Primary Presacral Neuroendocrine Tumors Presented by Lumbosacral Pain: a Case Report

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Abstract: Primary presacral neuroendocrine tumors (NETs) are exceedingly rare and often present with extensive metastases, posing significant challenges for clinical management. We report a case of a presacral neuroendocrine tumor in a 68-year-old male who presented with lumbosacral pain. Enhanced MRI revealed a soft tissue mass at the sacrococcygeal region, while whole-body enhanced 18F-PET/CT identified small intratumoral vessels and involvement of the adjacent rectal posterior wall, mesorectal fascia, presacral fascia, and sacrococcygeal bones, accompanied by multiple lymph node metastases and widespread metastases to the lungs, liver, and bones. A CT-guided biopsy confirmed the diagnosis of a grade 2 (G2) neuroendocrine tumor. Given the tumor's extensive metastasis and aggressive nature, surgical intervention was deemed unsuitable, and the patient was treated with sulfatinib. Sulfatinib shows significant potential in managing advanced neuroendocrine tumors, providing an effective therapeutic option for patients with such complex and high-risk conditions.

***Keywords*:** neuroendocrine tumors, diagnostic imaging, presacral tumors

1. Introduction

Neuroendocrine tumors (NETs) are a heterogeneous group of malignant tumors originating from neuroendocrine cells, commonly found in the gastrointestinal tract, pancreas, and lungs. Small intestine neuroendocrine tumors are the most frequent gastrointestinal NETs, followed by pancreatic neuroendocrine tumors[1]. However, primary presacral neuroendocrine tumors (pNETs) are extremely rare, with unclear incidence and epidemiological characteristics[2]. We present a case involving a 68-year-old male diagnosed with a primary presacral neuroendocrine tumor through a pathological biopsy, with multiple metastases to adjacent lymph nodes, lungs, liver, and bones. The anatomical complexity of the presacral region often leads to late-stage detection, increasing the challenges in diagnosis and treatment. Due to its rarity, there is limited research on the imaging and pathological features of presacral neuroendocrine tumors, posing significant challenges for early identification and management by clinicians[3]. This report aims to provide a detailed account of a rare case of presacral neuroendocrine tumor, highlighting its clinical presentation, imaging findings, and pathological characteristics to enhance understanding and management of this uncommon tumor.

2. Case Report

A 68-year-old male presented with lumbosacral pain of six months' duration, initially ignored but worsening significantly over the past month, prompting him to seek medical attention at a local hospital. CT imaging revealed a large presacral soft tissue mass, partially extending to the right side of the sacral canal. He was subsequently referred to our hospital for further evaluation.

Upon admission, the patient underwent comprehensive and systematic examinations. Physical examination revealed no significant abnormalities. Laboratory tests showed elevated levels of alkaline phosphatase (ALP) at 147 U/L, C-reactive protein (CRP) at 16.4 mg/L, and gamma-glutamyl transferase (GGT) at 92 U/L. Notably, common tumor markers including carbohydrate antigen 199 (CA199), carbohydrate antigen 125 (CA125), carcinoembryonic antigen (CEA), total prostate-specific antigen (PSA), and neuron-specific enolase (NSE) showed no significant abnormalities.

The patient underwent enhanced magnetic resonance imaging (MRI) of the lower abdomen. The MRI revealed a heterogeneous soft tissue mass measuring approximately 63 mm × 53 mm × 67 mm at the sacrococcygeal region (Figure 1). The mass appeared hypointense on T1-weighted imaging and heterogeneously hyperintense on T2-weighted imaging with restricted diffusion and marked heterogeneous enhancement upon contrast administration, involving the rectum. Multiple bone metastases were observed in the bilateral iliac bones, ischia, proximal femurs, fifth lumbar vertebra - second sacral vertebra. Additionally, multiple lymph node metastases were noted in the left obturator region and para-aortic areas. The imaging diagnosis suggested rectal carcinoma with multiple bone and lymph node metastases.

