

Case Report

Neuroendocrine tumor arising from tailgut cyst with spinal cord tethering:
case report and literature reviewTetsuryu Mitsuyama, MD, PhD^{a,b,*}, Motoo Kubota, MD, PhD^b, Yoshiaki Nakamura, MD^c,
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Abstract**BACKGROUND CONTEXT:** Neuroendocrine tumors (NETs) from tailgut cysts are rare; only 15 cases have been reported until now. A tailgut cyst with spinal cord tethering has not been previously reported, although both diseases are congenital anomalies in the early stage of gestation.**PURPOSE:** To report a rare case of NET from tailgut cyst associated with spinal cord tethering and review the literature.**STUDY DESIGN:** Case report and literature review.**METHODS:** We describe the clinical course of a 53-year-old man, who presented with gluteal pain and bladder dysfunction. Magnetic resonance images showed that a tumor of the sacral spinal canal extended into the retrorectal space and connected to a thickened fatty filum terminale, which was tethering the spinal cord.**RESULTS:** Because of tumor malignancy on a computed tomography-guided biopsy and the imaging data of involvement of presacral lymph nodes, we performed total removal of the tumor. Pathologic examination revealed NET (Grade 2) arising from a tailgut cyst. The patient received somatostatin analog therapy after surgery, followed by local radiation because of the further enlargement of the lymph nodes. Later, we started everolimus therapy for the metastases to the retroperitoneal lymph nodes. He presented with no local recurrence or further disease progression at 28 months after surgery. The review indicated that tumors in Grade 2 or 3 showed progressive clinical course after surgery and three of seven patients with biopsy were misdiagnosed.**CONCLUSIONS:** The correct preoperative diagnosis of NETs from tailgut cysts is difficult, but extremely important because Grade 2 or 3 tumors show disease progression even after surgery. Presacral congenital tumors, such as tailgut cysts, have the potential of malignant transformation into neuroendocrine tumors or adenocarcinomas. Comorbidity of spinal cord tethering and tailgut cyst suggests some relationship to common developmental errors in embryogenesis. © 2015 Elsevier Inc. All rights reserved.**Keywords:**

Embryologic failure; Malignant transformation; Neuroendocrine tumor; Somatostatin analogue; Spinal cord tethering; Tailgut cyst

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E-mail address: tmitsuyama@nij.twmu.ac.jp (T. Mitsuyama)**Introduction**

A tailgut cyst is a rare benign developmental lesion from the remnants of an embryonic hindgut [1]. It rarely undergoes malignant transformation, such as neuroendocrine tumor (NET), carcinoma, and adenocarcinoma [2]. Neuroendocrine tumors, defined as epithelial neoplasms with predominant neuroendocrine differentiation, are relatively rare

tumors arising from most organs of the body [3]. Most of these tumors are more indolent than other epithelial malignancies; however, a subset of them behave aggressively and are resistant to treatment [4]. Neuroendocrine tumors from tailgut cysts are very rare and only 15 cases have been reported with clinical details in the medical literature [5–19]. We describe here a new case and summarize the clinicopathologic features of NETs from tailgut cysts with a literature review. In addition, a tailgut cyst with spinal cord tethering, to the best of our knowledge, has not been previously reported. We discuss this comorbidity in the context of embryogenesis.

Case presentation

History and examination

A 53-year-old man presented with 1 year history of left gluteal pain, impaired defecation urge, difficulty in starting urination, and sensory disturbance in the perianal and gluteal areas. The gluteal pain was related to prolonged upright position. He showed weakness of anal sphincter muscles and Valsalva voiding; however, he was not incontinent for urine and feces. No skin lesion was detected on his back and buttocks. He realized to have coccygeal deviation since childhood and previous lumbar radiographs had shown erosion of his coccyx (Fig. 1). He had no associated anomalies in the central nervous system and other organs. In addition, he had no family history of presacral tumors and did not present with sacral agenesis or anorectal anomalies. Magnetic resonance images revealed an extradural tumor in the sacral spinal canal (Fig. 2, A–E). It was mostly hypointense both on T1- and T2-weighted images and moderately enhanced with gadolinium. The tumor extended anteriopcaudally to the

