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## 症 例

### Calcification in Carcinoma of the Stomach: Report of a Case

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#### Abstract

By upper gastrointestinal series, a 57 years-old woman was pointed out to have scattered calcifications along the greater curvature of the stomach. On computerized tomography, the calcifications distributed in the irregularly thickened gastric wall. With a diagnosis of calcified mucinous adenocarcinoma showing Borrmann type III, total gastrectomy with splenectomy was carried out. The characteristics of this lesion were briefly presented with a review of the literature.

#### Introduction

Malignant neoplasms involving the thyroid, kidneys, lungs, ovaries and other organs are occasionally associated with calcium deposits, which are easily demonstrated by plain roentgenogram and other imaging techniques<sup>1,2</sup>). However, a gastric carcinoma seldom develops calcifications extensive enough to be clearly visible by imaging techniques. The scattered calcium deposits found in cancer of the stomach show a spotty, sand-grain, stippled, fine granular or dotted appearance along the gastric contour by scout film of the abdomen and/or upper gastrointestinal series<sup>3-5</sup>). On computerized tomography (CT) of the abdomen, miliary and punctate calcifications diffusely distributed in the irregularly thickened gastric wall are pathognomonic signs for this condition<sup>6,7</sup>). Here, we report the case of a patient who underwent gastrectomy with a review of the literature.

#### Case

A 57 year-old housewife with a 5 year history of intermittent nausea and dull epigastralgia was admitted on May 26, 1990. The upper gastrointestinal series taken at another clinic showed circular rigidity and stricture of the stomach from the body to the antrum with scattered calcium deposits along the greater curvature (Fig. 1). Her personal history and family history were unremarkable.

Key words: Calcified gastric wall, Calcified gastric cancer, Advanced gastric cancer, Mucin-producing cancer, Imaging modalities

索引用語: 胃壁石灰化, 石灰化胃癌, 進行胃癌, 粘液産生癌, 画像診断手技

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Physical examination showed a well-nourished woman of 158 cm in height, weighing 63 kg, with a blood pressure of 120/80 mmHg, a regular heart rate of 84/min and regular respiration. She had no jaundice, the conjunctivae were slightly anemic, no abnormal breath sounds or heart murmurs were audible and no lymph node enlargement was detected over the entire body surface. On abdominal palpation, no abnormality was found. The liver, kidneys and spleen were not palpable.



Fig. 1 Calcifications adjacent to the greater curvature of stomach on the film of upper gastrointestinal series (arrows)

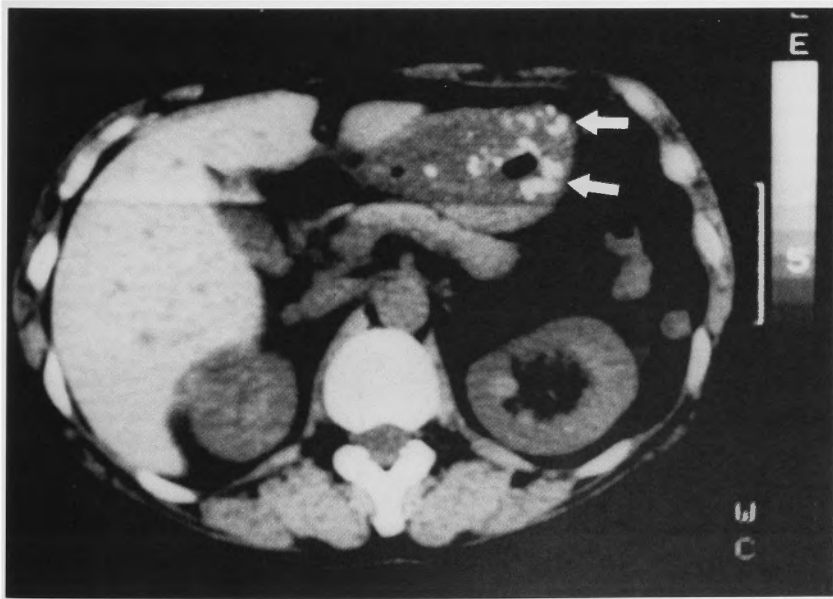


Fig. 2 Calcifications in the thickened gastric wall visualized by CT (arrows)

Hematology data revealed moderate anemia with a hemoglobin concentration of 7.8 g/dl. The presence of an adenocarcinoma showing Borrmann type III was confirmed by gastrofiberscopic examination. CT of the abdomen revealed marked thickening of the gastric wall containing scattered calcifications (Fig. 2). On ultrasonography of the abdomen, the wall thickening was observed, but the calcifications were unclear.

