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Gastric carcinoma with shadow cell differentiation in metastatic lymph nodes☆,☆☆

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ABSTRACT

A case of gastric carcinoma showing shadow cell differentiation (SCD) in metastatic regional lymph nodes was presented. The tumor histologically revealed features of poorly differentiated adenocarcinoma with focal squamoid components. The metastatic lymph node lesion exhibited similar histological features and was partially intermingled with shadow cell nests (SCNs) that were reminiscent of those seen in cutaneous pilomatricoma (PMX). Immunohistochemically, tumor cells around SCNs exhibited nuclear accumulation of beta-catenin and similar staining patterns for apoptosis-related molecules as those observed in PMX. This is the first report of gastric carcinoma with SCD and re-confirmed the common characteristics of carcinoma with SCD, such as modes of cell death and nuclear accumulation of beta-catenin.

1. Introduction

Shadow cells are morphologically characterized, specialized keratinized cells differentiating toward the hair matrix [1]. A shadow cell nest (SCN) is a characteristic histological feature commonly found in cutaneous pilomatricoma (PMX), craniopharyngioma, and odontogenic cysts [2], while it is rarely observed in some gonadal teratomatous tumors [3,4]. Extracutaneous and non-teratomatous carcinomas with shadow cell differentiation (SCD) are extremely rare and have been reported to arise from the endometrium [5,6], ovary [7], colon [5,8], lung [9], gallbladder [10] and urinary bladder [11,12]. However, there have been no reports of gastric carcinoma (GC) exhibiting SCD, as far as we know. This paper presents the first case of GC exhibiting SCD found in lymph node metastatic foci. The histogenesis as well as molecular pathogenesis of SCD is also discussed.

2. Case report

2.1. Clinical course

A 57-year-old Japanese man noticed tarry stools and general fatigue. Two months later, he visited a clinic and was diagnosed with anemia (hemoglobin: 8.0 g/dL). A large, well-circumscribed ulcerated tumor was found at the posterior wall of the lower gastric body by endoscopic examination. A biopsy specimen exhibited a histopathological features of poorly differentiated adenocarcinoma. He underwent a subtotal gastrectomy, reconstruction via the Roux-Y method, and regional lymph node dissection. Six months later, multiple metastatic nodules were found in the right lobe of his liver, and he underwent a partial hepatectomy. During postoperative follow-up, other metastatic nodules appeared in the residual lobe of the liver and lungs. He wanted to undergo immunotherapy and was transferred to another hospital. Thereafter, his clinical course has remained unknown.

2.2. Pathological findings of the tumor

The primary lesion was a well-circumscribed ulcerated tumor that measured 9.5 × 8.5 cm and was located in the greater curvature to posterior wall of the gastric body (Fig. 1A). Histologically, the tumor was partially necrotic and was composed of atypical neoplastic cells that formed solid nests and partially exhibited trabecular or microglandular patterns. Papillary or tubular growth patterns were not observed. Altogether, these components suggested poorly differentiated adenocarcinoma (Fig. 1B). Squamoid nests were intermingled among the adenocarcinomatous components, and there were transitions between the two (Fig. 1C). Immunohistochemical examination, however, revealed only a small number of p63- and p40-positive cells in the squamoid nests, indicating that this tumor was not adenosquamous carcinoma. SCNs found in the metastatic regional lymph node lesions described below were not observed in the primary tumor, as far as we examined. The tumor exhibited relatively expansive growth and involved the entire gastric wall thickness, with partial exposure on the serosal surface. Lymphatic and venous invasion was prominent.

☆ The author declares that there is no conflict of interest in this study.
☆☆ This work was performed according to the ethical criteria required by the institutional review board of Suwa Red Cross Hospital.

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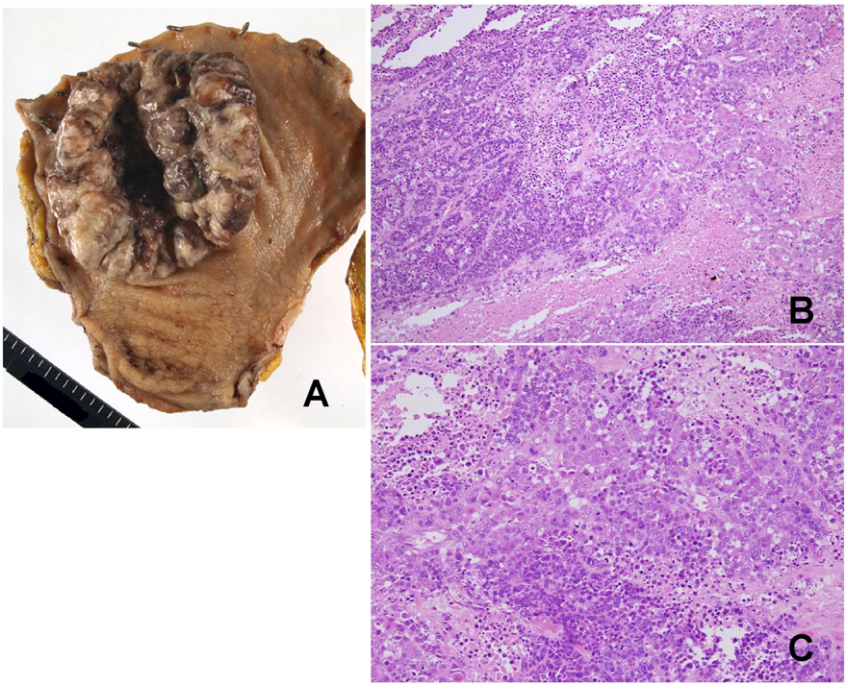

