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Case Report

CASE REPORT

Case report: potential treatment of metastatic amphicrine carcinoma of the rectum with FOLFOXIRI chemotherapy

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Abstract

Amphicrine carcinoma (AmC) is a unique epithelial tumor displaying exocrine and endocrine features in the same cell. It shows an adenocarcinoma-like cellular form and has endocrine granules. There are few reports describing chemotherapy for AmC. Here, we describe a case with metastatic AmC from the rectum that was treated with FOLFOXIRI chemotherapy. A 64-year-old man was diagnosed with a submucosal lesion on the scar produced after an endoscopic mucosal resection, which had been performed for adenocarcinoma of the rectum 2 years before. The endoscopic submucosal dissection revealed AmC. The abdominoperineal resection including lymph nodes dissection was performed. Thereafter, computed tomography showed multiple liver metastases, and FOLFOXIRI was administered. The best overall response was partial response, and progression-free survival was 8.7 months. After 16.0 months since first-line chemotherapy the patient died. We can therefore conclude that FOLFOXIRI may be effective for AmC of the rectum.

INTRODUCTION

Amphicrine carcinoma (AmC) was firstly reported by Ratzenhofer in 1977 [1]. AmC is a unique epithelial tumor with both exocrine and endocrine features in the same cell, showing an adenocarcinoma-like cellular form but also having intracellular endocrine granules. AmC is sometimes confused with mixed adenoendocrine carcinoma (MANEC) in the World Health Organization classification of neuroendocrine tumors from 2010. However, MANEC is defined as carcinoma having components of adenocarcinoma and neuroendocrine carcinoma (30% or more) in different cells. There are reports on pathological findings or surgical management of AmC, but few reports on chemotherapy for metastatic AmC [2–8].

We describe a case of metastatic rectal AmC treated with FOLFOXIRI.

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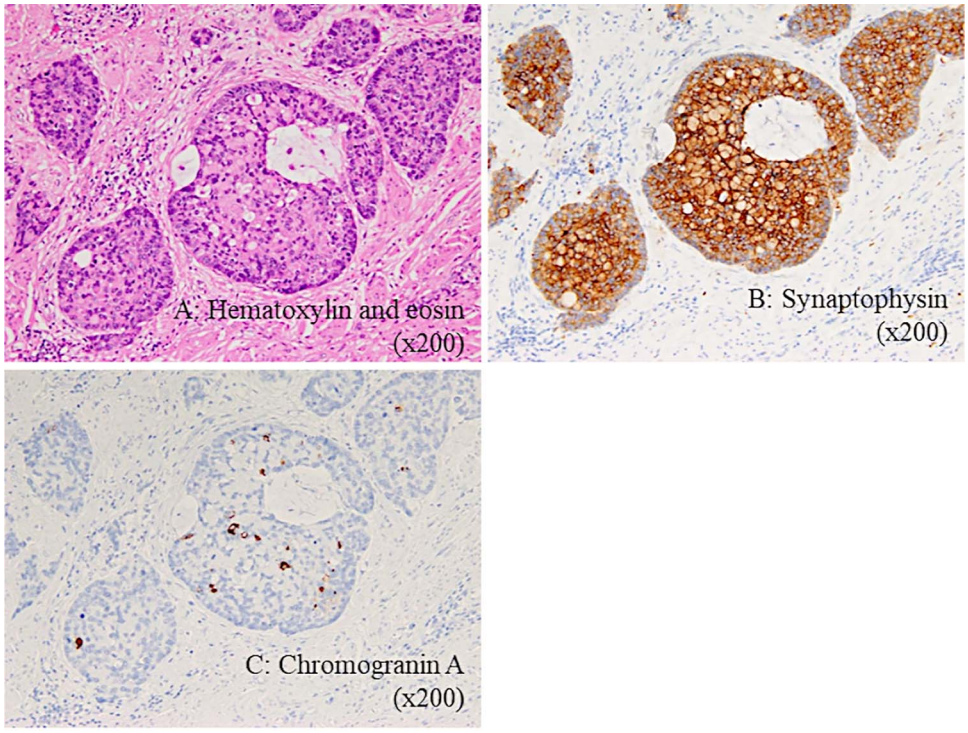

Figure 1: Pathological findings of the surgically resected rectum: (**A**) histopathological examination revealed that tumor cells with eosinophilic cytoplasm having circular irregular nuclei and signet cells containing abundant mucus were mixed and proliferated; (**B**) synaptophysin was diffusely positive; (**C**) chromogranin A was focally positive.

