

Figure 2 High power showing glandular structures composed of a double layer of epithelial and myoepithelial cells.

represent metastasis from an unsuspected and undiscovered occult thyroid carcinoma.

The presence of glandular elements embedded in the centre of the bone marrow in the present case initially lead to consideration of a diagnosis of metastatic adenocarcinoma. However, metastatic tumour was ruled out due to the lack of the nuclear features of malignancy and of a stromal desmoplastic response and the presence of a double layer of epithelial and myoepithelial cells in several of the glandular structures. Clinical examination and limited radiological investigation did not reveal a primary site of malignancy. The epithelial nature of the structures was confirmed on immunohistochemistry and positive staining for α -smooth muscle actin highlighted the presence of a layer of myoepithelial cells.

We believe these non-neoplastic glandular structures to be an artefact produced by the trauma of the biopsy procedure. Small fragments of squamous epithelium derived from skin are a well described artefact in bone mar-

row trephine biopsy specimens, especially when performed by an inexperienced operator. Such fragments are generally found at the end of a trephine biopsy specimen and their occurrence has been described in many of the textbooks of bone marrow pathology.⁵ However, the presence of non-neoplastic glandular structures in bone marrow has not been stressed. A further unusual point in the present case was that glandular structures were embedded in the centre of the bone marrow, completely surrounded by haemopoietic elements. Morphologically, they resembled dermal sweat gland structures. The presence of adjacent fragments of skeletal muscle, also embedded within the centre of the marrow, led us to conclude that both glandular and muscular elements had been displaced there during the biopsy procedure. Although skeletal muscle fibres were present in this instance, it is possible that cases might be encountered where glandular structures are present without muscle elements. If a serious misdiagnosis of metastatic malignancy and unnecessary investigation is to be avoided, pathologists and haematologists should consider non-neoplastic glandular structures in cases where epithelial elements show bland nuclear features and an absence of stromal desmoplasia. Such epithelial elements are likely to be of dermal sweat gland origin.

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Clear cell adenocarcinoma of the colon

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Abstract

A case of clear cell adenocarcinoma of the colon is reported. The histological examination of both the surgical specimen and of the metastases at necropsy showed columnar or polygonal cells with vesicular nuclei. The cytoplasm was usually clear with multiple, often empty looking vacuoles. From a panel of histochemical and immunohistochemical reactions,

carcinoembryonic antigen and tissue polypeptide antigen showed strong positivity. The histochemical and immunohistochemical differential diagnosis with another common clear cell tumour, namely clear cell renal adenocarcinoma, is discussed.

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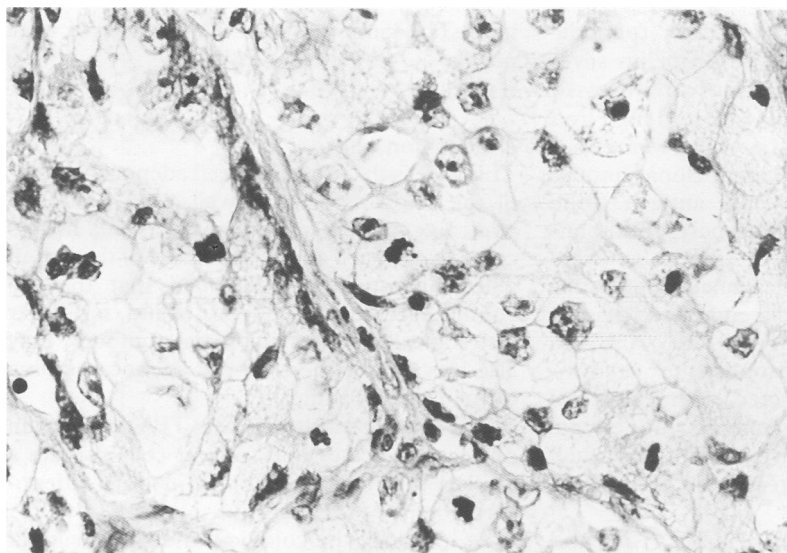


Figure 1 Clear cell adenocarcinoma of the colon showing glandular arrangement (haematoxylin and eosin, $\times 360$).

