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CASE REPORT

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Simultaneous appearance of an adenomyoma and pancreatic heterotopia of the stomach

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Abstract Adenomyomas of the stomach are rare tumours characterised by duct/gland-like structures embedded within a smooth muscle stroma. Although the histogenesis of adenomyomas remains unclear, the histological appearance has justified the assumption that these are abortive forms of pancreatic heterotopia. We report an unusual case with simultaneous and independent appearance of both adenomyoma and pancreatic heterotopia of the stomach including immunohistochemical characterisation, supporting the concept of a common histiogenetic origin of both lesions.

Key words Adenomyoma · Pancreatic heterotopia · Stomach

Introduction

Adenomyomas (AM) of the stomach are rare, benign tumours, characteristically composed of ductular structures, lined by tall, monomorph epithelia and a prominent smooth muscle stroma [12]. Since the epithelial component resembles those of pancreatic ducts, several authors suggested that AMs are best considered as an abortive variant of pancreatic heterotopia (PH) with a missing exocrine or endocrine component [7, 18, 26]. Generally, pancreatic heterotopia is a unifocal lesion, but very few reports about multifocal occurrences exist [10, 20]. According to the concept that AM represents a special, incomplete variant of PH, one may expect to find some case with multifocal lesions, showing both variants. To the best of our knowledge, we present the first case of simultaneous appearance of AM and PH, including an immunohistochemical characterisation, supporting a common histogenesis of both lesions.

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Clinical history

A 48-year-old man presented with a history of epigastric pain and vomiting. Upper gastrointestinal X-ray examination revealed a fixed contrast filling defect of the lesser curvature of the antral region, and gastroendoscopy demonstrated two independent, up to 2-cm large, submucosal tumours located at the transition from corpus to antrum ventriculi (Fig. 1). Biopsies from both lesions only showed antral mucosa fragments without tumour-representative tissue. Local excision of both lesions was performed 1998, and frozen sections revealed the diagnosis of an AM and PH. The postoperative course and the follow-up 1.5 years after the surgical procedure were uneventful.

Material and methods

Specimens were fixed in 4% buffered formalin, embedded in paraffin and stained with hematoxylin and eosin. Immunohistochemical stainings were made by an indirect immunoperoxidase technique according to a standard protocol with antibodies against cytokeratin 7, 8, 18, 19 (Sigma, Deisenhofen, Germany), carcinoembryonic antigen (CEA), chromogranin A, α_1-antitrypsin, antichymotrypsin (Dako, Hamburg, Germany) and CA 19-9 (Cisbio, Dreieich, Germany).

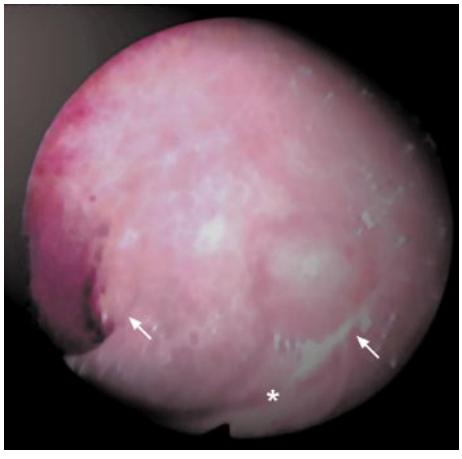

Fig. 1 Gastroendoscopic appearance of the antrum ventriculi. Two independent submucosal tumors, bulging the mucosa, are labelled with *arrows* (angulus ventriculi mucosa fold is labelled with an *asterisk*)

