

Presacral Ganglioneuroma: Diagnostic Considerations and Therapeutic Strategy

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Key Words

Ganglioneuroma · Presacral ganglioneuroma · Retrorectal tumors

Abstract

Presacral ganglioneuroma is an extremely rare tumor of neural crest origin. To the best of our knowledge, less than 20 cases have been reported previously. The present study reports on a presacral ganglioneuroma, 10.5 × 8 × 4 cm in size, that was found incidentally in a 35-year-old man with prior history of diverticulitis. He was admitted to our hospital due to lower left abdominal pain. Abdominal computed tomography and magnetic resonance imaging confirmed the extension of the lesion from the S2 level to the coccyx. The mass had low signal intensity on T1-weighted images and heterogeneous high signal intensity on T2-weighted images with no intraspinal or rectal extension. T2-weighted images demonstrated a compartmentalized solid tumor with cystic components. Complete tumor resection with free surgical margins was achieved using an abdominal approach. The patient remains asymptomatic 2 years after surgery. We emphasize on clinical features, radiologic appearance and surgical treatment of this rare entity. The clinical and pathologic features of previously reported studies are also briefly reviewed.

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Introduction

Ganglioneuroma (GN) is a benign, slow growing and rare tumor of neural crest origin. GN may develop as a result of progressive maturation of more primitive lesions, such as

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neuroblastoma, or may be diagnosed as primary GN [1, 2]. It can be found anywhere along the sympathetic nerve chain, and the most common locations are the posterior mediastinum (41.5%), retroperitoneum (37.5%), adrenal gland (21%) and neck (8%) [3]. A presacral location of GN is extremely rare. Here, we present the case of a 35-year-old man with a presacral GN (10.5 × 8 × 4 cm in size) and prior history of diverticulitis.

Case Report

A 35-year-old man presented to our hospital due to mild lower left abdominal pain lasting for 2 weeks. He reported one episode of uncomplicated diverticulitis 5 years ago, and his past medical history was unremarkable. He did not suffer from back pain or other neurologic symptoms and was physically active. Changes in bowel habits were not present. Routine blood tests, serum tumor markers (carcinoembryonic antigen, cancer antigen 19-9, and cancer antigen 125), α -fetoprotein and plasma and urine catecholamines were within normal range.

Abdominal ultrasonography incidentally revealed a huge solid pelvic mass, with well-defined borders. Abdominal computed tomography (CT) confirmed the presence of a well-circumscribed solid tumor in the presacral region, measuring 10 × 8.5 cm in size and presenting smooth edges and no calcifications (fig. 1). Pelvic magnetic resonance imaging (MRI) confirmed the extension of the lesion from the S2 level to the coccyx (fig. 2). The mass had low signal intensity on T1-weighted images and heterogeneous high signal intensity on T2-weighted images with no intraspinal or rectal extension. In addition, we were able to demonstrate by T2-weighted images that it was a compartmentalized solid tumor with cystic components (fig. 3). Colonoscopy examination revealed the presence of diverticulum in the sigmoid colon without inflammation and tumor involvement of the rectum.

The patient was submitted to surgical laparotomy without a preoperative fine-needle biopsy (FNA). An abdominal approach was used with the patient in the modified Lloyd-Davies position. The lesion was approached transperitoneally with presacral mobilization of the rectum, and complete tumor resection with free surgical margins was achieved. The specimen included a tumor of 10 × 8.5 × 4 cm in size, surrounded by a thin fibrous capsule, with elastic consistency, a compact form, and a grayish and partially brownish color.

After microscopic examination and immunohistochemical study, the diagnosis of mature GN was established. The neoplasm contained mature ganglion cells and Schwann cells together with collagen (fig. 4). Ganglion cells were distributed diffusely throughout the tumor or arranged in small clusters. There was no neuroblastomatous component. Mitoses were very rare. The immunophenotype of the neoplasm was as follows: synaptophysin (+), neuron-specific enolase (+), S-100 (+), neurofilaments (+), vasoactive intestinal polypeptide (+), protein 27 (+), myeline basic protein (–), and epithelial membrane antigen (–). The index of cellular proliferation ki-67 was <1%.

The patient had an uneventful recovery and was discharged on the 12th postoperative day. Repeat MRI at 12 and 24 months after surgery and neurologic examination were unremarkable.

Discussion

In adults, presacral tumors are uncommon lesions with an incidence rate of approximately 1/40,000 admissions [4]. They are derived from a variety of embryologic origins,

may be congenital or acquired and can be classified as congenital, inflammatory, neurogenic, osseous or miscellaneous [5]. Even though the majority of these lesions are benign, malignant tumors can be also found in the presacral-retrorectal space. GN is a benign tumor of neural crest origin that is very rarely found in the presacral space with less than 20 cases reported in the literature so far (table 1).