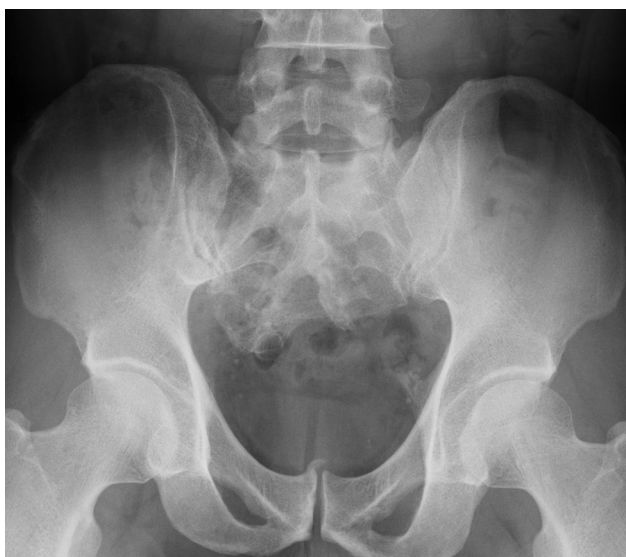


Fig. 1. Pelvic X-ray showing erosion of the coccyx.

retrorectal space with some cystic components and rostrally to the caudal end of the thecal sac. It connected to a thickened fatty filum terminale, which was tethering the spinal cord and showing partially high intensity both on T1- and T2-weighted images. Computed tomography (CT) scans showed enlargement of the sacral spinal canal with scalloped vertebral bodies. Positron emission tomography revealed mild accumulation of the radioisotope in the sacral tumor (standardized uptake value: 2.11–2.35) without any abnormal accumulation at other sites, and whole-body CT scans with contrast-enhancement detected no distal metastasis. Serum levels of key tumor markers were within normal limits. Bone erosion and tethered cord suggested a congenital malformation, whereas progressive neurologic symptoms and the mild tracer accumulation in positron emission tomography were features suggestive of malignancy. It was difficult to narrow the differential diagnosis of this tumor only with neuroradiologic findings. We performed a CT-guided biopsy to obtain a pathologic diagnosis, which was necessary to formulate a surgical strategy.

Biopsy

Hematoxylin-eosin stained section of the biopsy specimen showed dense proliferation of round cells. The proliferation rate, as highlighted by the Ki-67 immunohistochemical stain, was 15%. The tissue was positive for vimentin and slightly positive for pan-cytokeratin. It was negative for epithelial membrane antigen, S-100 protein, and CD99 antigen. The biopsy did not lead to a definitive diagnosis, although some tumors such as schwannoma, chordoma, ependymoma, and Ewing sarcoma were excluded. Rhabdoid tumor remained as a possible pathologic diagnosis at biopsy; however, it was less likely because it usually develops in infants and young children. Tumor removal was necessary for a final pathologic diagnosis that will determine the treatment strategy. In view of the high Ki-67 index, a retrospective review of all neuroimaging revealed an enlargement of the presacral lymph nodes because of regional metastases (Fig. 2E). We planned maximum tumor removal because of its increased proliferative ability and metastatic potential to the regional lymph nodes.

Operation

We performed osteoplastic sacral laminectomy. The tumor occupied most of the epidural space and covered the caudal portion of the thecal sac. The extradural tumor invaded into the intradural space and continued to the thickened fatty filum terminale at its rostral end (Fig. 3, Left). At first, we divided the filum terminale to untether the spinal cord. Next, we dissected the intradural tumor from adjacent nerve roots and totally removed it. Then, we removed most of the extradural tumor with detachment of the extradural

