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CASE REPORT

Complete response of esophageal small cell carcinoma amrubicin treatment

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Abstract Small cell carcinoma of the esophagus (SmCCE) is a rare and aggressive disease known to have a poor prognosis. SmCCE patients are generally treated with a chemotherapeutic regimen for small cell lung cancer. Salvage therapy for patients with relapsed or refractory tumors has not yet been established. A 63-year-old man with extensive SmCCE was treated with chemotherapy consisting of cisplatin (CDDP) and irinotecan (CPT-11). After the second course of CPT-11/CDDP, the celiac lymph node increased in size. Amrubicin (AMR) as second-line chemotherapy was started. The patient had a complete response after the fifth course of AMR, resulting in an 8-month progression-free survival after initial administration. This case suggests that, as in small cell lung cancer, AMR is effective for SmCCE.

Keywords Chemotherapy · Small cell carcinoma of the esophagus · Amrubicin

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Introduction

The main types of esophageal cancer are squamous cell carcinoma and adenocarcinoma, with small cell carcinoma being rare. The incidence of small cell carcinoma of the esophagus (SmCCE) had a range of 0.6–2.4 % [1–3]. Generally, SmCCE is known to show aggressive behavior and to have a poor prognosis. Because of the rarity of SmCCE, the standard therapy is uncertain. Its characteristics are similar to those of small cell lung cancer (SCLC), such that the same therapeutic strategies are generally recommended. Distant metastases often occur in patients with SmCCE, and systemic chemotherapy plays an important role. Several chemotherapy regimens have been reported, including cisplatin (CDDP) plus etoposide (VP-16), CDDP plus irinotecan (CPT-11), and CDDP plus fluorouracil (5-FU) [4, 5].

Second-line chemotherapy for patients with relapsed or refractory SmCCE is more uncertain than the first-line chemotherapy. Amrubicin chloride (AMR) is a synthetic anthracycline and a potent topoisomerase II inhibitor that has been demonstrated to be effective for previously treated SCLC [6–9].

Herein, we present the case of a patient of refractory SmCCE who showed a good clinical response to AMR monotherapy.

Case report

A 63-year-old man presented with dysphagia. He had no relevant medical history. He had consumed 5.4 U of alcohol per day for 30 years, mainly rice wine, and smoked 30 cigarettes per day for 40 years. Endoscopy revealed a large ulcerated tumor from the lower esophagus to the

esophagocardial junction and an ulcerative lesion in the cardia suspected to be tumor invasion (Fig. 1). The esophageal tumor was biopsied. Hematoxylin and eosin staining revealed focal proliferation of small round atypical cells with hyperchromatic nuclei (Fig. 2a, b). The tumor cells were positive for synaptophysin and neural cell adhesion molecules (Fig. 2c, d). The tumor was negative for chromogranin A. Therefore, a pathological diagnosis of small cell carcinoma was made. Contrast-enhanced neck, chest, and abdominal computed tomography (CT) demonstrated a large tumor of the lower intrathoracic and abdominal esophagus. Metastases of paratracheal, juxtaesophageal, left subclavicular, and celiac lymph nodes were also detected (Fig. 3). The concentrations of serum neuron-specific enolase (NSE) and pro-gastrin-releasing peptide (Pro-GRP) were elevated to 48.3 ng/ml and 881 pg/ml, respectively. The TNM stage was III (T4N1M0).

Under a diagnosis of advanced SCC of the esophagus invading the gastric cardia with distant lymph node metastases, combination chemotherapy was started. The chemotherapy regimen consisted of a 4-week cycle of irinotecan (CPT-11) at a dose of 60 mg/m^2 on days 1, 8, and 15 and cisplatin (CDDP) at a dose of 60 mg/m^2 on day 1. After the first cycle of this regimen, CT showed that wall thickness and all the lymph nodes were reduced, and the serum NSE level was decreased to 5.8 ng/ml. After the second cycle, CT revealed that the celiac lymph node had increased in diameter from 37 to 58 mm (a 57 % increase), although the sum of the diameters of target lesions had decreased from 108.8 to 67.8 mm. Serum NSE was again elevated to 25 ng/ml, indicating disease progression clinically.

