Incidental finding of synchronous neuroendocrine tumor of appendix and rectal adenocarcinoma. A case report and literature review

Abstract

Objectives: Colorectal cancers represent the predominant malignancies affecting the gastrointestinal tract. In contrast, appendiceal tumors occur less frequently. Among them, appendiceal neuroendocrine tumors (ANETs) account for approximately 50% of cases and are often detected incidentally during unrelated procedures.

Case presentation: We present an extremely rare case of an incidental neuroendocrine tumor of the appendix discovered during surgery for rectal adenocarcinoma and provide a review of the relevant literature. A 70-year-old patient with radiologically and endoscopically diagnosed rectal cancer underwent a low anterior resection with total mesorectal excision and a temporary diverting ileostomy following preoperative chemotherapy and radiation therapy. Intraoperatively, a small appendiceal mass was discovered and excised. Histopathological examination confirmed a well-differentiated NET of the appendix measuring 0.4 cm in diameter.

Conclusions: This case report emphasizes the importance of thorough intraoperative examination during colorectal surgeries and highlights the need for increased awareness of appendiceal NETs among surgeons.

Keywords: adenocarcinoma; appendix; case report; neuroendocrine tumor; rectum.

Introduction

Colorectal cancer (CRC) represents the most prevalent malignant tumor of the gastrointestinal tract and ranks as the third most common malignancy in humans [1]. The lifetime risk of developing colorectal cancer in the general population is estimated to be approximately 4–5% [2]. The development of CRC is attributed to mutations in specific genes, including oncogenes, tumor-suppressor genes, and DNA repair genes [3]. Several risk factors contribute to CRC, such as advanced age, family history of colorectal cancer or inflammatory bowel disease, obesity, smoking, alcohol consumption, and others [4].

Neuroendocrine tumors (NETs) comprise a heterogeneous group of neoplasms originating from neuroendocrine cells dispersed throughout the body [5]. NETs can develop in various organs, such as the gastrointestinal tract, pancreas, and lungs. Within the realm of gastrointestinal NETs, the appendix represents an uncommon primary site, accounting for less than 5% of all cases [6]. Appendiceal NETs are predominantly asymptomatic and frequently discovered incidentally during appendectomy or other abdominal surgeries [7]. Formerly known as carcinoids, neuroendocrine tumors constitute the majority of appendiceal tumors, representing approximately 50% of cases. NETs are primarily localized at the tip of the appendix, presenting as lesions smaller than 1 cm in size. Lesions exceeding 2 cm in diameter carry an increased risk for metastasis to regional lymph nodes, the liver, or other organs [8]. The synchronous occurrence of an appendiceal NET with colorectal cancer is a relatively rare
phenomenon and can manifest as either synchronous or metachronous NET [9].

In this case report, we present an unusual case of an asymptomatic appendiceal neuroendocrine tumor discovered incidentally during surgery for rectal adenocarcinoma. Our aim is to highlight the importance of thorough intraoperative examination and increased awareness among surgeons when encountering colorectal malignancies. Furthermore, we will provide a review of the relevant literature to offer insights into the diagnosis, management, and prognosis of patients with synchronous colorectal adenocarcinoma and appendiceal NETs.

Case report

A 70-year-old patient presented to a gastroenterologist with a 2-year history of abdominal pain and intermittent subocclusive symptoms. There was no reported weight loss or systemic symptoms. His family history was unremarkable for any gastrointestinal malignancies.

On physical examination, the patient appeared to be in good general health, with stable vital signs. A digital rectal examination revealed an ulcerative and infiltrative tumor approximately 5 cm from the anal verge. Laboratory investigations, including a complete blood count, indicated mild anemia, while coagulation profile, and liver function tests, were within normal limits. Carcinoembryonic antigen (CEA) levels were mildly elevated at 5.5 ng/mL (normal range: <5 ng/mL).

The patient underwent a colonoscopy that revealed a circumferential, ulcerated mass in the rectum causing significant luminal narrowing. Biopsies were performed, and histopathological analysis confirmed the presence of rectal adenocarcinoma. Further staging was performed using computed tomography (CT) scans of the chest, abdomen, and pelvis. These investigations did not show any signs of distant metastasis or lymphadenopathy. CT scans revealed thickening of the distal rectal wall with possible infiltration into the perirectal fat (Figure 1). Thus, the initial staging of the rectal adenocarcinoma was determined as T3N0. Based on these findings, the patient's case was reviewed by the Multidisciplinary Team Meeting to determine the most suitable treatment plan. The patient underwent neoadjuvant chemoradiotherapy with 5-fluorouracil and leucovorin. Post-treatment control abdominal and pelvic MRI showed a reduction in tumor size (Figure 1), indicating a positive response to the therapy. As a result, the Multidisciplinary Team Meeting recommended surgical intervention. He underwent a low anterior resection with total mesorectal excision and a temporary diverting ileostomy. During surgery, the surgeon conducted a comprehensive intraoperative examination of the abdominal cavity and incidentally discovered a small, firm mass at the tip of the appendix that had not been detected in prior radiological examinations. The decision was made to perform an appendectomy, and the specimen was sent for histopathological evaluation. A fast pathological evaluation was not performed during the operation due to factors such as the small size and asymptomatic nature of the lesion. In this particular case, an immediate evaluation would not have significantly impacted the surgical approach or management plan, as the appendectomy was already deemed necessary based on the intraoperative findings.