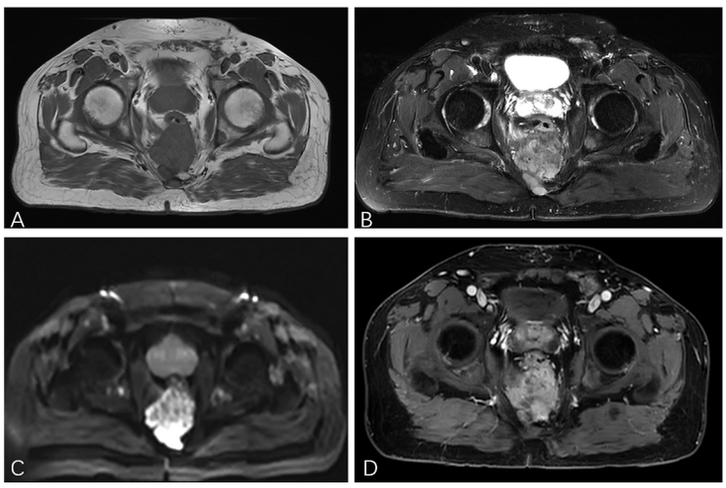

Figure 1. MR Images showed a 64 mm × 53 mm cystic and solid mass in the presacral region. (A) Axial T1-weighted MR Images showing a mass with hypointensity. (B) Axial fat-suppressed T2-weighted MR Images showing a mass with hyperintensity. (C) Diffusion-weighted images showing diffusion restriction. (D) Axial contrast-enhanced T1-weighted images showing significant enhancement.

To evaluate the systemic condition, a PET/CT scan was performed (Figure 2). The scan revealed an irregular soft tissue mass in the presacral space, involving the serosal surface of the adjacent rectal posterior wall, bilateral mesorectal fascia, presacral fascia, and sacrococcygeal bones, with SUVmax of 8.1. The enhanced scan showed significant enhancement, with Hounsfield units (HU) increasing from 47 to 75 post-contrast, and multiple small arteries within the lesion during the arterial phase. Multiple abnormal FDG-avid enlarged lymph nodes were seen along the presacral, bilateral iliac, and para-aortic regions, with SUVmax of around 8.6. Multiple FDG-avid nodules were detected in both lungs, with SUVmax of about 6.2. A multi-loculated cystic mass measuring 32 mm × 22 mm × 20 mm was identified in segment 6 of the liver, with significant arterial phase enhancement and a slight reduction in enhancement during the venous and equilibrium phases (Figure 3). Widespread osteoblastic bone changes were also noted.

