MUCOCOELES OF THE APPENDIX
Their underlying epithelia, behaviour and associated tumours
by
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MUCOCOELE is a descriptive term for mucus accumulation in the distended lumen of an organ, and does not indicate the underlying pathology. This paper describes four distinct pathological entities identified in a series of 65 mucocoeles of the appendix.

The first category, designated as retention cyst, is due to simple obstruction of the lumen often associated with post inflammatory fibrosis or a faecalith. The diagnosis is restricted to those cases in which there is no evidence of any epithelial abnormality in the mucosal lining of the appendix other than flattening.

The second category, designated as metaplastic polyp, is characterised by mucosal glands whose deeper aspect resembles normal appendicular epithelium, but towards the lumen the glands become dilated and lined by goblet cells and cells with pink staining cytoplasm with pale vesicular nuclei and only an occasional mitotic figure. Papillary infolding gives a characteristic serrated appearance (Fig. 1).

The third category is designated mucinous cystadenoma. These tumours are identical to tubular and tubulo-villous adenomas seen in the colon. They exhibit a glandular or pure villous histology, and the neoplastic epithelium shows mild, moderate or severe dysplasia. Mucin production is usually very prominent and may lead to a flattened epithelium (Fig. 2).

(left) FIG. 1 Metaplastic polyp H and E × 60
(above) FIG. 2 Mucinous cystadenoma H and E × 60
The fourth category is that of cystadenocarcinoma. This is a mucinous adenocarcinoma which may show evidence of origin from a mucinous cystadenoma. The histology is fundamentally no different from mucinous adenocarcinomas of the colon, but when in the confined space of the appendix, luminal obstruction and accumulation of mucus leads to the formation of a mucocoele.

Rupture of a mucocoele may occur, with spillage of mucus into the peritoneal cavity. The outcome varies with the cause of the mucocoele and the potential to produce peritoneal dissemination.

Two recent series report an unsuspected association between appendiceal cystadenomas and separate primary tumours of the colon, either adenomas or carcinomas.¹ ² One of these² suggests that the finding of appendiceal cystadenomas necessitates the subsequent screening of the large intestine for further neoplasms. These findings and conclusions are contrasted with this series. The simultaneous occurrence of mucinous cystadenomas of the appendix and ovary is also studied.

**MATERIALS AND METHODS**

A review of 65 cases of mucocoele of the appendix diagnosed in the histopathology laboratory of the Belfast City Hospital between 1968 and 1981 was carried out. Appendices showing only mild dilatation without evidence of mucus retention in the lumen, including three cases of primary adenocarcinoma without excessive mucus production, were eliminated from the study. Paraffin blocks from formalin fixed material with multiple transverse sections were available from all cases for review, and were stained by haematoxylin-eosin. Follow-up information was obtained from the hospital records for periods varying from eight months to fourteen years. The follow-up period was greater than two years in 55 of the cases.

**RESULTS**

Examination of the 65 cases of mucocoele allowed their separation into four well defined categories which were designated as retention cyst, metaplastic or hyperplastic polyp, mucinous cystadenoma and cystadenocarcinoma.

1. **Retention cyst**

This group comprised 26 cases. The ages of the patients ranged from five to 74 years; 14 were women and 12 were men. The majority had evidence of chronic inflammation and fibrosis, but no hyperplastic or neoplastic changes were identified in the appendiceal mucosa. One retention cyst was an incidental finding in a right colon removed for adenocarcinoma of the caecum. In four cases mucus had penetrated into the muscle coat and in a further eight cases perforation had occurred, with periappendicular mucus spillage. In none of these eight cases were epithelial cells identified in the mucus outside the serosa, and resolution followed appendicectomy. There were no simultaneous ovarian tumours.

2. **Metaplastic polyp**

This group comprised six cases. The ages of the patients ranged from 28 to 71 years; four were women and two were men. Only two of the patients were over 50 years of age. The histological picture was identical to the better recognised metaplastic polyp occurring in the colon.

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In three cases the metaplastic polyp was the sole lesion in the appendix. In the remaining three cases it was accompanied by a mucinous cystadenoma, and one of these bore secondary serosal deposits of a caecal adenocarcinoma. Two of the cases which showed a metaplastic polyp and a mucinous cystadenoma in the appendix were associated with intact ovarian mucinous cystadenomas, and in both perforation of the appendix occurred, with periappendicular mucus spillage. One was complicated by post-operative drainage of mucus from the peritoneal cavity which eventually resolved. Epithelial cells were not identified in the peritoneal cavity.

3. Mucinous cystadenoma

This group comprised 31 cases, plus the three mentioned above associated with metaplastic polyps. The ages of the patients ranged from 20 to 81 years; 18 were women and 13 were men. In three cases mucus had penetrated into the muscle coat, and in a further 14 cases perforation had occurred, with periappendicular mucus spillage. Epithelial cells were not identified in the extraneous mucus. Three of the cases were complicated by post-operative drainage of mucus from the peritoneal cavity, but this resolved.

4. Cystadenocarcinoma

This group comprised two cases. The patients were 37 and 68 years of age and were both male. The older patient presented with a cyst-like mass of mucus circumscribed by a calcified fibrous tissue shell at the base of the appendix. No residual epithelial lining or evidence of tissue invasion was found, and the diagnosis was based on the malignant epithelial fragments in the mucus deposits outside the lesion, and this was confirmed by the subsequent clinical course. He survived for four years, and over this period required repeated evacuation of mucus from secondary peritoneal implants in the abdominal cavity. The younger patient died within a year of appendicectomy from disseminated malignancy.