The histopathological examination of the appendiceal mass revealed a well-differentiated neuroendocrine tumor measuring 0.4 cm in diameter, with no evidence of lymphovascular invasion. Immunohistochemical staining was positive for synaptophysin, CD56, NSE, and chromogranin A, confirming the diagnosis of a NET (Figure 2). The resected rectal specimen showed a an invasive, low-grade (histological grade 1 and nuclear grade 1) rectal adenocarcinoma, with clear resection margins and no involvement of the 5 lymph nodes examined. Immunohistochemical staining revealed tumor cells positive for CK20, CDX2, MUC2, and negative for MUC1, MUC5AC, CK7 (Figure 3).

The patient's postoperative recovery was uneventful, and he was discharged on the seventh day after the surgery. The patient was referred to the Multidisciplinary Team Meeting for further assessment and management. Adjuvant chemotherapy was not recommended due to the good response of the rectal adenocarcinoma to neoadjuvant chemoradiotherapy and the favorable prognosis of the appendiceal NET. The patient was scheduled for regular follow-up appointments, including clinical examinations, CEA levels, and imaging studies, to monitor for any potential recurrence or metastasis. A chest, abdominal, and pelvic CT scan performed during the 6-month follow-up showed no evidence of disease recurrence or systemic dissemination.

Discussion

The incidental discovery of an appendiceal NET during surgery for rectal adenocarcinoma is an extremely rare occurrence. Our case highlights the importance of a thorough intraoperative examination in patients undergoing colorectal surgery to ensure the detection of synchronous tumors. The management of patients with synchronous colorectal adenocarcinoma and appendiceal NETs can be challenging due to the rarity of these cases and limited data available in the literature.
Colorectal cancer is the third most common malignancy in humans globally, with over 1.9 million cases reported in 2020 [1]. It is also the second most frequent cause of cancer-related deaths, accounting for around 935,000 deaths annually [10]. The incidence of CRC is higher in developed countries, which is associated with factors such as obesity, alcohol and cigarette consumption, unbalanced diet, family history of CRC or inflammatory bowel disease, gender, race, age, intestinal flora disorders, and socioeconomic status [4]. Mutations in oncogenes, tumor suppressor genes, and DNA repair process genes play a crucial role in the development of CRC [11].

Neuroendocrine tumors can occur in all organs, but neoplastic lesions of the appendix are relatively rare. Synchronous or metachronous tumors of the colon account for about 25% of all appendix tumors [12]. The common embryonic origin of the appendix, colon, and rectum suggests that malignant alterations of the colon or rectum can negatively impact the appendix [12].

The diagnosis of appendiceal NETs is typically confirmed through histopathological examination, with immunohistochemical staining for synaptophysin and chromogranin A, as demonstrated in our case [13]. Generally smaller than 1 cm, these lesions are often undetected by routine radiological procedures, which is similar to the case presented in our study [14]. The diagnostic challenges associated with detecting smaller neuroendocrine tumors arise from various factors, including their small size, indolent nature, and the limited sensitivity and specificity of conventional imaging techniques such as computed tomography (CT), magnetic resonance imaging (MRI), and somatostatin receptor scintigraphy (SRS) [15]. To address these challenges, it is crucial to refine and enhance radiological techniques, develop novel imaging methods like high-resolution imaging or specialized contrast agents, and integrate functional imaging techniques, such as positron emission tomography (PET), with anatomic imaging methods. Additionally, exploring the potential of biomarkers for early detection may facilitate the development of minimally invasive diagnostic tests, ultimately improving early detection and patient outcomes.

The prognosis of appendiceal NETs depends on factors such as tumor size, grade, and stage [12]. Tumors smaller than 1 cm in diameter, like the one reported in our case, generally have a favorable prognosis, with a low risk of metastasis and recurrence. Simple appendectomy is considered adequate treatment for such small, well-differentiated tumors [16]. In contrast, right hemicolectomy is recommended for tumors larger than 2 cm or those displaying aggressive features, such as lymphovascular or perineural invasion [17].