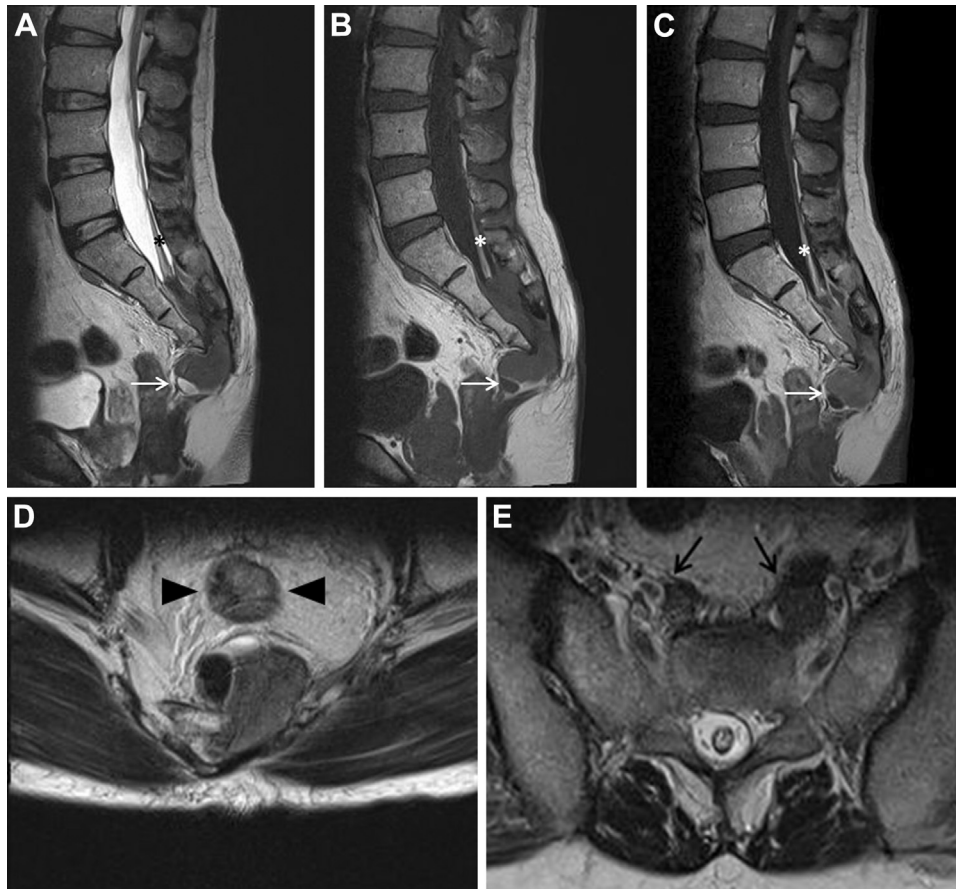


Fig. 2. Sagittal magnetic resonance images (*upper panels*) revealing a tumor occupying the extradural space of the sacral spinal canal and caudally extending into the presacral space with cystic components (arrows). The tumor invades into the dural sac and connects with a thickened filum terminale (asterisks), which is tethering the spinal cord. The tumor shows low intensity both on (A) T2-weighted and (B) T1-weighted images. (C) Most of the tumor homogeneously uptakes contrast and the walls of cystic components are strongly enhanced on Gd-contrast T1-weighted image. (D) Axial T2-weighted images show the tumor expanding into the fat tissue around the rectum (arrowheads) through the sacral hiatus and (E) the enlargement of presacral lymph nodes (arrows).

nerve root sleeves by widening of the intervertebral foramina (Fig. 3, Middle). Finally, we extirpated the caudal part of the tumor with detachment of the perirectal fatty tissue

(Fig. 3, Right). We achieved total removal of the tumor through the aforementioned steps. The sacral laminae were replaced after the dural closure.

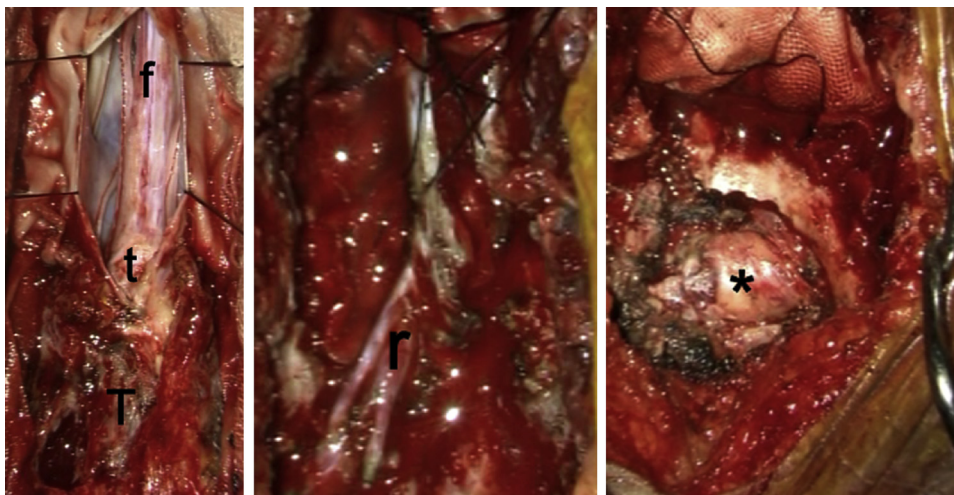


Fig. 3. Intraoperative photographs. (Left) Extradural tumor (T) invaded into the intradural space and the rostral part of the tumor (t) is continuing to the end of a fatty thickened filum terminale (f) in the intradural space. (Middle) Extradural nerve roots (r) are exposed after tumor removal. (Right) Caudal part of the tumor is removed from the perirectal fat tissue (asterisk).

