Gastrointest Radiol 3, 391–395 (1978)

Gastrointestinal Radiology

Heterotopic Submucosal Gastric Cysts:

Report of Two Cases, One in Association with Carcinoma

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Abstract. Two cases of heterotopic submucosal gastric cysts, one with a coexisting superficial spreading carcinoma, are described. This is an uncommon entity with which radiologists should be familiar. An association between such cysts and carcinoma has been predicated previously. The induction of submucosal gastric cysts in monkeys fed polychlorinated biphenyls is cited, and the potential significance of this observation with regard to such lesions in humans is discussed.

Key words: Gastric cysts – Gastric carcinoma – Polychlorinated biphenyls – Polybrominated biphenyls – Gastric malformation.

Diffuse involvement of the gastric submucosa by cystic glands, first described by Harris in 1869 [1], is an unusual condition of uncertain etiology. Although there have been only rare isolated reports of such lesions from this country [2], Iwanaga et al. [3] recently described 12 cases from Japan in which this was associated with gastric carcinoma. The frequency of gastric lesions, particularly carcinoma, among the Japanese might suggest that the concurrence of these lesions could be due to chance. However, we noted coexistence of the two lesions in one of the two cases described below, and a similar concurrence was presented in another recent report [4]. These observations suggest that these lesions may be associated.

Case Reports

Case 1. J.W., a 56-year-old white woman, was admitted on 12/16/75 for evaluation of a urinary tract infection. She had had a previous diagnosis of medullary sponge kidney. During the evaluation, she was found to be anemic with a hematocrit of 25, and her stools were persistently positive by guaiac test.

Radiologic examination of her upper gastrointestinal tract showed a broad-based, multinodular polypoid lesion arising from the greater curvature of the gastric antrum (Fig. 1). A discrete ulcer was not visualized. Gastroscopy showed an infiltrating lesion involving the greater curvature of the distal antrum and a polyp of the second part of the duodenum. The latter measured less than 1 cm in diameter. Biopsies of the two areas were interpreted as gastric adenocarcinoma and adenomatous hyperplasia of the duodenum. The patient subsequently was treated by subtotal gastrectomy. She was alive without evidence of recurrent neoplasm 6 months after operation.

The gastrectomy specimen consisted of the distal 15 cm of stomach with attached omentum. At the distal portion of the stomach was a mucosal defect 3 cm in diameter. The base of this lesion was covered by light tan tissue, and the edges were heaped up. The entire gastric mucosa had a somewhat cobblestone appearance, merging proximally with a more normal-appearing mucosal pattern of large rugal folds.

Microscopically, the area of gastric involvement consisted of mucosa diffusely replaced by adenocarcinoma with several layers of neoplastic cells lining the gastric glands (Fig. 2A). The neoplasm was largely noninvasive; however, in some areas neoplastic glands invaded lamina propria as well as superficial submucosa. Numerous large cysts were evident in the submucosa beneath the adenocarcinoma. These varied in size and shape, and many contained watery material. The cysts were lined by columnar epithelium with basally oriented nuclei and abundant, partly vacuolated cytoplasm. This epithelium lacked nuclear atypism or abnormal mitoses. All of these cysts were submucosal in location, and none were demonstrated to communicate with mucosa. Invasive neoplasm was focally evident adjacent to the cysts (Fig. 2B). Gastric mucosa manifested extensive and diffuse chronic inflammation with lymphocytes and focal intestinalization.

On 7/5 77 a specimen of subcutaneous fat (approximately 10 g) was removed from the patient's anterior abdominal wall and analyzed for content of polychlorinated and polybrominated biphenyls. These were found to be 0.164 and 0.086 ppm, respectively.

Case 2. C.S., a 67-year-old white man, was admitted on 1/17/55 because of weakness, fainting spells, and black stools. He gave a history of "ulcers" for 30 years and had been hospitalized on two occasions during the preceding year because of anemia and melena. X-ray examinations on those occasions were "negative," but endoscopy had revealed two superficial prepyloric ulcers.