The importance of considering an asymptomatic appendectomy in cases of incidentally discovered appendiceal tumors cannot be overstated, as undetected tumors can lead to future complications such as perforation, obstruction, or even metastasis [18]. In the present case, timely appendectomy intervention helped avert these potential complications and secured a better prognosis for the patient. Furthermore, the histopathological analysis of the excised appendix offered crucial insights into the tumor's characteristics, which were vital for establishing the most suitable management approach and follow-up regimen.

The treatment of patients with synchronous occurrence of colorectal adenocarcinoma and appendiceal neuroendocrine tumors presents several limitations, primarily due to the rarity of such cases and the distinct biological behaviors of the two tumor types. Colorectal adenocarcinomas generally require a more aggressive treatment approach, including neoadjuvant chemoradiotherapy, surgery, and potentially adjuvant chemotherapy [19]. On the other hand, small, well-differentiated appendiceal NETs, like the one described in our case, often have an indolent clinical course, and simple appendectomy may suffice as treatment [7]. Balancing the treatment approaches for these two malignancies can be challenging, as the management of one tumor type should not compromise the treatment of the other. Additionally, limited data is available in the literature to guide clinicians in the optimal management of such patients,
**Figure 2**: Histological and immunohistological examination of appendicular NET. (A) Histological examination of the resected specimen revealed appendicular NET (black arrows) (Hematoxylin-eosin stain; original magnification ×40, scale bar=100 µm). Immunohistological results revealed that the tumor chromogranin (black arrow) (B), CD56 (black arrow) (C), synaptophysin (black arrow) (D), and NSE (black arrow) (E) were positive (original magnification ×40, scale bar=100 µm).
which makes it difficult to develop evidence-based, standardized treatment protocols. Furthermore, the diagnostic challenges associated with detecting smaller NETs may lead to underdiagnosis and undertreatment, ultimately impacting patient outcomes. Finally, the potential for adverse effects and complications arising from the treatment of one tumor type may further complicate the management of the other, necessitating a highly individualized and multidisciplinary approach to optimize patient care and prognosis.

Our patient underwent a successful low anterior resection with total mesorectal excision for the rectal adenocarcinoma and an appendectomy for the incidentally discovered appendiceal NET. The favorable prognosis of the appendiceal NET and the good response of the rectal adenocarcinoma to neoadjuvant chemoradiation led to the decision not to administer adjuvant chemotherapy. However, it is important to note that only five lymph nodes were isolated during the surgery. The lower number of isolated lymph nodes in our case could be attributed to factors such as individual patient anatomy. Additionally, the patient had received neoadjuvant therapy, which may have influenced lymph node retrieval during surgery. Despite the lower number of isolated lymph nodes, the multidisciplinary team closely monitored the patient’s progress to ensure appropriate follow-up and care. Striving for a higher number of isolated lymph nodes in rectal cancer surgery remains essential for accurate staging and optimal patient outcomes. Comprehensive postoperative follow-up and surveillance, including clinical examinations, CEA levels, and imaging studies, will be crucial for early detection of any potential recurrence or metastasis, ensuring the best possible outcome for the patient.

We acknowledge several limitations in our work, which should be considered when interpreting the results. First, our case report is based on a single patient experience,
limiting the generalizability of our findings. Further studies involving larger patient populations are needed to validate and expand upon our observations. Second, the low number of isolated lymph nodes during the patient’s surgery could impact the accuracy of staging and prognosis evaluation. Lastly, the rarity of synchronous colorectal adenocarcinoma and appendiceal NETs presents challenges in developing standardized diagnostic and management protocols. Our case report highlights the importance of individualized, multidisciplinary approaches to patient care, which can help overcome these challenges and improve patient outcomes.

Conclusions

In conclusion, this case report presents a rare synchronous occurrence of appendiceal neuroendocrine tumor (NET) and rectal adenocarcinoma, emphasizing the importance of comprehensive intraoperative examination and multidisciplinary collaboration. The tailored approach to patient care, involving neoadjuvant chemoradiation therapy and appropriate surgical intervention, highlights the significance of individualized treatment plans. The favorable outcome demonstrates the potential for successful management when meticulous intraoperative examination is combined with a multidisciplinary approach. This report serves as a valuable reminder for clinicians to maintain a high level of suspicion for concomitant malignancies in patients with known tumors, ultimately contributing to the improvement of patient outcomes and long-term prognosis.

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Availability of data and materials: The data supporting the findings of this study are available from the corresponding author upon reasonable request. Some restrictions may apply to the availability of the data and materials due to privacy and ethical considerations.

References


