Correspondence

Clear cell adenocarcinoma of the colon arising in endometriosis: a rare variant of primary colonic adenocarcinoma

Colonic adenocarcinomas composed predominantly or exclusively of cells with clear cytoplasm are extremely rare. Considerable diagnostic difficulties can arise in distinguishing primary colonic clear cell adenocarcinoma and metastatic carcinoma from sites such as ovary or kidney. Here, we describe a case of primary colonic clear cell adenocarcinoma that probably arose in endometriosis. The possible presence of endometriosis was only appreciated on review and after the examination of multiple levels and extra histological sections. A 65 year old woman presented with crampy lower abdominal pain and the passage of blood and mucus from the rectum. Barium enema showed an apparently malignant stricture of the rectosigmoid and she underwent an anterior resection. Preoperative serum CA125 was not measured. At surgery, the clinical impression was that of a primary colorectal tumour. Small haemorrhagic nodules were present on the pelvic and abdominal peritoneum, suggestive of endometriosis. There were multiple metastatic lesions within the liver. Both ovaries and kidneys appeared normal.

The surgical specimen consisted of a 30 cm length of colon. A polyoid ulcerated tumour covered the mucosa and infiltrated through the full thickness of the colonic wall. Histology of the tumour showed an ulcerated surface. The tumour was composed entirely of cells with abundant clear cytoplasm and prominent cell membranes (fig 1A). Several growth patterns were present. Much of the tumour had a pronounced papillary pattern, with hyalinised cores covered by tumour cells (fig 1A). Tubular and solid areas were also identified. There was moderate nuclear pleomorphism and low mitotic activity, with a formal mitotic count revealing 1–2 mitoses/10 high power fields. Areas of necrosis were present and there was extensive lymphovascular permeation, both within the tumour and within submucosal and serosal lymphatics away from the tumour. Calfied psammoma bodies and intracytoplasmic periodic acid Schiff (PAS) positive eosinophilic hyaline inclusions were also present. The adjacent colonic mucosa showed no dysplastic features. The tumour infiltrated through the full thickness of the colonic wall into the surrounding fat.

Histological diagnosis was colonic adenocarcinoma, keratin negative. Cystic spaces lined by cells with clear cytoplasm were also identified. The tumour was composed predominantly of clear cell adenocarcinoma that probably arose in endometriosis of the colon, a rare variant of primary colonic clear cell adenocarcinoma. Clear cell adenocarcinoma of the colon is a rare tumour that has occasionally been described as arising in endometriosis. It is often associated with pelvic endometriosis in 50–70% of cases and a quarter of ovarian clear cell carcinomas can be shown to arise in endometriotic cysts. It should therefore be no surprise if occasionally a clear cell carcinoma of ovarian type should arise in endometriosis, and several such cases have been reported. Endometrioid type adenocarcinoma has occasionally been described arising in colonic endometriosis, and we are aware of a single previous report of clear cell carcinoma arising in endometriosis of the sigmoid colon.

In our patient, the strong positivity of tumour cells with CA125 provides evidence of Mullerian derivation. Although focal immunoreactivity can be present in primary colonic carcinoma, positivity to this extent is unusual. The strong immunoreactivity for CK7, combined with CK20 negativity, is also in keeping with an ovarian type primary, the converse pattern of staining being expected in a primary colonic neoplasm. A further histological pointer to an ovarian type tumour was the presence of calcified psammoma bodies. The ovaries and kidneys appeared grossly normal at laparotomy, helping to exclude the possibility of a colonic metastasis from an ovarian or renal primary.

In summary, we describe an unusual case of primary colonic clear cell adenocarcinoma that has probably arisen in endometriotic endometriosis. When confronted with an endometriotic tumour with the histological appearances described above, pathologists should consider a primary of ovarian type and an origin in endometriosis. The demonstration of endometriosis might require the examination of multiple levels and extra histological sections. Even then, residual endometriosis might not be definitely dem-
onstrated because it may be completely obliterated by tumour. Confirmation that a tumour is of ovarian type may be critical, because chemotherapeutic regimens will differ from those administered for a typical colonic adenocarcinoma.