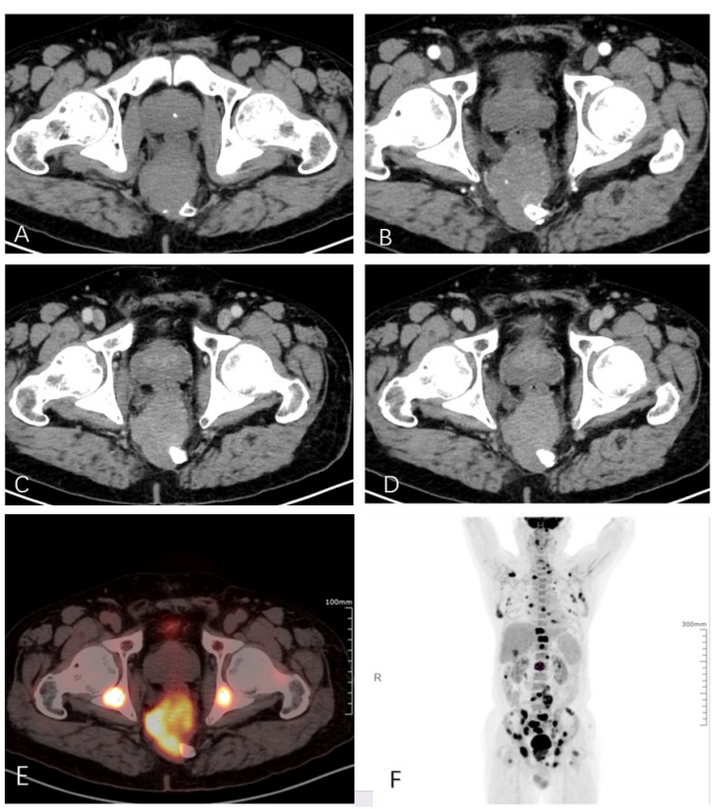

Figure 2. 18F-PET/CT image showing a mass located in the presacral region. (A) Axial unenhanced CT image showing an irregular mass invading the posterior wall of the rectum. (B) Axial contrast-enhanced CT image showing enhanced small vessel shadow in the mass (C) Venous phase (D) Delayed phase (E) 18F-FDG metabolism map (F) Maximum intensity projection.

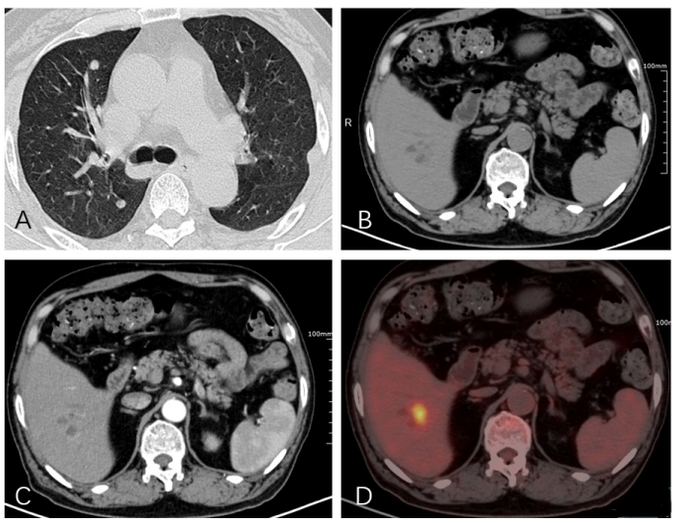

Figure 3. (A) Axial lung window showing bilateral lung metastases. (B) Axial CT image showing cystic and solid mass in the liver (C) Marked enhancement of the solid part in the arterial phase (D) Active metabolism of the intrahepatic mass.

To further diagnose the nature and origin of the tumor, a CT-guided biopsy of the presacral tumor was performed. Hematoxylin and eosin (HE) staining revealed nest-like and trabecular structures of tumor cells with mild cellular morphology and no significant nuclear atypia (Figure 4). Immunohistochemical staining showed positivity for cytokeratin (CK) (AE1/AE3), CD56, chromogranin A (CgA), synaptophysin (Syn), P53, somatostatin receptor 2 (SSTR2), and succinate dehydrogenase B (SDH-B), and negativity for CK7, and PSA. The Ki-67 index was approximately 5%. Based on histopathological and immunohistochemical findings, the tumor was definitively diagnosed as a grade 2 (G2) neuroendocrine tumor. Given the extensive metastasis indicated by PET/CT and the advanced clinical stage, surgery was not a viable option. Following clinical guidelines, the patient was started on oral targeted therapy with sulfatinib at a daily dose of 300 mg.

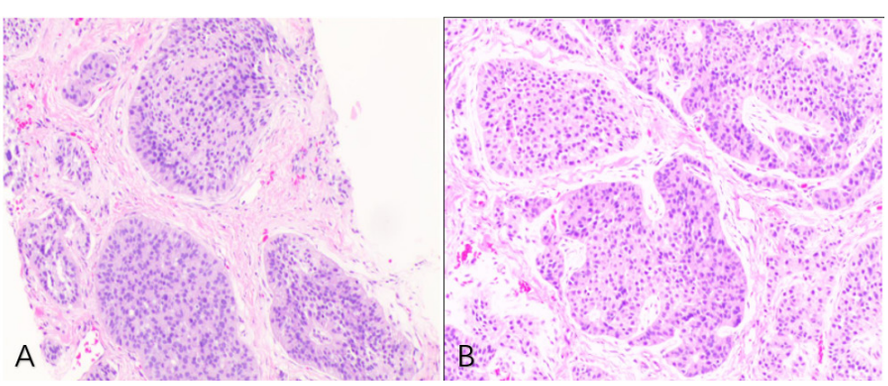

Figure 4. Pathological results (A-B) HE staining showed that the tumor cells were distributed in nests without obvious nuclear atypia.

