule. Resection of the capsule inevitably results in the sacrifice of some sympathetic fibers, but the contralateral sympathetic plexus remained intact. Intermittent nerve stimulation at 2 mAmp was used intraoperatively to aid in identification and dissection of the lumbosacral plexus and sciatic nerve. After intralesional debulking, the intrapelvic portion of the tumor was removed. The tumor was also dissected into the left S-2 neural foramen, but residual tumor was left behind in an attempt to preserve the nerve root and prevent possible cerebrospinal fluid leakage from the distal thecal sac. Follow-up MR imaging revealed gross-tumor resection except for the S-2 foraminal residual disease. Approximately 100 ml of blood was lost during the procedure. The pathological diagnosis of ganglioneuroma was confirmed.

Postoperative Course. One year later, the patient experienced left lower-extremity pain. An increase in size of the residual foraminal tumor was demonstrated on MR imaging. At this time, a sacral laminectomy and S-2 foramotomy were performed. The tumor was excised and the S-2 nerve root was preserved. Pathological examination again confirmed the diagnosis of ganglioneuroma. Postoperatively, the patient suffered no dysfunction. During the last 6 years, she has experienced minimal back pain, and her most recent imaging studies obtained at 4-year follow-up evaluation demonstrated no evidence of recurrence.

Discussion

Ganglioneuromas are benign slow-growing lesions that arise from sympathetic ganglion cells and are considered to be part of the neuroblastoma group. The cell of origin is derived from embryonic neural crest cells, which are destined to form autonomic nerve tissue. Ganglioneuroblastosomas and neuroblastomas are also included in this classification. Although neuroblastomas are composed of neuroblasts (undifferentiated neural crest cells), ganglio-

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**TABLE 1**

Summary of data obtained in five consecutive cases of presacral ganglioneuroma*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Symptoms</th>
<th>Signs</th>
<th>Imaging Finding</th>
<th>Surgery</th>
<th>Postop Status</th>
<th>Follow-Up Duration/Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65, F</td>
<td>3–4 mos of bilateral hip pain</td>
<td>none</td>
<td>retroperitoneal exposure; STR because tumor adhered to sciatic nerve</td>
<td>residual tumor capsule on imaging; dysesthetic pain</td>
<td>2 yrs, pain free &amp; no recurrence</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>21, F</td>
<td>1 wk of severe left flank pain</td>
<td>none</td>
<td>retroperitoneal exposure; STR because tumor adhered to LSP; 7500-ml blood loss</td>
<td>residual tumor capsule on imaging; leg pain required sacral lam &amp; for root decompression</td>
<td>2 yrs, no recurrence but complex regional pain syndrome in left LE; returned to college</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>21, M</td>
<td>none</td>
<td>none</td>
<td>5-cm presacral tumor extending laterally from L1–2</td>
<td>residual tumor capsule on imaging; left leg pain</td>
<td>3 yrs, no recurrence but chronic foot pain (on long-term disability)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>19, F</td>
<td>long-term constipation &amp; lower-back pain</td>
<td>none</td>
<td>intraperitoneal exposure w/ presacral mobilization of rectum; STR because tumor adhered to L5–S5 roots</td>
<td>no residual tumor on imaging; persistent bowel symptoms; pain resolved</td>
<td>18 mos; no recurrence</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>28, F</td>
<td>2 mos of lower-back pain</td>
<td>none</td>
<td>intraperitoneal exposure w/ presacral mobilization of rectum</td>
<td>LE pain 1 yr later attributed to recurrence w/in S2–3 foramen; sacral lam &amp; for w/ CR</td>
<td>6 yrs, pain free &amp; no recurrence</td>
<td></td>
</tr>
</tbody>
</table>

* CR = complete resection; for = foraminotomy; lam = laminectomy; LE = lower-extremity; LSP = lumbosacral plexus; STR = subtotal resection.
neuromas consist of mature ganglion cells and other mature tissue and are considered benign. A histopathological examination of a ganglioneuroma shows large, mature neurons in a stroma composed of Schwann cells (Fig. 2). It is believed that these tumors represent a continuum and that ganglioneuromas are the final stage in the maturation of neuroblastomas. In patients with neuroblastomas that have matured into ganglioneuromas the prognosis is excellent. There are also several reports in the literature in which authors have described malignant transformation of ganglioneuromas either spontaneously or after radiation therapy.

Ganglioneuromas can arise anywhere along the sympathetic chain. Common locations include the mediastinum, retroperitoneum, and adrenal gland. The presacral location is rare, with only nine previously reported cases. Stout, et al., reviewed a series of 234 ganglioneuromas located in multiple areas and reported that they are more common in females and that 60% of patients were younger than 20 years of age at the time of diagnosis. Our findings were similar. As in our small case series, most lesions occur in isolation, but an association with neurofibromatosis and multiple endocrine neoplasia syndrome Type IIB has been reported.