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Retroperitoneal extraskeletal osteosarcoma

Extraskeletal osteosarcoma are rare malignant mesenchymal neoplasms characterised by the direct production of osteoid or bone by tumour cells. By definition, they are located in the soft tissues without primary bone or cartilage involvement. The most common location of these tumours is the lower extremity, especially the thigh, followed by the upper extremity and the retroperitoneum.

We report the radiological presentation of a retroperitoneal extraskeletal osteosarcoma, which may be helpful in the consideration of its differential diagnosis. A 68 year old man presented with a painless palpable mass in the right side of the abdomen. A previous trauma was denied. The patient was not on anticoagulant medication. Except for a cholecystectomy in 1986, his medical history was unremarkable. Physiological examination revealed a firm mass measuring approximately 10 × 10 cm. Laboratory findings were within normal limits, with the exception of a slightly raised alkaline phosphatase concentration of 140 U/litre (normal range, 40-120).

Plain radiography of the abdomen demonstrated a large ill defined dense lesion projecting over the right side of the pelvis. Contrast enhanced helical computed tomography (CT) of the abdomen identified a large, non-homogeneous soft tissue mass in the right side of the retroperitoneum (fig 1). The tumour measured 9 × 12 × 14 cm. The major part of the mass was predominantly mineralised; the lateral side showed a large soft tissue mass with low density in the centre suggestive of a necrotic component. The radiological features suggested an osseous, rather than chondroid, nature because of the poorly defined and homogeneous aspect of the mineralisation. The upper border of the mass was in close anatomical proximity to, but clearly separate from, the adjacent right kidney on three dimensional reformattting. The tumour definitely did not arise from adjacent osseous structures and the psoas muscle was compressed by the tumour.

Magnetic resonance imaging (MRI) demonstrated a mass surrounded by a pseudocapsule near but not originating from the lower pole of the right kidney. In addition to the ossified zone, the mass contained areas of necrosis, old haemorrhage, or secondary lacunae formation filled with protein substance indicated by intermediate signal intensity on T1 weighted sequences and very high signal intensity on T2 weighted images. Based on the clinical history and radiographic findings, the diagnosis of an extraskeletal osteosarcoma was suggested.

Macroscopically, the tumour sample revealed a 19 × 12 × 9 cm tumour including the resected margins, partly bony, partly firm, partly weak of consistency, with a white pink colour. There was a large cystic area, measuring 7 × 6 cm filled with serous fluid.

Microscopically the tumour was composed of storiform oriented bundles of spindle shaped tumour cells, admixed with areas of polygonal shaped tumour cells with abundant deposition of primitive osteoid matrix in between (fig 2). The osteoid matrix showed a trabecular arrangement and was focally admixed with chondroid forming areas. In these fields, the tumour cells showed lacunae. In all areas the tumour cells showed moderate pleomorphism and mitotic activity of up to eight mitoses/10 high power fields, the areas of necrosis were seen. No relation with a pre-existing nerve could be documented. Immunohistochemically, the tumour showed diffuse reactivity with antibodies against vimentin and focal reactivity with antibodies against the S-100 protein in the chondroid containing fields and the spindle cells. Antibodies directed against neurofilaments and p53 showed no reactivity. The differential diagnosis included high grade extraskeletal osteosarcoma, malignant peripheral nerve sheath tumour with heterologous elements, and dedifferentiated liposarcoma. A combined liposarcomatous part was not identified. Because of the lack of an identifiable nerve component, the absence of focal reactivity only with S-100, and neurofilaments being negative, the diagnosis was extraskeletal osteosarcoma.

Extraskeletal osteosarcoma is a rare tumour, constituting approximately 1% of all soft tissue sarcomas and approximately 4% of all osteosarcomas. Although primary osteosarcomas of bone occur predominantly in the first decades of life, extraskeletal osteosarcoma are rarely encountered under 40 years of age.

