Acta Med. Okayama, 2004
Vol. 58, No. 6, pp. 275-278

Acta Medica Okayama
http://www.lib.okayama-u.ac.jp/www/acta/

Case Report

A Case of Small Cell Gastric Carcinoma with an Adenocarcinoma Component Operated Curatively

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We present a case of a primary advanced gastric tumor that was composed of 2 different pathological components: small cell carcinoma and moderately-differentiated adenocarcinoma. The patient was still alive four years after the surgery was performed, without recurrence. A large part of the tumor consisted of a diffuse sheet of small cell carcinoma, which transitioned into another small portion consisting of moderately-differentiated tubular adenocarcinoma components. Therefore, this case raised the possibility that small cell gastric carcinoma may originate from totipotential stem cells of the stomach. Although small cell carcinoma progresses aggressively, and patients with it have an extremely poor prognosis, this patient recovered uneventfully after the surgical resection, and has remained in good health, without any recurrences.

Key words: gastric tumor, small cell carcinoma, adenocarcinoma

Small cell gastric carcinoma (SCGC), although rare, is one of the most aggressive cancers found, and patients with this diagnosis have an extremely poor prognosis. There are 2 types of SCGC, a pure-type and a composite-type admixing glandular and/or squamous differentiation [1]. We report the case of a 78-year-old man who suffered from composite-type SCGC, and who was curatively operated on.

Case report

A 78-year-old Japanese man was admitted to our hospital with hematemesis. The history was notable for epigastric discomfort for 2 weeks before admission. On physical examination, there was no swelling of the lymph nodes, and no abdominal tenderness or mass.

Laboratory data on admission were as follows: red blood cell count (RBC) $281 \times 10^4/\mu l$, hemoglobin (Hb) 9.0 g/dl, white blood cell count (WBC) $9100/\mu l$ with a normal differential, platelets 192,000/μl, total protein 5.0 g/dl, albumin 3.3 g/dl, LDH 198 IU/l, CEA 1.7 ng/ml.

Upper gastrointestinal endoscopy revealed a large ulcerated Borrman type III tumor on the anterior wall near the cardia of the stomach. Although there was no active bleeding upon examination, the source of bleeding was unclear. Biopsies of the tumor demonstrated moderately-differentiated tubular adenocarcinoma. An upper gastro-

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intestinal radiograph also revealed a large ulcerative tumor on the anterior wall, and segmental narrowing of the upper body of the stomach. Preoperative chest radiography and whole-body computerized tomography (CT) showed no metastatic lesions. Total gastrectomy with splenectomy and regional lymph node dissection was performed. The surgical findings were T2, N1, P0, H0, M0, Stage II, PM (−), DM (−), with a curability of A [2]. Surgical pathology revealed a 3.0 × 4.5 cm ulcerated Borrmann type III tumor on the anterior wall near the cardia. In addition, there was a IIc lesion on the lesser curvature next to the tumor (Figs. 1a, b). The 2 lesions were contiguous in cut surface sections. Therefore, we classified this case as a Borrmann type V (unclassified type) that measured 4.5 × 7.5 cm in postoperative diagnosis. Microscopically, the Borrmann type III tumor was composed of two components. The majority of the tumor consisted of a population of small cells that had hyperchromatic, dark round, and oval or spindle-shaped nuclei with scant cytoplasm (Fig. 2a). These small cells were homogeneous in size and shape, had proliferated diffusely, and were arranged in sheets with fine fibrous connective tissue. In addition, numerous abnormal mitotic figures were present. The other component of the tumor was composed of moderately-differentiated tubular adenocarcinoma, which was continuous with the IIc lesion. The IIc lesion was also composed of moderately-differentiated tubular adenocarcinoma (Fig. 2b). In the immunohistochemical studies conducted, the small cells were positive for neuron-specific enolase (NSE) and chromogranin A staining, whereas the adenocarcinoma cells were negative. Grimelius staining and Fontana-Masson staining were negative in both cell populations. Based on these histological and immunohistochemical features, we diagnosed this case as a SCGC with adenocarcinoma. Although chemotherapy was not performed, by request of the patient, he recovered uneventfully after surgery, and was in good health, without evidence of recurrence, 4 years after the surgery.