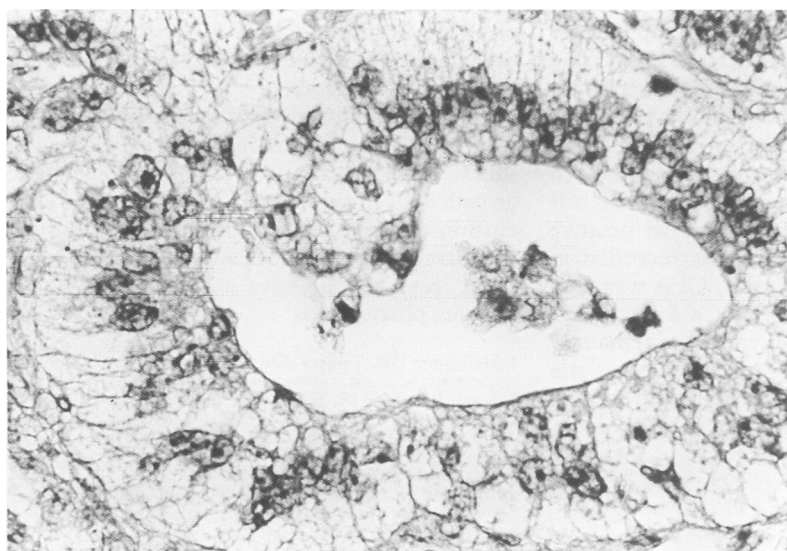


Figure 2 Another area of the tumour showing clear cells and vesicular nuclei with prominent nucleoli (haematoxylin and eosin, $\times 360$).

In 1964, Hellstrom and Fischer¹ described a case of adenocarcinoma of the sigmoid colon, composed of clear tumour cells which resembled the physaliferous (clear) cells of chordoma tumours. Since the original description by Hellstrom and Fischer, three other cases of clear cell adenocarcinoma of the large intestine have been reported.^{2,3} Subsequently a case of clear cell carcinoma of the anal canal was found.⁴

The importance of the clear cell adenocarcinoma of the colon is that the tumour may be histologically confused with a colonic metastasis from a primary clear cell adenocarcinoma of the kidney.¹⁻³ However, clear cell tumours may have different origins and include malignant melanoma, lymphoma, sarcoma, and carcinomas (for example, of thyroid, prostate, and uterine cervix⁴).

The purpose of this paper is to report and illustrate this unusual tumour of the large bowel.

Case report

A 68 year old man was admitted to the emergency ward with symptoms of total bowel obstruction. During the past four months, the patient had developed periods of diarrhoea alternating with periods of severe constipation. Three weeks before admission, the patient had nausea, periodical abdominal pain, meteorism, and 7 kg weight loss. At admission, a barium enema revealed an stenotic tumour mass in the splenic flexure. A derivative transversostomy was done and two weeks later a left hemicolectomy was carried out. The post-operative course was uneventful. Six months later, the patient complained of diffuse abdominal pain. Ascites and liver metastases were found on clinical examination. The patient deteriorated rapidly and died seven months after the hemicolectomy. A necropsy examination was done.

GROSS EXAMINATION

Hemicolectomy

The surgical specimen of the colon measured 44 cm in length and contained a centrally located tumour 6 cm in length. The tumour was exophytic, with a cobblestone-like surface. The cross section showed transmural invasion. Ten enlarged lymph nodes were found.

Necropsy

The necropsy examination showed metastatic tissue in the lungs, liver, peritoneum, both adrenal glands, and para-aortic lymph nodes. Blood stained ascites (3000 ml) was collected. The skin, thyroid, lymph nodes, and kidneys were macroscopically and microscopically normal.

