

Case Report

Running Title: Synchronous Neuroendocrine Tumor and Mucinous Tumors of the Appendix

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Synchronous Neuroendocrine Tumor and Mucinous Tumor of the Appendix in 76-Year-Old Woman

Seyed Jalal Eshagh Hoseini[♦], MD

Surgery Department, Qom University of Medical Sciences, Qom, Iran

♦Corresponding Author

Eshagh Hoseini SJ, MD

Surgery Department, Qom University of Medical Sciences,

Qom, Iran Telephone number: 00982536122854

Fax: 00982536122851

Email Address: jalaleshaghoseini@gmail.com

Abstract

A 76-year-old woman presented with a one-year history of intermittent right lower abdominal pain, little weight loss, and palpable mass in the right lower quadrant of the abdomen. Pelvic ultrasound scan identified a lobulated hypo-hetero-echoic mass with some calcified foci. Computed tomography scan revealed a low-attenuated lesion-like mass in the perineal region, which suggested a cystic localized tumor. Colonoscopy showed sub-mucosal lesion in the cecum. The patient underwent Laparotomy, and a right hemicolectomy (include ileum) with ileocolic anastomosis was performed. She was treated successfully. In the Histological examination, two mass-like lesions were found to attach to the appendix. In the proximal portion of the appendix, there were cystic structures that showed a low-grade appendiceal mucinous neoplasm. The tip of the appendix showed a well-differentiated neuroendocrine tumor (carcinoid tumor). In this unusual case, even though the initial origins of these two tumors are quite different, two tumors appeared in a single histological section.

Keywords: Synchronous, Mucinous, Carcinoid tumor, Appendix

Introduction

Synchronous neoplasms are rare tumors in a single patient, which are diagnosed simultaneously or within six months of each other. Synchronous tumors are quite interesting medical cases, on which a large number of studies and reports have been carried out.¹ Appendiceal neoplasms are relatively rare and

usually detected in 0.7 to 2.5% of histological evaluation of appendectomy specimens.² Carcinoid tumors are the most prevalent appendiceal neoplasm, accounting for more than half of all the malignancies of the appendix and almost accidentally found in appendectomy specimens. Carcinoid tumors are associated with other gastrointestinal tumors and ovarian

tumors.³ Mucinous appendiceal neoplasms (MANs) are commonly discovered in middle-aged and older adults. The majority of patients with mucinous appendiceal tumors are asymptomatic or have non-specific signs or symptoms.⁴ Medical and surgical approaches differ in each tumor and are particular to tumoral behaviors. Distant metastasis of each tumor is seen in other organs of the body, and therefore, it is necessary to investigate and follow up on a possible invasion for each tumor.⁵

In this report, we described the case of a 76-year-old woman with two different tumors located in the appendix.

Case Presentation

A 76-year-old emigrant woman presented with one-year history of intermittent right lower abdominal pain. She did not have a recent change in bowel habitus, diarrhea, melena, hematochezia, or a change in appetite. She had a slight weight loss and a history of urinary symptoms, such mild dysuria and frequency. She did not mention any previous illness or cancer about herself or her family. In addition, she was using opioid analgesics. On examination, the abdomen was soft and non-tender, with a palpable mass of approximately 10 × 5 cm in the right lower quadrant, which was freely mobile. Digital rectal examination was normal. Blood tests showed that CEA (tumor marker) was equal to 3.71 ng/ml. Pelvic ultrasound scan was performed, which identified a lobulated hypo-hetero-echoic mass (72 × 133 mm) with some calcified foci. Computed tomography revealed a low-attenuated lesion-like mass in the pericecal region that was measured to be about 48 × 43 mm and contained some small calcified fleck with certain enhanced foci. The aforementioned characteristics suggested a cystic localized tumor and no lymph node invasion or metastasis. (Figure 1) Colonoscopy revealed a 10-mm submucosal lesion with the possibility of benign or gastrointestinal stromal tumor lesion; however, there was the possibility of external pressure. A biopsy of the lesion was performed. (Figure 2) The pathologic result was insignificant. The patient underwent Laparotomy, right hemicolectomy (include ileum), and ileocolic

anastomosis, through which two large appendiceal masses were identified. (Figure 3D)

