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CASE REPORT

Well-Differentiated Neuroendocrine Tumor of the Appendix Presenting as Acute Phlegmonous Appendicitis: A Case Report

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ABSTRACT

A 26-year-old man underwent appendectomy for acute phlegmonous appendicitis, and postoperative histopathology revealed a well-differentiated appendiceal neuroendocrine tumor (NET) (G1, 1.3 cm, Ki-67 <1%), confined to the subserosa without mesoappendiceal invasion or lymphovascular/perineural involvement. Surgical margins were clear, and the patient recovered uneventfully. According to guidelines, right hemicolectomy is selectively considered for 1-2 cm tumors with high-risk features. As none were present, appendectomy was deemed sufficient following a multidisciplinary team review. This case highlights the importance of thorough histopathological assessment and individualized management of incidentally detected appendiceal NETs within the 1-2 cm gray-zone category.

Keywords: Appendiceal neuroendocrine tumor, appendix, acute appendicitis, histopathology, incidental tumor, case report

Introduction

Appendectomy remains one of the most common emergency surgical procedures worldwide. Although most cases are straightforward inflammatory conditions, unexpected neoplasms of the appendix may be encountered histologically.[1,2] Neuroendocrine tumors (NETs) are the most common primary neoplasms of the appendix, representing 0.3%-0.9% of all appendectomy specimens.[3,4] They typically occur in young adults, often with female predominance, and are usually diagnosed incidentally. Most appendiceal NETs are well-differentiated, have an indolent course, and are considered to have a favorable prognosis when small (<2 cm). However, larger lesions or those with mesoappendiceal or serosal invasion may require further oncological evaluation and extended surgical resection.[1,2,5]

We present a case of appendiceal NET discovered during histological examination following appendectomy for acute phlegmonous appendicitis.

Case Presentation

A 26-year-old male patient was admitted as an emergency case due to acute abdominal pain with a 2-day history of symptoms. The pain started in the epigastrium and localized to the right iliac fossa. The patient was febrile (38°C), with nausea, repeated vomiting, and loss of appetite. Past medical history was negative for hepatic, renal, or malignant diseases, and no drug allergies were reported. The patient had marked tenderness in the right lower quadrant on superficial and deep palpation. Laboratory results were as follows: white blood cell count =8×10^9/L, neutrophil-to-lymphocyte ratio (NLR) =2.55, C-reactive protein (CRP) = 56.5 mg/L, procalcitonin = 0.08 ng/

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mL, CRP-to-albumin ratio =1.26, and total bilirubin =22.9 µmol/L. Peripheral blood smear showed normal erythrocyte morphology, and viral hepatitis serology was negative. Contrast-enhanced abdominal computed tomography demonstrated an edematous appendix with absent luminal visualization, mild periappendicular fat stranding, and three calcified fecaliths (up to 8 mm) at the cecal ostium (Figure 1). Such findings are consistent with phlegmonous appendicitis.[6]

Appendectomy was performed. Intraoperatively, the appendix was inflamed and phlegmonous. A swab from the appendiceal lumen and mucosal sample was taken for microbiology. Culture yielded *Pseudomonas aeruginosa*, *Enterococcus spp.*, and *Escherichia coli*.

Histopathology confirmed the appendix measured 7.0×0.6 cm, with mesoappendiceal fat up to 2.5 cm. Serosa was dull with purulent deposits. Toward the tip, a whitish solid mass (1.3 cm diameter) was noted. On microscopy, the appendiceal wall showed ulcerated mucosa with luminal hemorrhagic-purulent contents and transmural acute inflammation. The whitish solid area consisted of nests of uniform oval cells with light cytoplasm and "salt-and-pepper" chromatin infiltrating through all layers into the subserosa. Mitotic figures were rare (1/10 high-power field) (Figure 2). Immunohistochemistry confirmed the following: chromogranin a (+) (Figure 3), synaptophysin (+) (Figure 4), Ki-67 <1% (Figure 5).

The final diagnosis was as follows: well-differentiated NET of the appendix, G1, pT3, with subserosal and no mesoappendiceal invasion, clear surgical margins, and no lymphovascular or perineural invasion.

