LETTERS TO JCP

# Reduplication cyst of appendix with mucinous carcinoma and Müllerian metaplasia: a case report

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This report describes a case of mucinous carcinoma and Müllerian metaplasia arising within an appendiceal duplication cyst found incidentally during an emergency Caesarian section. Intestinal duplication cysts are rare and although there are occasional reports of malignant transformation, this is the first case where Müllerian metaplasia was found concurrently with a malignancy. There was no previous history of endometriosis and no other abnormalities were found at surgery. Treatment included surgical excision. The patient is alive and well two years after removal of the cyst.

A 33 year old woman with a previously normal vaginal delivery and uncomplicated second pregnancy underwent an emergency Caesarian section. During the surgical procedure a mesenteric cyst was found in the pelvis. The cyst appeared to be attached to the mesoappendix and was separate from the ovaries. No other pelvic or peritoneal pathology was apparent and there was no free peritoneal fluid. There was no relevant past medical history; in particular, there were no previous signs or symptoms of endometriosis.

The cyst weighed 100 g and was 7 cm in maximum dimension. The cyst capsule was intact and attached to the mesoappendix, although not obviously connected to the appendix itself. Slicing through the cyst revealed that it was filled with blood and necrotic material (fig 1A). On light microscopy, the cyst wall was thickened, fibrous, and calcified, with no evidence of a breach of the capsule. The cyst contained several epithelial foci, differentiating along separate lineages. Large areas of a single layer of mucinous epithelium were present (fig 1B), which in places showed foci of atypical change amounting to both borderline and invasive mucinous adenocarcinoma (fig 1C). Small areas of neoplastic endometrioid epithelium were present and several foci of Müllerian type stroma were seen (fig 1D). Widespread evidence of old haemorrhage and inflammation were present, although there were no foci of endometriosis.

> "There were no previous signs or symptoms of endometriosis"

Immunohistochemical staining revealed the foci of mucinous carcinoma to show strong cytoplasmic positivity for

**Abbreviations:** CK, cytokeratin

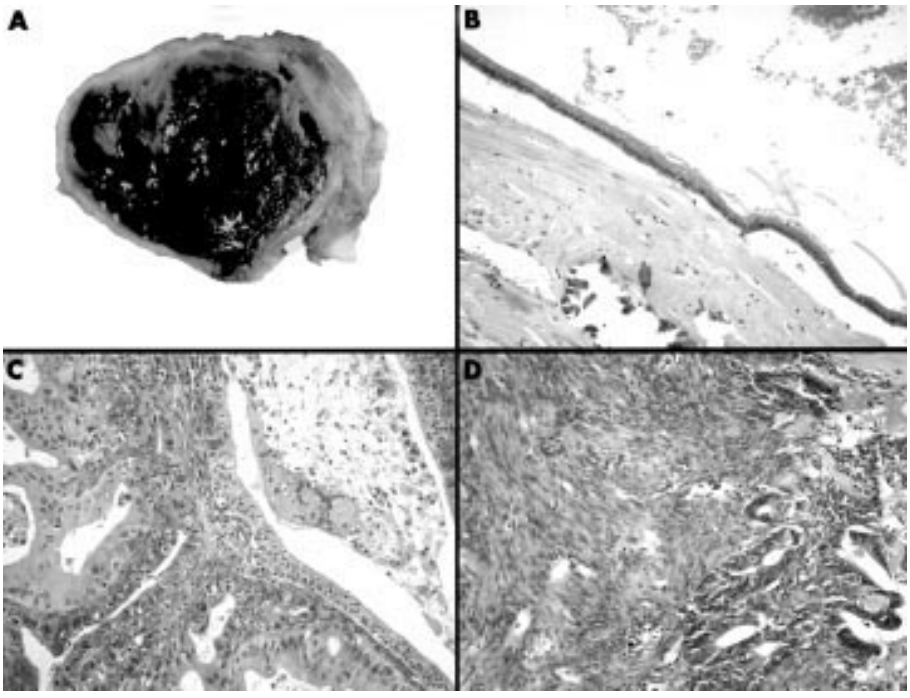


**Figure 1** (A) Cyst with necrosis and haemorrhage. (B) Haematoxylin and eosin stained sections showing a single layer of mucinous epithelium. (C) Haematoxylin and eosin stained sections of mucinous carcinoma. (D) Haematoxylin and eosin stained sections of endometrioid foci.

