REPORTE DE CASO

Mixed Neuroendocrine-NonNeuroendocrine Neoplasm of the Sigmoid colon: the first case reported in Perú

Neoplasia mixta neuroendocrina-no neuroendocrina del colon sigmoides: primer caso reportado en Perú

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ABSTRACT
Mixed Neuroendocrine-NonNeuroendocrine Neoplasms (MiNENs) are rare and aggressive entities, with scarce reports worldwide, especially from Latin America. We describe the first documented case of sigmoid MiNEN in Perú in a 77-year-old woman with a history of hypertension, diabetes, and osteoporosis who presented with left lower quadrant pain and abdominal distension. Colonoscopy revealed polyps, one of which was histologically consistent with a large-cell neuroendocrine carcinoma (NEC) and a high-grade tubular adenoma, each accounting for ≥30% of the lesion, fulfilling MiNEN criteria. Immunohistochemistry confirmed the diagnosis with an Antigen Kiel 67 [Ki-67] index of 70%. Positron Emission Computed Tomography (PET/CT) demonstrated focal uptake without nodal involvement. The patient underwent laparoscopic radical sigmoidectomy with colorectal anastomosis; histopathology confirmed submucosal invasion and metastasis in 5/14 lymph nodes. She was subsequently started on adjuvant carboplatin/etoposide chemotherapy and remains under oncological follow-up. This case underscores the diagnostic and therapeutic challenges of colorectal MiNENs, highlights the role of PET/CT as well as multidisciplinary management, and emphasizes the importance of considering radical resection even after endoscopic removal, given the high risk of recurrence and aggressive biological behavior.
Keywords: *Neoplasms, Complex and Mixed; Neuroendocrine Tumors; Immunohistochemistry (source: MeSH NLM).*

RESUMEN
Las Neoplasias Mixtas Neuroendocrinas-No Neuroendocrinas (MiNENs) son tumores infrecuentes y agresivos, con escasos reportes a nivel mundial, sobre todo provenientes de América Latina. Presentamos el primer caso documentado de MiNEN sigmoideo en Perú en una mujer de 77 años, con antecedentes de hipertensión, diabetes y osteoporosis, quien presentó dolor en fosa iliaca izquierda y distensión abdominal. La colonoscopia evidenció pólipos, uno de ellos compatible con carcinoma neuroendocrino de células grandes y adenoma tubular de alto grado, cada uno representando ≥30% de la lesión, cumpliendo criterios de MiNEN. La inmunohistoquímica confirmó el diagnóstico (Ki-67: 70%). La PET/CT mostró captación focal sin compromiso ganglionar. Se realizó sigmoidectomía radical laparoscópica con anastomosis colorrectal; la histopatología confirmó infiltración submucosa y metástasis en 5/14 ganglios linfáticos. Posteriormente inició quimioterapia adyuvante con carboplatino/etopósido y permanece en seguimiento oncológico. Este caso subraya los retos diagnósticos y terapéuticos de los MiNENs colorrectales, destaca el papel de la PET/CT y del manejo multidisciplinario, y enfatiza la necesidad de considerar la resección radical incluso tras la resección endoscópica, debido al alto riesgo de recurrencia y su comportamiento biológico agresivo.
Palabras clave: *Neoplasias Complejas y Mixtas; Tumores Neuroendocrinos; Inmunohistoquímica (fuente: DeCS BIREME).*

INTRODUCTION

MiNENs, terminology originally proposed in 2016 [(1)], but added to the World Health Organization (WHO) classification in 2019 [(2)], are exceptionally uncommon entities in which two morphologically recognizable components, i.e. a neuroendocrine (NE) neoplasia and a non-neuroendocrine (NNE) epithelial neoplasm, cohabit in the same tumor mass. Importantly, each of the two components: 1) must be malignant and 2) should represent at least 30% of the

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neoplastic burden [2]. Moreover, the NE component of MiNENs can be morphologically either well-differentiated neuroendocrine tumors (NETs) or poorly differentiated NECs. In addition to morphology, the assessment of the proliferative rate (including both mitotic count and the Ki-67 index) is extremely important for correct identification of the NE component. On the other hand, the NNE component may show histologic features of adenocarcinoma (reported in 90% of the cases) [3], signet ring cell carcinoma or squamous cell carcinoma. Furthermore, MiNENs have been classified into three categories (high, intermediate and low) according to the grade of each cellular component, which may have prognostic implications similar to pure tumors of the same grade (Table 1) [4].

