Malakoplakia and colorectal adenocarcinoma

AW Bates, S Dev, SI Baithun

Summary
We report a case of malakoplakia in association with colonic adenocarcinoma. Tumour-associated malakoplakia in the gastrointestinal tract is a rare finding, generally confined to the colon. It may be locally aggressive, with invasion of pericolic tissues, but is always located adjacent to the tumour. This contrasts with the often more diffuse, multifocal distribution of colonic malakoplakia in association with other pathologies.

Keywords: malakoplakia, colon, adenocarcinoma

Malakoplakia, an inflammatory condition first described by Michaelis and Gutmann in 1902,¹ is characterised by collections of histiocytes containing laminated, calcified Michaelis–Gutmann inclusion bodies. Though the mucosa of the urinary bladder is the typical site, malakoplakia has also been described in a variety of other locations including the gastrointestinal tract, lymph nodes, brain, skeleton, skin, breast, tonsils, pancreas and middle ear.^{2,3}

The gastrointestinal tract is the most common site for malakoplakia outside the urinary tract, and comprises 11% of all cases according to McClure.² Rarely, malakoplakia is associated with colonic carcinomas or adenomas: malakoplakia is present adjacent to the tumour and apparently represents a local response to it. It has, however, been suggested that small foci

of malakoplakia, which may be overlooked in routine practice, occur quite frequently. Gastrointestinal malakoplakia not associated with tumours may be more widespread or multifocal,⁴ though there is no consistent pattern. A variety of co-existing conditions including inflammatory bowel disease, ulcer, systemic lupus erythematosus, alcoholic liver disease, tuberculosis and combined immunodeficiency have been described in individual cases; inflammatory and infective conditions predominate, and underlying suppression of immune function may be a common factor in pathogenesis.²

We describe a case of malakoplakia of the sigmoid colon in association with adenocarcinoma and review the features of cases previously reported in the literature. The histology of a consecutive series of 102 colectomy specimens resected for colonic adenocarcinoma was reviewed to determine whether microscopic foci of malakoplakia were present.

Case report

A 67-year-old Asian man was admitted to hospital with a one-week history of colicky lower abdominal pain and constipation. Over the preceding three years a pyrexia of unknown origin had been extensively investigated without a cause being found, and repeated blood, sputum, urine and stool cultures were negative. The patient was a known asthmatic treated with 30 mg prednisolone a day for the previous year.

Table Malakoplakia and colorectal carcinoma: summary of reported cases

	Age/sex	Site	Tumour stage	Distribution of malakoplakia
Department of Morbid Anatomy, London Hospital Medical College and Department of Histopathology, St Andrew's Hospital, London, UK AW Bates SI Baithun	82 F	recto-sigmoid	Dukes B	no extra-mural spread
	80 M	rectum	Dukes B	spread to peri-colic fat
	45 F	rectum	not known (carcinoma)	colonic serosa
	72 F	sigmoid	adenoma	not known (biopsy)
	88 M	sigmoid	Dukes B (at least)	not known
	75 M	rectum	villous adenoma	confined to lamina propria
	64 M	rectum	not known (carcinoma)	not known
	72 M	rectum	not known (carcinoma)	not known
	71 F	transverse colon	Dukes B	spread into gastric wall
	79 M	rectum	Dukes B	peri-colic fat & lymph nodes
Department of Surgery, St Andrew's Hospital, London, UK S Dev	73 M	rectum	Dukes B	peri-colic fat
	59 F	rectum	Dukes B	not known
	83 M	rectum	Dukes B	spread to peri-colic fat
	65 M	sigmoid	Dukes B	spread to peri-colic fat
	77 M	recto-sigmoid	Dukes B	single nodule
	51 M	sigmoid	Dukes B	single microscopic focus
	74 M	caecum	Dukes C	single nodule
	67 M (present case)	sigmoid	Dukes B	spread to peri-colic fat

Figure Michaelis–Gutmann bodies within peri-tumoural histiocytes after staining for calcium (Von Kossa, $\times 60$)

On physical examination the patient was obese, with a pyrexia of 38.2°C. There was hypogastric tenderness and guarding and a 4 cm mass was palpable in the left iliac fossa. At sigmoidoscopy an ulcerated mass was seen 23 cm from the anal margin. A biopsy showed adenocarcinoma and a sigmoidectomy was performed. The pyrexia settled postoperatively.

The specimen consisted of 17 cm of colon with a 6 cm circumferential mass of firm, white tissue which extended into the peri-colic fat.

Histology sections showed a moderately differentiated adenocarcinoma arising from a severely dysplastic tubulo-villous adenoma. Tumour focally breached the muscularis propria, but there was no evidence of nodal, intravascular, or lymphatic spread. Partially surrounding the tumour and forming the bulk of the circumferential mass were sheets of histiocytes admixed with lymphocytes, which extended into peri-colic fat to the resection margin of the specimen. These histiocytes had granular cytoplasm and contained Michaelis–Gutmann bodies which stained with periodic acid Schiff and calcium stains (figure); positive immunohistochemical staining with CD 68 confirmed their histiocytic lineage. No organisms were identified intracellularly in Gram, Ziehl–Neelsen or silver-stained preparations.

Review of similar cases

We reviewed the histology from 102 colonic resections for adenocarcinoma received over a three-year period. Calcium stains were performed on areas showing atypical histiocytes. In only two cases were extensive collections of histiocytes present adjacent to the tumour, but in no case were inclusion bodies identified.