Pathological findings

The resected surgical specimens comprised a 3 × 2-cm portion of terminal ileum and a 19-cm long colon with a 5.5 × 0.7 cm appendix. Two mass-like lesions were attached to the appendix; the proximal one was 7 × 7 × 4 cm and the other one was 8 × 7 × 5 cm. In the histological examination of the proximal portion of appendix, there were two cystic structures showing a low-grade appendiceal mucinous neoplasm. (Figure 3B) The cysts were sloughed in the most areas. In the preserved area, the cyst had been lined by crowded columnar cells with elongated, hyperchromatic basal nuclei and also mucin-rich cytoplasm ... Loss of muscularis mucosa was noted. There was no peritoneal involvement and Lymphovascular space invasion.

At the tip of appendix, there was a well differentiated neuroendocrine tumor (carcinoid tumor). (Figure3C) This tumor was composed of nest and small sheets of rather monomorphic cells with round uniform nuclei, stippled chromatin, and moderate granular cytoplasm. Mitosis was found to be rare. The resection margins were uninvolved and there was an invasion to sub-serosal tissue without involvement of visceral peritoneum. Lymphovascular space invasion was not identified. These two neoplasms were seen in a single histological section (Figure 3D).

The patient applied for adjuvant chemotherapy, but did not accept the proposed method. She had no problems in the follow-up for four months and after that, the patient returned to her country. We did not detect any evidence of carcinoid syndrome in lab test data.

The Ethics Committee of Qom University of Medical Sciences approved this study (Ethics code: IR.MUQ.REC.1400.093).

Discussion

Colorectal adenocarcinoma is one of the most prevalent tumors in both men and women, which can be fatal. Colorectal cancer-associated mortality rate is about 145,000 annually in the United States.⁶ Due to the high prevalence of colorectal cancer, screening programs have been

considered for early detection of this cancer. Neuroendocrine tumors (NET) are relatively uncommon in the gastrointestinal tract (about 0.5%). NET is associated with symptoms similar to those of adenocarcinoma, including anemia, abdominal pain, and obstructive symptoms. In all synchronous cases, the symptoms and signs are related to the adenocarcinoma while NET was often asymptomatic.⁷ Synchronous gastrointestinal adenocarcinoma and neuroendocrine in the pancreas has been reported, but colorectal adenocarcinoma and NET at the same time are scarce. Carcinoid and non-carcinoid tumors were first reported simultaneously in 1949,⁷ and similar cases have been reported since then. A study was published by Jessica Winn in Colombia in 2017; by that time, 17 cases of synchronous carcinoid and adenocarcinoma had been identified. Simultaneous involvement of two tumors in one segment has seen in only two patients (one in the rectum and the other in the ileum).⁸ In synchronous tumors in the GI tract, the sigmoid and then the rectum is the most common site of adenocarcinoma and the most common site of NET is in the small intestine, followed by the rectum. In 2021, Lancellotti identified 28 cases of NET tumor and concomitant adenocarcinoma in a literature review. It was 4: 3 more common in men. No cases of NET and adenocarcinoma in the appendix have been reported simultaneously.⁷

The incidence of Secondary Primary Malignancy (SPM) is 2.3% in patients with NET. There are various theories to explain simultaneous tumors in the gastrointestinal tract, which include common stem cells and the effect of some hormones, such as gastrin and cholecystokinin on tumor formation.⁹ Aoyagi et al. speculated that there was an association between tubular adenocarcinoma and NET.¹⁰ Shenoy surveyed 11 patients in 2013 and found that the growth factors secreted by the NET through the paracrine model play a key role in the development of SPM in the colorectal region.¹¹

Treatment of adenocarcinoma is based on the principles of oncosurgery. However, various factors affect the treatment of NET and its treatment management includes endoscopic resection, simple appendectomy, and

oncological colectomy and in advanced cases, debulking and target therapy.