The patient had an uneventful recovery and was discharged on postoperative day 2 in good general condition. After receiving the pathohistological findings, the case was presented to the multidisciplinary tumor board (MDT). According to guidelines, right hemicolectomy (RHC) is selectively considered for 1-2 cm tumors with high-risk features. As none were present, appendectomy was deemed sufficient following a multidisciplinary team review. The patient was scheduled for regular follow-ups.

Discussion

Appendiceal NETs are most frequently encountered incidentally in appendectomy specimens for suspected appendicitis. In many cases, the presenting symptoms result from luminal obstruction by the tumor, leading to inflammation, as in this case.[3,4] The diagnosis is rarely made preoperatively because imaging and laboratory parameters typically reflect only inflammatory changes. Our patient presented with moderately elevated inflammatory markers (CRP =56.5 mg/L, NLR =2.55) and mild hyperbilirubinemia, findings consistent with complicated appendicitis but not specific for underlying neoplasia.[6,7]

Histological examination confirmed a well-differentiated NET (G1), characterized by uniform cytology, low mitotic activity, and a low Ki-67 proliferation index. Importantly, the tumor infiltrated the entire appendiceal wall into the subserosa (pT3), which has prognostic and therapeutic implications.[1,2] Both the European Neuroendocrine Tumor Society (ENETS) and North American Neuroendocrine Tumor Society (NANETS) agree that tumors <1 cm are adequately treated with appendectomy alone, whereas those >2 cm generally warrant RHC with lymphadenectomy due to a significantly higher risk of nodal metastases.[1,2] The main area of controversy lies in the

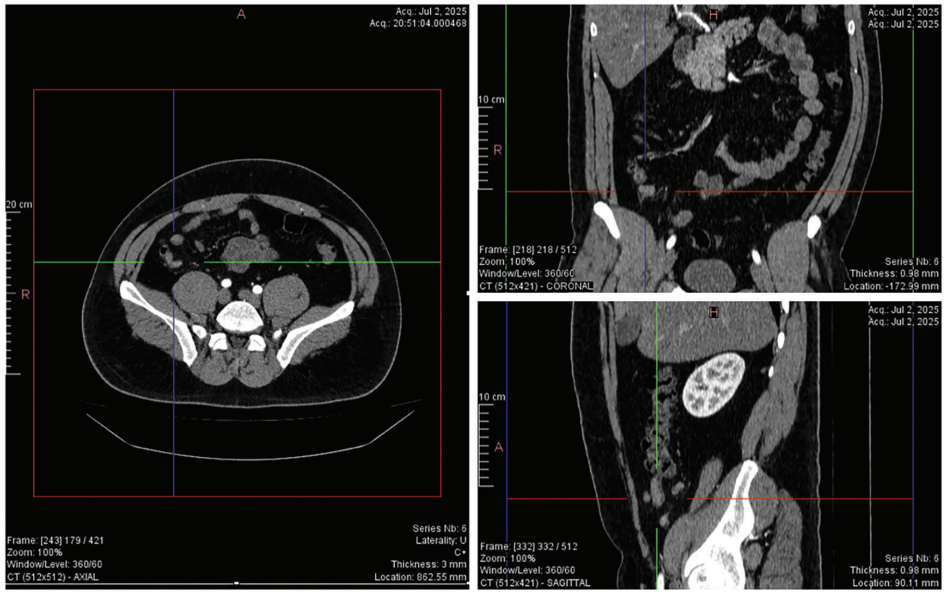

Figure 1. Contrast-enhanced abdominal computed tomography horizontal, coronal, and sagittal views, demonstrating an edematous appendix with absent luminal visualization, mild periappendicular fat stranding

management of tumors measuring 1-2 cm, the so-called "gray zone."

