Colonic Carcinoma Associated with Malakoplakia

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ABSTRACT

Malakoplakia is an unusual chronic inflammatory response first described in the genitourinary tract by Michaelis and Gutmann in 1902. It is now known to occur in other locations including the gastrointestinal tract, skin, lungs and the central nervous system. Malakoplakia has been frequently misdiagnosed clinically as a malignant lesion. Similarly, when it occurs in the gastrointestinal tract (eg colon) in association with adenocarcinoma, it may lead to clinical and radiological overstaging of the tumour.

Keywords: Adenocarcinoma, colon, malakoplakia

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RESUMEN

La malacoplaquia es una respuesta inflamatoria crónica poco común, primeramente descrita en la zona genitourinaria por Michaelis y Gutmann en 1902. Ahora se sabe que puede presentarse en otros lugares, tales como el aparato gastrointestinal, la piel, los pulmones y el sistema nervioso central. La malacoplaquia ha sido con frecuencia mal diagnosticada clínicamente como una lesión maligna. De manera similar, cuando se produce en el aparato gastrointestinal (por ejemplo, el colon) en asociación con un adenocarcinoma, puede llevar a que se sobredimensione la etapa del tumor desde el punto de vista clínico y radiológico.

Palabras claves: Adenocarcinoma, colon, malacoplaquia

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CASE REPORT

The patient was a 69-year old female with medical history of diabetes mellitus, hypertension and arthritis. Surgical history included a Caesarean section 28 years previously, laparoscopic cholecystectomy in September 2008, repair of suture sinus tract in December 2008, vaginal hysterectomy in 2010 and the most recent being a supra-umbilical hernia repair (with mesh) done in February 2013. She presented to hospital ten weeks later with abdominal pain for two days, with increasing intensity, and diarrhoea. Computed tomography (CT) imaging showed thickening and enhancement of the middle portion of the descending colon with features suggestive of a primary colonic lesion, which involved adjacent

loops of small bowel. No discrete lymph nodes were identified and no free air or free fluid was seen within the abdominal cavity. A colonoscopy study was scheduled in view of the CT findings, which showed a friable, stenotic tumour, 68 cm from the anal verge, which extended 10 cm proximally obstructing approximately 80% of the bowel lumen. Histological examination of a biopsy of the lesion showed adenocarcinoma. Other significant laboratory findings included decreased haemoglobin (10.6 mg/dL), elevated carcinoembryonic antigen (19.46 ng/ml) and C-reactive protein (36.9 mg/dL).

Because of the CT findings, the working preoperative diagnosis of this patient was stage IV colon cancer. Definitive surgical management in this case was guided by not only the radiological staging, but also by intra-operative findings, which showed loops of small bowel firmly adherent to the descending colon, possibly representing an advanced stage of the disease. A left hemicolectomy with en-block resection of the jejunum was performed. The surgical specimen was subsequently submitted to the histopathology laboratory.

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The postoperative recovery of the patient was adequate and she was eventually discharged, to be followed-up by the surgical and oncology teams, once diagnosis and pathological staging was complete.

The surgical specimen was received in 10% buffered formalin, and included a segment of large bowel, 20 cm in length, with a firmly adherent segment of small bowel 8.0 cm in length. External examination showed a segment of small bowel firmly attached to the serosa of the colon by firm, irregular, tan grey tissue. The colonic segment was opened along its longitudinal axis, revealing a firm, fungating, grey tumour, 6 cm in greatest dimension, arising from the mucosa, and which on transverse sections appeared to invade the bowel wall. The subjacent pericolic fat showed a poorly demarcated, firm, grey infiltrating lesion which appeared to be continuous with the invasive colon tumour, and the muscle wall of the adjacent small bowel appeared to be involved. The small bowel mucosa was elevated at that point but did not appear to be involved by the tumour. Multiple matted and discrete lymph nodes were identified in the pericolic tissue.

Representative sections were taken from the descending colon tumour, the pericolic tissues, the adherent loop of small bowel, and the large and small bowel margins. Regional lymph nodes were also sampled. These were processed routinely, and 5.0 µm sections were cut and stained with haematoxylin and eosin (H&E).

Microscopic examination of sections taken showed a well-differentiated adenocarcinoma with invasion of the wall of the colon as far as the muscularis propria without extension into the pericolic fat. Present at the leading edge of the tumour (Fig. 1) were extensive sheets of histiocytes which extended outwards in an infiltrative fashion to involve the wall of the colon adjacent to the tumour, the pericolic fat

Fig. 1: At the tumour margin (lower half), there is an abrupt change to sheets of macrophages with scattered inflammatory cells [H&E $\times 100$].

and the muscular layer of the adherent small bowel. The histiocytes were large with small round nuclei and abundant, acidophilic, granular cytoplasm.

Also present within the infiltrate but in lesser numbers were lymphocytes, plasma cells and scattered eosinophils. Many of the histiocytes contained round, basophilic intracytoplasmic concretions pathognomonic for malakoplakia – the Michaelis-Gutmann bodies (Fig. 2). Examination of the lymph nodes showed no evidence of metastatic adenocarcinoma, but malakoplakia was present. Hence, based on the histologic evidence, the patient was diagnosed with well differentiated invasive adenocarcinoma of the colon, Dukes' A, pT2 pN0, (American Joint Committee on Cancer (AJCC), 7th edition), associated with malakoplakia of the large and small bowel and lymph nodes.

Fig. 2: Many histiocytes contain rounded laminated concretions – the Michaelis-Gutmann bodies (arrow) [H&E $\times 400$].

DISCUSSION

The association of malakoplakia and colonic adenocarcinoma is rare, with the majority of cases described in the literature occurring in the rectum and sigmoid colon (1, 2) and with a male predominance of 4:1 (1). Only one other case has been reported in the descending colon.

Largely, because of its rarity, the pathogenesis of the malakoplakia in cases of adenocarcinoma is uncertain. Possible causes include infections *eg E coli* and *Klebsiella* spp, an abnormal immune response and a disorder of macrophage response related to defective lysosomal function (3). Alteration in the normal gut flora and an unusual stromal response to tumour are other postulated mechanisms. Although there have been claims of an association between steroid use and malakoplakia (4), relatively few such cases have been reported.

Where the two conditions co-exist, malakoplakia almost always occurs adjacent to the invasive tumour and is usually a localized phenomenon, lending some support to the hypothesis of an unusual stromal response to the carcinoma. In our case, the malakoplakia extended from the invasive

margin of the tumour, a feature which is in keeping with other reports (2, 5). Malakoplakia also involved the muscularis propria, pericolic fat and regional lymph nodes. The adherence to loops of small bowel in turn mimicked direct tumour invasion – both on CT imaging and at surgery.

Previous reports have commented on the likelihood of overstaging the cancer where there is pericolic involvement and adherence to other intra-abdominal structures *eg* bladder, pelvic wall or small bowel (1, 4, 6) and we would wish to emphasize this point. Overstaging may result in attempts at palliative therapy or to referral of the patient for neoadjuvant chemotherapy. Extensive examination of the tumour in our patient revealed no spread beyond the muscularis propria and no metastases to regional lymph nodes, placing it as a Dukes' stage A tumour (pT 2, AJCC).

The largest meta-analysis of cases of malakoplakia and colonic adenocarcinoma (1) shows that Dukes' stage B tumours are overwhelmingly the most common stage at surgery and our case is one of the few reported cases of a

Dukes' stage A tumour associated with malakoplakia. Apart from the possibility of errors in staging and treatment of the cancer, malakoplakia itself does not appear to alter the prognosis of the tumour.

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