There is a possibility of complications in the types of treatments used for cancer (such as radiotherapy), which sometimes lead to irreversible consequences. Cioffi et al. presented a patient with intestinal obstruction. After laparotomy and resection of ileum, histopathologic data proved the presence of a mixed adenocarcinoid tumor.¹² Henry reported renal teratoma coexisting with both carcinoid tumor and adenocarcinoma.¹³ Yamauchi et al. reported a 41-year-old Japanese man suffering from ascending colon tumor that was well-differentiated adenocarcinoma accompanied by carcinoid tumor, categorized as MANEC (mixed adenoneuroendocrine carcinoma).¹⁴ Michelle D Reid et al. discussed the high-grade versions of appendiceal goblet cell carcinoids ('adenocarcinoma ex-goblet cell carcinoids'). In their study, the tumors were almost gynecologic-based, which predominantly occurs in females (74%), stage IV (65%) disease.¹⁵

The prevalence of carcinoid tumor has been reported to be 0.5%. The most common affected sites are the appendix and ileum.¹⁶ The most frequently reported site affected by colorectal adenocarcinoma is rectosigmoid and its occurrence in the appendix is relatively rare.

Conclusion

Having a full colonoscopy and imaging prior to colorectal cancer surgery is of particular importance. On the other hand, colonoscopy for detection of another lesion, such as a gastrointestinal neuroendocrine tumor, could be recommended for detection of synchronous adenocarcinoma similarly.

Informed consent

Written informed consent for publishing this case report was obtained from the patient.

Conflict of Interest

None declared.

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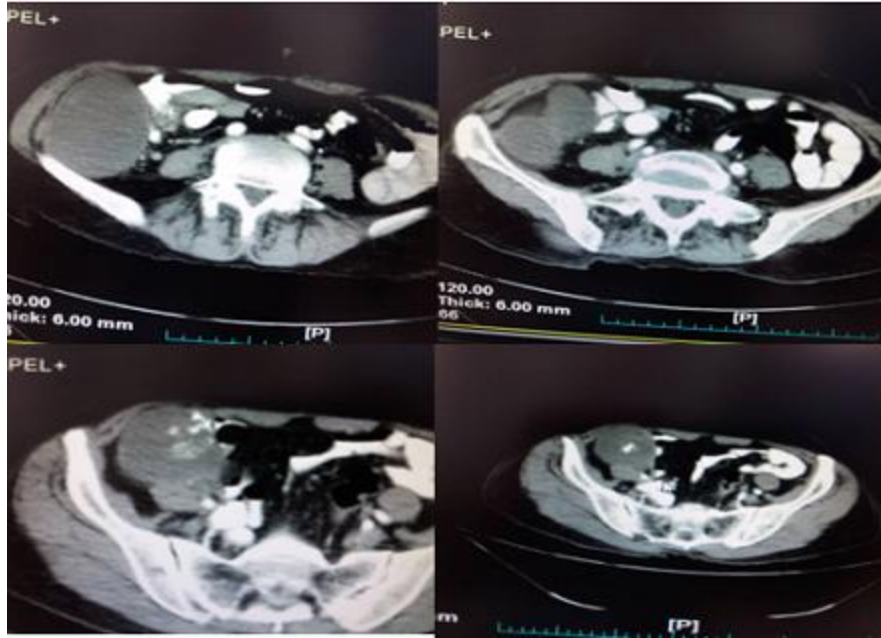


Figure 1. Abdominopelvic CT scan showed two masses in the right lower quadrant near the cecum.