For this group, ENETS and NANETS advocate a selective approach; RHC should be considered if high-risk features are present, such as mesoappendiceal invasion >3 mm, positive or close resection margin, tumor located at the appendiceal base, lymphovascular or perineural invasion, or higher proliferative index.[1-3] The ENETS 2023 update emphasizes a multifactorial risk assessment and stresses the importance of MDT discussion.[1] Similarly, NANETS guidelines (2022-2024) support individualized management and discourage routine RHC in the absence of high-risk factors.[2]

In contrast, the National Comprehensive Cancer Network guidelines tend to be more permissive, often accepting appendectomy alone for 1-2 cm tumors, even in the presence of some risk features[4], whereas European Society for Medical Oncology guidance generally mirrors the ENETS/NANETS approach but also defers to MDT decision-making.[5]

Outcomes data reinforce this selective strategy. Large retrospective studies show no consistent overall survival benefit for routine RHC in 1-2 cm NETs, especially when margins are negative and no additional risk factors exist.[6,7] Nonetheless, RHC offers the advantage of nodal staging and may reduce locoregional recurrence risk in selected patients.[6,7]

Our patient's tumor measured 1.3 cm, was well differentiated (G1, Ki-67 <1%), and extended through the wall into the subserosa (pT3). This fulfills one of the potential risk factors —depth of invasion— but the crucial discriminator in most guidelines is the millimetric depth of mesoappendiceal invasion (>3 mm). Our pathology report described "subserosal infiltration" without mesoappendiceal, lymphovascular, or perineural invasion.

This case highlights the clinical challenge of managing appendiceal NETs in the 1-2 cm gray zone. Although mesoappendiceal invasion was absent (only subserosal invasion with intact serosa), the absence of additional high-risk features (negative margins, no lymphovascular or perineural invasion) supports appendectomy alone, consistent with ENETS and NANETS guidance.

According to ENETS and NANETS, if mesoappendiceal invasion is >3 mm or if margins are positive/close, RHC would be advised. In the absence of these features, and given the favorable biology (G1, Ki-67 <1%), appendectomy alone may be adequate, with clinical surveillance. An MDT evaluation remains critical to guide final management.[1-3]

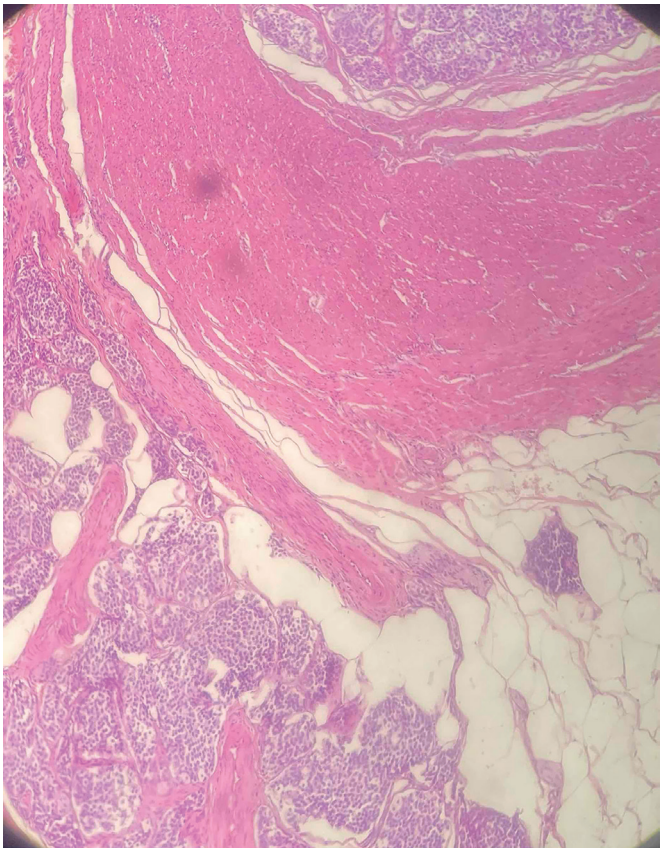

Figure 2. H&Ex100 Mural and subserosal infiltration. Nests of uniform oval cells with light cytoplasm and "salt-and-pepper" chromatin, infiltrating through all layers into the subserosa
H&E: Hematoxylin and eosin