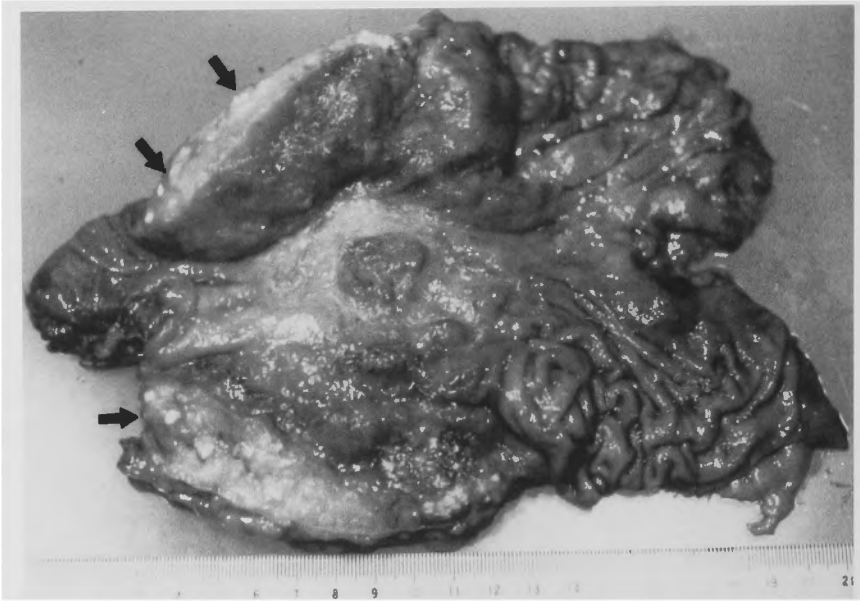


Fig. 3 Calcifications in the section of resected carcinoma of the stomach (arrows)

