

COLONIC AND BREAST CARCINOMAS - ASSOCIATION OR METASTASES ? REPORT OF A CASE

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ABSTRACT

There is an increased incidence of colonic carcinoma in patients with breast carcinoma but colonic involvement secondary to breast carcinoma can also occur. The differentiation of the organ of origin (breast vs colon) of the abdominal tumour can be difficult and may benefit from the use of immunohistochemical staining with monoclonal antibodies that react preferentially with colon cancer (JGT) and breast cancer (3E1.2, BC2,BC3). Measurement of Mammary Serum Antigen (MSA) level as detected by the anti-breast monoclonal antibody (3E1.2) was also useful in the classification of tumours of uncertain origin.

Keywords: Breast carcinoma, Colon carcinoma, Metastases to colon, Immunoperoxidase, Monoclonal antibodies.

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INTRODUCTION

Association of colorectal and breast cancer has been reported: there is an increased incidence of colonic carcinoma in patients with breast cancer⁽¹⁾ and the risk of breast cancer also increases in patients with colorectal cancer^(2,3). In addition, metastatic disease originating from breast cancer may involve the gastrointestinal tract (usually stomach and much less commonly, colon), most of them from infiltrating lobular carcinoma of the breast⁽⁴⁻⁸⁾. More recently, it has been suggested that

endoscopic intestinal biopsy can adequately diagnose the metastatic involvement from breast cancer and thus avoid unnecessary surgery⁽⁹⁾.

This case describes the diagnostic difficulties encountered in differentiating primary colon cancer from metastatic breast cancer involving colon even at laparotomy and with routine histology of the tissue. It illustrates the usefulness of monoclonal antibody technology in the practical management of the patient. A newly described monoclonal antibody-based serum test called Mammary Serum Antigen (MSA) has been shown to be useful in the management of breast cancer⁽¹⁰⁾: elevated MSA level has been noted in a high proportion (75%) of patients with localized breast cancer and changes in MSA level can precede clinical disease progression or recurrence. The role of immunohistochemistry in the classification of tumours of uncertain origin through the analysis of their antigenic profiles has also been reported^(11,12).

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CASE REPORT

A 54-year old post-menopausal woman had a total mastectomy and axillary dissection two years previously for invasive ductal carcinoma which measured pathologically 25 x 22 mm. The primary breast carcinoma was histologically a grade 2 tumour by Bloom and Richardson criteria⁽¹³⁾ with extensive metastases in ten of the 22 axillary lymph nodes.

She received adjuvant therapy with Tamoxifen and remained disease-free until two years after surgery when symptoms of upper abdominal pain associated with anorexia, weight loss and constipation developed. Clinical examination revealed a fixed, non-tender abdominal mass below the right costal margin. There was no clinical evidence of disease elsewhere. A contrast-enhanced computed tomography of the abdomen (Fig. 1a) showed a large mass containing gastrograffin and air bubbles in the region of the ascending colon. The liver was normal. In addition, an annular stenosing lesion of the ascending

Fig 1(a)
Computed tomography of the abdomen showing the presence of a large mass (→) in the region of the ascending colon.

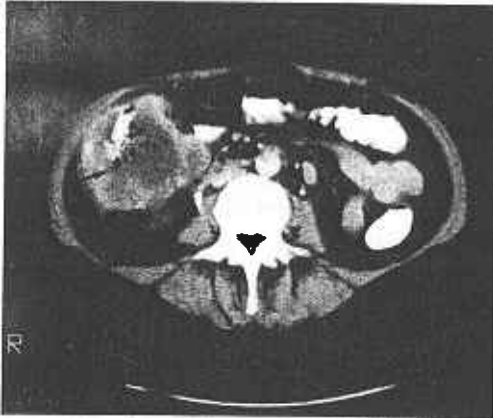
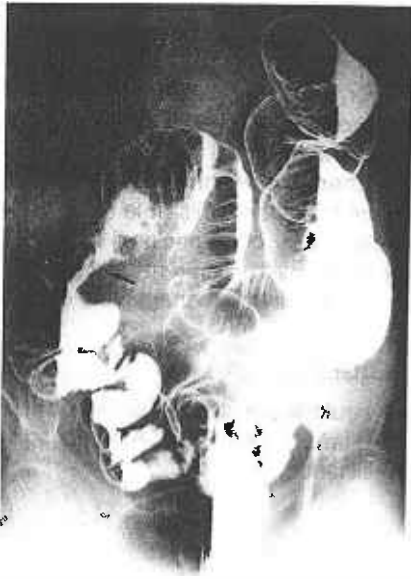