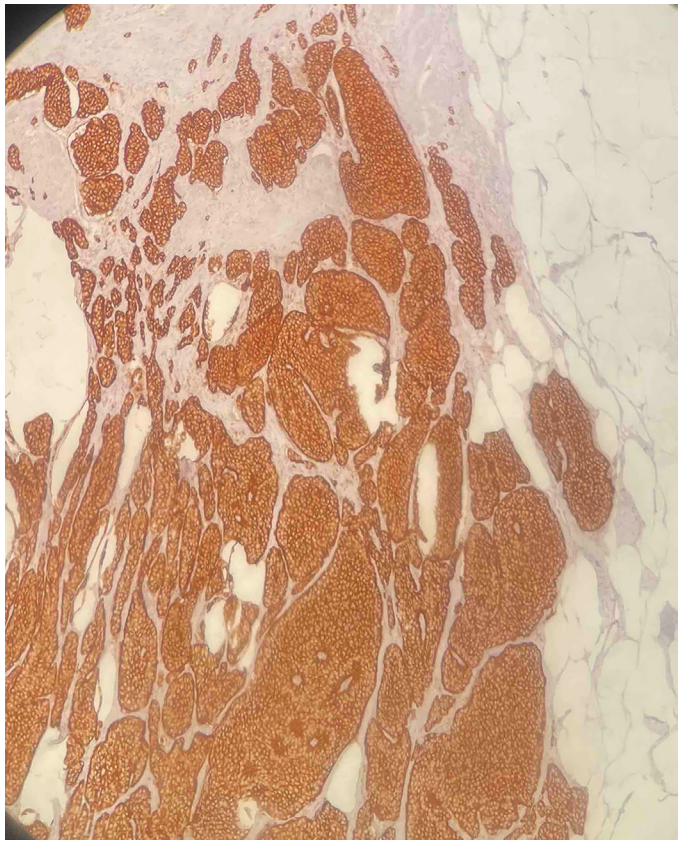

Figure 3. Chromogranin x100. Chromogranin is positive in tumor tissue

Limitations: As a single case report, the findings have limited generalizability and cannot determine definitive management strategies. Larger series and prospective studies are required to refine risk stratification and surgical decision-making.

To strengthen the clinical relevance, we have added a comparative summary table (Table 1) of previously reported appendiceal NET cases, focusing on the 1-2 cm "gray zone." This expanded comparison further underscores that

Table 1. Comparative summary of published case reports of appendiceal neuroendocrine tumors and our case

	Reference/case (year)	Age/gender	Tumor size and grade*	High-risk features present	Management performed	Outcome/follow-up notes
1	This case (2025, this report)	26-year-old male	1.3 cm, G1 (Ki-67 <1%)	No mesoappendiceal invasion; clear margins; no LVI; no PNI	Appendectomy alone; MDT review	Uneventful recovery; no recurrence
2	Appiah et al.[8], (Incidental Grade 2 ANET)	28-year-old male	0.5 cm, G2 (Ki-67 ~5%)	Confined to submucosa; negative margins; no LVI	Appendectomy only	Good outcome; followed clinically
3	Bayhan et al.[9], (4026 appendectomies)	Multiple cases	Mean ~0.85 cm (range 0.3-2.5 cm)	Some with MAI/serosal invasion; rare LVI	Appendectomy for most; RHC if >2 cm or risk features	No recurrences in small, low-risk tumors, 1-year follow up
4	Hasan et al.[10], (young patient with nodal spread)	19-year-old female	G2 (size not clearly stated)	LVI present; metastatic lymph nodes	Appendectomy + RHC	6/27 nodes positive; limited 3-months follow-up
5	Villa et al.[11], (collision tumor with LAMN)	31-year-old female	ANET T3, G1, Ki-67 <1% (with LAMN)	Mesoappendiceal invasion; positive LAMN margin	Appendectomy + RHC	5-year follow-up; no recurrence

*LAMN: Low-grade appendiceal mucinous neoplasm, LVI: Lymphovascular invasion, PNI: Perineural invasion, MAI: Mesoappendiceal invasion, ANET: Appendiceal neuroendocrine tumor, RHC: Right hemicolectomy, MDT: Multidisciplinary tumor board

