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Pathology

Incidental Finding of Synchronous Rectal Adenocarcinoma and Intestinal Neuroendocrine Tumor: A Case Report and Literature Review

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Abstract **Case Report**

Synchronous colorectal adenocarcinoma and neuroendocrine tumor (NET) represent a rare and unique phenomenon. These lesions are often incidental findings, typically diagnosed through histological examination rather than based on clinical symptoms, physical findings, or macroscopic appearance. We describe a case of a 83-year-old man who presented with complains of abdominal pain, intermittent subocclusive symptoms and two episodes of bleeding per rectum. Colonoscopy revealed an ulcerative infiltrating mass in the rectum. During the staging assessment, a CT of the abdomen and pelvic images showed the presence of a second tumor located in small intestine and formed a wall thickening. The patient underwent a low anterior rectal resection with total mesorectal excision and an intestinal resection. Based on histomorphology and immunohistochemistry, the rectal tumor was diagnosed as well-differentiated adenocarcinoma, whereas the intestinal tumor was diagnosed as neuroendocrine tumor. Our goal is to highlight the critical role of thorough extension assessment and meticulous intraoperative evaluation in the management of colorectal malignancies.

Keywords: Synchronous, Neuroendocrine, Adenocarcinoma, Rectum.

INTRODUCTION

Synchronous primary tumors are defined as two or more different tumors histologically, discovered at the same time or within a period of 6 months [1].

Colorectal cancer is the third most common malignant tumor of the gastrointestinal tract worldwide [2]. In the general population, the lifetime risk of developing colorectal cancer is estimated at around 4-5%. Its development is linked to mutations in specific genes, including oncogenes, DNA repair genes and tumor-suppressor genes [3].

NETs are a heterogeneous group of neoplasms originating from secretory cells of the diffuse neuroendocrine system which can develop in various organs [3]. NETs of the small intestine are often discovered by accident [4], 12% to 22% of patients are metastatic at presentation [3].

The synchronous occurrence of colorectal cancer with intestinal NET is a relatively rare phenomenon. Although, only a few cases have been reported [5].

Herein, we present an unusual case of an asymptomatic intestinal neuroendocrine tumor discovered incidentally during rectal adenocarcinoma extension assessment that were diagnosed by colonoscopy. Furthermore, we will discuss pathogenesis of NETs suggesting the coexisting of two histologically distinct tumors by a review of the literature and comparing it with previously reported cases.

CASE PRESENTATION

A 83-year-old man presented to the department of gastroenterology with a 3-month history of abdominal pain and intermittent subocclusive symptoms, with two episodes of bleeding per rectum. He also reported a significant loss of weight and appetite.

The medical history was essentially negative except for arterial hypertension. The patient had never smoked or drank and no familial history of malignancy was noted.

On physical examination, the patient appeared to be cachexic, but not icteric, he was tachycardic, with heart rate up to 110 bpm. There were no abdominal masses felt, and no cervical or inguinal lymphadenopathy was palpated, and per-rectal examination was unremarkable.

A digital rectal examination revealed an infiltrative tumor in lower rectum.

Results of laboratory investigations showed a mild anemia, while the rest of the parameters were within normal range.

The patient underwent a colonoscopy that revealed an ulcerative infiltrating mass in the rectum, approximately 5 cm from the anal verge, involving 60% of the circumference. Rest of the rectum and the colon were normal.

Colonoscopic biopsy specimens of the tumor were performed, and histopathological analysis confirmed the presence of well differentiated adenocarcinoma.

Further staging was performed using computed tomography (CT) scans of the chest, abdomen, and pelvis. A CT of the abdomen and pelvic images were reviewed with the radiologist, they showed the presence of two different tumors in different locations. The first tumor was located in the lower rectum and formed an ulcerative infiltrating mass with proximal dilatation. The second tumor was located in small intestine and formed a wall thickening surrounding by a prominent lymph node.

The patient was then referred to department of Visceral Surgery, his case was reviewed by the Multidisciplinary Team Meeting to determine the most suitable treatment plan. He underwent neoadjuvant chemoradiotherapy before surgical resection. At laparotomy, a low anterior rectal resection with total mesorectal excision and an intestinal resection and temporary diverting ileostomy were performed.