Fig 1(b)
Double contrast barium enema showing an annular stenosing lesion (→) of the ascending colon.



colon was demonstrated by double contrast barium enema (Fig. 1b). At laparotomy, a large necrotic tumour involving the hepatic flexure of the colon was noted and was found to be adherent to but not invading the right lobe of the liver and the right renal capsule, and encasing, but not obstructing, the third part of the duodenum. Multiple involved lymph nodes in the mesentery were noted but there was no liver metastases. It was unclear at operation whether the origin of the tumour was primarily colonic and invading the surrounding tissues or primarily extra-colonic involving the colon. A right hemicolectomy was performed but some residual tumour remained in the region of the duodenum.

PATHOLOGY

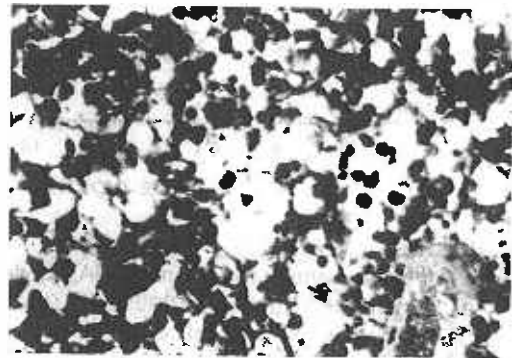
The specimen consisted of a portion of terminal ileum measuring 15cm and right colon measuring 36cm. There was a circumferential ulcerated tumour involving 6cm of the ascending colon with extensive extracolonic spread and there was residual tumour on the serosal aspect of dissection. Microscopically, poorly differentiated

adenocarcinoma cells invaded the entire colonic wall from the mucosa through the muscular coat into the serosa and there was metastases to three of the mesenteric lymph nodes. Comparison of the histology of the colonic tumour with that of the original infiltrating ductal carcinoma (grade 2) failed to establish the origin of the abdominal tumour (primary colon vs metastatic mammary).

Immunoperoxidase staining⁽¹⁴⁾ of the formalin-fixed, paraffin-embedded sections of the colonic tumour and original breast carcinoma with monoclonal antibodies (3E1.2, BC2, BC3) which are predominantly reactive with breast cancer-associated antigens^(14,15), and with anti-CEA monoclonal antibodies (I-1, JGT) which are predominantly reactive with colon carcinoma⁽¹⁶⁾ (unpublished observations) were performed. The colonic tumour had strong staining patterns with anti I-1 and JGT but weak staining with 3E1.2, BC2 or BC3, as judged by the proportion of carcinoma cells stained and the intensity of staining (Fig 2).

By contrast, the original primary breast carcinoma had a strong staining with anti-breast carcinoma antibodies 3E1.2, BC2 and BC3 but very weak staining with anti-CEA antibody (JGT) and had staining with I-1. The overall staining patterns of the colon tumour tend to suggest that it was of primary colonic origin. In addition, Mammary Serum Antigen level had been serially measured as part of the post-mastectomy follow-up protocol (Fig 3) and there was no significant change in the MSA level throughout the illness and this would further suggest that the abdominal tumour was not of metastatic mammary origin.

