Malakoplakia is an infrequent inflammatory reaction that characteristically affects the genitourinary tract and that, at least on clinical and macroscopic grounds, may occasionally simulate malignancy. Other organs and systems, however, can also be involved. In the gastrointestinal tract, malakoplakia is usually associated with other concomitant diseases such as ulcerative colitis, diverticular disease, adenomatous polyps, and carcinoma. The association of malakoplakia and adenocarcinoma of the colon and rectum is a rare event, with no more than 20 cases reported in the international literature. We present a series of six cases along with a review of the literature on this association.

**Materials and Methods**
From 1998 to 2002, 755 surgical specimens of colon-rectum with adenocarcinoma were registered in our hospital. We reviewed the clinical records and radiological exams (barium enema and CT studies) of every case. All the surgical specimens were examined and sampled following international standards. We retrospectively reviewed the histological slides with special attention to the stromal reaction at the infiltrating edge of the neoplasm. We selected six cases that fulfilled the classic histologic criteria of malakoplakia. Aside from hematoxylin and eosin, other stainings evaluated for this study included periodic acid Schiff (PAS), Prussia blue, silver methenamin, von Kossa staining, and CD68. Colorectal adenocarcinomas were graded and staged using the 2002 TNM classification.

**Results**
Males and females (age range, 48 to 71 years; mean 63.5 years) were equally affected (3:3) (Table 1). The patients presented with characteristic symptoms of colonic neoplasms (obstruction, melena, abdominal pain), and had typical radiologic images (Figure 1). All the cases were followed-up clinically between 3 and 25 months. Three patients died due to complications of the disease and three were alive at the last contact.

Grossly, four cases were of the stenosing type with severe narrowing of the lumina and circumferential desmoplastic reaction and two cases were exophytic. They measured between 3.5 and 8.0 cm in maximum diameter (mean: 5.5 cm), were located at the right colon (one case), left colon (three cases), and rectum (one case). Another case was multicentric, with three different tumors on the right (two foci) and left (one focus) colon.

All the cases were conventional intestinal-type adenocarcinomas, and most of them were at an advanced stage at diagnosis (pT3-4). A dense mixed inflammatory infiltrate was detected at the invading edge of all neoplasms (Figure 1). A closer view revealed leukocytes, lymphocytes, plasma cells, and histiocytes haphazardly intermingled with stromal cells. Frequently, histiocytes contained intracytoplasmic eosinophilic inclusions (Michaelis-Gutmann bodies) that also stained with PAS, Prussia blue, von Kossa, and silver techniques. Lymph nodes showed metastatic seed in three cases but no trace of malakoplakia was detected in any case.

**Discussion**
Malakoplakia is a classical term that defines a particular stromal inflammatory reaction that pursues a benign, although chronic, course. Von Hansemann first described it in a necropsy study in 1903, when he found a macrophagic infiltrate with PAS positive intracytoplasmic inclusion bodies in the urinary bladder of a 66-year-old man who died of...
Table 1. Reported cases malakoplakia and colorectal adenocarcinoma.

| Case | Age/sex | Presenting symptom | Location | Macroscopic growth pattern | Histology | G  | TNM grading and staging | Follow-up (months) |
|------|---------|-------------------|----------|---------------------------|-----------|----|--------------------------|---------------------|
| 1    | 67/M    | Weight loss       | Left colon| Stenosing                 | Intestinal-type | G2 | pT3/pN0                  | 25, alive          |
| 2    | 71/M    | Weight loss       | Multifocal| Stenosing                 | Intestinal-type | G3 | pT2/pN0                  | 5, DOD              |
| 3    | 66/F    | Weight loss       | Left colon| Exophytic                 | Intestinal-type | G1 | pT3/pN1                  | 12, alive           |
| 4    | 48/F    | Obstruction       | Rectum   | Stenosing                 | Intestinal-type | G3 | pT4/pN2/M1-hep           | 7, DOD              |
| 5    | 58M     | Obstruction       | Right colon| Stenosing                | Intestinal-type | G2 | pT3/pN1                  | 3, DOD              |
| 6    | 71/F    | Melena            | Left colon| Exophytic                 | Intestinal-type | G1 | pT2/pN0                  | 3, alive            |

DOD: died of disease

Figure 1. Low-to-high power view sequence (original magnifications: x15, x40, and x100) of case 3 showing the interface between adenocarcinoma and inflammation at the same area (A, B, and C). Histologic detail (original magnification x400) of the malakoplakia showing typical Michaelis-Gutmann bodies stained with Pas (D), Prussian blue (E), and von Kossa stains (F) (arrows in D and F).
pulmonary tuberculosis. The author coined the term malakoplakia, which means “soft plaque”. Posterior

[AUTHOR: Do you mean posterior of the urinary bladder? Is this common phraseology?] ultrastructural studies showed that these inclusion bodies were composed of mineralized organic material arranged in concentric layers surrounded by a simple, lysosomic-type, membrane.13

Although urogenital and gastrointestinal tracts are amongst the most frequently involved locations, involvement of other organs such as the pancreas, lymph nodes, skin, lung, adrenal, vagina, and brain, have also been reported.6 Mean age is around 45 to 50 years, and males are slightly more affected than females.

Despite the fact that its origin still remains a matter of controversy, a significant number of patients with malakoplakia suffer from other “debilitating” processes, such as cancer or immunodepression due to AIDS, tuberculosis, sarcoidosis, renal transplantation, or chemotherapy.6 Prolonged steroidal therapy in neoplastic patients has been incriminated in the development of peritumoral malakoplakia in some cases.6 On the other hand, as a large number of microorganisms are seen in the lesion, an infectious origin has been repeatedly proposed.14 In fact, some bacteria, mainly coliforms, frequently appear, partially disintegrated, in the histiocytic phagolysosomes.8 In immunocompromised patients other organisms like virus and fungi have been also identified.14

From a practical point of view, the relevance of this lesion resides in that it can present a pseudotumoral appearance not only on clinical and radiological exams, but also in the surgical room or on the pathological gross exam. Typically, malakoplakia grows as a hard and solid mass with geographic contours and smaller satellite nodules. When accompanying carcinomas at any site, it can be very difficult to ascertain by the naked eye which is the neoplasm and which the inflammation.

Some authors hypothesize that the coincidence of malakoplakia with adenocarcinoma of the colon and rectum might start with distortion of the local flora induced by the tumor.8 The specific location of the malakoplakia in the vicinity of the neoplastic invading border, but not mixing with it, favors this theory. This peculiar arrangement of the binomy neoplasm–inflammation may make it difficult for the pathologist to ascertain the exact location of wall infiltration by the neoplasm. Furthermore, there are some cases of malakoplakia that also affect regional lymph nodes or even other abdominal organs. In these examples the inflammation may give the false impression of metastatic seed, thus complicating even more the correct diagnosis.8 However, the opposite situation may also occur. Actually, some authors advise of the necessity for a careful search for colorectal neoplasia when malakoplakia appears on histologic grounds.8

To summarize, malakoplakia associated with adenocarcinoma of the colon and rectum is an incidental histologic finding that seems to have no influence on the prognosis and survival of patients. This association has been very rarely reported in the literature. Although rare, the coincidence of these two conditions may be more frequent that previously believed probably because, in routine practice, pathologists pay attention to the neoplasm without considering the associated inflammation.

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