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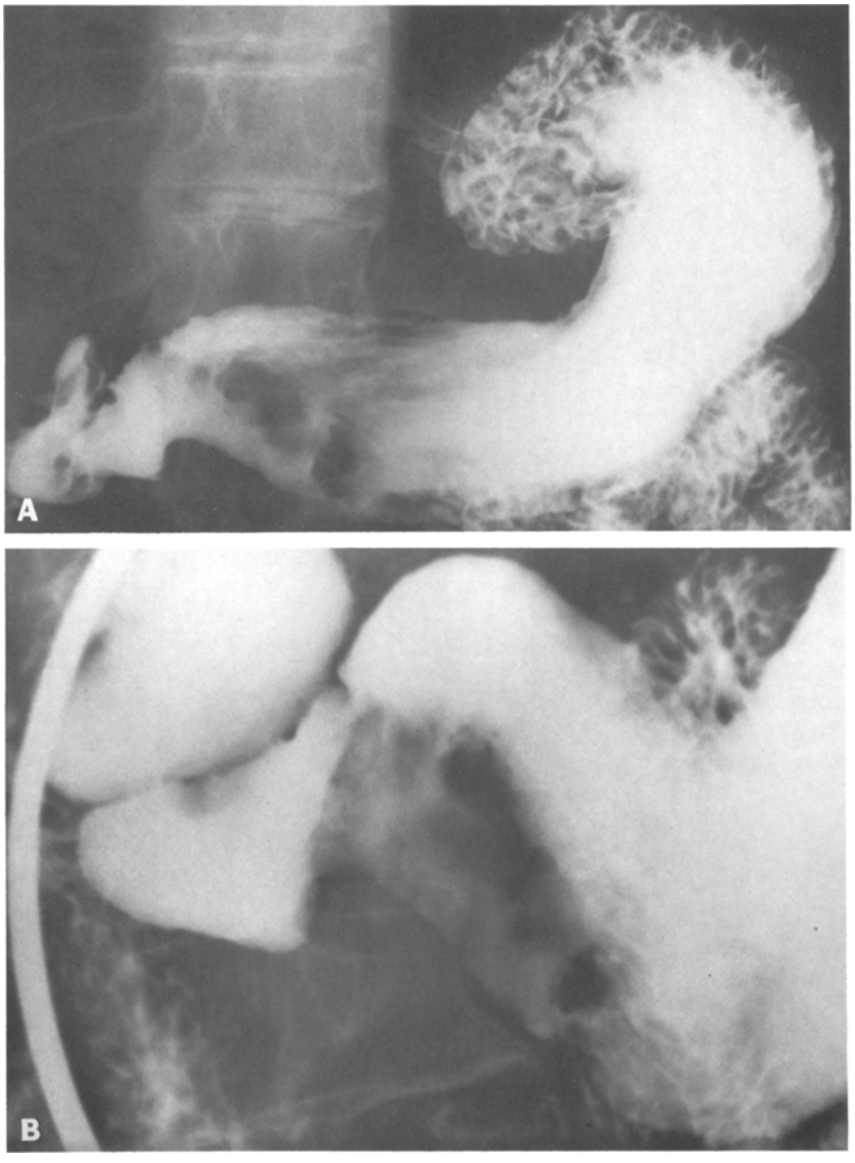


Fig. 1. *Case 1.* **A** There is a multinodular, polypoid filling defect in the antrum. The rugal folds are thickened in the areas adjacent to the proximal and distal margins of the lesion.
B Posteroanterior view, antrum, with compression. The lesion is circumscribed with relatively sharp margins and arises largely from the greater curvature. It appears to consist in part of thickened rugal folds, suggesting a large submucosal component. A discrete ulcer is not evident