Fig 2(a)
Immunoperoxidase staining of the colonic tumour with anti-colon carcinoma monoclonal antibody, JGT



DISCUSSION

This case illustrates the potential difficulties in defining the organ of origin (breast vs colon) of adenocarcinoma involving the colon. Such a differentiation is important because treatment depends on the organ of origin. Colonic involvement by metastatic breast cancer indicates a systemic disease and requires systemic therapy. The accurate classification of poorly differentiated adenocarcinoma using traditional haematoxylin-eosin (H & E) staining requires the availability of well-fixed and thinly sectioned tissues. In many cases, such preparations do not provide sufficient information to venture beyond a diagnosis of poorly differentiated adenocarcinoma of uncertain origin, like in the case reported. These problems are further exacerbated in poor quality tissues obtained

Fig 2(b)
Immunoperoxidase staining of the colonic tumour
with anti-breast carcinoma monoclonal antibody
3E1.2 (original magnification x 160).

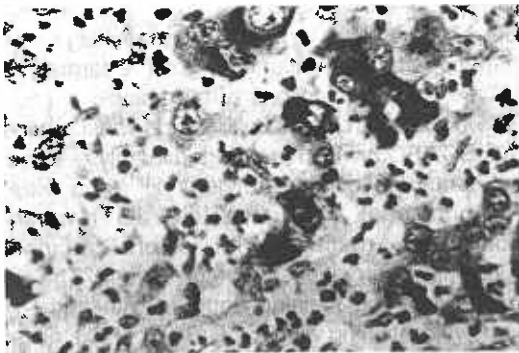
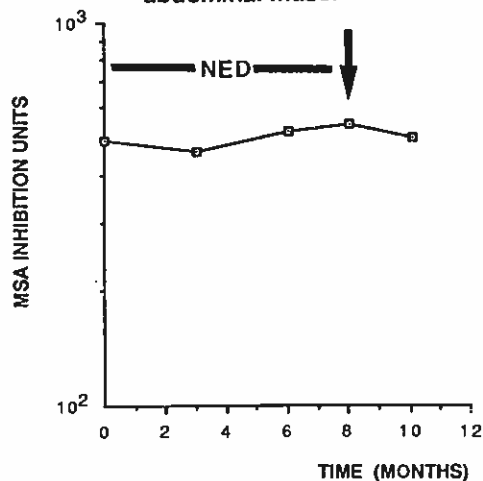


Fig 3
Monitoring the clinical course with serial Mammary
Serum Antigen (MSA) levels. NED indicates no
evidence of disease, ↓ indicates detection of
abdominal mass.



by endoscopic biopsies. Comparison of the H & E stained sections of the original primary breast cancer tissue and the subsequent cancer involving the colon is also difficult because of the potential heterogeneity between primary tumour and its metastases and the possible "downgrading" of the histology related the biological behaviour of the tumour⁽¹⁷⁾.

In this case, the preferential reaction of the carcinoma tissue with the anti-colon cancer antibody (JGT) and the lack of reaction with monoclonal antibodies reactive with breast associated antigens (3E1.2, BC2, BC3) strongly suggest that the carcinoma was of separate origin from the colon. By contrast, the original primary breast cancer tissue had a strong reaction with antibodies 3E1.2, BC2, BC3 and no reaction with JGT, as assessed by immunoperoxidase staining. Changes in MSA level tend to correlate with the clinical course (progressive disease, stable disease, disease regression and no evidence of disease) in breast cancer and the MSA level is uncommonly raised in colon cancer⁽¹⁰⁾. In this case, there was no significant change in the MSA level throughout the illness and after resection of the abdominal tumour. This further indicates that the abdominal tumour was unlikely to be metastases from the original breast carcinoma.

It is, however, important to be aware that monoclonal antibodies do not detect "cancer specific" antigens but rather, they react with normal or modified tissue antigens which are either preferentially or inappropriately expressed upon malignant cells. It is apparent from this case that cautious use of monoclonal antibodies with a preferential reaction with different cancers has proved to be a useful adjunct in the management of patient.

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ERRATUM

HEPATITIS B VACCINATION – THE PRESENT STATUS by I Yap, R Guan (Singapore
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In Table I (pg 303) for the age group <10 yrs, the dosage for Engerix-B should be 10 µg not 20 µg.