

Case Report

Signet-Ring Cell-Like Amphicrine Cell Carcinoma of the Stomach

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A poorly differentiated adenocarcinoma containing diverse components, tubular, signet-ring cell and neuroendocrine elements, in a 79-year-old man is described. Endoscopy examination revealed a Borrmann type IV tumor in the antrum. Histologically, scattered foci of tubular and signet-ring cells and a greater number of neuroendocrine elements were observed. The tumor cells were positive for chromogranin A, neuron specific enolase (NSE) and carcinoembryonic antigen (CEA). Furthermore, about one third of the tumor cells were demonstrated as amphicrine differentiation by double staining with chromogranin A and periodic acid-Schiff (PAS). Amphicrine cell carcinomas with exocrine and endocrine differentiation in the stomach is rare and poor prognosis.

The present case suggests that amphicrine cell carcinomas can occur in signet-ring cell morphogenesis, and that a multipotential stem cell is an origin of this unusual variant of neuroendocrine carcinoma.

Key Words: amphicrine cell carcinoma, stomach

Introduction

Poorly differentiated adenocarcinoma with neuroendocrine differentiation is an unusual phenomenon. In gastric tumors, it has been called various terms depending on predominant form and differentiation¹⁻⁴⁾, such as scirrhous argyrophil cell carcinoma and mixed glandular-endocrine cell carcinoma. Ratzenhofer and Leb⁵⁾ first suggested the term "amphicrine" to describe cells containing both neuroendocrine granules and mucin products in rabbit gastric mucosa. Amphicrine cell carcinomas are an unique variant of neuroendocrine carcinomas^{6,7)}. Divergent cell

differentiation coexpressed in the same cell has been neither well established nor fully accepted⁸⁾. It has been reported that gastric tumors with amphicrine differentiation are rare and commonly have a poor prognosis^{4,9)}.

We report a rare case of gastric amphicrine cell carcinoma associated with signet ring cell carcinoma, and discuss the cell origin of the amphicrine carcinoma.

Clinical Summary

A 79-year-old male visited a private hospital, complaining of nausea and vomiting. An upper gastrointestinal radiograph did not reveal a cause for his symptoms. Endoscopic examination revealed a Borrmann type IV tumor located in the antrum. A biopsy procedure disclosed signet-ring cell carcinoma. He was then referred to the First Department of Surgery, Nagasaki University Hospital. But, the operation could not be performed because his condition was unsatisfactory due to low blood pressure and pneumonia. His condition gradually deteriorated and he died 15 days later after admission.

Pathological Findings

An autopsy revealed 6.0 x 6.0 cm tumor with ulceration in the antrum of stomach. Metastases were detected in the perigastric and peripancreatic lymph nodes, measuring 1.5 x 1.0 cm in maximum size, and involved direct invasion into the duodenum and pancreas head.

Histologically, tumor invaded gastric wall and the serosal surface. The tumor showed a poorly differentiated adenocarcinoma with neuroendocrine differentiation, foci of signet-ring cells and a tubular appearance. Most of the tumor cells showed various sizes of cytoplasm with small droplets of mucin (Fig.1A). Nuclei were

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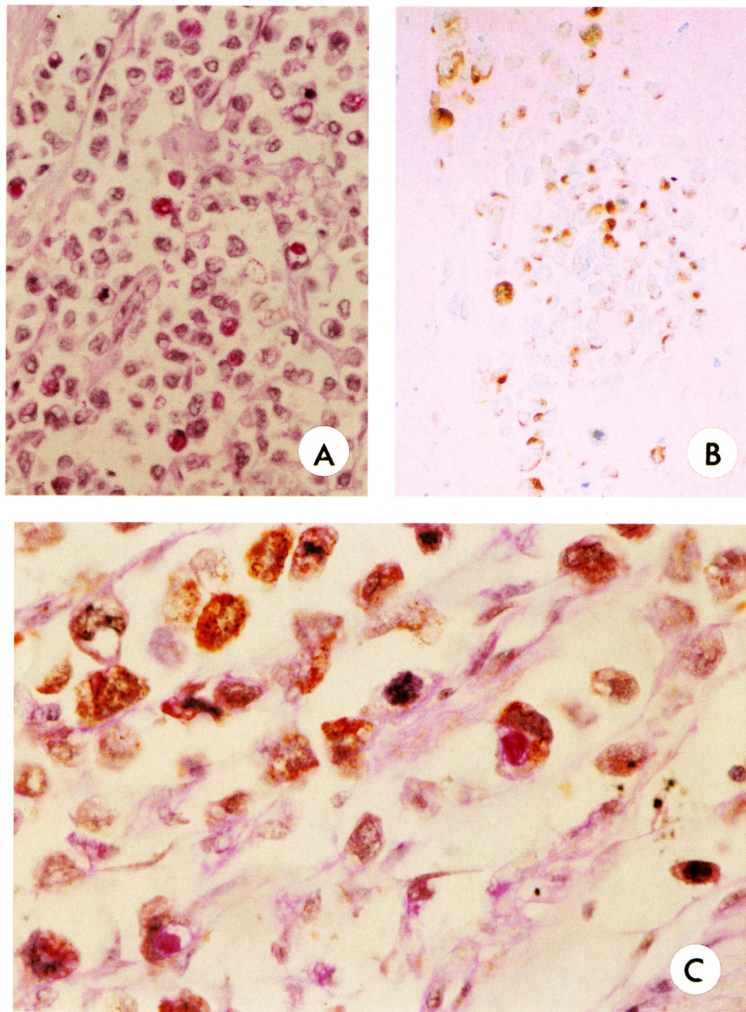