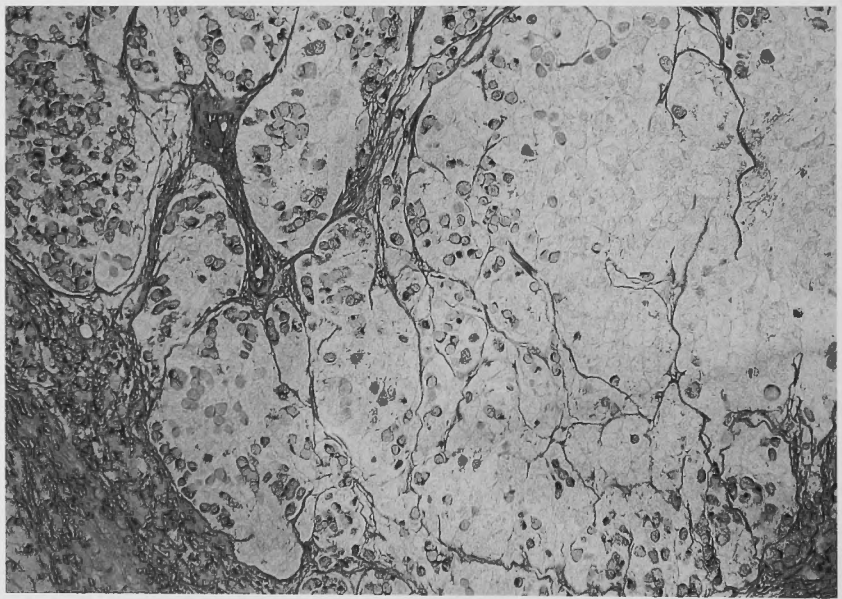
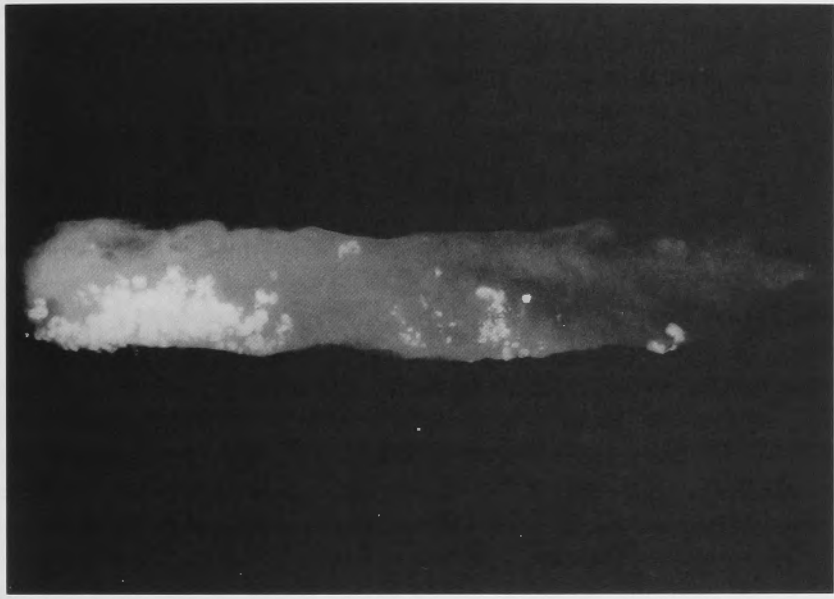
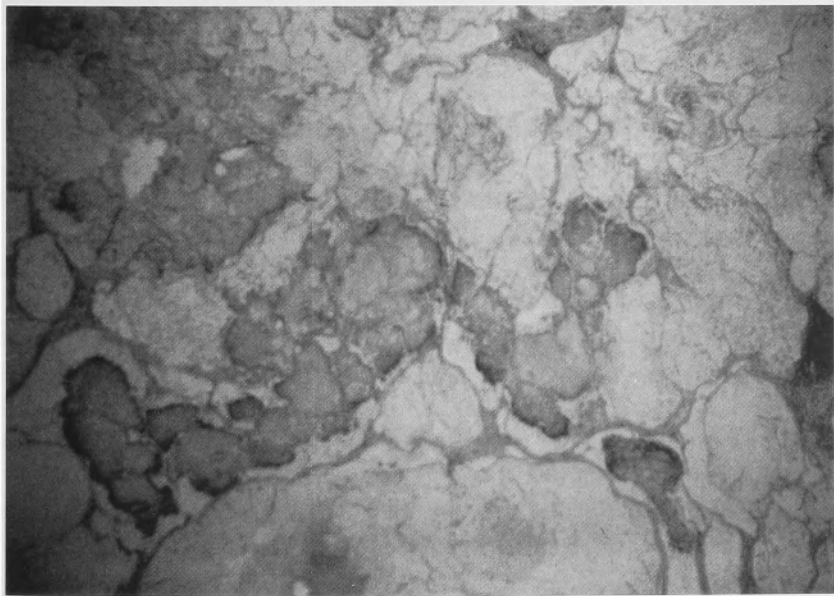


Fig. 4 The portion of mucinous adenocarcinoma of the stomach (H & E, original magnification  $\times 100$ )

On June 25, 1990, total gastrectomy with splenectomy was carried out. The resected stomach was involved by a Borrmann type III carcinoma and multiple calcium deposits of less than 3 mm were found in the thickened wall (Fig. 3). Microscopic sections revealed poorly differentiated adenocarcinoma which had invaded mainly the mucosal portion and a mucinous adenocarcinoma adjacent



**Fig. 5** Calcifications in the portion of gastric carcinoma opacified by a low voltage radiograph



**Fig. 6** Dark areas showing calcifications among the so-called mucous lakes in the photomicroscopic section (Kossa stain, original magnification  $\times 100$ )

to the calcium deposits in the deep layers (Fig. 4). Metastases had developed in several lymph nodes, however, no calcification was associated with them. According to the diagnostic criteria<sup>8)</sup>, the carcinoma was classified as MA, S<sub>2</sub>, N<sub>2</sub>, P<sub>0</sub>, H<sub>0</sub>, Borr. III, OW (-), AW (-), Stage III, R<sub>2</sub>, relative curative resection, n<sub>(2)</sub>, INF $\gamma$ , se ly<sub>3</sub>, v<sub>1</sub>, ow (-), and aw (-). A low-voltage radiograph of the resected specimen also clearly showed the calcium deposits (Fig. 5). The deposits (Fig. 6) were composed of 68% calcium phosphate and 32% calcium carbonate according to infrared spectrophotometry data.

Postoperatively, the patient developed left pleural effusion, which was drained through a catheter and rapidly subsided. Although the patient was discharged on July 7, 1990, she had died of the cancer recurrence two years and four months after the discharge. Autopsy was not allowed.