Establishing the real incidence of MiNENs in the general population is still an unmet need in medicine due to inconsistent reporting and varying nomenclature over the past several years; however, Song *et al.* [5] recently reported, in a database analysis of 767 patients: no sex predominance, patients were mainly diagnosed between the ages of 50 and 70 (55.4%, median age of 60 years) and interestingly, even though, it is well known that MiNENs may affect multiple organs; it has an anatomical preference for the distal digestive tract, being the appendix the most common site.

This report details a case of sigmoid MiNEN confirmed through both histological and immunohistochemical analysis in a 77-year-old female. The patient underwent laparoscopic radical sigmoidectomy and is now receiving adjuvant chemotherapy (carboplatin/etoposide). The report highlights that this is the first documented instance of such a case in Perú. Written consent for publication was provided by the patient.

CASE REPORT

A 77-year-old female with a past medical history of hypertension, type 2 diabetes mellitus, and osteoporosis presented with a 3-month history of recurrent episodes of left lower quadrant abdominal pain associated with abdominal distension. Colonoscopy revealed three polyps in the left colon and sigmoid colon, which were resected endoscopically without complications. Histopathological evaluation of the endoscopic specimen revealed findings consistent with a large-cell NEC associated with high-grade tubular adenoma. Importantly, with each component comprising at least 30% of the neoplasm, fulfilling criteria for a MiNEN. Immunohistochemistry demonstrated Caudal-type homeobox 2 (CDX2) and Special AT-rich sequence-binding protein 2 (SATB2) positivity in the invasive component, Cytokeratin 20 (CK20) positivity in the adenomatous component, focal synaptophysin expression, and a Ki-67 index of 70%.

The patient was referred to the surgical service for evaluation. A subsequent PET/CT demonstrated minimal focal uptake at the endoscopically resected surgical bed (Figure 1) without evidence of lymph node involvement. Based on the PET/CT and the prior histologic findings obtained during the colonoscopy, a multidisciplinary decision was made to proceed with surgical management.

Table 1. Proposed grading of MiNENs [4].

Grades	Neuroendocrine component	Non-Neuroendocrine component
Low	Well-differentiated NETs Grade 1: Ki-67 <3, MI <2/10HPF Grade 2: Ki-67 3-20, MI 2-20/10 HPF	Adenoma
Intermediate	Well-differentiated NETs Grade 1: Ki-67 <3, MI <2 Grade 2: Ki-67 3-20, MI 2-20	Adenocarcinoma, Mucinous carcinoma, Signet ring cell carcinoma.
High	Poorly differentiated NEC (small/large cell) Grade 3: Ki-67 >20 Anaplastic/undifferentiated	Adenoma, Adenocarcinoma, Squamous cell carcinoma, Adenosquamous carcinoma, Mucinous carcinoma, Signet ring cell carcinoma