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A 64-year-old male underwent endoscopic mucosal resection (EMR) for a sessile type lesion (0-Is) in the rectum 2 years before presentation. The histological diagnosis was adenocarcinoma invading into the muscularis mucosae. The tumor was close to the vertical stump, and there were some areas where it was difficult to determine the stump due to the influence of cauterization. Adjuvant chemotherapy was not applied because it was determined the pathological curative resection had been performed. Upon presentation to the clinic, he was diagnosed with a submucosal lesion on the EMR scar from the rectum to anal canal on the anal transition zone. Histopathological examination suggested a local recurrence of rectal adenocarcinoma. He was referred to our hospital for definitive diagnosis and treatment a month after the endoscopic biopsy. FDG-positron emission tomography/computed tomography (CT) showed 2-fluoro-2-deoxy-D-glucose (FDG) accumulation of pelvic lymph nodes (maximum standardized uptake value [SUVmax] 4.7) but not in the rectum.

Two months after the endoscopic biopsy, an endoscopic submucosal dissection (ESD) for diagnostic purposes was performed for the local recurrent lesion. Histopathological examination revealed tumor cells with round atypical nuclei and eosinophilic cytoplasm and signet cells in the epithelium. Synaptophysin was diffusely positive in tumor cells of both histological types, and chromogranin A was focally positive by immunohistochemistry. This indicated the tumor had both exocrine and endocrine features in the same cell. The final diagnosis was rectal AmC.

A month later, endoscopic ultrasound of pelvic lymph nodes and a colonoscopy were performed. Pelvic lymph nodes accumulated FDG could not be detected, but the local recurrence of AmC on the ESD scar was shown. A month later, an abdominoperineal resection including dissection of lymph nodes was performed, resulting in R0 resection. Findings of the histopathological examination of surgically resected specimens were similar to those of the previous endoscopic biopsy. CDX-2 and synaptophysin were diffusely positive, chromogranin A and MUC2 were focally positive and MUC5AC and MUC6 were negative (Fig. 1). The recurrent rectal AmC was partially exposed to the surface layer and invaded into veins and lymphatic vessels. Tumor cells were also found in pelvic lymph nodes. Comprehensive genetic testing showed mutation of KRAS codon 61 Q61R, CCND1 amplification, FGF19 amplification and FGF3 amplification.

A month after surgical resection, CT showed liver metastases (Fig. 2A). FOLFOXIRI was chosen as first-line palliative chemotherapy. Heterozygosity for the UGT1A1∗28 allele was recognized. The regimen of FOLFOXIRI was folinic acid [L-LV; 200 mg/m^2, on day 1] + irinotecan [CPT-11; 150 mg/m^2, on day 1] + oxaliplatin [L-OHP; 85 mg/m^2, on day 1] + fluorouracil [5-FU; 2400 mg/m^2, continuous infusion for 46 h]. Compared with the original FOLFOXIRI regimen, CPT-11 and 5-FU were reduced due to concerns of adverse side effects. The best overall response (BOR) was partial response (PR) (−37.5%) after six cycles of FOLFOXIRI (Fig. 2). After six cycles of FOLFOXIRI, the treatment regimen was changed to FOLFIRI due to peripheral neuropathy. After 12 cycles of FOLFIRI, the disease progressed. The progression-free survival (PFS) was 8.7 months. After progression, FOLFOX plus bevacizumab (Bmab) was administered. The BOR was stable disease (+6.5%) after four cycles of FOLFOX plus Bmab. After eight cycles of FOLFOX plus Bmab, disease progression was confirmed, resulting in PFS of 4.4 months. He died due to the primary disease 16.0 months after the induction of FOLFOXIRI.