3. Discussion

The presacral space, located between the rectum, sacrum, peritoneal reflection, and levator ani muscles in the pelvic cavity, is a complex anatomical region[4]. It contains structures such as the sacral plexus, iliac vessels, and connective tissues that support various organs, making it a site for diverse pathologies, including developmental cysts, teratomas, neurogenic tumors, chordomas, and other skeletal tumors[5,6]. However, primary neuroendocrine tumors originating from the retroperitoneum are exceedingly rare[3,7]. The retroperitoneal space allows tumors to grow significantly before causing symptoms like sacrococcygeal/perianal pain and bowel dysfunction, which often leads to the detection of relatively large retroperitoneal neuroendocrine tumors[8].

In imaging studies, retroperitoneal neuroendocrine tumors typically present as morphologically varied masses. Small tumors often appear as round or oval homogeneous solid masses, whereas larger tumors tend to be lobulated and heterogeneous with cystic, hemorrhagic, and necrotic areas. Due to their rich capillary network, these tumors usually show significant uniform or heterogeneous enhancement on contrast scans. Differential diagnoses for retroperitoneal neuroendocrine tumors include presacral chordomas, rectal cancer, and secondary metastatic cancer. Chordomas typically occur in the sacrococcygeal

and cranial base regions, presenting as osteolytic lesions on CT and MRI, sometimes with soft tissue components and calcifications[9]. Rectal cancer often presents with bleeding, changes in bowel habits, and symptoms of intestinal obstruction, characterized by irregular rectal wall thickening and mass formation, often accompanied by lymphadenopathy and distant metastasis[10]. Secondary metastatic cancers can originate from various primary tumors such as lung, breast, and prostate cancers, presenting with multiple lesions and often with evidence of the primary tumor[11]. In our case, the patient, a 68-year-old male, had no history of tumors. Colonoscopy did not reveal any significant organic lesions. The tumor, located in the retroperitoneal presacral region, exhibited a lobulated appearance with heterogeneous enhancement and multiple small arteries on the enhanced scan, thus not supporting the three differential diagnoses mentioned above. Given the absence of evidence for tumors in common sites such as the gastrointestinal tract and pancreas, the widespread distribution of multiple pulmonary nodules, and extensive metastases to the liver and bones, the primary diagnosis was a presacral neuroendocrine tumor with extensive local and distant metastases.

Neuroendocrine tumors are a group of tumors originating from the diffuse neuroendocrine cells throughout the body, characterized by a wide range of clinical manifestations[12]. The 2019 World Health Organization classification divides neuroendocrine tumors into two categories: well-differentiated, low-proliferation tumors such as carcinoids, and poorly differentiated, high-proliferation tumors such as small cell or large cell neuroendocrine carcinomas. This classification is crucial for assessing tumor grading and potential disease prognosis, based on the degree of differentiation and proliferative activity (i.e., Ki-67 index and mitotic count). Tumors are classified as low grade (G1) when the Ki-67 index is <3% and mitotic count is <2 per 10 high-power fields (HPF), intermediate grade (G2) when the Ki-67 index is 3-20% and mitotic count is 2-20 per 10 HPF, and high grade (G3) when the Ki-67 index is >20% and mitotic count is >20 per 10 HPF[13]. According to this classification, the patient was diagnosed with a well-differentiated, intermediate-grade (G2) neuroendocrine tumor.