**HPF high-power field, MI mitotic index.

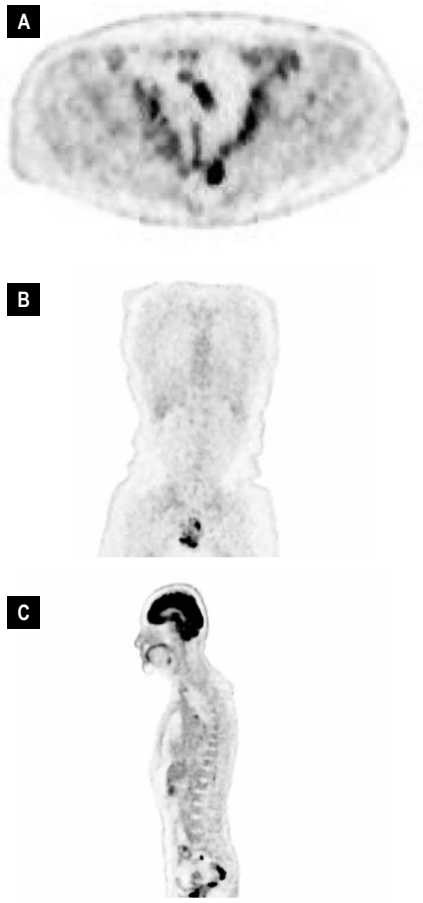

Figure 1. PET/CT findings. **A.** Axial view. **B.** Coronal view. **C.** Sagittal view. Approximately at 12 cm from the anal margin, along the rectum, there is an area of nodular thickening of the left rectal wall, intramural in location and showing intense metabolic activity (SUVmax 24.44), with an approximate diameter of 7 mm.

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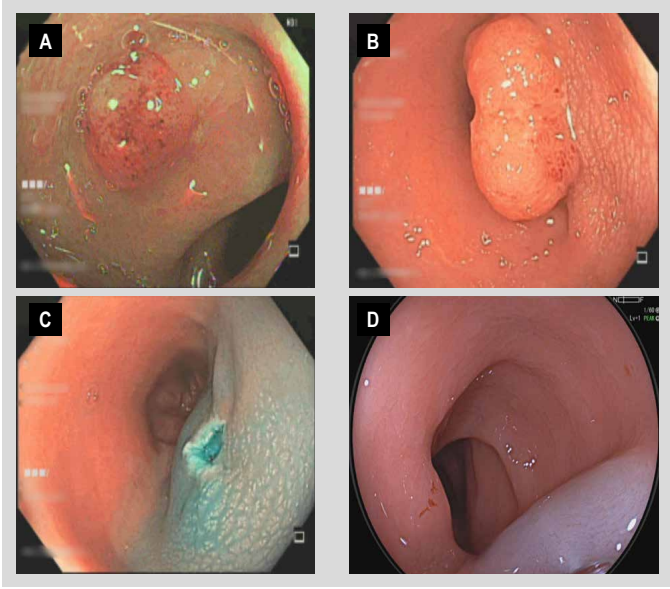

Figure 2. Colonoscopy findings. **A.** First colonoscopy: Left colon and sigmoid: three small polyps (~6 mm). **B.** First colonoscopy: Complex adenomatous polyp measuring 2.0 × 2.5 cm (Yamada II, Paris/Emura 0-I sp, pattern II). **C.** First colonoscopy: The complex lesion was located approximately at 12 cm from the anal verge and was marked with Indian ink. **D.** Second colonoscopy: showing scar at the site of previous endoscopic resection. The mucosa appears preserved, with no evidence of recurrence or residual disease. The area was subsequently marked with Indian ink.

In that regard, a second colonoscopy (Figure 2) was scheduled in order to: 1) evaluate the preceding resected sigmoid mucosa and. 2) tattoo the area prior to any surgical procedure. The patient underwent an elective laparoscopic radical sigmoidectomy (Figure 3) with colorectal anastomosis. Her postoperative course was uneventful. Histopathological examination of the resected specimen showed submucosal infiltration by poorly differentiated carcinoma with metastatic involvement in 5 of 14 regional lymph nodes, thereby confirming the MiNEN diagnosis. The immunohistochemical profile (Figure 4) was concordant with the initial biopsy, with synaptophysin and SATB2 positivity and a Ki-67 proliferative index of 70% (i.e. high-grade MiNEN [4]). The patient was subsequently referred to the oncology service, where she is currently receiving systemic chemotherapy.