Pathologic Findings

Two surgical specimens were received in two separate containers for microscopical examination. The first vial contained a rectal resection specimen that measured 24 cm in length with a diameter varying between 2 and 7 cm. Upon opening the specimen, an infiltrating and ulcerated tumor measuring 4x4 cm is observed, located in the lower rectum. The dissection of the perirectal fat reveals 13 lymph nodes, the largest measuring 0.8 cm in its longest axis.

The second vial contained a 6 cm long and 2 cm wide piece of intestinal resection, along with an attached lymph node measuring 4x3.5x3 cm. Upon opening the specimen, a whitish, budding lesion measuring 1.2x1 cm was observed.

Histopathological examination of step serial sections and immunohistochemical study based on morphology were performed for both tumors.

The histological study of the rectal tumor was consistent morphologically with well-differentiated adenocarcinoma, showing a carcinomatous tumor proliferation with a glandular architecture, arranged in tubular structures, clusters, and cribriform masses. They are bordered by tall cylindrical cells showing moderate cytonuclear atypia with numerous mitotic figures.

The depth of invasion was submucosa with clear resection margins.

There were no evidence of lymphovascular invasion and no involvement of the 13 lymph nodes examined.

The histological examination of the sections taken from the identified intestinal tumor reveals a proliferation with a lobular architecture, distinct from the rectal tumor. It is structured into trabeculae, cords, acini, and occasionally exhibits an insular arrangement. The tumor cells are monomorphic, of medium size, with oval nuclei containing granular chromatin (salt-and-pepper). Their cytoplasm is abundant and eosinophilic. Mitosis count was 1/10 high power field.

This tumor infiltrates the intestinal wall and reaches the subserosa with clear resection margins.

Cancer metastasis was found in 1 lymph node out of the 2 dissected regional lymph nodes.

Synaptophysin and chromogranin a immunohistochemical stains had the best performance to classify and characterize NETs. This immunohistochemical panel in the rectal tumor, that had typical morphology of adenocarcinoma, was completely negative, confirming the diagnosis. On the other hand, neuroendocrine markers were diffusely positive in the intestinal tumor and the Ki-67 proliferation index was low, estimated at 1%.

Based on histomorphology and immunohistochemistry, the rectal tumor was diagnosed as well-differentiated adenocarcinoma and was staged as pT2N0MX, and the intestinal tumor was diagnosed as neuroendocrine carcinoma grade 1. Therefore, we concluded that the patient had developed simultaneously

a rectal adenocarcinoma and an intestinal neuroendocrine carcinoma.

DISCUSSION

Neuroendocrine tumors (NETs) are a diverse group of tumors that can develop in various epithelial organs throughout the body. They account for approximately 0.5% of newly diagnosed neoplasms. Their incidence has increased over time, due to advancements in diagnostic techniques. The most frequent primary sites for NETs are the gastrointestinal tract (62%-67%) and the lungs (22%-27%). The most commonly documented gastrointestinal NETs are located in the colon and rectum (69%), followed by the small intestine (36%), stomach (10%), appendix (5%), and esophagus (0.4-2%) [6].

NETs can occur either synchronously or metachronously with other secondary primary malignancies (SPMs), even in the absence of a genetic predisposition syndrome. 80% of them were recognized in the gastrointestinal tract (27% in the large intestine) [6].

Adenocarcinomas were the most common type of primary malignant tumor occurred at the same time with NETs (49.4%), followed by GIST (13.5%) and other NETs in different gastrointestinal tract segments (7.9%) [6].

The pathogenesis of NENs associated with SPMs remains unclear. Several hypotheses have been proposed, including the possibility of a shared carcinogenic factor that promotes the development of both tumors [11]. Another theory suggests the involvement of a common stem cell that could undergo similar genetic mutations (such as c-kit or p53), leading to the development of various types of gastrointestinal cancers [7]. Interestingly, the presence of NETs markers has also been detected in other types of carcinomas [8, 9]. In a recent study, Kato *et al*., reported a case of positive CK20 in NET in a patient with a synchronous colorectal adenocarcinoma and suggested a possible link between colorectal neuroendocrine carcinoma and adenocarcinoma [10].