Fig. 1. (A) Gross appearance of gastric tumor. There is a huge, well-circumscribed tumor with central ulceration at the greater curvature to posterior wall of the gastric body. (B)(C) Histology of gastric tumor, showing features of poorly differentiated adenocarcinoma with a squamoid component (H.E. stain).

Metastases were found in 7 regional lymph nodes. Although the histological features were mostly similar to those of the primary tumor (Fig. 2A), p63- and p40-immunoreactive tumor cells in the squamous nests were more frequent than observed for the primary lesion (Fig. 2B and C). Squamous components, however, were less than 10% of the tumor, being not enough to suggest a diagnosis of adenosquamous carcinoma. Among the squamous areas were intermingled shadow cells, which formed nests or were scattered in isolation (Fig. 3). The shadow cells exhibited the same morphological features as those in cutaneous PMX; they had preserved cell shapes with eosinophilic cytoplasm and ghost-like nuclear contours. Some shadow cells had apoptotic nuclei (Fig. 3, inset). Transitions between SCNs and squamous components were often observed.

2.3. Immunohistochemical characterization of SCD

Formalin-fixed, paraffin-embedded tissue sections of stomach and lymph nodes containing carcinoma were stained for beta-catenin, single-stranded DNA (ssDNA), cleaved caspase-3, cleaved lamin A and caspase-14, as previously described [12,13], to characterize SCD including the modes of cell death. SCNs were not immunoreactive for any antigens examined. Nuclear accumulation of beta-catenin (beta-catenin(N)) was observed in areas of poorly differentiated adenocarcinoma in the primary lesion as well as metastatic sites (Fig. 4A), whereas membranous localization of beta-catenin (beta-catenin(M)) was noted in some of the squamous cells just adjacent to SCNs (Fig. 4A). Viable tumor cells around SCNs were negative for cleaved caspase-3 (Fig. 4B), while some of them

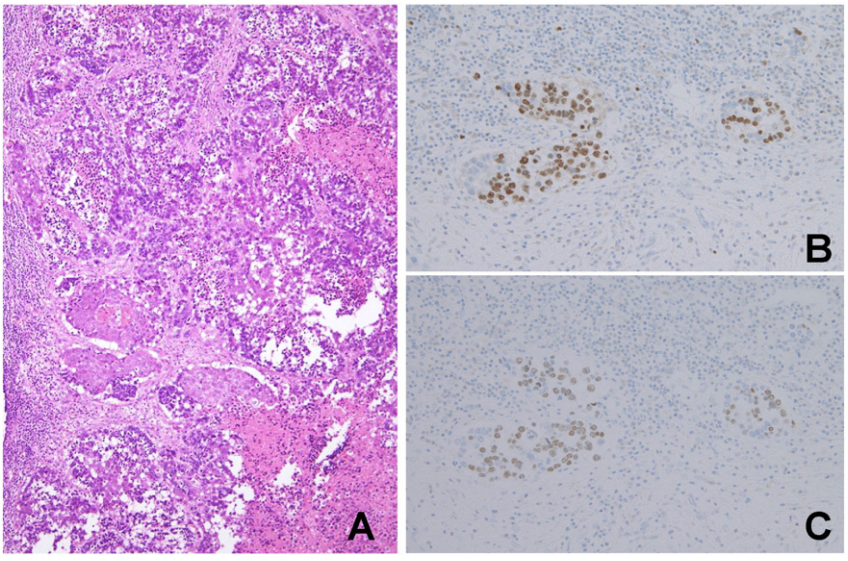

Fig. 2. Metastatic tumor in the regional lymph node. (A) Histological features similar to those in the primary tumor (H.E. stain). (B)(C) Tumor cells in the squamous foci are immunoreactive for p63 (B) and p40 (C).