Previous studies indicate that most neuroendocrine tumors grow slowly with low risks of local invasion and metastasis, and have relatively low mortality rates[14]. Surgical resection is the preferred treatment for well-differentiated neuroendocrine tumors that are confined locally or have a small metastatic tumor burden. Radical surgical resection is the first-line treatment for primary neuroendocrine tumors, but data show a high recurrence risk of 13.7%-43% post-radical resection of pancreatic neuroendocrine tumors, with recurrent patients often developing distant metastases and poorer survival outcomes[15]. For metastatic neuroendocrine tumors, systemic treatment options are considered to control disease progression, including radiolabeled peptide therapy (such as 177Lu-DOTATATE), somatostatin analogs (SSA), and targeted therapies (such as everolimus). These treatments can provide palliative benefits. Therefore, a multidisciplinary approach combining surgery, radiotherapy, chemotherapy, and targeted therapy may significantly impact patient prognosis[16, 17].

In this patient, the extensive involvement of multiple vital organs and widespread metastasis made radical surgical resection unfeasible. Considering the differences between neuroendocrine tumors in China and other countries, and the current clinical situation domestically, sulfatinib emerged as a new treatment option[18]. Sulfatinib, with its anti-angiogenic and immune-modulating mechanisms, has significant implications for inhibiting tumor growth and extending survival in patients. Phase III clinical trials in China have shown that sulfatinib significantly prolongs progression-free survival and improves objective response rates in patients with advanced neuroendocrine tumors[19]. Thus, it offers an effective treatment choice for patients with such high-complexity and high-risk profiles.

4. Conclusion

We report an exceptionally rare case of primary presacral neuroendocrine tumor (G2) involving the serosal surface of the adjacent rectal posterior wall, bilateral mesorectal fascia, presacral fascia, and sacrococcygeal bones, with metastases to the lungs, liver, and multiple bones throughout the body. This case highlights the importance of considering primary retroperitoneal neuroendocrine tumors in the differential diagnosis when encountering irregular solid masses in the presacral region. Early diagnosis and treatment are crucial for improving patient survival and quality of life. Accumulating and summarizing experiences from future cases will provide valuable references for clinicians, advancing the diagnostic and therapeutic approaches for presacral neuroendocrine tumors.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] K. Öberg, and D. Castellano, Current knowledge on diagnosis and staging of neuroendocrine tumors. Cancer and Me-

