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Papillary Adenocarcinoma of the Stomach with Psammoma Bodies: Report of Two Cases

Calcification of gastric carcinoma is unusual and most of the reported cases were of the mucinous type. This report describes two cases of papillo-tubular adenocarcinoma of the stomach with psammomatous calcification confined only to the papillary portion. Calcification was so heavy that specimen X-ray was able to clearly delineate its distribution. Microscopically, the calcification was confined to the papillary carcinoma area and was not found in the area of the tubular adenocarcinoma. Polymorphic calcific bodies were found in the supportive stroma of papillae and extrapapillary spaces as concentrically laminated psammoma bodies. They were also found in tumor cells as minute corpuscles. The mechanism of neoplastic mineralization in these cases seemed different from ontogenic calcification of mucinous gastric carcinoma and we postulated the mechanism of psammomatous calcification which is referred as intracellular calcification.

Key Words : *Stomach neoplasms; Adenocarcinoma, papillary; Calcinosis; Psammoma body*

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INTRODUCTION

Calcification of the neoplasm is not unusual, and occurs predominantly in the form of dystrophic calcification in areas of necrosis and hemorrhage, or in psammomatous deposits in certain tumors of the thyroid, thymus, ovary, breast, pancreas, meninges, and endometrium (1-4). This phenomenon has been reported with extreme rarity in gastrointestinal carcinomas such as duodenal carcinoid, gastric adenocarcinoma and colorectal adenocarcinoma (5-8). Review of calcifying gastric carcinomas revealed that most of them were of the mucinous variant and featured a dystrophic pattern of calcification in the mucinous substance (8-14). Although papillary carcinoma in the thyroid or ovary occasionally exhibits psammoma bodies, papillary carcinoma of the stomach is not well known to demonstrate such psammoma bodies. We herein describe two unusual cases of gastric adenocarcinoma with heavy psammomatous calcification confined in the area of papillary adenocarcinoma.

CASE REPORT

CASE 1

A 49-year-old man complained of postprandial epigastric discomfort which started two years prior to admission. On physical examination, there were no positive findings except for dull epigastric tenderness. Laboratory data were normal. Upper gastrointestinal radiologic study and gastroscopy confirmed a large ulcerofungating tumor mass in the pyloric antrum, and the endoscopic biopsy from the tumor showed adenocarcinoma. Physical findings and laboratory workups, including liver scintiscan showed no evidence of distant metastasis. A subtotal gastrectomy was performed.

The resected stomach contained a ulcerofungating tumor mass (Borrmann type 2), ovoid in shape and 6 × 4 cm sized, in the antrum along the lesser curvature. The tumor infiltrated deeply into the serosa and perigastric adipose tissue, and the resection margins were not involved. The cut surface of the tumor was grayish white, granular, and partly gritty. Mucinous area was not demonstrated. Specimen X-ray of the formalin-fixed tissue showed diffuse, dense opacity mainly in the anterior half of the tumor, and the specimen X-ray, using mammography film, disclosed conglomerated, sandy speckles (Fig. 1).

Microscopically, the tumor was composed of two histologic types; tubular and papillary adenocarcinomas. The former resided at the posterior wall, and was a moderately differentiated type. The latter was found in the anterior wall where the psammomatous calcification was confined. Histologic mapping (Fig. 2) revealed a distribution pattern of calcifica-