Pathologic findings

The tumor consisted of solid and cystic components (Fig. 4 A and B). The proliferation of round cells with eccentric nuclei was forming trabecular or alveolar growth patterns in some parts of the solid components. Immunohistochemical staining was strongly positive for chromogranin A and focally positive for synaptophysin (Fig. 4 C and D). The proliferation rate (Ki-67 index) was 12.5%. The cystic component showed columnar or squamous cells lining. A subset of these cells was positive for chromogranin A or synaptophysin and another subset showed mitoses (Fig. 4 E). The cystic content was mucoid. These pathologic findings indicated a NET arising from epithelial cells of a tailgut cyst. It was classified as Grade 2 according to its Ki-67 index [20]. In addition, it was positive for somatostatin receptor Type 2 with circumferential membrane staining in most of the tumor cells, graded as score 3 [21].

Postoperative course

Gluteal pain disappeared soon after the surgery; however, he deteriorated to urinary retention and loss of sensation during defecation. He needed a urinary catheterization and a scheduled purgative. Subcutaneous fluid collection at the level of the cavity of the removed tumor enlarged after the postoperative mobilization. It showed no reduction in size, although its bacterial culture was negative and its cell counts were less than three per microliter when sampled with fine needle. Therefore, we repaired the cerebrospinal fluid leakage from the caudal end of the dural sac (the area of intradural tumor invasion) with a myofascial patch on the dura and packing with a fat tissue 3 weeks after surgery. He also started a postoperative treatment with octreotid, a long-acting somatostatin analog, 20 mg every 4 weeks. He returned to work 6 months after surgery with partial improvement of the initially deteriorated urinary and bowel dysfunction.

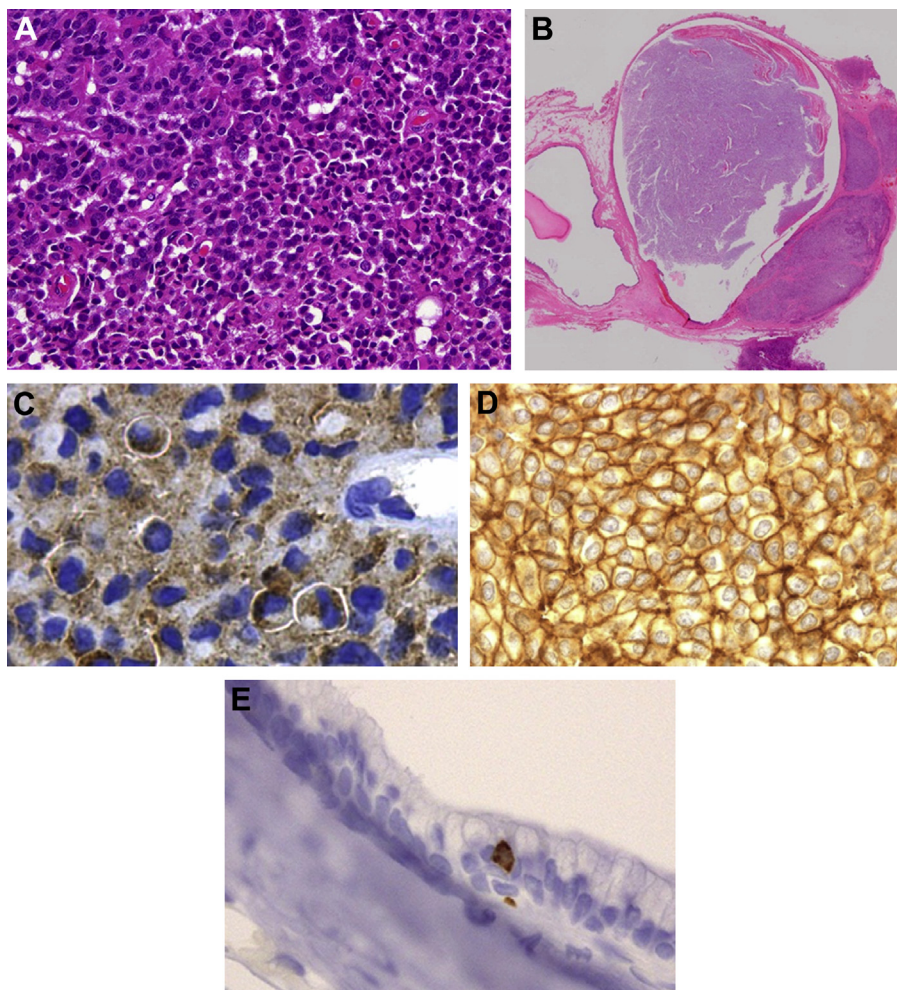


Fig. 4. Photomicrographs of the tumor revealing (A) a neuroendocrine tumor with a trabecular growth pattern and (B) a tailgut cyst with epithelial cells lining on hematoxylin-eosin stained sections. Tumor cells are positive for (C) chromogranin A, (D) synaptophysin, and somatostatin receptor Type 2. Some of cells, which are lining the cyst, are positive for (E) chromogranin A.

