Papillary mucinous adenoma arising in adenomyomatous hyperplasia of the gall bladder

G Y Lauwers, S J Wahl, G V Scott, S J DeRoux

Abstract
A case of papillary mucinous adenoma arising in adenomyomatous hyperplasia (AMH) of the gall bladder is reported. The lesion was unsuspected and discovered by routine palpation of the gall bladder during laparotomy. The adenoma developed within fundal AMH and showed cytological atypia. This case illustrates that neoplastic proliferation is indeed possible in AMH and challenges the classical opinion that AMH is devoid of neoplastic potential.

Results
On gross examination, the fundus of the acalculous gall bladder showed a dome shaped, cystic lesion measuring 2 x 1.3 x 1 cm. Microscopically, the gall bladder mucosa showed normal luminal folds lined by a single layer of columnar epithelium. The stroma was slightly fibrotic and contained lymphocytes in small clusters. AMH was identified within the wall of the fundus as the typical multiple anastomosing, epithelium lined extrusions extending between bundles of hyperplastic smooth muscle. Foveolar type mucinous metaplasia of the hyperplastic epithelium was also present. A large cyst measuring 11 x 5 mm was observed in continuity with AMH. Its lining was composed of tall mucinous cells with focal formation of papillae (figs 1 and 2). A large villous polyoid lesion formed of anastomosing fronds protruded into the cystic space. The fibrovascular stroma of the papillae was infiltrated by lymphocytes and plasma cells. Most of the fronds were lined by a single layer of benign mucus cells, although focal cellular tufting and nuclear atypia were present.

Keywords: Gall bladder, cancer, adenomyomatous hyperplasia, adenomyomatosis, mucinous adenoma.
HISTOCHEMICAL AND IMMUNOHISTOCHEMICAL FEATURES

The surface epithelium of the gall bladder was positive on staining with alcian blue and negative with PAS and mucicarmine. In contrast, the metaplastic foveolar epithelium of the AMH and the papillary adenoma was positive on staining with PAS, both before and after pre-treatment with diastase, highlighting neutral mucus cells. Occasional cells were positive on staining with alcian blue and mucicarmine. Immunohistochemical staining with chromogranin antibodies did not reveal endocrine cells in the metaplastic foveolar epithelium or the adenoma.

Discussion

A case of low grade papillary mucinous adenoma arising in AMH, showing foveolar type mucinous metaplasia, is reported. In contrast to the surface epithelium of the gall bladder, the foveolar type metaplastic epithelium of the AMH and the adenoma lacked acid mucins but were positive for neutral mucin. The histological and histochemical similarity support the conclusion that the papillary mucinous adenoma arose from the AMH. To the best of our knowledge, the present case is the first detailed description of such neoplastic change arising within AMH. In 1982, Von Matting et al. described a so-called “benign papillary cystadenoma of the gall bladder fundus”, suggesting a similar lesion, but their report did not contain a precise microscopic description. AMH, regarded as a hyperplastic lesion, combines excessive surface epithelial proliferation with exuatinon of the mucosa through a thickened muscular wall. This acquired process can be diffuse, segmental, or localised with a propensity for the fundus. Its frequency has been reported to vary between 2 and 25% in both surgical and radiological retrospective studies. More commonly recognised in women, its incidence increases with age. Although most lesions are asymptomatic, non-specific cholecystitis-like symptoms have been reported. Cyst formation secondary to inflammation, fibrosis, and inspissated bile has also been described. Abscess formation has been the most frequently reported complication.

The association between AMH and gall bladder cancer is unclear. Although regarded classically as a benign process, recent publications have challenged this opinion. Ootani et al. redefined the association between AMH and gall bladder cancer. In their series 11.4% of gall bladder cancers developed in the fundal compartment, distal to the stricture induced by AMH. They suggested that segmental AMH was a causative factor in gall bladder cancer, but indicated that this relation was not true for diffuse or fundal AMH. Of more interest in the light of the present report are the eight cases of gall bladder cancer which developed directly in AMH. The following are of particular relevance: four of the eight gall bladder cancers developed in localised AMH of the fundus; mucinous metaplasia was present in two of these four cases; and in one case the carcinoma arose from a papillary adenoma similar to the case presented in this report.

The case presented here, supported by the recent reports of gall bladder cancer arising in AMH, suggests that AMH may have neoplastic potential. In some cases at least an adenoma could be one of the intermediate steps in the carcinogenic sequence. The possibility that mucinous metaplasia in AMH is indicative of a predisposition to neoplasia requires investigation. That the histological features of our case are reminiscent of the mucinous cystadenoma of the appendix is of particular interest.

The clinical significance of our finding is limited at present. AMH is a frequent finding during surgery and has an excessively low malignant potential (if any greater than normal epithelium). None the less, awareness of the possibility of malignant degeneration might be
Induction of interleukin-8 secretion from gastric epithelial cells by a cagA negative isogenic mutant of Helicobacter pylori

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Abstract

The ability of Helicobacter pylori strains to induce interleukin-8 (IL-8) gene expression and protein secretion from gastric epithelial cell lines in vitro is variable. This cellular response is associated with bacterial expression of the CagA protein present in type I H pylori strains. To determine the role of CagA in this host cell response, an isogenic cagA negative mutant, N6.XA3, was constructed. The cagA negative isogenic mutant and the wild-type parental cagA positive strain, N6, were co-cultured with AGS, ST-42 and KATO-3 gastric epithelial cell lines and secreted interleukin-8 assayed by enzyme linked immunosorbent assay. In all three cell lines there was no significant difference in the IL-8 secretion induced by the cagA negative isogenic mutant, N6.XA3, and the wild-type parent strain, N6. These studies show that CagA is not the inducer of IL-8 secretion from gastric epithelial cells. As all wild-type CagA positive strains studied to date induce IL-8, the bacterial factor(s) inducing this inflammatory response is closely associated with the expression of CagA.

Keywords: Interleukin-8, Helicobacter pylori, CagA, epithelial cells, gastritis.

The CagA surface protein of Helicobacter pylori is highly immunogenic and is expressed in about 60 to 70% of H pylori strains.1,2 Mucosal IgA antibody recognition of this protein has been linked with peptic ulcer disease and the activity of gastritis3 and systemic IgG responses to CagA are also elevated in ulceration.4 Strains of H pylori which have the gene coding for CagA and express this immunogenic protein usually coexpress the vacuolating cytotoxin (VacA).5 Strains with this genotype/phenotype have recently been classified as type I bacteria.6 Type II strains lack the cagA gene and express neither the CagA protein nor the VacA protein.7 While the VacA protein is thought to be an important mediator of gastric mucosal damage, this protein does not elicit gastric inflammatory cell infiltration in animal models.8
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doi: 10.1136/jcp.48.10.965

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