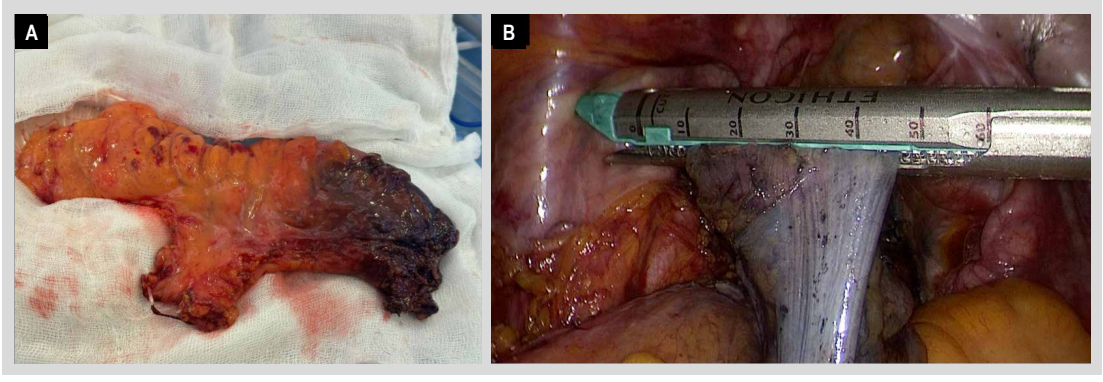

Figure 3. Surgical Specimen. **A.** Sigmoid colon marked with India ink prior to intestinal resection. **B.** Radical sigmoidectomy specimen measuring 14.0 × 2.5cm with an 8.0 cm mesentery. The serosa was smooth and glistening, without macroscopic alterations. Upon opening along the antimesenteric border, an irregular area measuring 0.6 cm in diameter was identified, located 2.5 cm from the distal surgical margin and 11.0 cm from the proximal surgical margin. The remaining colonic mucosa displayed preserved light brown folds.