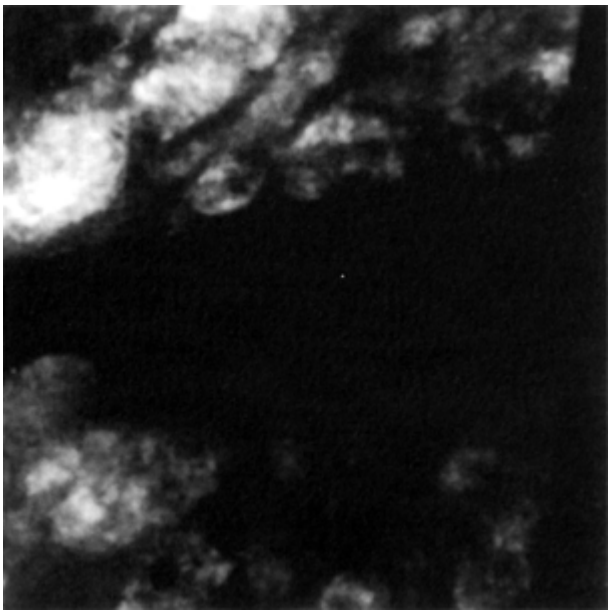

Fig. 1. Photomicrography of specimen X-ray using mammography (case 1). Multiple radio-opaque, conglomerated, punctate densities correspond well to the dark granular calcium deposits in the tumor nests.

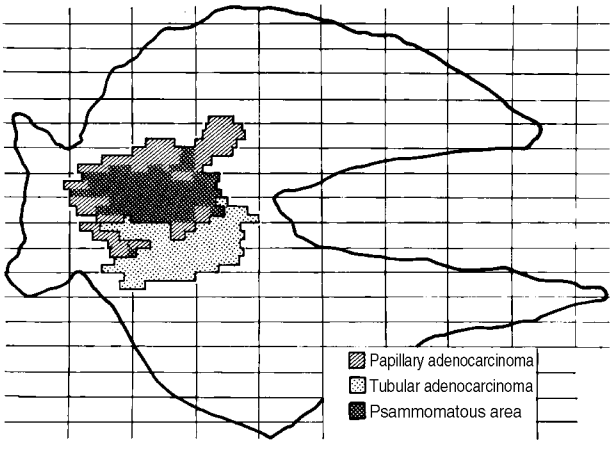

Fig. 2. Histotopographic map of the entire tumor tissue (case 1). Psammomatous calcification is totally confined within the papillary area.

tion and carcinoma by its histologic types. The psammoma bodies were deeply basophilic. They were concentrically laminated or mulberry shaped with dense central cores, measuring 4 to 44 μm (19.1 μm in average). They were found not only in the fibrovascular cores and extrapapillary spaces, but also within the tumor cells (Fig. 3). No metastatic lesion was found in 63 regional lymph nodes. The immediate postoperative course was uneventful. Five months after surgery, an epigastric mass was palpated and liver scintiscan revealed multiple space-occupying lesions. Ascites developed subsequently, but the follow-up was discontinued thereafter.

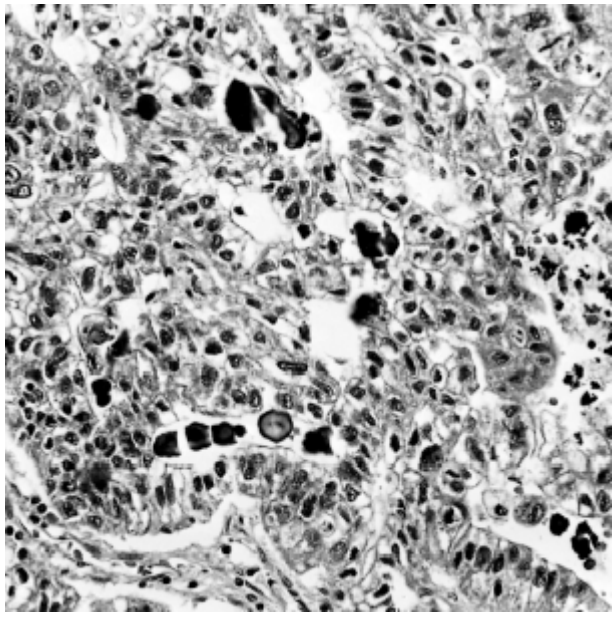

Fig. 3. A portion of papillary adenocarcinoma (case 1). Note numerous small amorphous or round calcospherule deposits in the tumor tissue. Psammoma bodies are located in the fibrous fronds and extrapapillary spaces (Hematoxylin-eosin, $\times$ 100).