Other theories propose that neuroendocrine cell tumors may contribute to tumor growth through a paracrine or autocrine loop, driven by the secretion of peptides (such as bombesin, somatostatin, glucagon, gastrin and cholecystokinin) or growth factors (including platelet-derived growth factor, insulin-like growth factor, transforming growth factor, epidermal growth factor and fibroblast growth factor). These secreted molecules can promote tissue growth, potentially leading to the transformation of normal cells into neoplastic ones [6].

Pearson and Fitzgerald reported the first recorded case of synchronous carcinoid and non-carcinoid gastrointestinal neoplasms in 1949 in an autopsy series [11]. Since then, large series of cases have documented the presence of NETs in gastrointestinal tract with synchronous and metachronous SPM tumor. In a literature review conducted by Cokmert *et al*., in 2013, there was a report of a high-grade neuroendocrine carcinoma located in the ampulla of Vater with synchronous sigmoid colon adenocarcinoma [12]. In 2019, a Data collected by R. Parra Medina *et al*., includes 78 case reports that described the presence of NETs in gastrointestinal tract with secondary primary synchronous tumors [6]. A.Lazovic *et al*., in 2023 reported a case of neuroendocrine tumor of the appendix discovered during surgery for rectal adenocarcinoma [3]. And most recently, in 2024, there was a case report by D.alagoo *et al*., of an early rectal adenocarcinoma with synchronous NET [13].

Curative surgery remains the "gold standard" of the management of localized NETs of the small intestine. After a complete excision, there is no indication for adjuvant treatment [14]. However, metastatic and non-resectable disease is treated with radiation therapy in combination with systematic chemotherapy [6]. On the other hand, adenocarcinomas generally require a more aggressive approach, which may include neoadjuvant chemoradiotherapy, surgery, and possibly adjuvant chemotherapy [3].

The management of patients with both intestinal neuroendocrine tumor (NETs) and colorectal adenocarcinoma presents several challenges, mainly due to the distinct biological behaviors of the two tumor types, the rarity of these cases and the limited data available in the literature to guide clinicians to the best treatment approach for such patients [3].

In our case, the patient underwent neoadjuvant chemoradiotherapy before surgery. For the rectal adenocarcinoma, the treatment approach was a low anterior resection with total mesorectal excision. Otherwise, a simple surgical resection of the small well-differentiated intestinal NETs was performed and may suffice as treatment.

CONCLUSION

The incidental finding of an intestinal NETs during the staging assessment for rectal adenocarcinoma is extremely rare. This case highlights the importance of a thorough extent of disease assessment and an intraoperative examination in patients undergoing colorectal surgery to identify any synchronous tumors.