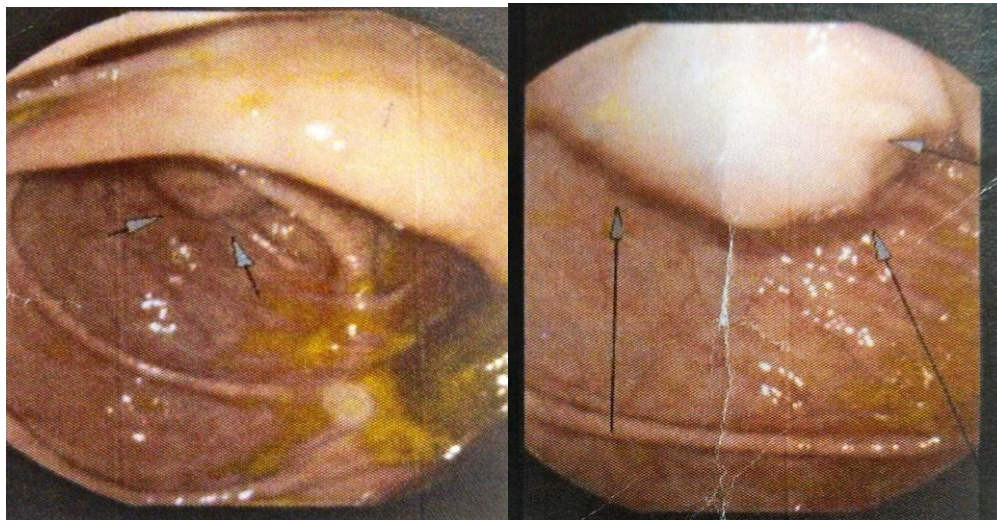


Figure 2. Colonoscopy findings showed a mass in the sub-mucosal layer, which was protruded into the lumen.

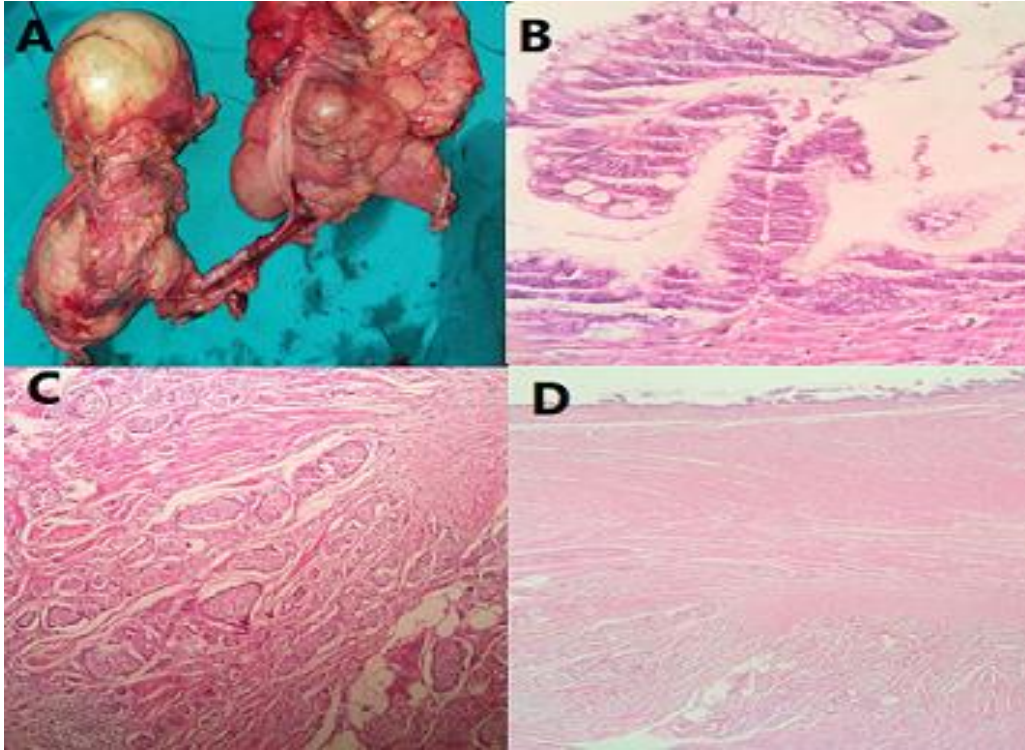


Figure 3. Histological examination of appendiceal tumors; (A) gross view (B) Mucinous tumor of appendix (H&E, $\times 400$); (C) Carcinoid tumor of appendix (H&E, $\times 400$); (D) Histopathological section where both tumors appeared simultaneously (H&E, $\times 100$).