CASE 2

A 62-year-old man had a 7-month history of dysphagia and weight loss (12 kg for 6 months). Physical examination revealed no positive findings. Laboratory data including serum calcium and phosphorus were normal. Radiologic study of the upper gastrointestinal tract and endoscopy showed a large ulcerofungating mass involving the cardia and distal part of the esophagus and an ulceration in the mid-esophagus. Biopsy was done in these lesions, and pathologic diagnosis was adenocarcinoma. Ultrasonography of abdomen and computed tomography of chest showed no evidence of metastasis except for a few enlarged lymph nodes in the left perigastric area. Total gastrectomy was performed.

The specimen was composed of a totally resected stomach. The stomach contained a 6 $\times$ 5 cm-sized ulcerofungating mass (Borrmann type 2) in the cardia and high body along the lesser curvature. The cut surface of the tumor was grayish white and granular and the tumor infiltrated deeply into the muscular layer and subserosa. Specimen X-ray using mammography film showed sandy speckles in some areas.

Microscopically, the tumor mass consisted of papillary adenocarcinoma admixed with a small portion of moderately differentiated tubular adenocarcinoma. Psammomatous

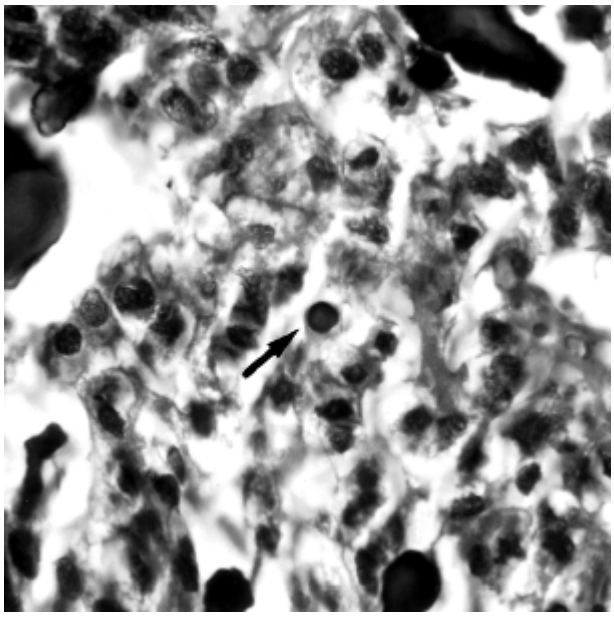

Fig. 4. A minute calcific body (arrow) is observed in the cytoplasm (case 2). (Hematoxylin-eosin, × 400).

calcification was confined to the papillary adenocarcinoma area and not seen in the area of the tubular adenocarcinoma. Calcific bodies were found in the extrapapillary space and fibrovascular core as concentrically laminated psammoma bodies which were seen singly or in clusters. Minute corpuscles were present in the cytoplasm of tumor cells and intracytoplasmic lumens (Fig. 4). The tumor cells infiltrated deeply into the subserosa and metastasis were found in 5 out of 20 perigastric lymph nodes. Metastatic lesions did not demonstrate psammoma body. The postoperative course was uneventful and adjuvant chemotherapy was performed.

DISCUSSION

The cases presented were of advanced gastric carcinomas with two distinct histologic types, of which the papillary carcinomatous component was only the seat of diffuse calcification. Spotty calcification in the gastric carcinoma is not a rare presentation and comprises 0.5% of surgically resected specimens and 4.4 to 10.2% in autopsy materials (9). However, heavy mineralization of gastric carcinomas, which can be visualized by a scout abdominal x-ray, is so rare that only approximately 72 cases of such calcifying carcinomas have been reported until now (8-18). Calcification usually occurs in diffuse or patchy distribution within the pools of mucinous adenocarcinoma, and psammomatous deposit in the carcinoma is extremely rare. There were seven case reports, most of them appeared in Japanese literature (15-18). To our knowledge, psammomatous gastric carcinoma outside Japan have not been documented.