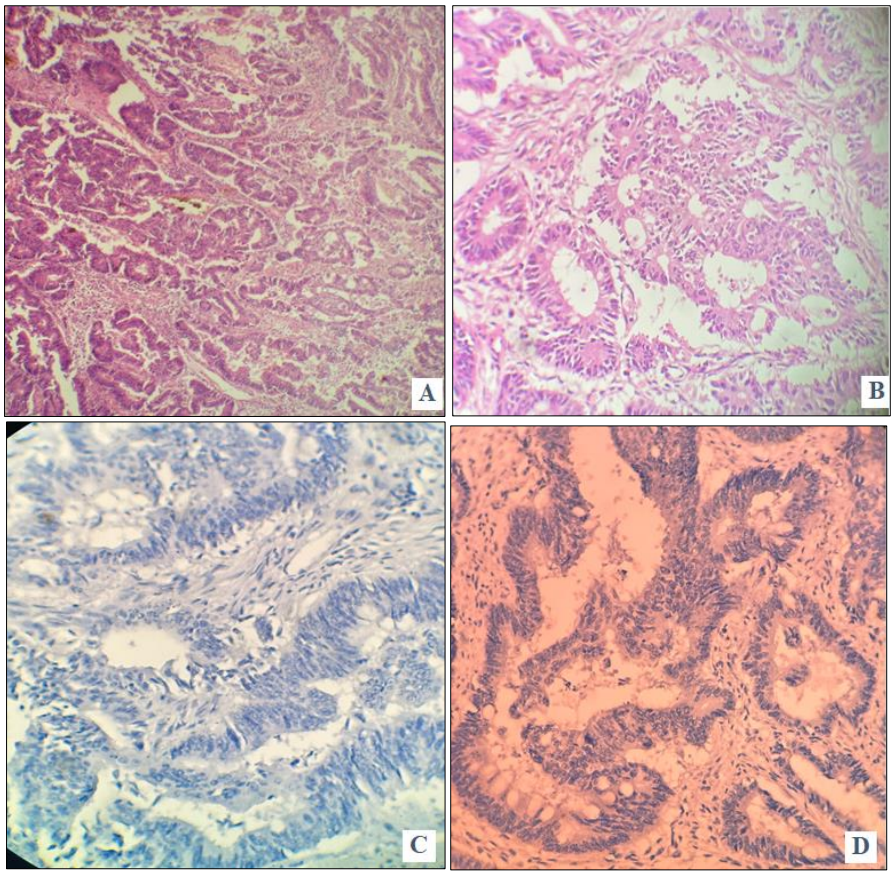

Figure 1: Histological aspects of rectal adenocarcinoma in Hematoxylin and Eosin staining (H&E) showing a glandular architecture, arranged in tubular structures, clusters, and cribriform masses: (A) H&E x 20; (B) H&E x 40; Immunohistochemical findings: Chromogranin A (C) and synaptophysin (D) are completely negative in the tumor

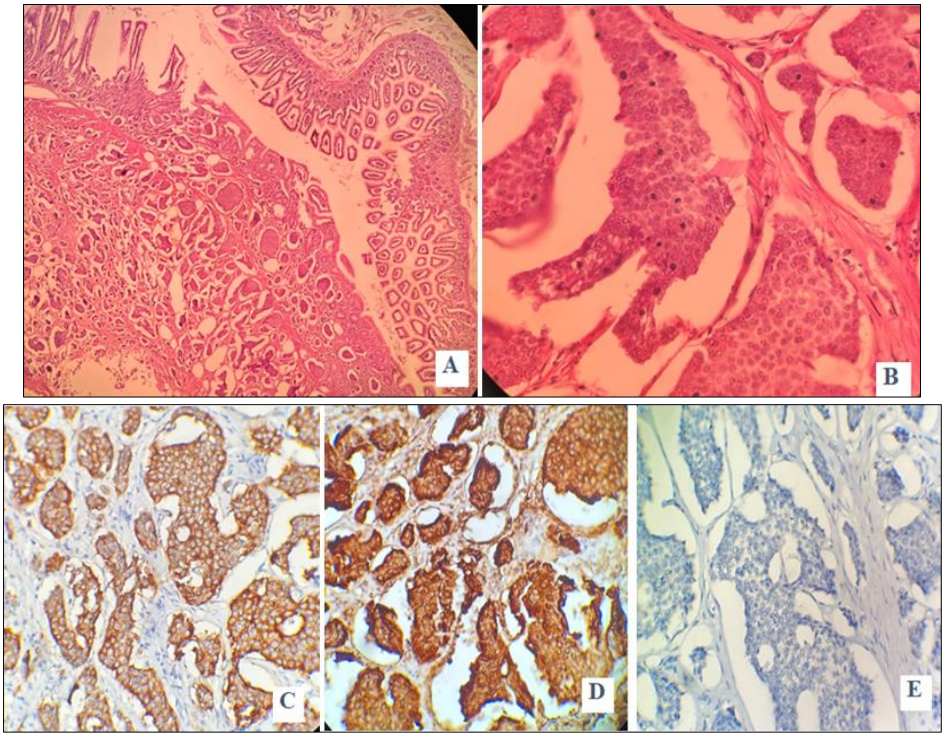

Figure 2: Histological aspects of intestinal adenocarcinoma in Hematoxylin and Eosin staining (H&E) showing a lobular architecture structured into trabeculae, cords, acini. (A) H&E x 10; (B) H&E x 40; Immunohistochemical findings: synaptophysin (C) and Chromogranin A (D) are diffusely positive in the tumor with a low Ki-67 proliferation index estimated at 1% (E)