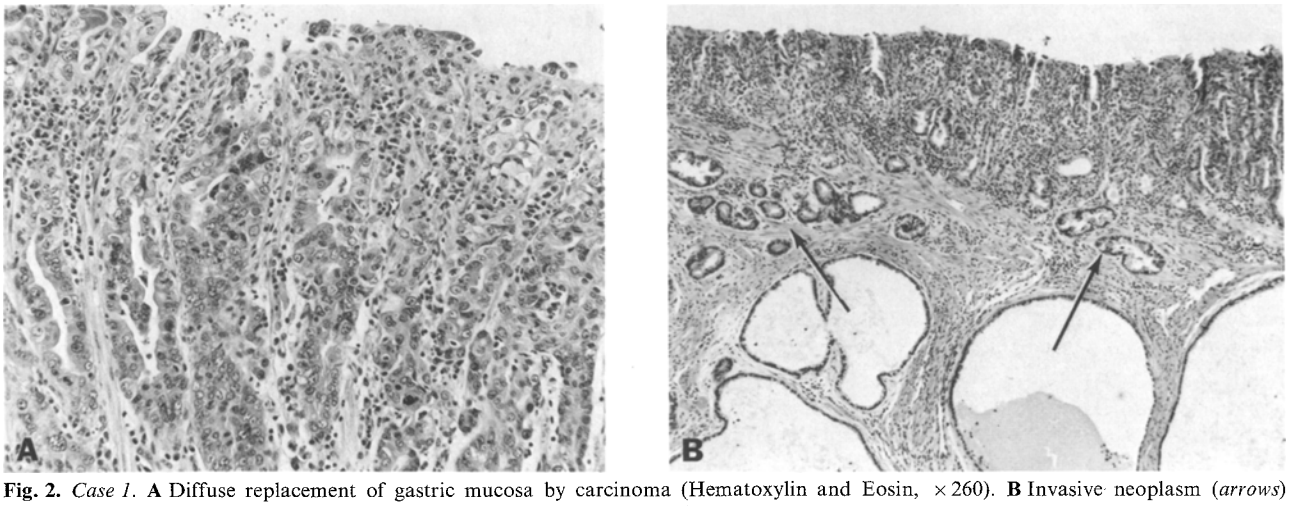
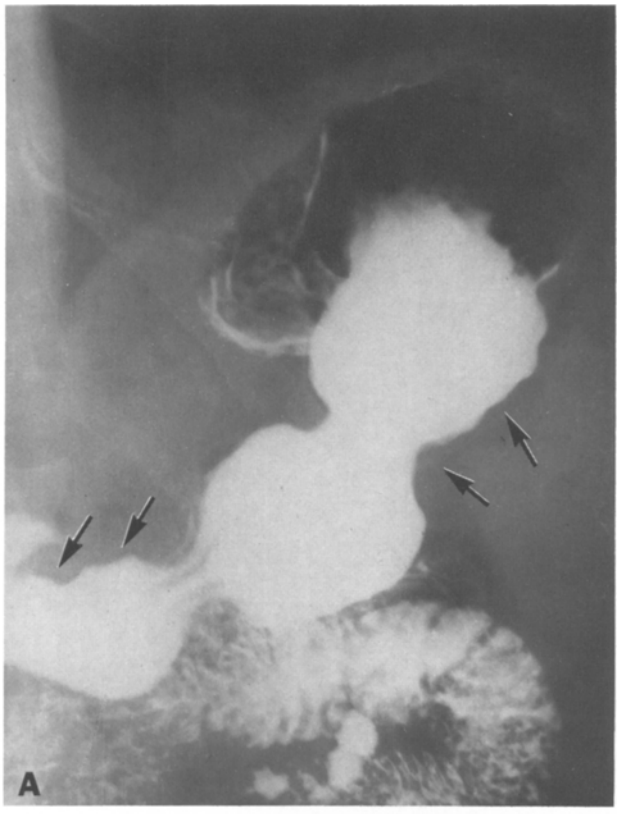


Fig. 2. *Case 1.* **A** Diffuse replacement of gastric mucosa by carcinoma (Hematoxylin and Eosin, ×260). **B** Invasive neoplasm (*arrows*) in lamina propria adjacent to benign cysts (Hematoxylin and Eosin, ×64)