Therefore, AMR as second-line chemotherapy was started 4 weeks after the administration of the second cycle of CPT-11/CDDP. A dose of 45 mg/m^2 was infused on days 1, 2, and 3 every 4 weeks. Grade 3 neutropenia was observed at each administration but without significant complications. CT thereafter revealed a reduction in size of the celiac lymph node from 60 to 10 mm in diameter after the fifth course (Fig. 4). To evaluate residual tumor viability, positron emission tomography (PET)/CT scan with [^{18}F]-fluorodeoxyglucose (FDG) was performed. The FDG-PET/CT scan showed negative uptake (Fig. 5).

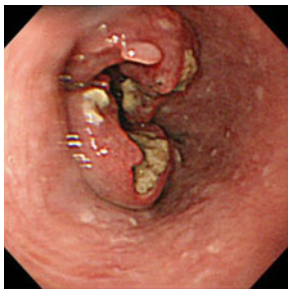

Fig. 1 Endoscopy showed a large ulcerated tumor from the lower esophagus to the esophago-cardial junction

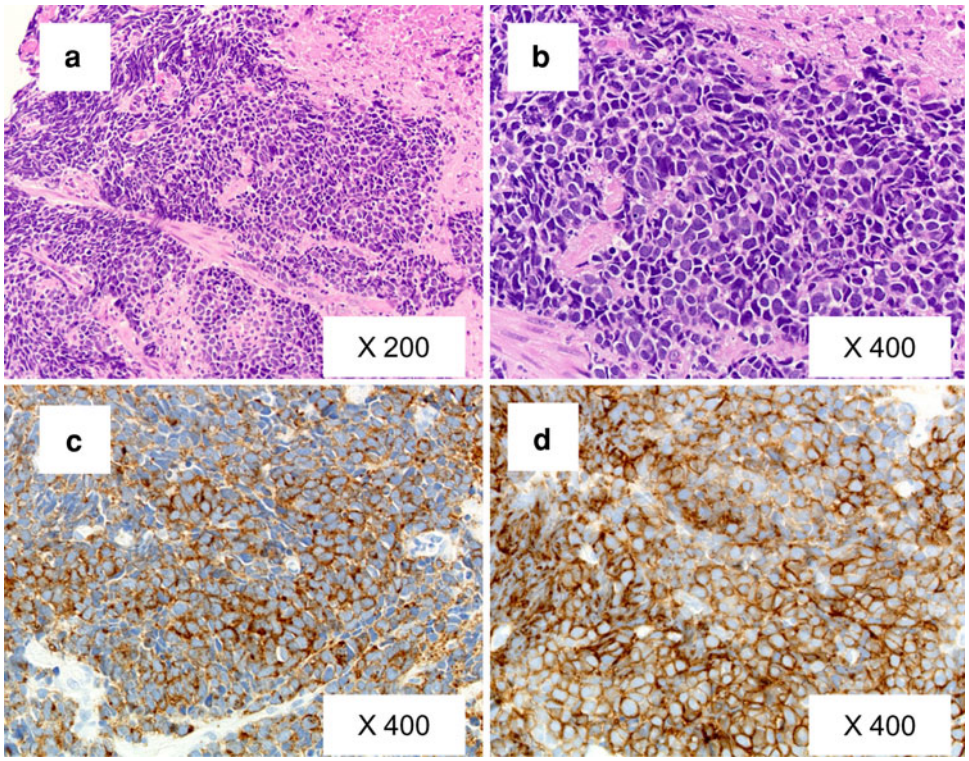

Fig. 2 Hematoxylin and eosin (H&E) staining showed focal proliferation of small round atypical cells with hyperchromatic nuclei (**a**, **b**). Immunostaining was positive for synaptophysin (**c**) and neural cell adhesion molecules (**d**)