Clinical Case Report

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Primary mixed adenocarcinoma and small-cell carcinoma of appendix

A case report (CARE-compliant)

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Abstract

Rationale: Primary extrapulmonary small-cell carcinoma (SCC) of appendix is reported very rarely. We report herein a case of mixed SCC and adenocarcinoma of appendix.

Patient's concern: A 70-year-old female was consulted to our Emergency Department with the right lower abdominal pain and low-grade fever for 2 days.

Diagnosis: Abdominal ultrasonography revealed the perforated appendicitis with periappendiceal abscess. Postoperative histology confirmed the diagnosis of mixed SCC and adenocarcinoma.

Interventions: After laparoscopic appendectomy, she underwent right hemicolectomy for radical surgery.

Outcomes: Laparoscopic appendectomy was performed and histological examination showed mixed SCC and adenocarcinoma. After confirming that there was no other organ metastasis, right hemicolectomy was performed for radical surgery. Five months after surgery, the patient expired due to multiple organ metastases.

Lessons: Further studies are required for better understanding of disease entities, and clinical trials are needed to define adequate treatment strategies for extrapulmonary SCC.

Abbreviations: EPSCC = extrapulmonary small-cell carcinoma, SCC = small-cell carcinoma.

Keywords: appendiceal carcimona, mixed adenocarcinoma and small-cell carcinoma

1. Introduction

The lung has been reported to be the primary origin in most cases of small-cell carcinoma (SCC). Extrapulmonary SCC has been described in different sites. Many different sites of origin have been described, including kidney, bladder, prostate, endometrium, salivary glands, nasal sinuses, and intestinal tract. But extrapulmonary SCC of appendix is reported very rarely. To the author's knowledge, only 2 cases were reported by Rossi et al (mixed type)[1] and O'Kane et al (pure type),[2] and this is the second reported case of a mixed SCC and adenocarcinoma of the appendix.

We report herein a case of mixed SCC and adenocarcinoma of appendix arisen in a 70-year-oldwoman and clinically presenting as an acute appendicitis with appendiceal abscess.

2. Case report

A 70-year-old female presented with the right lower abdominal pain and low-grade fever for 2 days. She had no other past history. The physical examination disclosed a tender mass over the right lower quadrant of abdomen with mild tenderness and rebound tenderness. Abdominal ultrasonography revealed the perforated appendicitis with periappendiceal abscess (Fig. 1). Under the impression of perforated appendicitis with periappendiceal abscess, she admitted and underwent laparoscopic appendectomy.

Immunohistochemistry performed on the appendix revealed positive staining for synapto physin (Fig. 2B) and chromogranin (Fig. 2C). Histological examination showed mixed SCC and adenocarcinoma with periappendiceal fat infiltration and resection margin was free from carcinoma. Abdominopelvic computed tomography was performed for further evaluation. It showed an enhanced, thickened cecal wall with fatty infiltration (Fig. 3). Tumor markers were carcinoembryonic antigen (CEA) 0.77 ng/mL and carbohydrate antigen 19-9 (CA 19-9) 2.0 U/mL. A chest computed tomography scan was normal. In the absence of an identified pulmonary tumor, a diagnosis of primary mixed SCC and adenocarcinoma was made.

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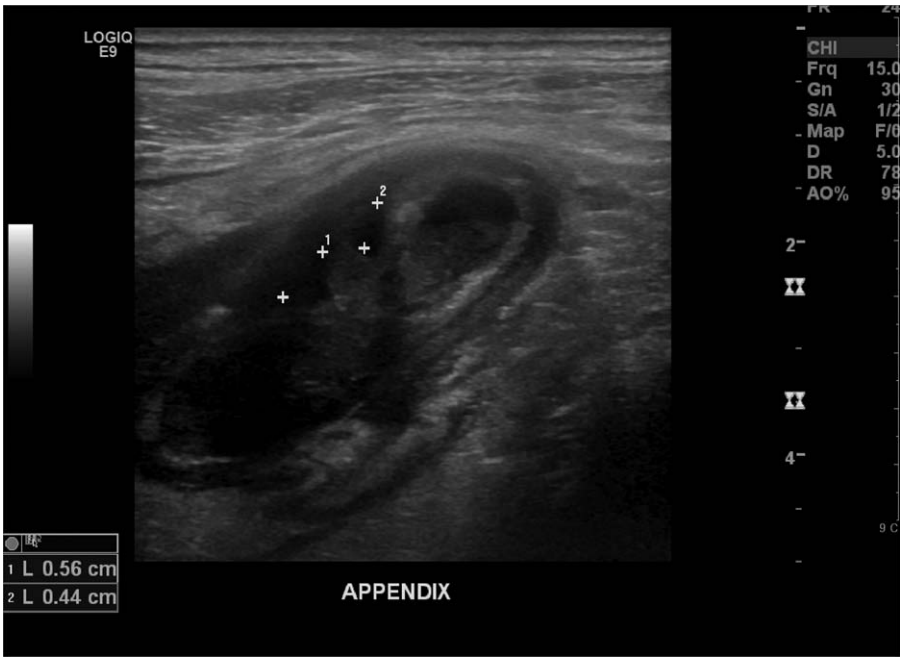

Figure 1. Ultrasonography scan shows thick walled appendix with perforation.