tastasis Reviews 30 (2011) 3-7.
[2] S. La Rosa, L. Boni, G. Finzi, D. Vigetti, N. Papanikolaou, S.M. Tenconi, G. Dionigi, M. Clerici, S. Garancini, and C. Capella, 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. Endocrine Pathology 21 (2010) 190-198.
[3] A. Lee, T.S. Suhardja, T.C. Nguyen, and W.M.-K. Teoh, Neuroendocrine tumour developing within a long-standing tailgut cyst: case report and review of the literature. Clinical Journal of Gastroenterology 12 (2019) 539-551.
[4] Z. Li, and M. Lu, Presacral Tumor: Insights From a Decade's Experience of This Rare and Diverse Disease. Frontiers in Oncology 11 (2021).
[5] J. Ghosh, T. Eglinton, F.A. Frizelle, and A.J.M. Watson, Presacral tumours in adults. The Surgeon 5 (2007) 31-38.
[6] E. Canelles, J.V. Roig, M. Cantos, J. García Armengol, E. Barreiro, F.L. Villalba, M.D. Ruiz, and V. Pla, Tumores presacros. Análisis de nuestra experiencia en 20 casos tratados quirúrgicamente. Cirugía Española 85 (2009) 371-377.
[7] K. Kodera, S. Eto, N. Fukasawa, W. Kai, T. Matsumoto, T. Hirabayashi, H. Kawahara, and N. Omura, Laparoscopic resection of a neuroendocrine tumor that almost fully replaced tailgut cysts: a case report. Surgical Case Reports 6 (2020).
[8] D. Shi, G.-Q. Dong, K.-R. Shen, Y. Pan, S.-M. Wei, Y. Chen, and R.-S. Yu, Primary cystic and solid neuroendocrine tumor of the retroperitoneum. Medicine 100 (2021).
[9] V. Ulici, and J. Hart, Chordoma. Archives of Pathology & Laboratory Medicine 146 (2022) 386-395.
[10] E. Dekker, P.J. Tanis, J.L.A. Vleugels, P.M. Kasi, and M.B. Wallace, Colorectal cancer. The Lancet 394 (2019) 1467-1480.
[11] R. Syed, J.A. Bishop, and S.Z. Ali, Sacral and presacral lesions: Cytopathologic analysis and clinical correlates. Diagnostic Cytopathology 40 (2010) 7-13.
[12] Ashley K. Clift, M. Kidd, L. Bodei, C. Toumpanakis, Richard P. Baum, K. Oberg, Irvin M. Modlin, and A. Frilling, Neuroendocrine Neoplasms of the Small Bowel and Pancreas. Neuroendocrinology 110 (2020) 444-476.
[13] I.D. Nagtegaal, R.D. Odze, D. Klimstra, V. Paradis, M. Rugge, P. Schirmacher, K.M. Washington, F. Carneiro, and I.A. Cree, The 2019 WHO classification of tumours of the digestive system. Histopathology 76 (2019) 182-188.
[14] J.-H. Fan, Y.-Q. Zhang, S.-S. Shi, Y.-J. Chen, X.-H. Yuan, L.-M. Jiang, S.-M. Wang, L. Ma, Y.-T. He, C.-Y. Feng, X.-B. Sun, Q. Liu, K. Deloso, Y. Chi, and Y.-L. Qiao, A nation-wide retrospective epidemiological study of gastroenteropancreatic neuroendocrine neoplasms in china. Oncotarget 8 (2017) 71699-71708.
[15] M.H. Shah, W.S. Goldner, A.B. Benson, E. Bergsland, L.S. Blaszkowsky, P. Brock, J. Chan, S. Das, P.V. Dickson, P. Fanta, T. Giordano, T.R. Halfdanarson, D. Halperin, J. He, A. Heaney, M.J. Heslin, F. Kandeel, A. Kardan, S.A. Khan, B.W. Kuvshinoff, C. Lieu, K. Miller, V.G. Pillarisetty, D. Reidy, S.A. Salgado, S. Shaheen, H.P. Soares, M.C. Soulen, J.R. Strosberg, C.R. Sussman, N.A. Trikalinos, N.A. Uboha, N. Vijayvergia, T. Wong, B. Lynn, and C. Hochstetler, Neuroendocrine and Adrenal Tumors, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 19 (2021) 839-868.
[16] J. Franko, W. Feng, L. Yip, E. Genovese, and A.J. Moser, Non-functional Neuroendocrine Carcinoma of the Pancreas: Incidence, Tumor Biology, and Outcomes in 2,158 Patients. Journal of Gastrointestinal Surgery 14 (2010) 541-548.
[17] A.K. Stueven, A. Kayser, C. Wetz, H. Amthauer, A. Wree, F. Tacke, B. Wiedenmann, C. Roderburg, and H. Jann, Somatostatin Analogues in the Treatment of Neuroendocrine Tumors: Past, Present and Future. International Journal of Molecular Sciences 20 (2019).
[18] A. Dasari, C. Shen, D. Halperin, B. Zhao, S. Zhou, Y. Xu, T. Shih, and J.C. Yao, Trends in the Incidence, Prevalence, and Survival Outcomes in Patients With Neuroendocrine Tumors in the United States. JAMA Oncology 3 (2017).
[19] J. Xu, L. Shen, C. Bai, W. Wang, J. Li, X. Yu, Z. Li, E. Li, X. Yuan, Y. Chi, Y. Yin, W. Lou, N. Xu, Y. Bai, T. Zhang, D. Xiu, X. Wang, Y. Yuan, J. Chen, S. Qin, R. Jia, M. Lu, Y. Cheng, Z. Zhou, J. Li, J. He, and W. Su, Surufatinib in advanced pancreatic neuroendocrine tumours (SANET-p): a randomised, double-blind, placebo-controlled, phase 3 study. The Lancet Oncology 21 (2020) 1489-1499.

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