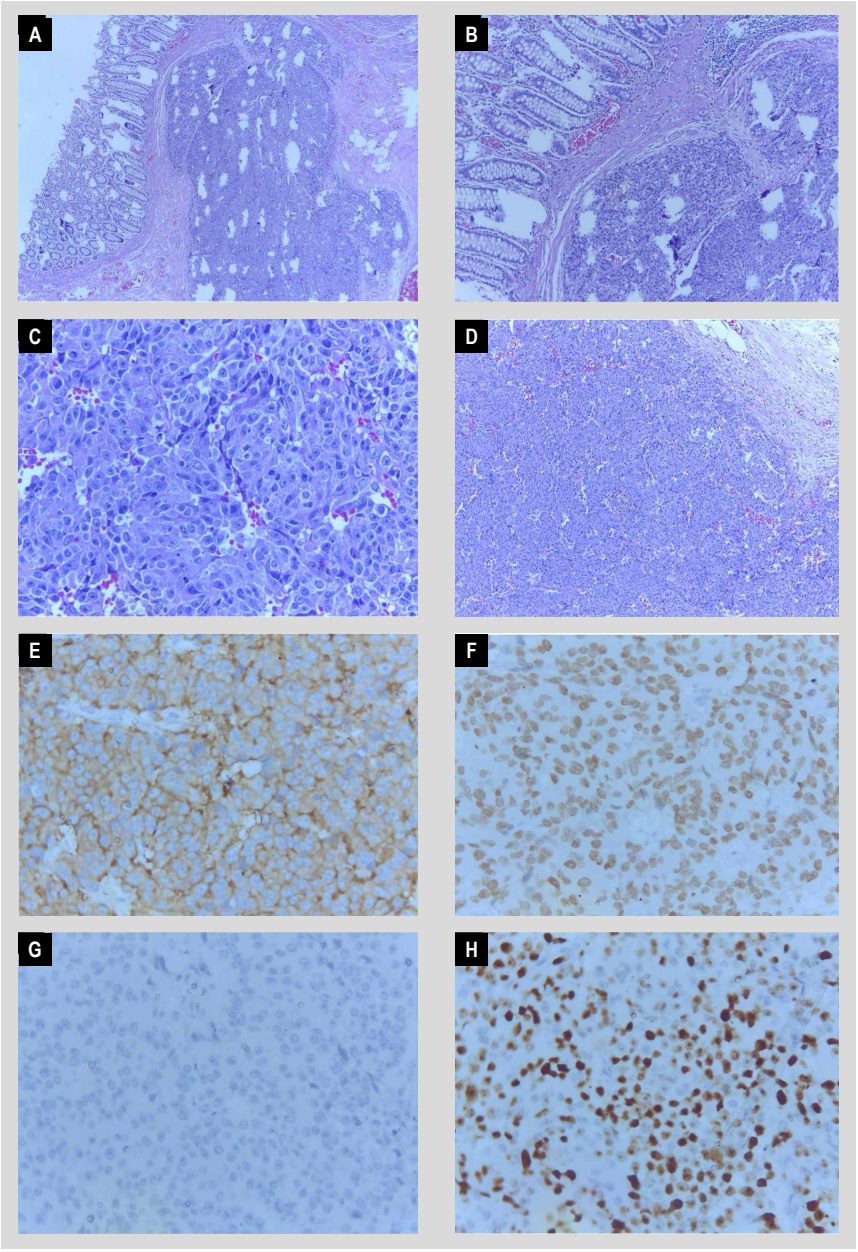

Figure 4. Histology: **A**. Colonic mucosa with preserved architecture and no epithelial dysplasia (H&E 4×). **B.** Submucosal solid, nodular neoplastic proliferation composed of cell nests infiltrating the stroma, consistent with large-cell neuroendocrine carcinoma (H&E 10×). **C.** Tumor cells are medium-to-large with well-defined borders, moderately abundant eosinophilic cytoplasm, and round-to-oval nuclei showing granular "salt-and-pepper" chromatin, evident nucleoli, and frequent mitoses (H&E 40×). **D.** One regional lymph node with metastatic neuroendocrine carcinoma (H&E 10×). Immunophenotype: **E.** Tumor cells were positive for both synaptophysin and **F.** SATB2. **G.** Tumor cells were negative for keratin. **H.** Tumor cells display a high proliferative index by Ki-67.

DISCUSSION

Establishing protocols for diagnosing and, most importantly, treating infrequent diseases is inherently challenging due to limited knowledge, resources, and the scarcity of cases.

Although MiNENs have been included in the WHO classification for several years, management guidelines still rely on retrospective studies, case reports, and case series; largely because the rarity of MiNENs makes prospective randomized trials difficult. Globally, less than 5% of all digestive NE neoplasms are MiNENs, with the majority of reports coming from Asia and Europe [6]. Data from the 2008 Surveillance of Rare Cancers in Europe (RARECARE) registry estimated the annual incidence of MiNENs at fewer than 0.01 cases per 100,000 individuals [7]. Evidence from Latin America is particularly limited, and to our knowledge, this appears to be the first reported case of

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sigmoid MiNEN in Perú, emphasizing the importance for regional data collection to enrich the current knowledge of this rare neoplasm.

As previously described, MiNEN diagnosis depends on histopathological evaluation and immunohistochemistry. In our patient, endoscopic polyp removal provided sufficient tissue to confirm the coexistence of a high-grade tubular adenoma and a large-cell NEC with a Ki-67 index of 70%. Immunohistochemical analysis further corroborated the diagnosis, showing focal synaptophysin expression along with CDX2 and SATB2 positivity in the NE component and CK20 expression in the adenomatous component. A subsequent PET/CT scan demonstrated minimal focal uptake at the endoscopically resected surgical bed without evidence of lymph node involvement. Recent evidence has shown that PET/CT is a crucial tool used in the multidisciplinary management of NE neoplasms, as the combination of morphological and functional imaging enhances diagnostic accuracy, facilitates the detection of small metastatic deposits, and guides treatment strategies [8]. Moreover, PET/CT has been demonstrated to be valuable in the preoperative staging of rectal cancer by revealing metabolic activity at the lesion site [9]. Based on the PET/CT results and the histologic evidence from colonoscopy, a multidisciplinary team determined that surgical resection was the most appropriate course of action.

This case illustrates why surgery was indicated despite initial endoscopic resection. Firstly, histopathology confirmed a high-grade MiNEN [10]; and secondly, PET/CT demonstrated minimal focal uptake at the resection bed, raising concern for residual disease. In this context, at least for our group, radical sigmoidectomy was justified for: 1) endoscopic removal alone carries a high risk of incomplete excision and local recurrence, particularly with high-grade tumors; 2) submucosal invasion and the high proliferative index further increase the probability of nodal spread and 3) the lack of robust evidence-based MiNEN guidelines direct us to individualize therapeutic options. Hence, a radical sigmoidectomy enables both definitive oncologic resection and accurate staging [11]. Indeed, histopathology of the surgical specimen confirmed submucosal infiltration and nodal metastases in 5/14 nodes, findings that would have been missed without the radical surgical approach. As a result, the procedure provided local control, prevented under-treatment, and allowed integration of systemic therapy into a multidisciplinary management plan.