MICROSCOPICAL EXAMINATION

Surgical specimen

Histological examination of the resected colon showed a clear cell adenocarcinoma breaking through the muscularis propria and infiltrating the subperitoneal tissues. The tumour had a mainly trabecular arrangement, although a tubuloglandular arrangement was occasionally observed in some areas. The trabecular areas were surrounded by tenous bands of connective tissue with thin vessels (fig 1). The tumour cells had either columnar or polygonal shapes and the clear cytoplasm contained small, apparently empty vacuoles. At high magnification ($\times 1000$) the small vacuoles were surrounded by a tenous basophilic network. Tumour cells adjacent to necrotic areas had larger vacuoles. The nuclei were vesicular, pleomorphic, and with one or more prominent nucleoli. Moderate numbers of atypical mitosis were present.⁵ In areas with glandular arrangement, the nuclei were located near the luminal aspect of the cell (fig 2).

Six of the 10 regional enlarged lymph nodes showed metastatic growth. The histological characteristics of the metastasis were the same as those of the primary tumour.

A panel of histochemical stains (periodic acid-Schiff technique (PAS)), Grimelius silver stain, oil red O in sections of unprocessed tissue, Alcian blue (AB) pH 2.5, and high iron diamine (HID) reactions, as well as immunohistochemical reactions (monoclonal mouse anti-human carcinoembryonic antigen clone A5B7 DAKO = CEA), tissue polypeptide antigen = TPA, rabbit anti-TPA: B1AB), were done. Immunohistochemical analysis on formalin prefixed paraffin wax embedded tissues showed no cross reactivity of CEA A5B7 to polymorphonuclear neutrophils or erythrocytes. The antibody reacted with colorectal adenocarcinomas (more intense in necrotic debris). PAS was negative, except for small cytoplasmic globules present in occasional tumour cells.

Oil red O, Alcian blue pH 2.5, HID, and Grimelius stains were non-reactive. Immunohistochemical studies showed strong positivity for CEA and TPA. TPA was strongly positive in all tumour cells, particularly in cytoplasm surrounding some of the vacuoles.

A sample from the tumour was prepared for transmission electromicroscopy (TEM). The occurrence of multiple, apparently empty vacuoles was confirmed at the TEM level.

A panel of histochemical and immunohistochemical reactions (see above) was applied to sections from three cases of clear cell adenocarcinoma of the kidney. A PAS positive reaction within the vacuoles was recorded in about 50% of the tumour cells; CEA was positive only in the Golgi area in a few cells in some areas, whereas the vacuoles remained unstained. The cell membrane as well as the cytoplasm (but not the vacuoles) were stained in a few tumour cells (<1%) in sections challenged with TPA.

Necropsy microscopical examination

Material taken from tumours in the liver, lungs, and omentum at necropsy showed identical structures to those found in the surgical speci-

men. The kidneys, prostate, and thyroid were normal.

Discussion

This case is the sixth clear cell adenocarcinoma of the colon reported. Jewell *et al*² described two cases of clear cell adenoma as well as two cases of clear cell adenocarcinoma of the colon. These investigators concluded that the adenoma-carcinoma sequence, valid for other histological types of colorectal tumours, may also be valid for the clear cell adenocarcinoma of the large intestine.

The strong positivity for TPA present in our case indicates that tumour cells contain a marker that has been found in other adenocarcinomas of the digestive tract.⁶

At histology the colonic tumour was similar with another clear cell adenocarcinoma: clear cell adenocarcinoma of the kidney. The three kidney adenocarcinomas tested here showed a positive reaction for mucopolysaccharides (PAS) and lipids (oil red O), whereas our case of clear cell adenocarcinoma of the colon showed occasional small globules with a PAS positive cytoplasmic substance.

This appears to be the first reported case of clear cell adenocarcinoma of the colon with follow up. The patient had massive metastatic growth at necropsy examination. While no conclusion can be drawn from one case report, it would seem that clear cell adenocarcinoma may be at least as aggressive as other large bowel tumour phenotypes.

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Introduction of computer assisted control of oral anticoagulation in general practice

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Abstract

The number of patients referred to hospital clinics for monitoring of oral anticoagulation continues to rise rapidly. Introduction of computer programs for the control of oral anticoagulation improves

the quality of anticoagulant control in hospital clinics. This approach has now been extended to include patients managed in general practice. Results confirm that the quality of anticoagulation can also be improved in these patients. A standard ap-