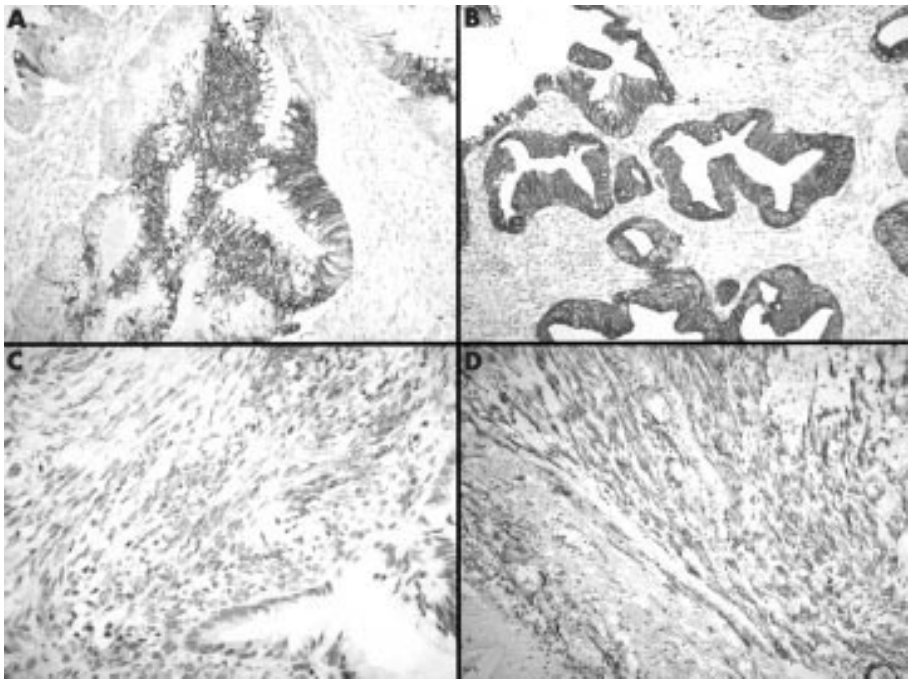


**Figure 2** (A) Immunohistochemical staining for cytokeratin 20 (CK20) within the mucinous carcinoma. (B) Immunohistochemical staining for CK7 in endometrioid epithelium. (C) Immunohistochemical staining for α inhibin within Müllerian stroma. (D) Immunohistochemical staining for actin (IA4) within the cyst wall.

cytokeratin 20 (CK20) only (fig 2A). The endometrioid areas were strongly positive for CK7 (fig 2B) and CA-125, and negative for CK20. The Müllerian stroma showed strong positive staining for smooth muscle actin and α inhibin (fig 2C), and the non-Müllerian stroma was positive for smooth muscle actin only (fig 2D).

The differential diagnosis on light microscopy was between a mucinous carcinoma in a reduplication cyst in which there is Müllerian metaplasia, mucinous carcinoma in an endometriotic cyst, and a mucinous carcinoma in a peritoneal cyst with metaplastic changes. The smooth muscle actin and CK20 positivity favoured a reduplication cyst, and the focal CK7 and CA-125 positivity supported the theory of Müllerian metaplasia. The lack of generalised CA-125 staining does not support the diagnosis of peritoneal cyst. The diagnosis was therefore considered to be a mucinous carcinoma in a reduplication cyst of the appendix with focal Müllerian metaplasia/neoplasia.

## DISCUSSION

Duplication cysts are uncommon and may occur at any level of the gastrointestinal tract.[1] They tend to be more frequently seen in the small intestine, especially the distal ileum.[2] They are lined by gastrointestinal epithelium, usually colonic, but also include squamous, gastric, and urothelial cells. They may be differentiated from other intra-abdominal cystic lesions by the presence of a normal gastrointestinal mucosal lining. Most cysts are located close to the mesenteric border or within the muscularis propria, and contain smooth muscle. Occasionally, they are widely separated from the intestine and are found in the retroperitoneum.[3 4]

> "The presence of malignancy including carcinoid tumours and adenocarcinomas is rarely reported within duplication cysts"

Theories explaining the origin of these cysts include failure of recanalisation of the bowel lumen after the solid epithelial phase of growth, persistence of epithelial outpouching, and impaired separation of the notocord from intestinal endoderm. Others have suggested that enteric duplication, segmental dilatation of intestine, and congenital diverticula may share a common pathogenesis.[5]

The presence of malignancy including carcinoid tumours[6 7] and adenocarcinomas[8 9] is rarely reported within duplication cysts. Although the finding of Müllerian tissue within urogenital cysts has been reported,[10] we believe this to be the first report of Müllerian metaplasia within an intestinal duplication cyst, which also contains malignant elements.