GN of the peripheral nervous system was first described in 1870 [6]. The classification of neuroblastic tumors is based on the International Neuroblastoma Pathology Classification System (the Shimada system) that was established in 1999 [7]. According to this classification, neuroblastoma, ganglioneuroblastoma and ganglioneuroma are subdivided in seven categories based on morphologic features with the objective of proposing a prognostically significant system. Neuroblastoma, ganglioneuroblastoma and GN are tumors arising from precursor cells of the neural crest that form the sympathetic nervous system and are called neuroblastic tumors [7]. The basic difference of these subtypes, that explains their various clinical behavior and their subsequent prognosis, is the degree of differentiation of their precursor cells [7, 8]. GN includes mature sympathetic ganglion cells and Schwannian stroma without neuroblasts or intermediate cells, neuroblastoma includes immature elements (primitive neuroblasts), and ganglioneuroblastoma has an intermediate cell population with both mature and immature cells [7, 8]. Subsequently, they are all considered as different maturational steps of a unique neoplasm. Neuroblastoma is the least differentiated malignant lesion with unfavorable prognosis, while GN is considered a benign tumor with excellent prognosis [9]. Neuroblastoma is often lethal, but 30% of patients have favorable outcomes, and this is explained by its unique biologic features of spontaneous regression and maturation to GN in a few cases [10]. Therefore, GN may present as a primary tumor or may be the result of progressive maturation of neuroblastoma or ganglioneuroblastoma, spontaneously or after chemotherapy or radiotherapy treatment [1].

GNs are equally distributed between males and females (1.13:1) [3]. They are often asymptomatic, but a variety of nonspecific symptoms have been attributed to local mass effects on adjacent structures. Especially, for presacral GNs, low back and leg pain, bilateral hip pain, constipation, amenorrhea and neurogenic bladder have been reported in various studies as main symptoms [6, 11–14]. Moreover, patients with GN (approx. 39%) may have increased levels of catecholamines in plasma or urine, due to hormonally active tumors, and may present with symptoms as hypertension or flushing [3]. For GN, median age at diagnosis is 6.5 years. For presacral location, median age at diagnosis is 35.5 years with a range from 8 to 70 years [3, 11]. Usually, presacral GNs have a mean diameter of 7 cm [11].

MRI and CT are the preferred methods for imaging of GNs. At CT, calcifications have been found in approximately 42–60% of GN. Although GN tends to be relatively homogeneous, the imaging characteristics of GN are similar to ganglioneuroblastoma and neuroblastoma, and therefore, a safe discrimination of these three tumors is not possible [8]. FNA can be used preoperatively, but it usually leads to inaccurate diagnosis. In the largest published series of five presacral GNs [14], the diagnosis of GN was not established preoperatively in any case, even though FNA biopsy was conducted in 3 patients. We did not perform FNA preoperatively because we agree that for retrorectal tumors a biopsy is required only if it will alter management and is therefore unnecessary if preoperative imaging provides sufficient information to allow appropriate surgical management [15]. Surgical resection is the optimal treatment of retrorectal tumors and provides a definitive histologic diagnosis [15].

Surgical management of retrorectal tumors includes three different approaches. The perineal approach that is performed with the patient in the Jack-Knife position, the abdominal approach, and the combined approach that includes both a laparotomy and sacral

transection [15]. Even though these lesions are rare, excision in many cases is technically demanding, and specific algorithms have been published in order to minimize complications. According to these, all lesions above the S3 level should be excised by means of an abdominal approach [15–17]. Below the middle of the S3 level, a posterior or combined approach is the ideal treatment, unless there is involvement of the pelvic viscera [15]. In cases of pelvic viscera involvement, abdominal approach with en block excision of the involved viscera is the treatment of choice. In our case, the lesion extended from the S2 level to the coccyx, and we achieved complete tumor resection via an abdominal approach in accordance to the previously published data.

Prognosis after surgical resection of GN, even if it is subtotal and there are macroscopic residuals, seems to be excellent. Adjuvant chemotherapy or radiotherapy is not indicated due to the benign nature of the disease [3, 11, 12]. Nevertheless, spontaneous malignant transformation of GN can be found in rare cases, so annual follow-up, that includes neurologic examination and pelvic magnetic imaging, is needed [11, 18].

Disclosure Statement

The authors declare that they have no conflicts of interest to disclose.