Fig. 1. (A) This tumor included diffuse signet-ring like cells with mucin in the cytoplasm (PAS). (B) Immunohistochemistry for chromogranin A was positive in carcinoma cells. (C) Simultaneous expression of neuroendocrine granules and mucin was observed in same cells by double staining of immunohistochemistry for chromogranin A and PAS staining.

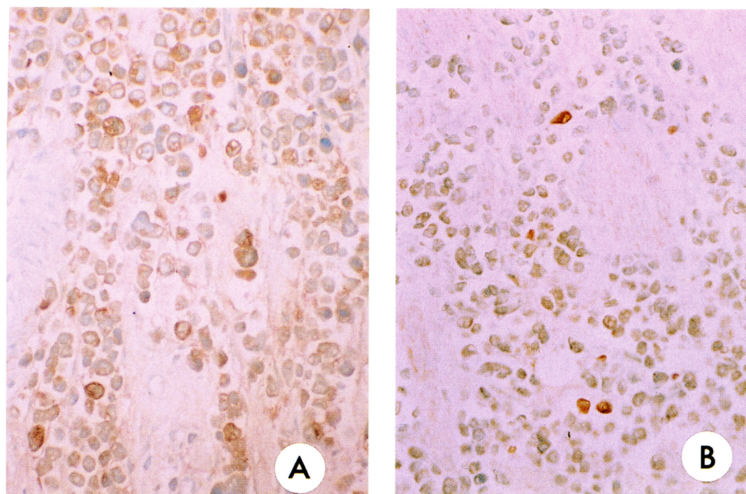


Fig. 2. (A) Immunohistochemistry for gastrin was positive in carcinoma cells. (B) CEA was positive in the scattered tumor cells.

hyperchromatic and showed mitotic figures in a high percentage. The endocrine origine was demonstrated by Grimelius (data not show) and immunohistochemistry for chromogranin A (Fig.1B). In addition, amphicrine differentiation in this case was clearly indicated by two sets of double staining of both Aluciane blue-chromogranin A (data not show) and PAS - chromogranin A (Fig.1C). Furthermore, a part of these cells were immunopositive for gastrin (Polyclonal, Dako, Carpinteria, USA)(Fig.2A), neuron specific enolase (Polyclonal, Dako) (data not show), and carcinoembryonic antigen (Polyclonal, Dako) (Fig.2B).

Discussion

The coexistence of endocrine and exocrine secretory products within single cells was first suggested by Feyrter⁸⁾ in his classic description of the "Diffuse endocrine epithelial system". Ratzenhofer and Leb⁵⁾ first suggested the term "amphicrine" to describe cells containing both neuroendocrine granules and mucin vacuoles in rabbit gastric mucosa. Chejfec *et al.*⁹⁾ offered evidence for neuroendocrine differentiation and mucin production within the same cells in two cases of well or moderately differentiated adenocarcinoma in the stomach. Yang and Rotterdam⁴⁾ described two cases a mixed glandular-endocrine cell carcinoma of the stomach and offered ultrastructural evidence for the coexistence of neuroendocrine granules and mucin droplets in the same cells.

The present case showed widespread, strongly-positive staining for chromogranin A and grimelius in the tumor cells. Furthermore, about 35 % of the tumor cells showed unequivocal evidence of neuroendocrine differentiation and mucin production within the same cell. In advanced cancer, the incidence of argyrophil cell differentiation is significantly higher in poorly differentiated types than in well differentiated types¹⁰⁾. Then, the association of

amphicrine cells with the poorly differentiated carcinoma might not be an unexpected event. As for prognosis, amphicrine carcinomas showed aggressive behaviour⁹⁾. Tahara *et al.*²⁾ reported ten cases of adenoendocrine cell carcinomas with a diffuse growth pattern and five patients died within the first year. Similarly, the present case advanced gastric cancer with diffuse regional lymph node metastases and resulted in a quick death.

This case suggests that amphicrine carcinoma originates from clonal cells which possess both character of exocrine and endocrine natures. Finally, the present case supports the idea that neuroendocrine carcinomas arise from immature multipotential stem cells in the endodermal origin^{10,11)}.

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