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REFERENCES

1. T.Alshammari, S.Alshammari, R.Hakami, M.Alali, T.Aljohani, M.A.Zayed, T.B.Traiki. Two Histologically Different Primary Malignancies: Synchronous Obstructive Descending Colon Adenocarcinoma and Appendicular Carcinoid Tumor. Am J Case Rep. 2020; 21: e921810.
2. J.N.Winn, A.Sathyamurthy, J.L.Kneib, J.A. Ibdah, V.Tahan. Synchronous Gastrointestinal Carcinoid Tumor and Colon Adenocarcinoma. Am J Case Rep. 2017; 18: 632-636.
3. A.Lazovic, M.D.Stojanovic, M.Milosavljevic, V.Stankovic, B.Milosevic, B.S.Stojanovic, M.Spasic, A.Cvetkovic, B.Stojanovic. Incidental finding of synchronous neuroendocrine tumor of appendix and rectal adenocarcinoma. A case report and literature review. De Gruyter. Oncologie 2023; 25(4): 435–44.
4. T.Achach, A.Trabelsi, M.Taher Yacoubi, B.Sriha, A.Ben Ali, S.Korbi. Adénocarcinome colique révélateur de tumeurs carcinoïdes multiples du grêle. Oncologie (Tech Science Press). 2010, Vol 12, p1.
5. S.Yumoto, Y.Miyamoto, T.Akiyama, Y.Kiyozumi, K.Eto, Y.Hiyoshi, Y.Nagai, M.Iwatsuki, Y.Baba, S.Iwagami, N.Yoshida, H.Baba. Synchronous NET and colorectal cancer development: a case report. Surgical Case Reports (2020) 6:10.
6. R.P.Medina, P.M.Lucero, J.J.Moreno, A.M.Morales, A.R.Rojas. Neuroendocrine neoplasms of gastrointestinal tract and secondary primary synchronous tumors: A systematic review of case reports. Casualty or causality?. PLOS ONE. (2019) 6:10.
7. A.O.Vortmeyer, I.A.Lubensky, M.J.Merino, C.Y.Wang, T.Pham, E.E.Furth, et al. Concordance of genetic alterations in poorly differentiated colorectal neuroendocrine carcinomas and associated adenocarcinomas. J Natl Cancer Inst. 1997; 89: 1448–53.
8. Yao G-Y, Zhou J-L, Lai M-D, Chen X-Q, Chen P-H. Neuroendocrine markers in adenocarcinomas: an investigation of 356 cases. World J Gastroenterol. 2003; 9: 858–61.
9. Romeo R, Pellitteri R, Mazzone V, Marcello MF. Chromogranin A expression in human colonic adenocarcinoma. Ital J Anat Embryol. 2002; 107: 177–83.
10. J.S.Park, L.Kim, C.H.Kim, B.W.Bang, D.H.Lee, S.Jeong, Y.W.Shin, H.G.Kim. Synchronous Large-Cell Neuroendocrine Carcinoma and and Liver, Vol. 4, No. 1, March 2010, pp. 122-125.
11. C.Pearson, P.Fitzegerald. Carcinoid tumors; a re-emphasis of their malignant nature; review of 140 cases. Cancer. 1949; 2: 1005–26, illust.
12. S.Cokmert, L.Demir, A.Akder Sari et al: Synchronous appearance of a high-grade neuroendocrine carcinoma in the ampulla of vater and sigmoid colon adenocarcinoma. Case Rep Oncol Med, 2013; 2013: 930359.
13. D.Alagoo, H.Sellappan, S.K.Rajanthran, N.Azizan, N.F.Johari, Z.A.Dzulkarnaen, F.Hayati. Synchronous early rectal adenocarcinoma and neuroendocrine tumour: A treatment strategy. Polish Annals of Medicine. 2024;31(2):105–108.
14. M.Dior, J.Dreanic, C.Prieux-Klotz, B.Brieau, C.Brezault, R.Coriat. Tumeurs neuroendocrines de l'intestin grêle: actualités sur le traitement médical. Presse Med. (2017).