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 carcinoma, 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-old woman 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 synaptophysin (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.
Figure 1. Ultrasound scan shows thick walled appendix with perforation.

Figure 2. (A) Mixed adenocarcinoma. (B) Synaptophysin positive stain. (C) Chromogranin positive stain.
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. The vast majority of SCC develop from the lung. Approximately 6.4% of all SCC is arisen in
adenocarcinoma of the appendix was reported by Rossi et al.\[1\] Recurrence of EPSCC is common.\[7\] Colorectal EPSCC is advanced stage due to the aggressive nature of the disease and after surgery). Clinical presentation of EPSCC is usually at an different (disease free and alive 65 months vs survival 6 months lymph nodes presented a metastatic deposit by the adenocarcinoma region (30%). Regional 2 adenocarcinoma, and SCC components were found as small component (about 70% of the tumor specimen) was the most commonly used, with response rates of up to 70%.\[7,10,11\] In section 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.

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