Presacral lymph nodes showed enlargement 10 months after surgery, in spite of no local recurrence (Fig. 5). He received radiation therapy (59.4 Gy/37 fr) to the presacral lymph nodes with increasing dose of octreotid to 30 mg. Although this treatment was effective to control the regional lymph nodes, CT scans 20 months after surgery revealed the swelling of the retroperitoneal lymph nodes. Therefore, we added 10 mg oral everolimus therapy for the metastasis to the distant lymph nodes. He was voiding by self-catheterization once a day and adjusted defecation by laxative drugs every few days without local recurrence or further disease progression when evaluated at 28 months after surgery.

Discussion

Tailgut cysts

Tailgut cysts, also known as retrorectal cystic hamartomas, are believed to originate from remnants of tailgut, the most distal portion of the embryonic gut [1,22]. They are multiloculated and lined with squamous, transitional, or glandular epithelium [23]. Tailgut cysts can rarely undergo malignant transformation from these epithelial components into NETs, carcinomas, adenocarcinomas, or sarcomas [1,2,23,24]. Mathis et al. [2] reported 31 patients with tailgut cysts and 4 of them (13%) had malignant

findings: adenocarcinoma in three and NET in one. They concluded that presacral tailgut cysts should be removed because of the risk of malignant transformation, because two of the four patients with malignancy had died through the follow-up period. In contrast, Hjermstad and Helwig [1] reported 51 patients with tailgut cysts and only 1 of them (2%) was accompanied with adenocarcinoma.

Tailgut cyst with spinal cord tethering

To our knowledge, this is the first report of a tailgut cyst with spinal cord tethering. Tailgut reaches its greatest development during the early sixth week of gestation and shortly regresses by the seventh week [22]. Tailgut cysts arise from the remnant of tailgut when incomplete involution occurs during this stage of embryogenesis [1,22]. In contrast, the secondary neurulation, in which the caudal part of spinal cord and cauda equina derive from the caudal eminence, is completed by the eighth week of gestation [25]. A thickened filum terminale, which is tethering the spinal cord, is attributed to an error of the tail bud during secondary neurulation. We hypothesized that some common developmental errors might be considered responsible for the comorbidity of tailgut cyst and a thickened filum terminale tethering the spinal cord, in view of the time and location of the embryologic failure.

Spinal cord tethering by a thickened filum terminale to the tailgut cyst in the present case had been asymptomatic, until being enhanced by the enlargement of the malignantly transformed tumor. This pathologic mechanism can probably explain why the gluteal pain, caused by spinal cord tethering, was resolved soon after untethering at surgery.

Neuroendocrine tumors

Neuroendocrine tumors consist of a spectrum of malignancies that can arise from neuroendocrine cells throughout the body, mostly in the gastrointestinal tract, lung, pancreas, and liver originating from the primitive gut [4]. They are classified into well-differentiated NETs and poorly differentiated neuroendocrine carcinoma. They are graded in accordance with the following definitions of Ki-67 index: 2% or less as Grade 1, from 3% to 20% as Grade 2, and more than 20% as Grade 3 [20]. In the review of 35,168 patients with NETs, the regional lymph node involvement was observed at diagnosis in 19% of them and distant metastasis in 20% of them [4]. Surgery is the only curative treatment for NETs; however, many patients have unresectable tumors or metastatic disease at the time of diagnosis [4,26]. Yao et al. [4] also reported prognosis of NETs in 35,097 cases: the median survival duration in patients with G1, G2, and G3 NETs was 124, 64, and 10 months, respectively. They pointed out that the primary tumor site was a powerful predictor of survival duration: the median survival durations with regional NETs varied from 360 months (appendicular tumors) to 14 months (liver tumors); the median



Fig. 5. Sagittal T2-weighted magnetic resonance imaging showing no recurrence of the tumor 10 months after surgery.

