Synchronous small cell carcinoma and adenocarcinoma of the rectum

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Abstract
Small cell carcinoma (SCC) is derived from neuroendocrine cells primarily found in the lung. Extra-pulmonary SCC is relatively rare, comprising <5% of all SCCs. Most extra-pulmonary SCCs are found in the gastrointestinal tract; however, SCC of the rectum is extremely rare. The tumour biology of rectal SCC is similar to that of pulmonary SCC, an aggressive tumour that results in frequent distant metastases associated with poor response to chemotherapy. Combination chemotherapy, based on regimens for pulmonary SCC, has been used to treat extra-pulmonary SCC, and surgical resection followed by radiation therapy has been suggested; however, an optimal treatment modality has not been established due to the rarity of these cases. Here, we present a case of synchronous SCC and adenocarcinoma of the rectum that was managed by radical surgery followed by chemotherapy, but recurred with rapid progression in the regional and distant lymph nodes.

INTRODUCTION
Small cell carcinoma (SCC) originates from neuroendocrine cells, frequently found in the lung. Neuroendocrine cells are distributed in various organs such as the gastrointestinal tract and the thyroid gland; thus, extra-pulmonary SCC, although very low in incidence, can be found throughout the body as a rare type of solid tumour [1]. Rectal SCC is among the rarest tumours, comprising <1% of colorectal malignancies [2, 3]. Moreover, synchronous rectal adenocarcinoma and SCC is extremely rare. Unlike typical colorectal cancer, the prognosis of rectal SCC is very poor because of its aggressive behaviour and poor response to chemotherapy [2]. Thus, an optimal treatment modality for rectal SCC is not established. Here, we present a case of synchronous rectal SCC and adenocarcinoma.

CASE REPORT
A 45-year-old man presented with a 1-week history of haematochezia. His medical history was unremarkable, except a 4-kg weight loss in the past 3 months. Upon admission, his vital signs were stable, and his laboratory results were within normal limits, including those for tumour markers. Colonoscopy revealed a 2.5 × 2.0 cm pedunculated lesion with surface ulceration located 10 cm from the anal verge (Fig. 1). Microscopic
examination obtained from colonoscopic biopsy revealed a vil-
lus adenoma. Abdominopelvic computed tomography (CT)
indicated a polypoid lesion at ~3 cm in the upper rectum; posi-
tron emission tomography (PET) revealed multiple metastases
to lymph nodes (LNs) along the inferior mesenteric artery,
mesorectum and superior rectal artery (Fig. 2). Under the pre-
sumptive diagnosis of advanced upper rectal adenocarcinoma,
low anterior resection with LNs dissection was performed.
Subsequently, the resected specimen was found to contain an
SCC mainly in the subserosa, and an adenocarcinoma with mus-
cle layer invasion (Fig. 3). Microscopic examination showed typ-
ical cytologic features of SCC—discohesive, small and round cells
with scanty cytoplasm. A concurrent, moderately differentiated
adenocarcinoma was also observed. Immunohistochemically, the
round-shaped tumour cells had positive results for two neuroen-
docrine markers—synaptophysin and CD56 (Fig. 4). The staging of
the lesion was T3N2b (10/15) with lymphovascular invasion; all
LNs were invaded by the SCC. He received intravenous chemother-
apy 3 weeks after surgery, with standard doses of irinotecan
and cisplatin. However, a month after chemotherapy, he had
local recurrence with regional LNs metastases on follow-up CT.
Intravenous chemotherapy was changed to 5-fluorouracil
(5-FU), etoposide and cisplatin. However, local recurrence with
regional LNs metastases had progressed. Despite third-line
intravenous chemotherapy with topotecan and radiotherapy,
multiple distant metastases to the right femur, left axilla, right
thyroid and neck, pericolic LNs and retroperitoneal LNs, caus-
ing bilateral hydronephrosis, developed 6 months postopera-
tively. The patient died of multiple metastatic disease soon
after nephrostomy tube insertion.

DISCUSSION

SCC, a subtype of neuroendocrine tumours, is the most poorly
derifferentiated of these tumours [4]. It originates from neuroen-
docrine stem cells, found in the gastrointestinal tract, lung,
thorax and other organs [1]. While pulmonary SCC is com-
mon, extra-pulmonary SCC is among the rarest tumours.
Although the gastrointestinal tract is one of the common sites
of extra-pulmonary SCC, rectal SCC is rare (<1% of all colorec-
tal malignancies) [2, 3]. Moreover, the incidence of synchron-
ous colorectal cancer is 5%; however, colorectal cancer showing different histologies is extremely rare [5].