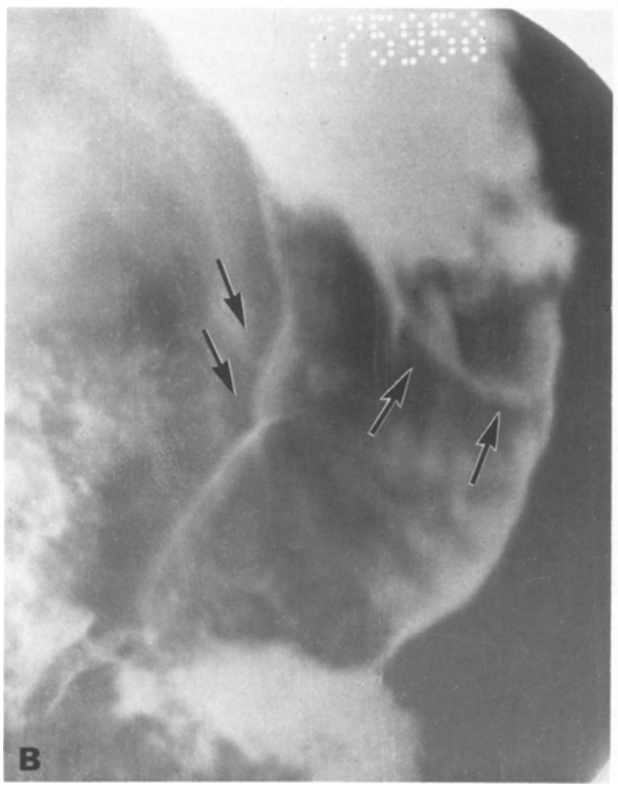
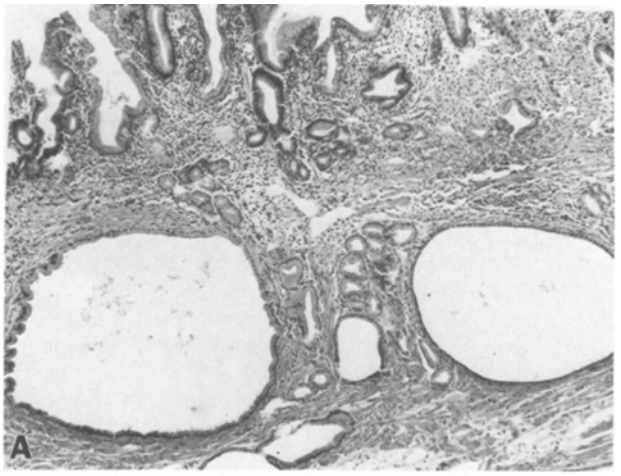


Fig. 3. *Case 2.* **A** Posteroanterior view of the stomach. Nodular distorted rugal folds with prominent ridges are evident in the cardia and fundus. There is a suggestion of nodularity of the wall in the body (*arrows*) and lesser curvature of the antrum (*arrows*). **B** Spot film, left posterior oblique, body of stomach, showing the inferior edge of one of the intramural masses on the greater curvature (*large arrows*). There is an additional shallow lesion on the adjacent lesser curvature (*small arrows*). These lesions were not appreciated at the time of the examination. (Reproduced from microfilm)



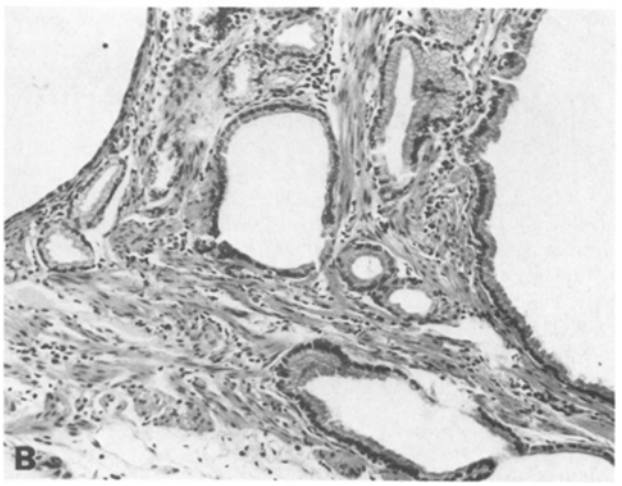


Fig. 4. *Case 2.* **A** Cysts in lamina propria surrounded by hyperplastic muscularis mucosae. Chronic inflammation is evident in mucosa (Hematoxylin and Eosin, ×64). **B** higher magnification indicating columnar epithelium lining cysts (Hematoxylin and Eosin, ×162)

On this admission his hemoglobin was 3.2 g% and gastric analysis after histamine stimulation showed no free acid.

Radiologic examination of the stomach again was interpreted as "negative, but in retrospect there was a smoothly marginated submucosal filling defect in the body of the stomach associated with thickening and irregularity of the rugal folds which extended from the body of the stomach to the fundus (Fig. 3). At subsequent operation a deformity of the first part of the duodenum was felt to represent scarring due to previous ulceration. There were inflammatory adhesions between the posterior wall of the stomach and pancreas. A subtotal gastrectomy and gastrojejunostomy were performed as treatment for "peptic ulcer disease." The nature of the gastric lesion was not appreciated at the time of the resection.