Table
Neuroendocrine tumors from tailgut cysts.

Author, year	Age (y)	Sex	BRD	Spinal canal invasion	Result of biopsy	Preoperative metastases	Grade	Ki-67 index	F/U (mo)	After treatment	Progression of metastases	Clinical features
Present case	53	M	+	+	Rhabdoid tumor	Presacral lymph nodes	2	12.5%	20	SSA, RT, mTOR	Retroperitoneal lymph nodes	Gluteal pain, Valsalva urine No urge to defecate
Zoccali et al., 2012 [5]	64	M	–	–	NET	—	1	Low-grade	3	—	—	Rectal pain and discomfort
Spada et al., 2011 [7]	41	F	–	–	—	Liver	2	18%	72	CTx, SSA PRRT	Adnexa Multiple bone	Rectal pain
Niazi et al., 2011 [8]	28	F	+	+	Epidermoid	—	1	Rare mitosis	12	—	—	Retained urine, anal tone weakness
Wöhlke et al., 2011 [6]	55	F	–	–	—	Lymph nodes Liver	2	20%	30	SSA	Paraduodenum Multiple bone	Perianal abscess, sacral pain
La Rosa et al., 2010 [9]	73	F	–	–	NET	—	1	<2%	9	—	—	Back and pelvic pain
Liang et al., 2008 [10]	51	F	–	–	Carcinoma	—	1	<1%	NA	—	—	Hip pain
Lee et al., 2007 [11]	40	F	–	–	Malignant NET	—	3	Malignant	6	—	Liver, brain	Acute anal pain
Matthieu et al., 2005 [12]	49	F	–	–	—	—	NA	NA	24	—	—	Rectal fullness, mucus emission
Jacob et al., 2004 [14]	42	F	–	+	—	—	NA	NA	NA	NA	NA	Painful constipation
Song et al., 2004 [13]	41	F	–	–	—	—	NA	NA	15	CTx, RT	Liver, CS	Perianal pain
Mourra et al., 2003 [15]	68	M	–	–	—	—	NA	NA	12	—	—	Anal pain
Prasad et al., 2000 [17]	69	F	+	–	—	—	NA	NA	24	NA	—	Painful bowel movement
Oyama et al., 2000 [16]	52	M	–	–	NET	—	NA	NA	6	—	—	Diarrhea, left leg pain
Horenstein et al., 1998 [18]	19	F	–	–	—	—	NA	NA	48	—	—	Pelvic pain
Lin et al., 1992 [19]	18	F	–	–	—	—	NA	NA	NA	NA	NA	Perianal pain

BRD, bladder and rectal disturbance; CS, cavernous sinus; CTx, chemotherapy; F/U, follow-up; mTOR, mammalin target of rapamycin inhibitor; NA, not available; NET, neuroendocrine tumor; PRRT, peptide receptor radionuclide therapy; RT, radiation therapy; SSA, somatostatin analog; M, male; F, female.

survival periods of rectal NETs with localized, regional, and distant diseases were 290 months, 90 months, and 22 months, respectively [4].

Systemic treatment options for patients with advanced NET have been limited. Somatostatin analogs have been shown to provide disease stabilization, prolonged survival, and antiproliferative effects [26,27]. The immunohistochemical status of somatostatin receptor Type 2A correlates with the response to somatostatin analog treatment [21]. Some malignant NETs are controlled with conventional radiation therapy [28]. The tyrosine kinase inhibitor, sunitinib, or the oral mammalian target of rapamycin inhibitor, everolimus, are recently reported to improve progression-free survival in patients with advanced pancreatic NET [26].

Because of high proliferation rate in the biopsy specimen and enlargement of the regional lymph nodes, we performed a total resection of the primary tumor. Postoperatively, we started somatostatin analog therapy for preventing local recurrence and metastatic progression. In addition, we increased the dose of somatostatin analog, combining with conventional radiation therapy for the enlarged regional lymph nodes. Later, we started everolimus therapy for distant metastases to the retroperitoneal lymph nodes.

Neuroendocrine tumors from tailgut cysts

Clinopathologic features of NETs from tailgut cysts are summarized in the Table. Of the 16 patients included in our case, 12 were woman and 4 were men, as tailgut cysts are prevalent in woman. Tumor extension into the sacral spinal canal was also reported in another case, however, without spinal cord tethering [8]. No patients complained of hormonal symptoms, although two-thirds of NETs were functioning tumors that produced a variety of hormones inducing a specific clinical syndrome [29]. Postoperative recovery of the bladder and rectal disturbances was seen in only one of three affected patients. The malignant potential of NETs is well illustrated by the following: two patients with preoperative distant metastases showed postoperative disease progression and two patients, who had no preoperative metastasis, developed a metastatic lesion after surgery, although none of them showed local recurrence [5–19]. All four patients with Grade 2 or 3 tumors presented with disease progression after surgery; this supports the correlation between pathologic grading and prognosis.