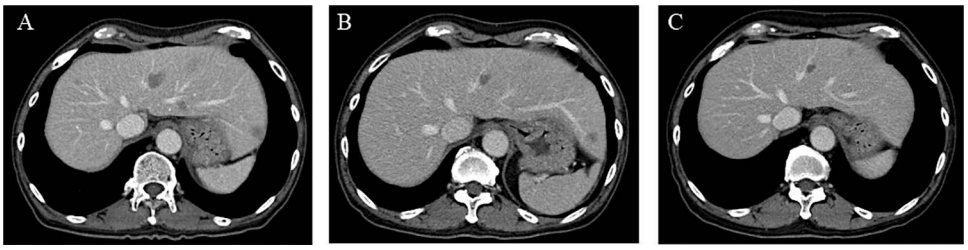

Figure 2: Comparison of computed tomography images of multiple liver metastases (**A**) before FOLFOXIRI, (**B**) after two cycles of FOLFOXIRI and (**C**) after six cycles of FOLFOXIRI. Tumor reduction was confirmed.

DISCUSSION

We describe a case of rectal AmC with liver metastasis treated by FOLFOXIRI.

AmC can arise from various organs throughout the body, especially the gastrointestinal tract. A total of 22 cases of colorectal AmC have been previously described in seven reports [2–8]. Three patients were treated with palliative chemotherapy [6, 8]. Karkouche *et al.* [6] reported a case in which PR was confirmed in first-line chemotherapy with XELOX, but response was not achieved in second-line chemotherapy with FOLFIRI. Huang *et al.* [8] reported two cases; one patient with liver and lung metastases received palliative radiotherapy and chemotherapy. Overall survival (OS) was 12 months. The other with liver metastasis received chemotherapy and has survived for >33 months. Details of treatment are not described. AmC is characterized by a mixture of pathological features of adenocarcinoma and neuroendocrine carcinoma. Some efficacious chemotherapy agents are suitable for both adenocarcinomas and neuroendocrine carcinomas, whereas some other chemotherapy agents only work for one type of tumor. In our case, FOLFOXIRI was chosen for first-line chemotherapy, with the expectation that it would work for both adenocarcinoma and neuroendocrine carcinoma as 5-FU is effective for rectal adenocarcinoma and CPT-11 and platinum agents are effective for both adenocarcinomas and neuroendocrine carcinomas. FOLFOXIRI is usually used for colorectal adenocarcinomas with an objective response rate, median PFS and OS reported as 66%, 9.8 months and 22.6 months, respectively [9]. In the present case, PR was achieved, and PFS was 8.7 months. As expected, FOLFOXIRI was as effective for AmC of the rectum as for colorectal adenocarcinoma. However, OS was 16.0 months, indicating that AmC has a worse prognosis than colorectal adenocarcinoma. If the resection had been performed earlier and adjuvant chemotherapy had been administered, metastases might not have appeared or might have appeared much later. But this does not affect the efficacy of palliative chemotherapy including PFS, OS and response. FOLFOXIRI as palliative chemotherapy was administered as soon as possible after metastases was confirmed. Therefore, multiple drug combination therapy effective for both adenocarcinoma and neuroendocrine carcinoma may be the best option for the treatment of rectal AmC.

ACKNOWLEDGMENT

None.

CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING

None declared.

ETHICAL APPROVAL

This case report was approved by Institutional Review Board of National Cancer Center Hospital (2017-229).

CONSENT

The patient is deceased. Patient and their family were provided the opportunity to opt out in homepage of National Cancer Center Hospital. In our hospital, we explain to all patients at their first visit that their medical records may be used for academic research and give them the opportunity to opt out. This report is in accordance with the ethical standards of Japan.

GUARANTOR

Y.H.

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