MiNENs are complex entities and their treatment remains controversial. In localized disease, surgery is the only potentially curative option. However, prognosis remains poor, with reported five-year survival rates of only 20% to 50% [12]. In our case, the tumor was classified as a high-grade MiNEN [4]. According to international guidelines, its management should be analogous to pure NECs, as the NE fraction dictates both prognosis and therapeutic response [12]. For patients with resectable non-esophageal gastroenteropancreatic NECs, guidelines recommend radical surgical resection combined with platinum-based adjuvant chemotherapy (cisplatin or carboplatin plus etoposide), while neoadjuvant chemotherapy followed by surgery remains an alternative in patients at high risk of postoperative morbidity [12,13]. Staging is performed using the American Joint Committee on Cancer (AJCC) TNM classification applied to the organ of origin [13]. Pathological assessment of the resection specimen revealed submucosal invasion (T1), metastatic involvement of 5/14 regional lymph nodes (N2a), and no distant metastases (M0), corresponding to stage IIIA disease. In line with the limited existing management guidelines, diagnosis and treatment were performed accordingly in our patient.

Recent case reports described management strategies similar to ours. Tanaka *et al.* [14] reported a descending colon MiNEN treated with laparoscopic resection followed by adjuvant platinum-based chemotherapy, which is consistent with the role of formal oncologic resection plus systemic therapy in localized high-grade colorectal MiNEN. Similarly, Fujimura *et al.* [15] reported a rectal MiNEN initially diagnosed by endoscopic resection, but due to submucosal invasion and positive margins, definitive surgery was performed, revealing stage IIIb disease with nodal involvement and emphasizing the importance of oncologic resection after endoscopic diagnosis. Likewise, similar surgical decisions have been reported by Mukai *et al.* [16]; in a case of MiNEN of the ascending colon, composed of adenocarcinoma and NET grade 1, where a laparoscopic colectomy with lymphadenectomy was accomplished. Consequent to these reports, the management in our case was similar, with radical sigmoidectomy after endoscopic tumor removal ensuring adequate staging and local control; additionally, the finding of nodal metastases supported the use of adjuvant platinum-based chemotherapy.

This research, however, has several limitations. The primary limitation is that it is a case report, which affects its methodology. Specifically, it lacks generalizability, cannot establish cause-and-effect relationships, and is particularly vulnerable to selection bias.

As a final point, this case highlights the diagnostic and therapeutic challenges of colorectal MiNENs, a rare and complex neoplasm. In our patient, a combination of histopathology, immunohistochemistry, multidisciplinary team expertise, and PET/CT was essential for accurate diagnosis, staging, and therapeutic planning. Radical sigmoidectomy ensured local control and revealed submucosal invasion with nodal metastases, supporting surgery in localized disease despite initial endoscopic removal [17]. Adjuvant platinum-based chemotherapy was initiated in accordance with current recommendations for high-grade MiNENs. Notably, this represents the first reported case of sigmoid MiNEN in Peru, emphasizing the need for regional data collection in order to improve understanding and management of this uncommon disease for the formulation of future management guidelines.