Discussion

SCGC is rare (0.1% of gastric carcinoma), and its prognosis is extremely poor because it tends to invade local structures and rapidly metastasize [3–5]. We here reported a case of SCGC with an adenocarcinoma component that was operated curatively.

In the lung, it has been reported that small cell carcinoma can be associated with adeno or squamous cell carcinoma; some of these tumors have exhibited multidirectional differentiation [6]. Matsusaka *et al.* first reported on the only 2 cases of SCGC in a review of about 2000 gastric carcinomas, one of which was a mixed tumor composed of small cell carcinoma, well-

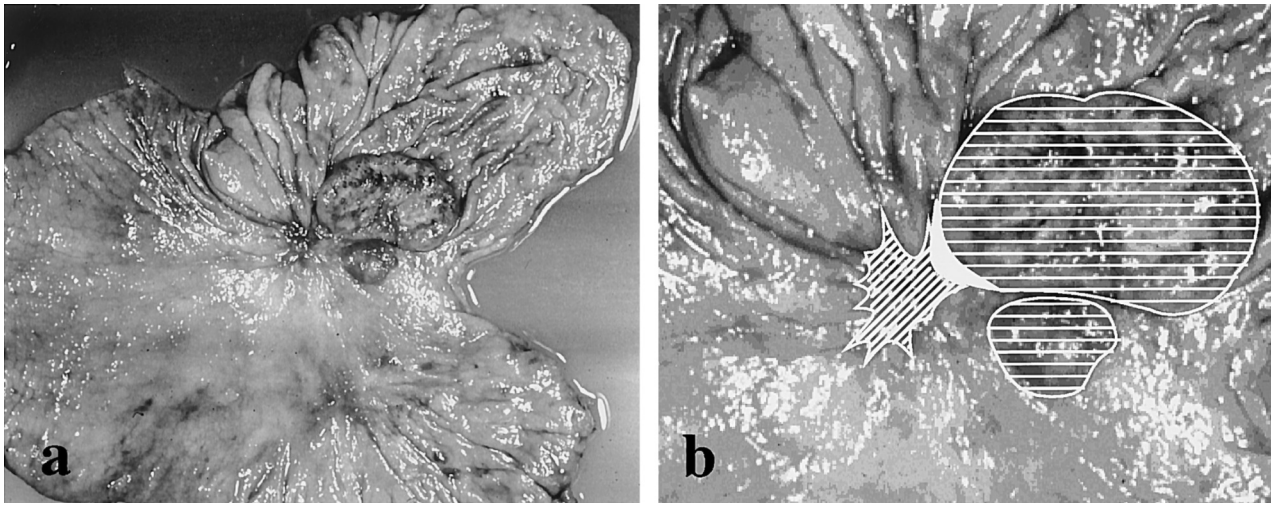

Fig. 1 Macroscopic findings. (a) A large Borrmann type III tumor in the anterior wall near the cardia, along the lessor curvature and IIc lesion next to the tumor. (b) Schema of the tumor. This tumor consisted of 2 components, small cell carcinoma ( ) and adenocarcinoma ( ). The 2 components were continuous in cut surface sections ( ).