Based on the small number of reported cases, it is difficult to estimate the natural course and prognosis of NETs from tailgut cysts. However, a subset of them, especially Grade 2 and 3 tumors, have malignant potential to show disease progression and resistance to treatment. Somatostatin analog treatment even after total removal of the tumor is recommended in case the specimen is positive for somatostatin receptor Type 2. Additional surgery is necessary for the local recurrence and newly found metastatic lesions. If they are unresectable, we have to do additional radiation therapy or chemotherapy. Meticulous postoperative check-

up with CT or magnetic resonance imaging is essential for early detection of local recurrence, enlargement of the residual tumor, and new metastatic lesions.

In NETs from tailgut cysts, the correct preoperative diagnosis is difficult even with biopsy. Three of seven patients were misdiagnosed at biopsy. The rarity and variety of sacral tumors makes the preoperative diagnosis even more difficult. However, there are some clues to be used in the preoperative diagnosis derived from our case. Scallop of sacral bone and spinal cord tethering are mostly associated with congenital tumors: teratoma, dermoid/epidermoid cyst, and tailgut cyst. The cystic component and presacral location indicate higher probability of a tailgut cyst. Furthermore, progressive neurologic symptoms and local lymph nodes swelling suggest tumor enlargement with malignant transformation from the epithelial cells of the tailgut cyst.

Conclusion

Presacral congenital tumors, such as teratoma, epidermoid, dermoid, and tailgut cysts, have a potential of malignant transformation from their epithelial components into NET or adenocarcinoma. For the complete differential diagnostic analysis in such cases, we should consider this rare pathology from the signs of congenital sacral abnormalities and progressive malignancy. In addition, in these cases, it is possible to have spinal cord tethering.

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References

- [1] Hjermstad BM, Helwig EB. Tailgut cysts. Report of 53 cases. *Am J Clin Pathol* 1988;89:139–47.
- [2] Mathis KL, Dozois EJ, Grewal MS, Metzger P, Larson DW, Devine RM. Malignant risk and surgical outcomes of presacral tailgut cysts. *Br J Surg* 2010;97:575–9.
- [3] Klimstra DS, Modlin IR, Coppola D, Lloyd RV, Suster S. The pathologic classification of neuroendocrine tumors: a review of nomenclature, grading, and staging systems. *Pancreas* 2010;39:707–12.
- [4] Yao JC, Hassan M, Phan A, Dagohoy C, Leary C, Mares JE, et al. One hundred years after “carcinoid”: epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. *J Clin Oncol* 2008;26:3063–72.
- [5] Zoccali M, Hart J, Fichera A. Image of the month. Low-grade neuroendocrine carcinoma arising from a tailgut cyst. *Arch Surg* 2012;147:93–4.
- [6] Wöhlke M, Sauer J, Dommisch K, Gorling S, Valdivia A, Hinze R. Primary metastatic well-differentiated neuroendocrine tumor arising in a tailgut cyst. [German]. *Pathologe* 2011;32:165–7.
- [7] Spada F, Pelosi G, Squadrone M, Lorizzo K, Farris A, de Braud F, et al. Neuroendocrine tumour arising inside a retro-rectal tailgut cyst: report of two cases and a review of the literature. *Ecancermedicalscience* 2011;5:201.