The pathogenesis of the tumour is unclear; the tumour may occur and be induced at sites that have received previous radiotherapy. In addition, a history of trauma has been reported in 12–30% of patients. There are cases described in which extraskeletal osteosarcoma is presumed to be preceded by myositis ossificans. Few reports of extraskeletal osteosarcoma have detailed the radiological findings of this rare neoplasm. The imaging techniques showed a large soft tissue tumour, for a large part, demonstrating ossification, located in the retroperitoneum. Another primary osteosarcoma of bone was not found elsewhere in the body. On T1 weighted sequences the tumour was heterogeneous and intense compared with muscle, and exhibited high signal intensity on T2 weighted imaging in the lateral part of the tumour, suggesting necrosis, haemorrhage, or secondary lacunae formation filled with protein substance. This latter correlated with the histological findings. Compression but no involvement of the psoas muscle, as visualised by CT, was confirmed.

The radiological differential diagnosis of extraskeletal osteosarcoma includes benign and malignant lesions that show mineralisation. The most important benign lesions are calcified haematomas and myositis ossificans. Several mesenchymal tumours can show reactive or metaplastic bone formation—for example, synovial sarcoma, epithelioid sarcoma, liposarcoma, and malignant peripheral nerve sheath tumour. Both possible benign lesions could be ruled out. The first because the patient definitely denied previous trauma. Furthermore, the patient did not use anticoagulant medication and the aorta was normal on all studies. Myositis ossificans was unlikely because there was no previous trauma and because of the large size of the lesion. Most myositis ossificans lesions measure 3–6 cm in size.

Figure 1  Axial contrast enhanced helical computed tomography (CT) scan compatible with the ultrasound image demonstrates a large mass with extensive mineralisation in the medial part of the tumour, as well as an area of decreased attenuation laterally compatible with necrosis. The psoas muscle is compressed. However, the tumour does not seem to arise from this structure.

Figure 2  Photomicrograph of the tumour mass demonstrates the spindle shaped tumour cells with abundant deposition of osteoid matrix (haematoxylin and eosin stained; magnification, ×200).
determines specific patient treatment. The most frequent histopathology result that factors that might cause interlaboratory variation of this type is worse than chance alone. These coefficients are used in the statistical analysis. An example of a contingency table is shown in Table 1. The authors may have done this in the final versions of their paper. They may have done this in the final versions of their paper.

The excellent paper by Rhodes and colleagues is mandatory for a definitive diagnosis. Furthermore, the data shown in the paper (for example, figs 8 and 9) demonstrate that in an obvious difference in staining, rather than interpretative variation, that accounts for the different results. None of these minor points should detract from the very important results of Rhodes et al, which have important implications for any laboratory running an immunohistochemical service assessing oestrogen and progesterone receptor expression.

The immunohistochemical demonstration of oestrogen and progesterone receptors

The excellent paper by Rhodes and colleagues provides a valuable insight into the factors that might cause interlaboratory variability in the immunohistochemical demonstration of oestrogen receptors, now probably the most frequent histopathology result that determines specific patient treatment. There is, however, one section of the paper where the statistical analysis may be causing confusion, rather than clarity.

In table 6, the degrees of agreement between the participant and organizing laboratory for oestrogen receptor expression using the “Quick score” method are given. For each level of expression a κ statistic is given, and the values of all these statistics are given, and the values of all these statistics are expressed as the degree of intra-observer (AR and BJ) agreement. Fleiss recommends that κ values between 0.4 and 0.75 represent fair to good agreement, and values exceeding 0.75, excellent agreement. The weighted κ statistics for intra-observer agreement in our study for the evaluation of the Quick scores of the participants’ assays and the organising laboratories’ assay on the same in house tumours, are 0.70 and 0.74, respectively, indicating good agreement by the same assessor when evaluating the same slides on different occasions. The weighted κ statistics for inter-observer agreement when assessing the participants’ and organising laboratories’ IHC results by Quick score evaluation in this study are 0.70 and 0.87, respectively, indicating excellent agreement. These findings support those of previous studies that have used the Quick score method of evaluation.

In summary, we conclude that the results of these additional tests suggested by Dr Cross and clarify those published in our original study. They emphasise that the significant differences observed in the Quick score evaluation of the IHC assay results for ER on in house tumours are caused by differences in the expression of oestrogen receptors.