Unlike typical colorectal adenocarcinoma, the pathogenesis
and risk factors of colorectal SCC remain unknown. Some stud-
ies reported that the tumour may derive from pluripotent neu-
roendocrine stem cells or cells in the pre-existing adenoma, as
has been reported for synchronous SCC with tubulovillous
adenoma [2].

The differential diagnosis of rectal SCC includes metastatic
lung SCC, basaloid carcinoma, cloacogenic carcinoma, lymph-
oma and other neuroendocrine tumours. However, histological
examination enables a definite diagnosis of rectal SCC [6].
Although CT findings of rectal SCC have been reported, it is dif-
ficult to differentiate these from typical rectal cancer using

Figure 2: PET-CT findings. Multiple metastases to LNs along the inferior mesen-
teric and superior rectal arteries (arrows) are noted.

Figure 3: Surgical specimen. Approximately 3.0 x 2.5 cm polypoid mass with
ulceration (arrow) is noted at 1.5 cm from the distal margin.

Figure 4: Pathological findings. (A) Lower power view shows two different tumours
(low dark and upper light) coexisting with collision area (arrow) (H&E x10). (B) Collision area reveals the border (arrows) between the moderately differentiated
adenocarcinoma (left) and the poorly differentiated SCC (right) (H&E, x200). (C) The
tumour consists of discohesive, small and round cells with scanty cytoplasm. No
gland formation is seen (H&E, x400). (D) The tumour cells are diffusely positive for
synaptophysin immunostaining (x100).
imaging studies [7]. Thus, histopathological examination of colonscopic biopsy samples is necessary. However, when the biopsy specimen is obtained from superficial parts, and present with different histologies, the diagnosis of SCC may be difficult. Histological features of extra-pulmonary SCC are identical to those of pulmonary SCC. They possess characteristically round- or spindle-shaped cells with intensely hyperchromatic nuclei and scant cytoplasm. Immunohistochemically, at least two neuroendocrine markers (neuron-specific enolase, chromogranin, synaptophysin or CD56) must have positive results for a definite diagnosis of SCC. Among them, synaptophysin is the most reliable marker [8]. In the present case, an initial diagnosis based on colonscopic findings and imaging studies was advanced rectal adenocarcinoma, although the tumour was small. However, histological evaluation of the surgical specimen enabled a definite diagnosis of synchronous adenocarcinoma and SCC of the rectum. The tumour had round-shaped cells with little cytoplasm, finely granular nuclear chromatin, and inconspicuous nucleoli, and immunohistochemically, the tumour cells are positive for synaptophysin and CD56.

Although metastatic patterns of rectal SCC remain uncertain because of rarity, extra-pulmonary SCC originating from the gastrointestinal tract commonly metastasize to the liver, LNs and bone marrow, irrespective of the staging. Thus, the mean survival time for patients with colorectal SCC is <1 year [2]. In the present case, although liver metastasis was not observed, multiple regional LNs metastases, followed by distant LNs and bone metastases developed within the 6-month survival period.

The optimal treatment for rectal SCC remains unknown. Since the response of these tumours to chemotherapy is similar to that of pulmonary SCC, combination chemotherapy with either irinotecan and cisplatin or etoposide and cisplatin may be administered to patients with rectal SCC. Former chemotherapy regimens for pulmonary SCC showed better results than latter ones, and the effect of chemotherapy with cisplatin and 5-FU for oesophageal SCC has been reported; however, optimal chemotherapeutic regimens for rectal SCC have not been established [9, 10]. Moreover, even though the combination of radical surgery and multi-treatment modalities including chemotherapy and radiation therapy has been suggested, the role of radical surgery is controversial for rectal SCC [2]. In the present case, we performed radical surgery followed by adjuvant chemotherapy. However, the aggressive tumour biology resulted in disease progression with poor response to chemotherapy.

In conclusion, rectal SCC is an extremely rare type of colorectal malignancy, and the prognosis is very poor due to its aggressive tumour biology. Thus, optimal treatment modality and the role of radical surgery need to be clarified in the future.

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CONFLICT OF INTEREST STATEMENT
None declared.

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