- [8] Niazi TN, Shah LM, Chin SS, Schmidt MH. Isolated intradural lumbosacral tailgut cyst with carcinoid features. *J Neurosurg Spine* 2011;14:382–7.
- [9] La Rosa S, Boni L, Finzi G, Vigetti D, Papanikolaou N, Tenconi SM, et al. Ghrelin-producing well-differentiated neuroendocrine tumor (carcinoid) of tailgut cyst. Morphological, immunohistochemical, ultrastructural, and RT-PCR study of a case and review of the literature. *Endocr Pathol* 2010;21:190–8.
- [10] Liang JJ, Alrawi S, Fuller GN, Tan D. Carcinoid tumors arising in tailgut cysts may be associated with estrogen receptor status: case report and review of the literature. *Int J Clin Exp Pathol* 2008;1:539–43.
- [11] Lee CM, Lee SH, Jeon CW, Ahn BK, Baek SU. Carcinoid tumor arising within a tailgut cyst: a case report. *J Korean Soc Coloproctol* 2007;23:65–7.
- [12] Mathieu A, Chamlou R, Le Moine F, Maris C, Van de Stadt J, Salmon I. Tailgut cyst associated with a carcinoid tumor: case report and review of the literature. *Histol Histopathol* 2005;20:1065–9.
- [13] Song DE, Park JK, Hur B, Ro JY. Carcinoid tumor arising in a tailgut cyst of the anorectal junction with distant metastasis: a case report and review of the literature. *Arch Pathol Lab Med* 2004;128:578–80.
- [14] Jacob S, Dewan Y, Joseph S. Presacral carotinoid tumor arising in a tailgut cyst—a case report. *Indian J Pathol Microbiol* 2004;47:32–3.
- [15] Mourra N, Caplin S, Parc R, Flejou JF. Presacral neuroendocrine carcinoma developed in a tailgut cyst: report of a case. *Dis Colon Rectum* 2003;46:411–3.
- [16] Oyama K, Embi C, Rader AE. Aspiration cytology and core biopsy of a carcinoid tumor arising in a retrorectal cyst: a case report. *Diagn Cytopathol* 2000;22:376–8.
- [17] Prasad AR, Amin MB, Randolph TL, Lee CS, Ma CK. Retrorectal cystic hamartoma. Report of 5 cases with malignancy arising in 2. *Arch Pathol Lab Med* 2000;124:725–9.
- [18] Horenstein MG, Erlandson RA, Gonzalez-Cueto DM, Rosai J. Presacral carcinoid tumors: report of three cases and review of the literature. *Am J Surg Pathol* 1998;22:251–5.
- [19] Lin SL, Yang AH, Liu HC. Tailgut cyst with carcinoid: a case report. *Zhonghua Yi Xue Za Zhi (Taipei)* 1992;49:57–60.
- [20] Rindi G, Arnold R, Bosman FT, Capella C, Klimstra DS, Klöppel G, et al. Nomenclature and classification of neuroendocrine neoplasms of the digestive system. In: Bosman FT, Carneiro F, Hruban RH, Theise ND, eds. *WHO classification of tumours of the digestive system*. Lyon, France: International Agency for Research on Cancer, 2010:13–4.
- [21] Volante M, Brizzi MP, Faggiano A, La Rosa S, Rapa I, Ferrero A, et al. Somatostatin receptor type 2A immunohistochemistry in neuroendocrine tumors: a proposal of scoring system correlated with somatostatin receptor scintigraphy. *Mod Pathol* 2007;20:1172–82.
- [22] Skandalakis JE, Gray SW, Ricketts R. The colon and rectum. In: Skandalakis JE, Gray SW, eds. *Embryology for surgeons*. Baltimore, MD: Williams and Wilkins, 1994:242–52.
- [23] Dahan H, Arrive L, Wendum D, Docou le Pointe H, Djouhri H, Tubiana JM. Retrorectal developmental cysts in adults: clinical and radiologic-histopathologic review, differential diagnosis, and treatment. *Radiographics* 2001;21:575–84.
- [24] Gonul II, Baglan T, Pala I, Mentes B. Tailgut cysts: diagnostic challenge for both pathologists and clinicians. *Int J Colorectal Dis* 2007;22:1283–5.
- [25] Larsen WJ. The fourth week. In: Sherman LS, Potter SS, Scott WJ, eds. *Human embryology*. Philadelphia, PA: Churchill Livingstone, 2001:86–91.
- [26] Chan JA, Kulke MH. New treatment options for patients with advanced neuroendocrine tumors. *Curr Treat Options Oncol* 2011;12:136–48.
- [27] Culler MD, Oberg K, Arnold R, Krenning EP, Sevilla I, Diaz JA. Somatostatin analogs for the treatment of neuroendocrine tumors. *Cancer Metastasis Rev* 2011;30(1 Suppl):9–17.
- [28] Furuta M, Hayakawa K, Kato S, Mitsuhashi N, Nakajima T, Niibe H. Malignant neuroendocrine tumor presenting a huge mediastinal mass controlled with radiation therapy. *Lung Cancer* 1998;22:55–8.
- [29] Oberg K, Castellano D. Current knowledge on diagnosis and staging of neuroendocrine tumors. *Cancer Metastasis Rev* 2011;30(1 Suppl):3–7.