In Japan, since the first report of KITAGAWA and KIMATA<sup>2)</sup> in 1963, calcifications have been demonstrated by scout film of the abdomen, upper gastrointestinal series, and/or abdominal CT in the neoplasm in more than 80 patients who had gastric carcinoma, including our own. Their ages ranged from 27 years<sup>9)</sup> to 80 years<sup>10)</sup>, and predominated in female patients approximately 1.6 times more frequent than in male patients.

Signs and symptoms were recorded in 64 patients. The main symptoms found were as follows: the abdominal mass was palpable in 25 cases (39.1%), abdominal pain was present in 23 cases (35.9%), abdominal distention in 16 (25.0%), 15 patients (23.4%) had lost weight, 12 (18.8%) had lost their appetite and 10 (15.6%) complained of dysphagia. Calcium deposits in the tumor were revealed by scout film of the abdomen in 56 patients (78.9%) and by upper gastrointestinal series in 38 (53.5%). In 39 patients the calcifications were also detected in the thickened gastric wall by abdominal CT.

Laboratory data of 37 patients showed serum calcium and phosphate values within the normal range, except for two cases of moderately elevated phosphate. There was one case of slightly elevated levels of serum parathormone<sup>11)</sup> and in another case the urine level of this hormone was slightly high<sup>2)</sup>.

Twenty-nine patients underwent total gastrectomy, five underwent partial resection and the procedures of gastrectomy were unrecorded in 8 cases. Eight patients underwent palliative procedures or exploratory laparotomy alone. The remaining 21 patients (29.6%) were judged inoperable. Of 58 macroscopic records, 23 of Borrmann type III and 35 of Borrmann type IV present and the wall containing calcium deposits was markedly thickened. Histopathologically, all patients but one case of moderately differentiated tubular adenocarcinoma<sup>10)</sup> showed signet-ring cells or mucinous adenocarcinoma. Among 47 patients whose metastases were recorded, eight patients (17.0%) also had calcium deposits in the lymph nodes.

Generally, the calcium deposits were composed of scattered numerous white irregular granules varying from several millimeters to less than one millimeter in diameter. Among the 15 patients in whom the concrements were analyzed by infrared spectrophotometry, concrements that consisted mainly of calcium phosphate, calcium carbonate, calcium oxalate and/or magnesium ammonium phosphate were found.

The postoperative follow-up was recorded in 12 of the 42 patients who had undergone some resections. Only four cases, a 28 year-old man<sup>12)</sup>, a 31 year-old woman<sup>13)</sup>, a 44 year-old woman<sup>14)</sup> and our own case have survived for two years or more.

### Discussion

Although the incidence has gradually declined in Japan, cancer of the stomach is still the most common cause of death due to malignancy and predominates in men, it is approximately 1.7 times more frequent in men than in women<sup>15)</sup>. According to YAMAGIWA<sup>16)</sup>, some calcium deposits in the neoplasm were histopathologically demonstrated in 0.5 percent of the resected specimens and in 4.4 percent of the autopsied specimens. On the other hand, MORIWAKI *et al*<sup>1)</sup> reported an incidence of 10.2% in 157 autopsied cases, and MATSUKI *et al*<sup>8)</sup> found calcifications in 8.4% in 107 gastrectomized cases of the carcinoma. From these data, the calcifications do not seem to be rare histopathological findings.

IMAI *et al*<sup>18)</sup> classified calcifications into three types; 1. psammomatous calcification containing clearly stratified calcium bodies, 2. mucin pool calcification showing fine granular calcium deposits in the mucous lake or necrotic tissues, and 3. unclassifiable type. In clinical practice, however, cases showing extensive and massive calcium deposits in the neoplasm by imaging techniques prior to laparotomy or autopsy have been quite rare and usually associated with mucin-producing carcinoma<sup>1,2,11,13,19)</sup>. In addition, TAKASAKI *et al*<sup>8)</sup> pointed out that these visible calcium deposits in cancer of the stomach histopathologically developed mucin pool calcification.

For the calcification in gastric carcinoma, one hypothesis based on the ontogenic calcification<sup>20)</sup> usually seen in the epiphyseal cartilage of growing bone which is mediated by a glycoprotein seems most plausible. The glycoprotein in mucin produced by cancer cells may participate in the reaction between the calcium ion and the phosphate ion, and the microsomes which are also present in mucin may supply the calcium. In some cases, so-called dystrophic calcification may develop, that is, tissue degeneration and necrosis due to rapid expansion of massive mucin-producing carcinoma inhibit tissue respiration and the resultant decrease of CO<sub>2</sub> makes the tissue alkaline and calcium salts may easily deposit<sup>2,21)</sup>.