### Take home messages

- We describe a case of mucinous carcinoma and Müllerian metaplasia arising within an appendiceal duplication cyst found incidentally during an emergency Caesarian section
- This is the first reported case where Müllerian metaplasia has been found concurrently with a malignancy

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# ECHO

## Uveal melanoma has what it takes to boost blood supply

Please visit the Journal of Clinical Pathology website [www.jclinpath.com] for link to this full article.

Soluble cytokines may enable tumour cells to stimulate the formation of blood vessels within melanomas of the uvea. Vascular endothelial growth factor-A (VEGF-A) and basic fibroblast growth factor (bFGF)—promotors of blood vessel development—have been shown histochemically in uveal melanomas.

VEGF-A occurred in low amounts in 22% (11/49) of melanomas, around small blood vessels deep in the tumour. bFGF was detected in 89% (42/47), located diffusely in the cytoplasm. Twenty tumours tested by reverse transcriptase PCR detected mRNA for each cytokine. The presence of VEGF-A and bFGF was not related to microvessel density or tumour cell type, location, or mitotic index. Primary cell cultures of three melanomas stimulated the growth of two established endothelial cell lines—one derived from rat brain and the other from human umbilical cord—in a dual culture system allowing diffusion of soluble substances but no mingling of the cells, suggesting "cross talk" between melanoma and endothelial cell lines . Stimulation was partially reduced with antibodies against bFGF or VEGF-A, or both, so other soluble cytokines might be involved.

Fifty uveal melanomas were excised from removed eyes. The cytokines were located immunohistochemically in formalin fixed, paraffin thin sections using several staining methods for VEGF-A, including a double antigen retrieval method to increase the chance of detection. The remaining unfixed tumour provided material for mRNA determination and tissue culture. The effects on growth of adding anti-bFGF or anti-VEGF-A antibody, or both, to the dual cell cultures was determined by ATP assay.

▲ *British Journal of Ophthalmology* 2002;**86**:440–447.

# ECHO

## Target for treating uveal melanoma

Please visit the Journal of Clinical Pathology website [www.jclinpath.com] for link to this full article.

The presence of growth factors in eyes may enable patients with melanoma of the uvea to retain their eyes. The detection of vascular endothelial growth factor-A (VEGF-A) in the ocular fluid of affected eyes bodes well for new treatments in trial stage for blocking VEGF-A . This should prevent neovacularisation of the iris and neovascular glaucoma—complications which mean removal of the eye. Neovacularisation of the iris, in particular, seems to follow radiation treatment.

VEGF-A measured by enzyme linked immunosorbent assay had a median concentration of 0.8 ng/ml in aqueous samples (range: undetectable–10 ng/ml) and in vitreous samples (0.75 ng/ml (undetectable–21.6 ng/ml), significantly more than aqueous samples from control eyes (0.17 ng/ml, 0.05–0.96 ng/ml). The highest concentrations of VEGF-A (>1 ng/ml) were evident in seven affected eyes. Six of these had neovascularisation and five had received radiation treatment for melanoma. VEGF-A was located by immunohistochemistry in the anterior eye in 54% of tumours. The amounts found in ocular fluids bore no relation to tumour size, microvessel density, staining of the anterior segment, or retinal detachment.

VEGF-A was measured in aqueous samples (30 eyes) and vitreous samples (19) from eyes removed because of melanoma and in aqueous samples taken from 16 control eyes during cataract surgery. Immunohistochemistry was used to locate VEGF-A in thin sections from tumours excised from extracted eyes. Eight of the eyes with tumours had neovascularisation of the iris and 21 had retinal detachment.

▲ *British Journal of Ophthalmology* 2002;**86**:448–452.