The specimen consisted of the distal 17 cm of stomach and included the pylorus. No definite ulcer was identified although the gastric wall appeared thick. Section through the gastric wall revealed a spongy texture.

Microscopically, the gastric mucosa was diffusely edematous, and was the seat of a variably intense infiltrate of lymphocytes and plasma cells. In some areas the lymphocytes formed nodules with reaction centers in the lamina propria. Cystic dilatation of gastric glands was evident throughout, not only in the lamina propria, but also in the submucosa, although the submucosal component was not evident in sections taken from the proximal margin of resection. The dilated glands of the submucosa were associated with small aggregates of nondilated glands. Cystic dilatation of glands was more remarkable in submucosa than in the basal portion of lamina propria, and muscularis mucosa surrounded the superficially located cysts (Fig. 4A). The cells lining the dilated submucosal gastric glands contained basally oriented nuclei and pink cystoplasm which was frequently vacuolated (Fig. 4B). Occasional cystic glands contained aggregates of polymorphonuclear leukocytes. Neoplasm was not evident. Sections through the pylorus revealed focal chronic inflammation but no ulcer. The cystic glands noted in the antrum were not present in the pyloric area.

Discussion

It has been suggested previously that such heterotopic gastric cysts represent a developmental glandular malformation or myoepithelial hamartoma [5]. Although it is difficult to deny the occurrence of such congenital lesions, it is also possible that a histologically similar lesion may be acquired, possibly secondary to chronic gastritis. The fact that these lesions appear to be associated with symptoms of gastritis and peptic ulcer disease and are generally found in older individuals tends to support this view.

A patient previously described by one of the authors and considered at the time to have had a congenital malformation [6] was quite similar to our Case 2. Both had diffuse involvement of the stomach by cysts in the submucosa and lamina propria, surrounded by chronic inflammatory cells, primarily plasma cells and lymphocytes. In view of our present observations and those of others, it is concluded that the previously reported case may well have been on an acquired basis.

Similar lesions have been described in the esophagus and colon [7, 8]. It has been postulated that obstructing secretions in association with chronic inflammation accumulate in mucosal glands and result in the formation of single or multiple cysts in these areas [3]. Diffuse intramural esophageal pseudodiverticulosis also may be a related condition, although its pathogenesis is controversial; presumably, in this condition the cells of the esophageal mucus glands, in response to chronic irritation, undergo squamous metaplasia which leads to blockage of the ducts and intramural glandular distention [9].

It is possible that there is a significant association between such gastric cysts and carcinoma. However, there is no evidence that the cysts are precancerous. In our case the cysts were subjacent to the neoplasm, but in the case described by Pillay and Petrelli [4] the neoplasm and cystic areas were intimately related. It has been suggested that repeated gastric ulceration and mucosal regeneration in association with chronic inflammation may give rise to submucosal cysts or carcinoma [3].

An intriguing aspect of this lesion is its possible association with high tissue levels of polychlorinated biphenyls (PCB) or polybrominated biphenyls (PBB). Allen and Norback [10, 11] recently produced such lesions, associated with overlying gastric mucosal hyperplasia, in rhesus monkeys that ingested PCB for 3 months. A similar experience has been reported by Rosenquist and Silverman [12]. It must be noted that the concentration of the biphenyls in the monkey experimental diet (300 ppm) was about 10 times the levels that have occurred in samples of milk (28 ppm) and fish (35 ppm) reported by the U.S. Food and Drug Administration [11]. Nevertheless, this concentration is much less than the levels that have occurred in food products due to industrial accidents (2,000 to 3,000 ppm), such as the "Yusho" incident in Japan [13]. Such studies in animals assume greater significance in view of the recent contamination of livestock in Michigan with PBB and the possibility that the biologic effects of the latter could be similar to those of PCB. Relatively low concentrations of both of these compounds were found in a biopsy of body fat from Case 1. The regression of PBB in body fat in humans has been given as 30% to 60% per year [14]. This would indicate that the tissue level of PBB in this patient at the time of gastric surgery in 1975 was well below that recently found to be within the usual range for Michigan residents.

[The range of concentrations of PBB in body fat at autopsy in 18 randomly selected Michigan residents was 0.12 to 0.73 ppm, and the average concentration was 0.31 ppm (T.H. Corbett and J.L. Simmons, *personal communication*).]

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Received: January 24, 1978; accepted: March 8, 1978