Table 1: Contingency table showing the overall level of agreement between the participants’ assays and the organising laboratory’s assay, on 152 breast carcinomas

<table>
<thead>
<tr>
<th>Participants’ IHC assays</th>
<th>Organising laboratory’s IHC assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative (0)</td>
<td>Low (2, 3)</td>
</tr>
<tr>
<td></td>
<td>Medium (4, 5)</td>
</tr>
<tr>
<td></td>
<td>High (6, 7)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
</tr>
</tbody>
</table>

For each level of expression a κ statistic is given, and the values of all these statistics are given, and the values of all these statistics are expressed as the degree of intra-observer (AR and BJ) agreement. Fleiss recommends that κ values between 0.4 and 0.75 represent fair to good agreement, and values exceeding 0.75, excellent agreement.

The authors’ reply

We would like to thank Dr Cross for his interest shown in our article and for his kind and constructive comments. Cohen’s κ statistic was used in our study to compare the degree of agreement between the immunohistochemical (IHC) sensitivity for oestrogen receptors (ER) achieved by 152 laboratories on in house breast tumours, to that achieved by the UK National External Quality Assessment Scheme for Immunocytochemistry (NEQAS-ICC) organising laboratories’ IHC assay on spare sections from the same cases, as evaluated by the “Quick score” method. As quite rightly deduced by Dr Cross, the rationale behind using κ statistics for this part of the study, in addition to the Wilcoxon’s matched pairs signed ranks test and the χ² goodness of fit test, was to emphasise the lack of agreement between the pairs of slides. This was reflected in the high expressing tumour as a low expressing tumour—is more important than misclassification between adjacent categories, a weighted κ statistic might be appropriate. It should also be remembered that the quick method of scoring will be subject to observer variability, but this was not the case in the paper (for example, figs 8 and 9) demonstrate that in an obvious difference in staining, rather than interpretative variation, that accounts for the different results.

None of these minor points should detract from the very important results of Rhodes et al, which have important implications for any laboratory running an immunohistochemical service assessing oestrogen and progesterone receptor expression.
ences in the sensitivity of the assays in different laboratories and not by observer bias.

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7 Cohen J. Weighted kappa: a nominal scale agreement with provision for scale disagreement or partial credit. Psychol Bull 1968;70:213–20.

Dietary dangers: ingestion of a bread bag clip

During a routine postmortem evisceration, a segment of jejunum of approximately 20 cm was noted to be doubled back upon itself, with fibrous adhesions joining the two halves of the loop creating a “U” shape. The segment of jejunum was opened along the antimesenteric border, and a bile encrusted foreign body was seen to be attached by a free bridge of mucosa where the bowel doubled back upon itself. The object was removed without damaging the mucosal bridge; removal of the encrusted bile showed the foreign object to be a plastic bread bag clip. There was no date on the clip. The bridge of free mucosa passed through the space behind the tooth-like pincers (fig 1). The amount of bile encrustation and the remarkable growth of a mucosal bridge through the clip suggest that it had been present in this particular segment of jejunum for a considerable time. Its presence was unrelated to the cause of death, which was given as coronary artery atherosclerosis, and there was no evidence to suggest that the presence of the bread bag clip had caused problems during life.

The segment of jejunum removed was sliced across, the cut running parallel to the place of circularis, to cut the mucosal bridge longitudinally. Sections were submitted for histopathological examination. A haematoxylin and eosin stain and an actin immunocytochemistry stain, to highlight muscle, were studied (fig 2). Although there was considerable postmortem autolysis, it was evident that the bread bag clip had been held within a mucosal lined eylet. The actin stain showed the muscularis propria curving to run below the base of the eylet; there was no muscularis propria running over the bridge of tissue that retained the clip. The muscularis mucosa similarly did not run in continuity across the top of the eylet; the eylet was within the lamina propria and the muscularis mucosa passes around and deep to it. There was a small amount of muscle within the tissue bridge itself but this did not appear to run in continuity across the top of the tissue bridge.

The mechanism of formation of this loop is difficult to determine. The bread bag clip has sharp tooth-like pincers, and would be expected to cause crushing and necrosis of the wall if attachment occurred. Re-epithelialisation of the bowel wall is recognised to take place after crush injury; this phenomenon has been exploited in the this phenomenon has been exploited in the

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Retroperitoneal extraskeletal osteosarcoma

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J Clin Pathol 2001 54: 77-78
doi: 10.1136/jcp.54.1.77

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