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Table 1. GN cases reviewed

First author, year	Age	Sex	Size	CT/MRI findings	Symptoms	Surgical approach	Resection	Follow-up
MacCarty, 1965 [19]	37	M	6 cm in diameter	No data	Pain	Midline sacral incision, coccygectomy and rectum mobilization	Complete	Asymptomatic after 9 years
Andersen, 1986 [20]	14	M	No data	No data	Pain –coexistence of acute appendicitis	Transperitoneal approach	Subtotal	Asymptomatic after 2 years
Richardson, 1986 [21]	71	M	No data	Low-density lesion in the midsacral level with a sclerotic margin	Neurogenic bladder, constipation	Sacral laminectomy, a second surgery followed which was not specified	Subtotal, second surgery	Volvulus of the cecum postoperatively, improved urination afterwards
Leeson, 1989 [6]	21	M	No data	Widening of the right sacral foramen	Dysuria, left leg numbness	Transperitoneal approach	Subtotal, second surgery	3 years asymptomatic
Stener, 1989 [22]	20	F	No data	No data	Pain	S2 to S3 sacral amputation	Complete	Asymptomatic after 20 years
Spirnak, 1993 [23]	8	M	13 × 8 × 5 cm	Low-density presacral mass	Progressive constipation	No data	Complete resection	Asymptomatic
Okai, 2001 [13]	70	M	9 × 5 × 4 cm	Inhomogeneous lesion with calcifications	Constipation, right flank pain, weight loss	Transperitoneal approach	Complete	Mild constipation persisted
Lam, 2002 [24]	11	M	No data	Extension of the lesion from S1 to S5	Constipation, back pain	Combined anterior and posterior approach	Complete	Asymptomatic after 4 years
Marmor, 2002 [25]	70	F	6 × 5.5 × 6 cm	No data	None	Posterior approach, en block excision with distal sacrum and coccyx	Complete	No data
Modha, 2005 [14]	65	F	9 × 3 cm	Extension of the lesion laterally from S1 to S2	Bilateral hip pain	Retroperitoneal approach	Subtotal	2 years asymptomatic
	21	F	12 × 7 cm	Extension of the lesion laterally from S2 to S3	Severe flank pain	Retroperitoneal approach	Subtotal	2 years no recurrence, chronic foot pain
	21	M	5 cm	Extension of the lesion laterally from S1 to S2	Asymptomatic	Transperitoneal approach	Subtotal	3 years no recurrence, chronic foot pain
	19	F	8 cm	Extension of the lesion into the midline from S2 to S3	Constipation and low back pain	Transperitoneal approach	Complete	18 months asymptomatic
	28	F	No data	Extension of the lesion into the midline from S2 to S3	Low back pain	Transperitoneal approach	Subtotal	6 years asymptomatic
Przkora, 2005 [2]	17	F	No data	Extension of the lesion from S2 to S3	Amenorrhea, weight loss	Posterior approach, partial resection of the sacrum, laminectomy	Complete	2 years asymptomatic
Cerullo, 2005 [11]	64	M	12 × 9 × 8 cm	Inhomogeneous mass extending from S2 to S3	Asymptomatic	Transperitoneal approach	Complete	8 months asymptomatic
Mounasamy, 2006 [26]	64	M	13.5 × 8.2 × 5.6 cm	Extension of the lesion from S1 to S4	Low back pain, right posterior thigh pain	Transperitoneal approach and laminectomy	Complete	12 months asymptomatic
	21	F	10 × 8 × 7 cm	Partially cystic, heterogeneous mass	Asymptomatic	Transperitoneal approach and laminectomy	Subtotal	4 years asymptomatic
Roganovic, 2010 [12]	12	F	9 × 8 × 7 cm	Presence of calcifications, heterogeneous mass	Lower abdominal pain	Transperitoneal approach	Complete	3 years asymptomatic

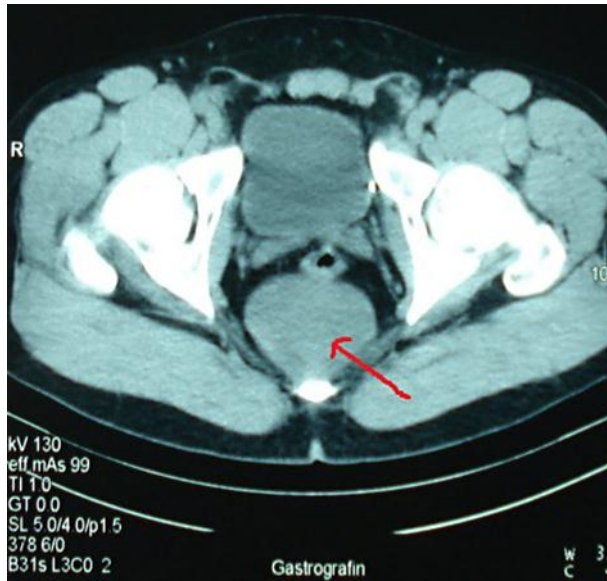


Fig. 1. Axial CT image of the lower pelvis. A well-circumscribed solid tumor is seen in the presacral region, with no signs of infiltration, in contact with the posterior wall of the rectum (arrow).