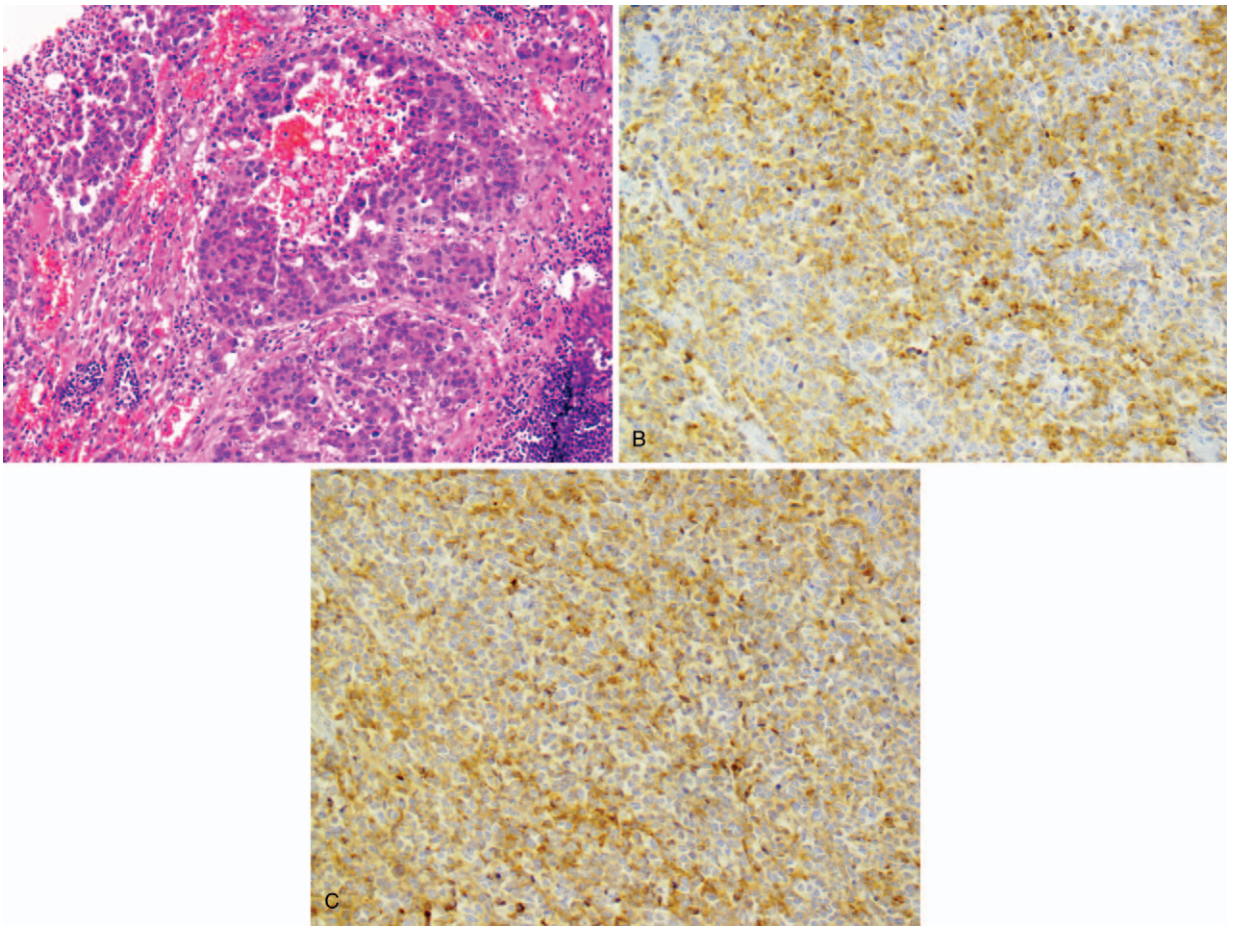

Figure 2. (A) Mixed adenocarcinoma. (B) Synaptophysin positive stain. (C) Chromogranin positive stain.