DISCUSSION

The pathogenesis of appendiceal mucocoele has been a subject for considerable debate. Some emphasise proximal luminal obstruction by post inflammatory fibrosis\(^3\),\(^4\) while others consider primary mucus-secreting neoplasms of the appendix to be paramount.\(^5\) Retention cyst, or simple mucocoele is due to obstruction of the proximal lumen with retention of mucus secretions, usually on a post inflammatory basis, although in one case in this study the luminal obstruction was caused by an adenocarcinoma of the caecum. Metaplastic polyps, cystadenomas and cystadenocarcinomas produce copious mucus, and may cause secondary obstruction, and may also be associated with inflammation and fibrosis. Any one of these mechanisms may dominate in a particular case.

Metaplastic or hyperplastic polyps were first described in the appendix in 1972,\(^6\) and are a rare cause of a mucocoele.\(^7\) The lesion is analogous to the metaplastic polyp in the colon, a common finding in older patients, where it has traditionally been regarded as degenerative,\(^8\) or a response to inflammation,\(^9\) with no neoplastic potential. More recently, a possible relationship has been proposed between metaplastic polyps and villous adenomas,\(^10\) the counterpart of cystadenomas in the appendix. It has been suggested that because areas of metaplasia may be found in villous adenomas, and because they exhibit similar enzyme patterns,\(^11\) some villous
adenomas may be derived from metaplastic nodules. Although in this study only six appendiceal mucocoeles contained metaplastic polyps, it is interesting that three were associated with cystadenomas.

Mucinous cystadenomas were the commonest cause of mucocoele in our study, exceeding simple non-neoplastic retention cyst, and caused the greatest distention of the lumen, often leading to a thin fibrous mucus-filled sac. Rupture with mucus spillage complicated fifteen of thirty-four cases, but epithelial cells were not present in the periappendicular mucus and follow-up did not identify any patients with progressive accumulation of mucus in the peritoneal cavity (pseudomyxoma peritonei). We consider the lack of epithelial fragments in the mucus is a useful negative finding in confirming the benign nature of this appendiceal tumour. Resolution has, however, occasionally been described in cases with apparently viable epithelial fragments in the periappendicular mucus and this has been attributed to misplaced epithelium following rupture and not to invasion.

The only cases of true progressive pseudomyxoma peritonei occurred in the two patients with cystadenocarcinomas and secondary carcinomatosis of the peritoneum. The clinical course was consistent. One died within a year of appendicectomy and the other died four years later following repeated clearance of mucus from the peritoneal cavity. It is therefore maintained, along with other authors, that the condition known as pseudomyxoma peritonei is caused by peritoneal dissemination of a mucus-secreting adenocarcinoma and rupture of a benign mucinous tumour is always self limited.

Wolff and Ahmed, and Higa et al in their reviews of the appendix described an association between mucinous cystadenomas of the appendix and separate primary neoplasms of the colon. Adenocarcinoma of the colon was found in 21.4 per cent and 19.5 per cent of cases respectively and in Wolff and Ahmed's study one third of the patients had multiple adenomatous colonic neoplasms. This series of 34 cystadenomas did not confirm the association. Only one patient had a simultaneous colonic adenocarcinoma and follow up of all cases for periods varying from one to fourteen years did not provide evidence of the subsequent development of colonic tumours, either benign or malignant. Thus from our findings the diagnosis of an appendiceal mucinous cystadenoma does not necessarily confer a high risk of colonic malignancy and the neoplasm has the same prognosis as a single benign epithelial tumour found elsewhere in the large intestine.

A similar association noted by Shanks of concurrent cystadenomas of ovary and appendix was observed in two of the 34 patients with cystadenomas. This was a much smaller proportion than Shanks who reported the concurrence in one third of cases and considered the association too great to be coincidental.

In conclusion, this study of 65 mucocoeles of the appendix showed four underlying pathological groups. Mucinous cystadenomas and non-neoplastic retention cysts predominated with metaplastic polyps and adenocarcinoma infrequent. The relationship of half the metaplastic polyps with cystadenomas was noted, a finding which is being increasingly identified in the intestine although the significance is uncertain. We conclude that pseudomyxoma peritonei is caused by peritoneal implants of a mucus-secreting adenocarcinoma, and rupture of a cystadenoma into the abdomen will resolve following removal of the tumour. The high incidence of
associated adenocarcinomas of the colon previously described in one fifth of patients with cystadenoma of the appendix was not confirmed, indicating that the prognosis of this tumour is that of a single benign neoplasm.

SUMMARY

The pathology of 65 cases of mucocoele of the appendix was studied. Mucinous cystadenoma (34 cases) and simple retention cyst (26 cases) were the commonest underlying conditions, with metaplastic polyp (six cases) and cystadenocarcinoma (two cases) seen infrequently. In three of these cases metaplastic polyps and cystadenomas occurred simultaneously. Rupture with mucus spillage was self limited in the benign conditions, and pseudomyxoma peritonei was only encountered after peritoneal dissemination of cystadenocarcinoma. The previously described association of mucinous cystadenomas with separate primary tumours of the colon was not confirmed.

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