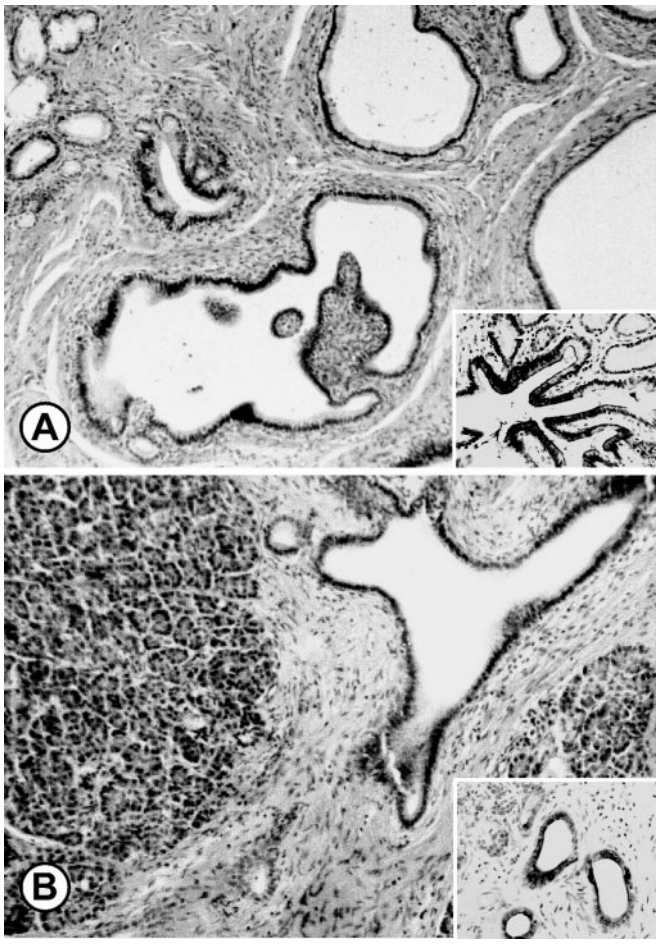

Fig. 2 Histological appearance of the adenomyoma (**A** proximal tumour) and pancreatic heterotopia (**B** distal tumour). The adenomyoma is characterised by branching, ductular structures embedded in smooth muscle bundles (Hematoxylin and eosin), whereas both ductular and typical exocrine glands are visible within the proximal tumour (Hematoxylin and eosin, original magnification ×100). A focal, membranous reactivity of the ductular epithelium against CA19-9 is demonstrated in both insets (×200)

Pathological findings

The specimen from the proximal tumour showed a 1.5-cm large, submucosal nodule with sharp margins and a greyish-white cut surface. Histological findings were glandular, in part branching, ductal structures, lined by a monomorph columnar epithelium, surrounded by bundles of smooth muscle tissue (Fig. 2A). Complete sectioning of this nodule failed to demonstrate exocrine or endocrine pancreatic structures. The distal tumour measured 1.1 cm and displayed a greyish-yellow cut surface, located in the submucosa, extending into the muscularis propria. Histology showed well-organised, pancreatic glands including typical ductular structures (Fig. 2B) and a few endocrine islets, reactive for chromogranin A. Ductal epithelia in both lesions displayed a typical pancreatic-duct like immunophenotype, characterised by a specific reactivity for cytokeratin 7, 8, 18, 19 and CA19-9, whereas no reactivity against CEA, α_1-antitrypsin and chymotrypsin were detectable. Glands with typical exocrine differentiation were focal positive for α_1-antitrypsin and chymotrypsin.

Discussion

AMs of the stomach are rare benign tumours composed of pancreatic-duct-like epithelial structures surrounded by a prominent smooth muscle component. The entity was first described by Cohen and Magnus-Alsleben in 1899 and 1903 [9, 19], respectively, and, as early as 1903, Thorel noted the morphological similarity of AMs and PHs [26]. According to Vandelli's review, 38 cases were recorded until 1993 [27]. Whereas AMs of the stomach are very rare, PH occurs with an incidence of 0.55–15.7%, most often in antral, pyloric, duodenal or jejunal location, as assessed by autopsy studies [3, 13]. Surgical studies found PH in approximately 0.2% of all laparotomies, usually as an incidental finding [4, 24]. Multifocal PH has been described, but appears to be rare [10, 20].

Based on the similarities of the epithelial component of AMs to pancreatic ducts, several authors suggested that these are closely related to PH [7, 18, 26]. In line with this concept, Derbyshire classified PHs into those with typical exocrine and endocrine glands, those with an incomplete exocrine component and those without exocrine differentiation, the latter representing AMs [12]. Pearson and Delhougne described an additional subtype composed of duct-like structures and endocrine islets [11, 23].