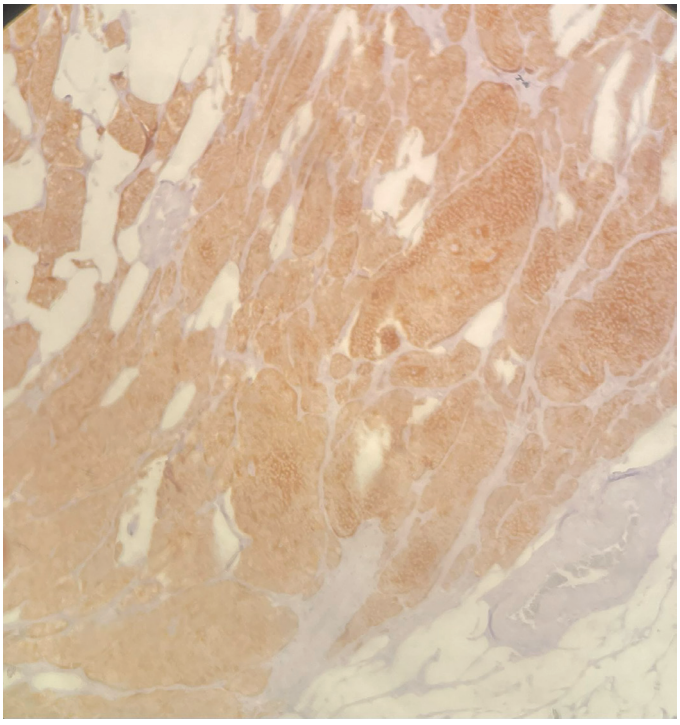

Figure 4. Synaptophysin x100. Synaptophysin is positive in tumor tissue

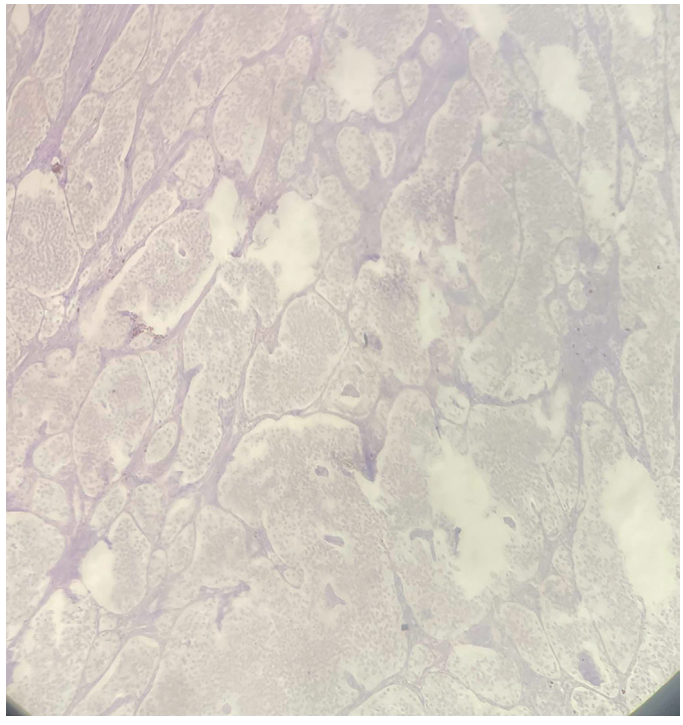

Figure 5. Ki-67 x100. Ki-67 proliferation index is very low (<1%) in tumor tissue

mesoappendiceal invasion, lymphovascular/perineural invasion, and positive or close surgical margins often drive the decision for RHC, whereas their absence—as in our patient—supports appendectomy alone.

Conclusion

We report a case of well-differentiated appendiceal NET presenting as acute phlegmonous appendicitis. Although rare, NETs should be considered in the differential diagnosis of appendiceal pathology. Histopathological examination remains essential for definitive diagnosis and guiding further management. Current ENETS and NANETS guidelines support selective RHC in tumors between 1-2 cm only when additional high-risk features are present. When viewed in the context of previously published reports (Table 1), our case supports the selective approach; RHC should be reserved for 1-2 cm tumors with additional high-risk features, and appendectomy alone may be sufficient in their absence. This reinforces the importance of precise histopathological assessment and individualized, multidisciplinary decision-making in the "gray zone."

Ethics

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: R.G., B.K., B.T., Concept: R.G., G.J., Design: R.G., G.J., Data Collection or Processing: R.G., B.K., V.J.M., B.T., N.J., Analysis or Interpretation: R.G., G.J., B.K., V.J.M., B.T., N.J., Literature Search: R.G., V.J.M., B.T., N.J., Writing: R.G., G.J., B.K., V.J.M., B.T., N.J.

Conflict of Interest: The authors declare that they have no conflicts of interest relevant to the content of this article.

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