The postulated mechanisms of calcification in gastric carcinomas are either metastatic calcification, dystrophic calcification or ontogenic calcification (8). Metastatic calcification is theoretically feasible in cases with persistent hypercalcemia with regard to functional parathyroid hormone (PTH) or PTH like substance-producing tumor. De Carvalho et al. (11) described two cases of calcified mucinous adenocarcinoma of the stomach, one of which showed hypercalcemia, but no further explanation was given in their case. Functional PTH-producing tumors often cause metastatic calcification in otherwise normal organs and rarely capsular calcification (19). However, we were not able to find any cases of calcifying gastric carcinoma producing functional ectopic PTH or associated with other PTH-producing tumor in the literature. Mirayama et al. (17) reported that a fairly high level of PTH-like substance was noted in the tissue extract of their gastric carcinoma with psammomatous calcification. But serum calcium level and PTH were normal and the mechanism of calcification was different from metastatic calcification.

Dystrophic calcification has been considered to be the major contributory mechanism in gastric carcinoma with multifocal tumor necrosis or hemorrhage. Previously, it has been suggested that there is a decrease in cellular metabolism, secondary to necrosis and ischemia resulting in relative alkalinity and subsequent calcification, since calcium salts, especially phosphates and carbonates, are soluble in acid solution but are much less soluble in alkaline solution (12). And denatured protein due to necrosis preferentially binds phosphate ions, which reacts with calcium ions to form calcium phosphate precipitate (14).

Because of a similarity of glycoprotein constituent in both mucinous adenocarcinoma and epiphyseal cartilage of the growing bone, which is believed to play an important role in calcification (10), ontogenic calcification has also been considered for calcified mucinous gastric carcinomas.

Histotopographic analysis of our two cases revealed that calcification occurred only in the papillary carcinomatous portion, and suggests that the mechanism for neoplastic mineralization in these cases are different from the one suggested in the mucinous variant of gastric adenocarcinomas. The mechanism of psammomatous calcification remains unclarified and seems pluralistic. The concepts previously reported can be categorized to extracellular calcification or intracellular calcification. It has been suggested that psammomatous calcification is a result of direct mineralization of round, whorled collagen bodies which have been suggested as the precursor lesion of psammoma bodies. This mechanism of calcification has been described in menigioma and desmoid tumor (20, 21). It has also been suggested that the initial foci of mineralization in psammoma bodies are extracellular matrix vesicles

derived from cellular degeneration with demonstrations of hydroxyapatite within matrix vesicles by ultrastructural study of psammoma bodies in meningocytic whorl (22). These two mineralization processes may belong to extracellular calcification category.

The mechanism of intracellular calcification has been demonstrated by ultrastructural studies. Mitochondria has been considered as then initial focus of intracytoplasmic calcification by releasing stored calcium and phosphorus (23). However, ultrastructural observation of needle-like crystalline deposits other than mitochondrial calcification was made by several investigators (4-6, 17). They were found especially in the tumor cells of papillary carcinoma of endometrium, duodenal carcinoid and non-mucinous carcinoma of stomach. Initial foci of calcification have been suggested to be cytoplasmic fibrils, osmiophilic intracytoplasmic deposits or lysozyme. Recently, it has been reported that the expression of osteopontin mRNA increases in macrophages within the necrotic area of breast cancer and osteopontin protein appears to play an important role in the development of calcifying foci (24).

We were able to find intracytoplasmic small calcific bodies and exfoliation of tumor cells in the extrapapillary spaces. Conglomerated calcific bodies and degenerated tumor cells were observed in the extrapapillary spaces. Although we did not examine this possibility by ultrastructural studies, the sequence of calcification in our cases may reflect intracytoplasmic calcification and subsequent active secretion of calcific bodies into extracellular spaces or shedding of tumor cells by degeneration.

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