Summary points

- malakoplakia is a rare complication of colorectal carcinoma
- malakoplakia in such cases may be aggressive and locally infiltrative, but standard resection of the tumour appears to be curative
- long-term steroid therapy may predispose to the development of peri-tumoural malakoplakia

Discussion

Though malakoplakia was extensive, it was apparently confined to the area adjacent to the carcinoma, and although the patient's immunosuppressive therapy may have predisposed to its development, this case falls into the minority in which malakoplakia is a peri-tumoural phenomenon. Of the 18 cases summarised in the table, the mean age at presentation was 71 years, comparable to that of uncomplicated adenocarcinoma, and the male to female ratio was approximately 5:2. The majority of the tumours were Dukes stage B adenocarcinomas and all but two were in the recto-sigmoid region. Two cases associated with adenomas are also included. In some, malakoplakia was present only as a microscopic focus, whereas other reports described extensive deposits extending into adjacent fat, lymph nodes, and, in one case, the stomach. In all cases malakoplakia was found adjacent to the tumour: involvement of sites distant from the tumour, in the gastrointestinal tract or elsewhere, was not described. This contrasts with the multifocal gastrointestinal lesions and involvement of other organs reported in non-tumoural malakoplakia.^{5,6} No patient had a documented immunosuppressive disorder, though in the only two cases where a drug history was given the patient was receiving long-term corticosteroids. The presence of malakoplakia does not appear to have prognostic significance in cases of colonic carcinoma⁷ and when the tumour is resected malakoplakia has not been reported to recur.

The finding of intracellular Gram-negative bacilli within the histiocytes of non-tumoural malakoplakia has supported a hypothesis that infective agents are involved in its pathogenesis^{5,8,9} and this may also apply to malakoplakia associated with carcinoma, where a local alteration in gut flora has been postulated as a mechanism.¹⁰ An alternative hypothesis, which could account for the restriction of malakoplakia to the area immediately adjacent to a tumour, and for its presence at the deep surface of the tumour away from the bowel lumen, is that malakoplakia represents a stromal response to tumour.³ Tumour-associated gastrointestinal malakoplakia has not been described outside the colon, though malakoplakia associated with other underlying conditions can occur in various sites including the stomach, ileum, and appendix. This difference may reflect a specific role of the colonic flora in its pathogenesis. However, when intracellular microorganisms have been

sought in cases of peri-tumoural malakoplakia, including the present case, they have not been detected.⁷ It may be that colonic cancer is the only gastrointestinal malignancy resected in sufficient numbers to reveal the low incidence

of malakoplakia. The rarity of tumour-related malakoplakia, and the history of immunosuppression in some cases, suggest that systemic as well as local factors are involved in its aetiology.

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Severe pneumococcal disease and temporary splenic dysfunction

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Summary
We report a patient presenting with pneumonia in whom temporary splenic dysfunction was diagnosed by counting pitted red blood cells. This under-recognised condition caused a transient immunosuppression which may have had serious implications for our patient’s recovery.

Keywords: splenic dysfunction, pneumococcal disease, immunosuppression

We present a case of a common disease that demonstrates a new immunological observation. The case highlights temporary hyposplenism (box 1) which we believe is an under-recognised condition which could contribute to morbidity and mortality.

Case report

In March 1994 a previously fit 40-year-old caucasian woman presented to the Accident and Emergency department at the Chelsea and Westminster Hospital with a four-day history of left shoulder tip and left pleuritic chest pain. At home, she had deteriorated despite antibiotics, and on arrival was unwell, dyspnoeic at rest, with a tachycardia of 130 beats/min. Her blood pressure was 140/70 mmHg and she had clinical evidence of consolidation throughout her left lung. Her blood gases showed a pO₂ of 6.7 KPa, pCO₂ of 5.21 KPa and her pH was 7.30. The chest X-ray showed extensive consolidation of her left lung and patchy changes in her right lung. She had no relevant medical history, no pre-existing clinical or laboratory evidence of immunosuppression, but she smoked 20 cigarettes a day. A diagnosis of pneumonia was made.

She was treated with high-dose intravenous broad spectrum antibiotics, including penicillin G, but she deteriorated rapidly and developed severe respiratory failure requiring intubation and ventilation. She was transferred to the intensive care unit, where she was noted to have a refractory hypoxia despite a FiO₂ of 1.0, with 10 cm H₂O PEEP and IPPV. Supplementary ventilation with the Hayek negative pressure oscillator was used and she required inotropic support.

The causative agent was confirmed by blood culture to be *Streptococcus pneumoniae* (serotype 14) which was fully sensitive to penicillin G. *Klebsiella* was also grown in the sputum several days later. In addition to the investigations required for clinical management, blood was taken to assess her spleen function and specific anti-pneumococcal antibody levels as part of an ongoing study. Splenic function was assessed by counting pitted red blood cells (PRBC) in the circulation by direct interference microscopy.¹ This method has been validated in many studies and a raised PRBC level is accepted as a marker of impaired splenic function.^{2,3} In our laboratory, a level

Causes of hyposplenism
<ul style="list-style-type: none">• trauma• sickle cell disease• malignancy• alcoholism and drug addiction• systemic lupus erythematosus• HIV infection• reticuloendothelial block

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