Ganglioneuromas are commonly asymptomatic, but patients can present with symptoms associated with local mass effect. Table 2 provides a summary of the age, sex, symptoms, treatment, and follow-up data for the nine previously reported patients. Most pelvic tumors were large and patients presented with constipation due to mass effect on the rectum or with pain due to sacral root and lumbosacral plexus involvement.

On radiographic and neuroimaging evaluation, ganglioneuromas are not readily distinguished from other nerve sheath tumors. Plain radiographs may demonstrate bone remodeling. Axial CT scanning may reveal a hypodense homogeneous lesion that might enhance after contrast administration. The tumor often exhibits microcalcifications. Magnetic resonance imaging reveals a hypointense homogeneous lesion on T1-weighted sequences and a hyperintense heterogeneous lesion on T2-weighted sequences. The tumor usually enhances significantly. Magnetic resonance imaging is the best noninvasive diagnostic study available to assess these lesions and their neighboring structures, helping in surgical planning. Lesions that are paraspinal often originate from nerves/nerve roots, which can also be identified. In all five patients in this series, the location of origin was identified and confirmed intraoperatively. Features such as the widening of the neural foramina and thickening of the nerve root help to narrow down the differential diagnosis of solid pelvic tumors to schwannoma, neurofibroma, meningioma, or ganglioneuroma. Numerous other cystic lesions of spinal origin can also be found in this location, but their CT and MR imaging characteristics are different. Other tumors, such as lymphomas, chondromas, teratomas, soft-tissue sarcomas, Ewing sarcomas, osteo- and chondrosarcomas, and metastases involve, invade, and erode bone. Therefore, MR imaging can help distinguish these lesions of spinal origin from those of pelvic origin, allowing correct diagnosis, appropriate counseling, and proper treatment planning. In addition, operative planning and the approach to the mass can be determined by evaluating the preoperative images.

On average, ganglioneuromas are approximately 7 cm in diameter, are encapsulated and firm, and are white to yellow in color. In all five patients in this case series the lesions were larger than 5 cm in widest diameter; all were firm and encapsulated. Three patients underwent FNAB sampling, but the results yielded an incorrect diagnosis. Jain, et al., stressed in their report that FNAB samples of the ganglioneuromas be obtained at multiple sites within the tumor and several specimens analyzed to ensure correct diagnosis. It is possible that inadequate samples were acquired during the FNAB procedures in our three patients, and thus the initial diagnosis was incorrect. Despite these inaccurate diagnoses, the pathological examination did not suggest a malignant tumor histology, radiosensitive tumor, or an origin in surrounding structures, such as the uterus or colon. Computerized tomography scanning guidance should be used during FNAB sampling.

As with other nerve sheath tumors, the presacral location lends itself to an anterior approach. Tumors located high and/or laterally in the pelvis are best resected via a retroperitoneal approach. Those located in the midline, lower in the pelvis, are approached transperitoneally with presacral mobilization of the rectum. This approach is associated with a higher risk of injury to the intraperitoneal organs and subsequent morbidity. For both procedures, the neurosurgeon and general surgeon must have a good working knowledge of the anatomy of the neural and vascular structures, as with the intestinal and urogenital organs that could be encountered (Fig. 3). Preoperative bowel preparations are necessary.

Of previously reported cases (Table 2), four patients underwent transperitoneal approaches alone; complete and subtotal resections were achieved in two patients each, respectively. In addition, in one patient a transperitoneal approach was combined with a sacral laminectomy, whereas in another a sacral amputation was also required. Complete resection was achieved in each case. Results were good in all these cases, and no recurrence or progressive residual radiographically documented tumor was demonstrated.

A posterior transsacral approach is not advised because of the potential morbidity to the dural sac and cauda equina. Additionally, the anterior pelvic structures (neurovascular, intestinal, and urogenital) could not be observed until after tumor removal by which time injury may al-

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Fig. 2. Photomicrograph of a ganglioneuroma showing large mature neurons in a neuromatous proliferation including spindle-shaped Schwann nuclei. H & E, original magnification × 180.
Because of the benign nature of this disease, adjuvant chemo- or radiotherapy is not indicated. Our follow-up period ranged from 18 months to 6 years. There has been no progression of disease or symptoms after more than 1 year of radiographic and neuroimaging follow up.

Conclusions

Presacral ganglioneuromas are rare, benign lesions but present when the mass is very large and symptomatic. Surgery is the primary means of diagnosis and treatment. An anterior approach to the tumor allows safe and adequate resection. It is helpful to have both a neurosurgeon and general surgeon involved in surgical planning and execution. The use of nerve stimulators and somatosensory evoked potential monitoring is essential to minimize somatic nerve injuries. An intracapsular resection may be acceptable if the tumor capsule is densely adherent to the lumbosacral plexus in patients who are neurologically intact. For at least a year postoperatively, patients should be followed at regular intervals to assess for recurrence.

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