REFERENCES

1. La Rosa S, Sessa F, Uccella S. Mixed Neuroendocrine-Nonneuroendocrine Neoplasms (MiNENs): Unifying the Concept of a Heterogeneous Group of Neoplasms. Endocr Pathol. 2016;27(4):284-311. doi: 10.1007/s12022-016-9432-9.
2. Klimstra DS, Kl€oppel G, La Rosa S. Classification of neuroendocrine neoplasms of the digestive system. In: World Health Organization. Classification of Tumours. Digestive system tumours. 5th ed. Lyon: IARC Press, 2019. 16-19 p.
3. Toor D, Loree JM, Gao ZH, Wang G, Zhou C. Mixed neuroendocrine-non-neuroendocrine neoplasms of the digestive system: A mini-review. World J Gastroenterol. 2022;28(19):2076-2087. doi: 10.3748/wjg.v28.i19.2076.
4. Jacob A, Raj R, Allison DB, Soares HP, Chauhan A. An Update on the Management of Mixed Neuroendocrine-Non-neuroendocrine Neoplasms (MiNEN). Curr Treat Options Oncol. 2022;23(5):721-735. doi: 10.1007/s11864-022-00968-y.
5. Song H, Yang S, Zhang Y, Hua Y, Kleeff J, Liu Q, *et al.* Comprehensive analysis of mixed neuroendocrine non-neuroendocrine neoplasms (MiNENs): A SEER database analysis of 767 cases. Front Oncol. 2023;12:1007317. doi: 10.3389/fonc.2022.1007317.
6. Díaz-López S, Jiménez-Castro J, Robles-Barraza CE, Ayala-de Miguel C, Chaves-Conde M. Mixed neuroendocrine non-neuroendocrine neoplasms in gastroenteropancreatic tract. World J Gastrointest Oncol. 2024;16(4):1166-1179. doi: 10.4251/wjgo.v16.i4.1166.
7. Frizziero M, Chakrabarty B, Nagy B, Lamarca A, Hubner RA, Valle JW, *et al*. Mixed Neuroendocrine Non-Neuroendocrine Neoplasms: A Systematic Review of a Controversial and Underestimated Diagnosis. J Clin Med. 2020;9(1):273. doi: 10.3390/jcm9010273.
8. Ebner R, Sheikh GT, Brendel M, Ricke J, Cyran CC. ESR Essentials: role of PET/CT in neuroendocrine tumors-practice recommendations by the European Society for Hybrid, Molecular and Translational Imaging. Eur Radiol. 2025;35(4):1903-1912. doi: 10.1007/s00330-024-11095-7.
9. Dahmarde H, Parooie F, Salarzaei M. Is 18F-FDG PET/CT an Accurate Way to Detect Lymph Node Metastasis in Colorectal Cancer: A Systematic Review and Meta-Analysis. Contrast Media Mol Imaging. 2020;2020:5439378. doi: 10.1155/2020/5439378.
10. Verdasca FR, Ferreira R, Montenegro A, Mendes JL, Furtado I, Escaleira R, *et al*. Mixed Neuroendocrine-Non-Neuroendocrine Neoplasms of the Rectum: A Case Report. Case Rep Oncol. 2024;17(1):587-595. doi: 10.1159/000538384.
11. Rinke A, Ambrosini V, Dromain C, Garcia-Carbonero R, Haji A, Koumarianou A, *et al*. European Neuroendocrine Tumor Society (ENETS) 2023 guidance paper for colorectal neuroendocrine tumours. J Neuroendocrinol. 2023;35(6):e13309. doi: 10.1111/jne.13309.
12. Sorbye H, Grande E, Pavel M, Tesselaar M, Fazio N, Reed NS, *et al*. European Neuroendocrine Tumor Society (ENETS) 2023 guidance paper for digestive neuroendocrine carcinoma. J Neuroendocrinol. 2023;35(3):e13249. doi: 10.1111/jne.13249.
13. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, *et al*. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin. 2017;67(2):93-99. doi: 10.3322/caac.21388.
14. Tanaka Y, Takagi M, Nakayama T, Kawada S, Matsushita R, Matsushita T, *et al*. Mixed neuroendocrine-non-neuroendocrine neoplasm of the colon treated with laparoscopic resection and adjuvant chemotherapy: a case report. Clin J Gastroenterol. 2025;18(2):314-323. doi: 10.1007/s12328-024-02089-5.
15. Fujimura H, Goto A, Izumiya Y, Ito S, Tanaka A, Itoh H, *et al*. Mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) of the rectum. Clin J Gastroenterol. 2025;18(2):324-329. doi: 10.1007/s12328-025-02099-x.
16. Mukai S, Hirata Y, Ishikawa S, Kai A, Kohata A, Okimoto S, *et al*. Mixed neuroendocrine-non-neuroendocrine neoplasms of ascending colon: A case report. Int J Surg Case Rep. 2020;76:125-129. doi: 10.1016/j.ijscr.2020.08.054.
17. Argilés G, Tabernero J, Labianca R, Hochhauser D, Salazar R, Iveson T, *et al*. Localised colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2020;31(10):1291-1305. doi: 10.1016/j.annonc.2020.06.022.