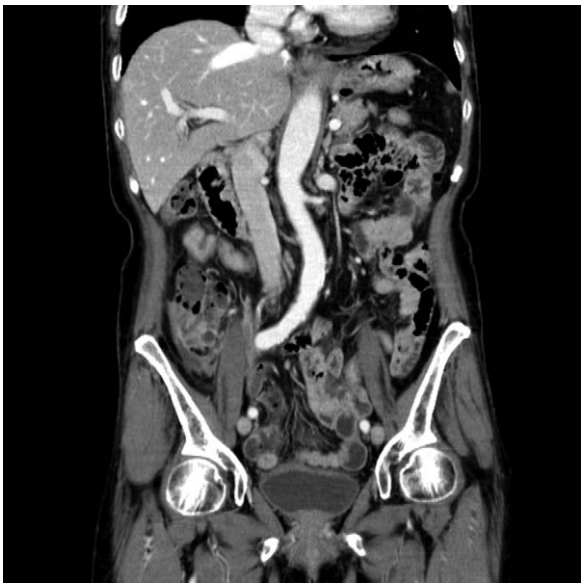

Figure 3. Coronal reconstructed computed tomography scan with intravenous contrast enhancement, enhanced thickened cecal wall with fatty infiltraton in right lower quadrnat of abdomen.

Two weeks after laparoscopic appendectomy, she underwent right hemicolectomy for radical surgery. Histological examination showed the residual carcinoma cannot be found in the colonic wall itself, and the metastatic tumor of lymph node showed features of neuroendocrine carcinoma and focal adenocarcinoma (metastases to 2 out of 38 nodes, stage IIIb). Chemotherapy was planned, but cancelled due to deteriorating symptomatology.

Four months after surgery, a computed tomography scan of the abdomen confirmed multiple liver metastases within both lobes of liver and huge mass in the right iliac fossa (Fig. 4A, B). There was associated lymphadenopathy extending through the ileocolic branch of the superior mesenteric artery and further large lymph nodes in the ascending colon and paraaortic regions. Furthermore, extrinsic pressure to the distal third of the right ureter was present with severe hydronephrosis (Fig. 4C). No lung parenchymal abnormality was identified. After 1 month, the patient expired due to multiple organ failure.

3. Discussion

SCC is thought to originate from neuroendocrine cells, which are found in the epithelium of many mucosal surfaces including the gastrointestinal tract.[3] The vast majority of SCC develop from the lung. Approximately 6.4% of all SCC is arisen in