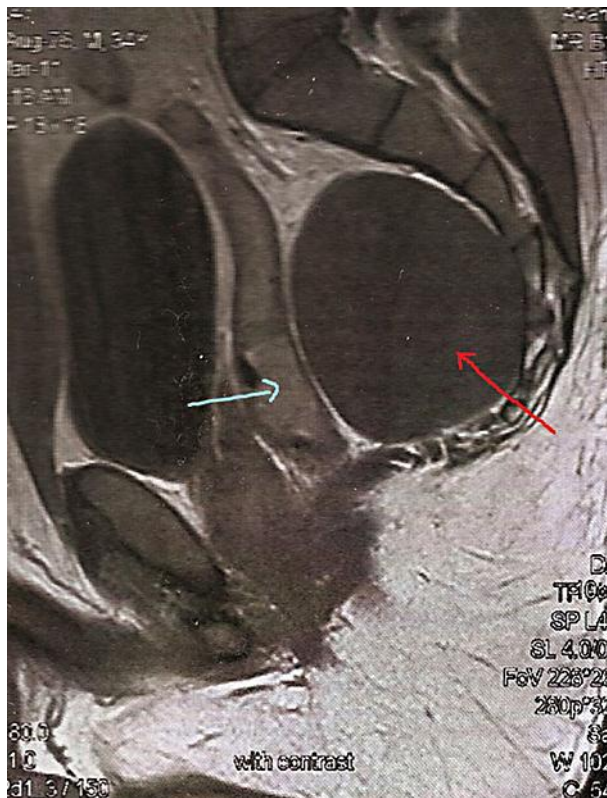


Fig. 2. Sagittal T1-weighted MRI image. A presacral tumor with low signal intensity is shown (red arrow). A fat plane can be seen between the tumor and the rectum, indicating that infiltration is not present (blue arrow).

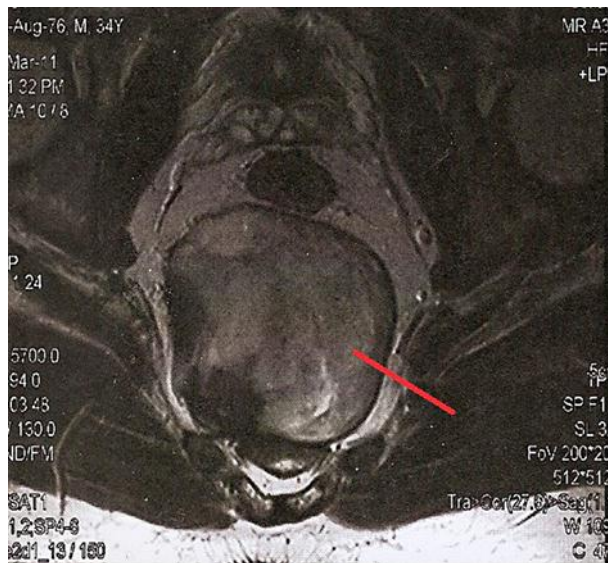


Fig. 3. Axial T2-weighted MRI image. An inhomogeneous compartmentalized solid tumor with cystic components is illustrated.

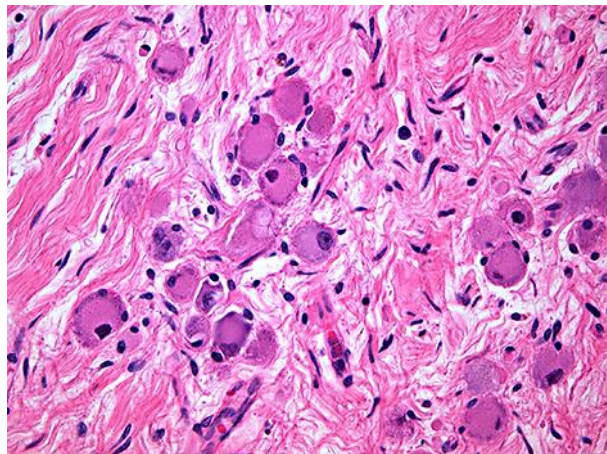


Fig. 4. Histopathologic findings. The tumor contains small clusters of mature ganglion cells surrounded by a Schwann cell-rich stroma (HE ×400).