In the present survey, levels of serum calcium and phosphate were not abnormally high in the majority of patients. Although there is one report in the English literature<sup>22)</sup> of a case presenting hypercalcemia, in general, the theory of metastatic calcification<sup>23)</sup> due to hyperparathyroidism, hypercalcemia or vitamin D intoxication for producing calcium deposits in cancer of the stomach is not valid.

In the present survey, the prevalence of relatively young patients may depend on the development of mucin-producing adenocarcinoma of undifferentiated type. Female patients predominated in contrast with the usual trend of cancer of the stomach. Signs and symptoms of patients were not different from usual advanced carcinoma. Diagnosis of gastric carcinoma was established by upper gastrointestinal series, fiberoptic gastroscopy and/or endoscopic biopsy, and calcium deposits in the neoplasm were easily demonstrated by scout film of the abdomen and/or upper gastrointestinal series. Irregular and patchy calcium deposits in the upper abdomen due to chronic pancreatitis, pheochromocytoma, tuberculosis of the adrenals or leiomyoma (sarcoma) of the stomach, etc. may be occasionally seen, but the scattered calcification in the cancer of stomach is characteristic except for rare cases of calcified mucin-producing carcinoma in the left-side colon<sup>24,25)</sup>.

In addition, since the first report of HASUO *et al*<sup>26)</sup> in 1979, the calcium deposits in the thickened gastric wall have been clearly visualized by CT. Cases in which the deposits were depicted by ultrasonography of the abdomen were few. Scattered fine granules in the irregularly thickened wall may be not strongly echogenic. Recently, one case in which the deposits were detected by en-

doscopy was reported<sup>13</sup>), however, the procedure is limited because of the hardened gastric wall in advanced carcinoma. In cases of calcified gastric carcinoma, it was often observed that the cancer extended into the submucosa and there was scirrhous infiltration in the muscle layer. Calcium deposits have been demonstrated in a superficially biopsied specimen by endoscopy in only one case<sup>27</sup>).

It is still unknown why the calcium deposits develop in only a very small number of patients affected by mucin-producing adenocarcinoma and why some metastatic lesions have similar calcifications. Although the beginning of calcification during cancer growth was obscure, radiographically non-visible calcium deposits in a gastric mucinous adenocarcinoma in the early stages were histopathologically demonstrated<sup>28</sup>. On the other hand, all gastric carcinomas in which calcification were demonstrated by imaging techniques were advanced.

All patients except those who had cancer of the residual stomach were affected by massive neoplasms of Borrmann type III or IV, of approximately 10 cm more and metastatic lesions were found in approximately two-thirds of the cases. Therefore, a radical gastrectomy including sufficient removal of the regional lymph nodes and/or adjacent viscera was possible for only a small number of patients. Although some form of resectional surgery was performed in approximately 60% of the reported Japanese cases, the outcome was poor in the majority of patients. However, the prognosis of patients with calcified gastric carcinoma did not differ from that of the patients with the usual carcinoma of a similar advanced stage<sup>12</sup>).

Occasionally, extension of calcium deposits during cancer growth was observed<sup>29,30</sup>. To detect calcium deposits in cancer of the stomach prior to their visualization on scout film of the abdomen and/or upper gastrointestinal series, high resolution CT may be useful<sup>26</sup>. Fine calcifications early visualized by such imaging techniques should not be overlooked to improve the surgical outcome.

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## 和文抄録

## 石灰化胃癌の1例

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57歳女性の上部消化管透視において、胃の大弯側に散在性の小斑点状の石灰化が指摘された。この石灰化は、腹部コンピューター断層撮影では不規則に肥厚した胃壁内に存在した。ポールマンⅢ型の石灰化胃粘液腺癌の診断で胃全摘・脾摘を行った。画像診断と肉眼標本によって石灰化を証明できた胃癌はまれであり、

本邦報告例では女性に多く、すべて進行癌であった。腫瘍の粘液産生がこの石灰化に関与すると考えられている。また、切除率や生存率がかなり低い疾患でもあり、自験例も術後2年半で癌再発により死亡した。文献的考察を加えて報告した。