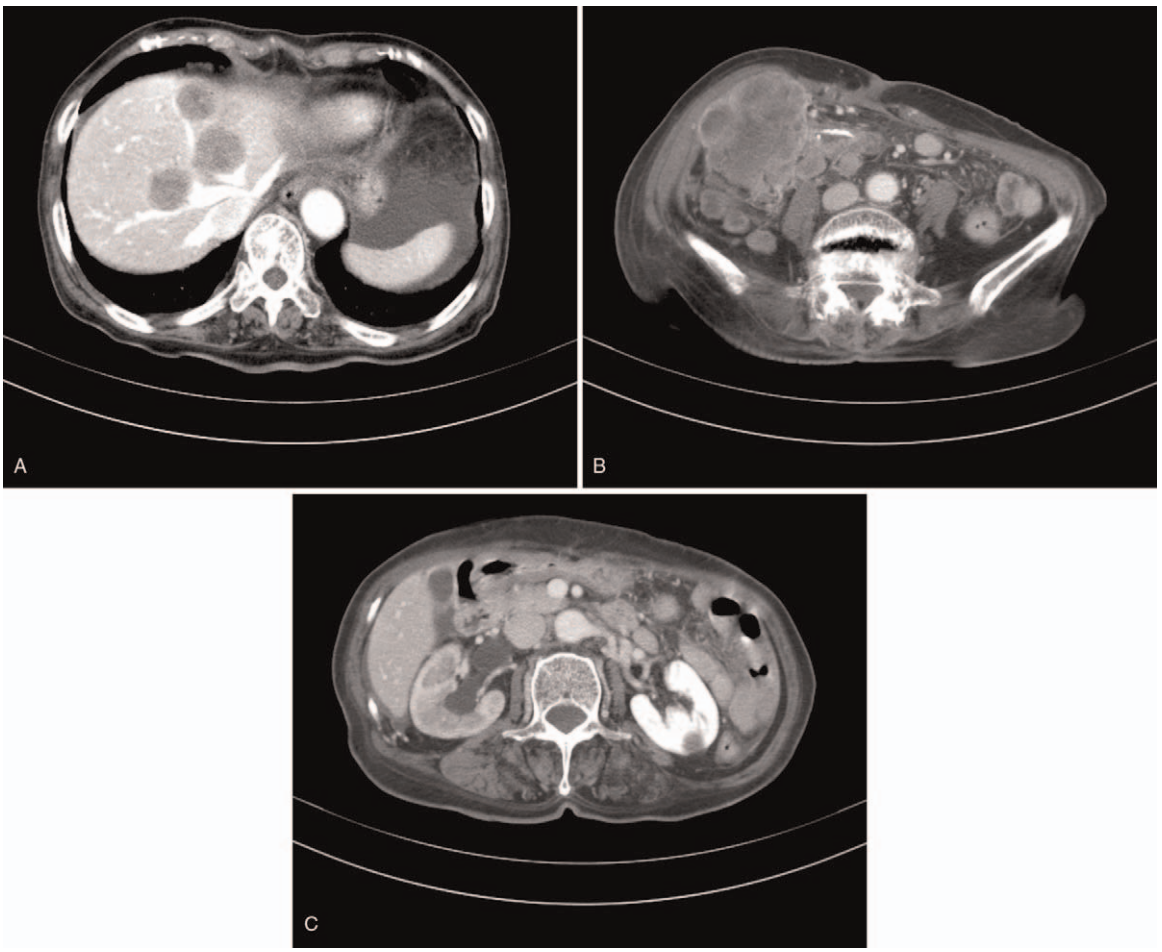

Figure 4. (A, B) Computued tomography scan 4 months after surgery shows marginal enhanced ovoid masses in both lobe of liver and huge fungating enhancing mass in right lower quadrant of abdomen. (C) Computued tomography scan at level of renal hilum after surgery shows dilated pelvocalyceal system and ureter with decreased renal parenchymal enhancement of right kidney.

extrapulmonary sites such as the gallbladder, esophagus, stomach, pharynx, larynx, pancreas, colon, rectum, skin, and cervix.[4]

Duke (1950) was the first to report on SCC of the colon. Colorectal extrapulmonary small-cell carcinoma (EPSCC) is rare with a proposed incidence of 0.3% of all colorectal cancer, according to the National Cancer Institute.[5] Yasui et al[6] reported that colorectal EPSCC was located in the cecum in 7 paitnets (18.4%), ascending colon in 7 patients (18.4%), transverse colon in 3 patients (7.9%), sigmoid colon in 3 patients (7.9%), rectum in 16 patients (42.1%), and proctos in 2 patients (5.3%). The majority of patients had SCC in the recutm. Pure SCC of the appendix is rare with only one previously reported case by O'Kane et al [2] and one case of mixed SCC and adenocarcinoma of the appendix was reported by Rossi et al.[1]

Primary neoplasm of appendix presents with clinical symptoms that are indistinguishable from those of acute appendicitis. Our case also presented with symptoms suggestive of acute appendicitis. It is difficult to distinguish computed tomography and other image study. Histologic examination is the only diagnostic method. If appendiceal SCC is confirmed by pathology, further investigative modalities with chest computed tomography imaging or bronchoscopy are mandatory to exclude a pulmonary origin. In our case, there were no lung lesions until the patient expired.

Similar to reported case by Rossi et al,[1] the major tumor component (about 70% of the tumor specimen) was the adenocarcinoma, and SCC components were found as small foci throughout the adenocarcinoma region (30%). Regional 2 lymph nodes presented a metastatic deposit by the adenocarcinoma component only. But the survival time was significantly different (disease free and alive 65 months vs survival 6 months after surgery). Clinical presentation of EPSCC is usually at an advanced stage due to the aggressive nature of the disease and recurrence of EPSCC is common.[7] Colorectal EPSCC is aggressive malignancy with early metastasis and have a 5-year survival is $<13\%$.[7,8] In our case, tumor had aggressive clinical course with locoregional (include multiple lymph nodes) and distant disease recurrence.

Multimodality therapy is required for the majority of patients to improve overall outcome.[9] Unfortunately, there are no definite chemotherapeutic regimens for EPSCC of the colon due to the small patient numbers. The chemotherapeutic regimens used for the treatment of EPSCC were similar to those of SCC of the lung because of its relative chemosensitive nature, combination chemotherapy regimens using cisplatin and etoposide are the most commonly used, with response rates of up to 70%.[7,10,11] In colorectal SCC, the mean survival times for patients who underwent resection only and for those who also underwent adjuvant chemotherapy were 67.0 and 121.4 weeks, indicating a longer survival time with adjuvant chemotherapy.[6]

In summary, we described herein a unique case of primary mixed adenocarcinoma and SCC of the appendix incidentally discovered during appendectomy for suspected appendicitis. Limitation of this study was failure of chemotherapy and gene mutation study. Further studies are required for better understanding of disease entities, and clinical trials are needed to define adequate treatment strategies for EPSCC.

Author contributions

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