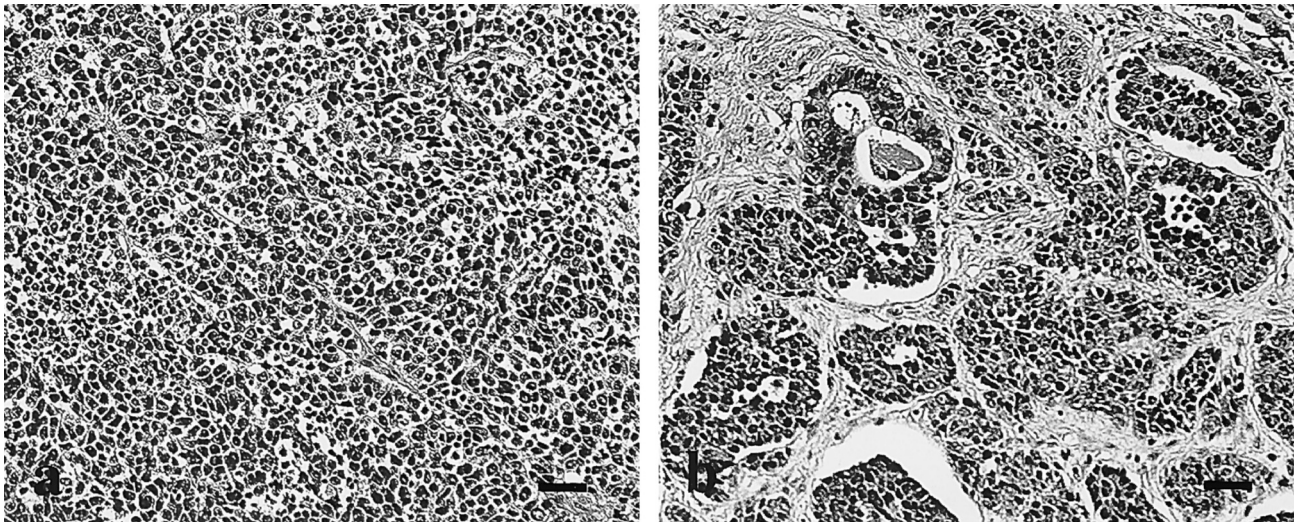

Fig. 2 Histological findings (HE staining). (a) The Borrmann type III tumor was composed primarily of small cell carcinoma (round or ovoid cells with hyperchromatic nuclei and scant cytoplasm). (b) The IIc lesion was composed of moderately-differentiated tubular adenocarcinoma. Bars indicate 50 μm.

differentiated adenocarcinoma, and mucous cell carcinoma [3]. Although small cell carcinoma is thought to originate from pre-existing neuroectodermal cells, pluripotent epithelial stem cells, or adenocarcinoma precursor cells, its origin is still unclear [7]. Some reports suggest that SCGC can be derived from the stem cells, since some cases of SCGC have been accompanied by adenocarcinoma components [1, 8, 9]. Experimental data has indicated that immature mucous cells (stem cells) of the stomach are capable of differentiating towards mature mucous, parietal, and chief as well as argyrophilic cells [10]. In addition, in genetic analysis of colorectal tumors, identical genetic alterations, such as a frequent loss of heterozygosity (LOH) for adenomatous polyposis coli (APC), deleted in colorectal carcinoma (DCC) or p53 genes, were found in both composite small cell carcinoma and the associated adenocarcinomas. Therefore, both tumors are considered to have the same cell origin [11]. Our case also supports the idea that neoplastic multidirectional differentiation of totipotential stem cells is possible in the stomach.

Since the behavior and growth characteristics of SCGC are similar to pulmonary small cell carcinoma, treatment with regimens specific for pulmonary small cell carcinoma may be the recommended choice for treatment of this tumor, instead of surgical resection [12, 13]. However, nearly 50% of the patients with SCGC underwent chemotherapy, and favorable clinical effects were not found. Furthermore, the non-small-cell components in the stomach are more resistant to chemotherapy that those same components in the lung [13]. Despite the fact that our patient requested not to receive chemotherapy, recurrence of the tumor has not been seen for the four years since surgery was performed. In light of our experience, earlier surgical resection is the most important and the followed adjunctive chemotherapy based on the regimen for pulmonary small cell carcinoma should be appropriate for the treatment of SCGC according to the conditions of the each cases.

It has also been reported that several endocrine cell tumors, including small cell carcinomas, were found to have originated from amine precursor uptake and decarboxylation (APUD) cells, and several transcriptional factors are important for the differentiation of APUD cells [14]. For SCGC, additional studies that include gene expressing profiling will be critical to revealing the cellular origin and pattern of differentiation of this type of tumor.

Acknowledgments. We would like to thank Dr. Don C. Rockey (of Duke University Medical Center, NC, USA) for his critical reading of this manuscript, and for his invaluable advice.

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