However, the use of different terms for adenomyomatous lesions of the stomach is not as unequivocal as proposed by Derbyshire. Some authors use the term AM also for epithelial lesions with prominent smooth muscle component and exocrine pancreatic glands. Various terms, such as myoepithelial hamartoma, myoglandular hamartoma, adenomyomatous hamartoma and adenomyosis have been used, reflecting different opinions about the histogenesis of these lesions [4, 8, 17, 25, 27].

However, several lines of evidence suggest a common histogenesis of AM and PH. First, the ductal epithelia of both lesions are morphologically indistinguishable. Second, the immunophenotype of the epithelial component in regard to the expression of pancreatic duct typical proteins (particularly cytokeratin 7, 8, 18, 19 and CA19-9) is identical, as reported in this study. Additionally, an identical reactivity of both lesions against anti-cytokeratin AE1/AE3 and *T. mobilensis* has been described by Babál et al. [2]. Further, taken the low incidence of AMs and PHs into account, it is unlikely that the described synchronous appearance of both lesions happened only by chance. We believe that the observed synchronism is best explained by the hypothesis of a multifocal PH with different morphological manifestations; however, a coincidental synchronicity cannot be excluded. According to these circumstances, the term "hamartoma", which designates an excessive focal overgrowth of mature normal cells and tissues in an organ or tissue of identical (i.e. orthotopic) cellular elements appears to be a misnomer.

With regard to the pathogenesis, a phyllogenetic and ontogenetic explanation for PH have been discussed. Comparative anatomy reveals different types of organisation of pancreatic cells in vertebrates: pancreas compactum (type homo-sapiens), pancreas diffusum (type rat), pancreas disseminatum (type cyprinids) and pancreas intrahepaticum (type carp) [5]. In terms of phylogenesis, PH in humans may be understood as an atavism, reminiscent of a pancreas disseminatum or intrahepaticum, the latter particularly in cases with extensive PH in the liver [5, 28]. Ontogenetically, the pancreas develops from a larger dorsal and a smaller ventral anlage, which are fused in the sixth week of gestation. PHs of the stomach and duodenum are thought to be derived from the dorsal anlage, whereas the ventral anlage appears to be the source of aberrant pancreatic tissue of the jejunum and ileum [4, 5].

Clinically, patients with AM and PH have, if at all, non-specific symptoms, including intermittent epigastric pain, nausea and vomiting. PH appears to be more frequently associated with ulcers, gastrointestinal bleeding and obstruction. Particularly intramucosal lesions larger than 1.5 cm are thought to cause clinically relevant symptoms [1]. Rarely, AM and PH may undergo malignant transformation [6, 16] or cystic dystrophy [14, 21].

Detection of the tumour is usually obtained by upper gastrointestinal barium X-ray, by gastroendoscopy or as incidental finding during laparotomy or autopsy. Radiographically, PH and AM are characterised by a small, sharply defined polypoid mass, often with a central umbilication and sometimes ducts, seen en profile, entering the central depression [7]. As observed in the presented case, PH and AM appear endoscopically as round or oval, sharply defined, submucosal masses, in part with central umbilication. However, central umbilication is neither a constant nor a specific feature of PH/AM [22] and, usually, endoscopic biopsies fail to obtain representative tumour tissue [15]. Careful interpretation is needed in cases with mucus retention in PH (“cystic dystrophy”), since this rare complication may be confused histologically with a high-grade mucinous carcinoma. A significant mucus-associated inflammation and fibrosis as well as missing epithelial atypias are helpful features to differentiate this complication of PH from its malignant counterpart [21].

Since radiographic imaging and endoscopic biopsies are usually not sufficient to differentiate the lesion from other submucosal tumours (e.g. gastrointestinal stroma tumour, carcinoid, lymphoma), endoscopic or surgical resection is required to reliably diagnose an otherwise undefined gastric lesion [4, 15, 27].

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