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Case report

Colitis cystica profunda associated with diverticulosis and calcification mimicking colorectal carcinoma: a case report and a brief literature review

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Summary

Colitis cystica profunda (CCP) is a rare, uncommon and nonneoplastic condition that can occur anywhere in gastrointestinal tract, but its main occurrence is in the rectum and sigmoid colon. It is characterized by the presence of mucin filled cysts, lined by benign epithelium, beneath the muscularis mucosae, usually confined to the submucosa, and it can clinically and radiologically mimic a neoplasm. Here we report a rare case of CCP in a patient with a 2-months history of abdominal pain and severe anemia, associated with diverticulosis. The knowledge of this entity and its differential diagnosis, in particular with the intestinal mucinous adenocarcinoma, is necessary, as it can be a clinically and histological mimic of a malignant neoplasm.

Key words: colitis cystica profunda, colorectal carcinoma, mucinous carcinoma, intestinal bleeding, diverticulosis

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Introduction

Colitis cystica profunda (CCP) is a rare, uncommon and nonneoplastic condition that can occur anywhere in gastrointestinal tract, but its main occurrence is in the rectum and sigmoid colon. It is characterized by the presence of mucin filled cysts, lined by benign epithelium, beneath the muscularis mucosae, usually confined to the submucosa, and it can clinically and radiologically mimic a neoplasm.
Here we report a rare case of CCP in a patient with a 2-months history of abdominal pain and severe anemia, associated with diverticulosis.
The knowledge of this entity and its differential diagnosis, in particular with the intestinal mucinous adenocarcinoma, is necessary as it can be a clinically and histological mimic of a malignant neoplasm.

Case description

A 65-year-old woman was admitted to our institute due to the presence, for several months, of abdominal pain that accentuated in the last two months, especially in the lower quadrants of the abdomen, with regular hive.

The patient had a family history of colon cancer and a history of atrial fibrillation that was under pharmacological treatment.
Laboratory tests showed severe anemia. Subsequently, the patient underwent a fecal occult blood test, which was weakly positive, followed by a colonoscopy. Colonoscopy showed a sigmoid colon with diverticula and traces of bright red blood material.
In the context of diverticulosis, a voluminous vegetating neoformation was found and biopsied.
Histological examination of the endoscopic biopsies identified only fragments of granulation tissue.
The CT examination confirmed the diffuse diverticulosis of the sigmoid colon, associated with wall thickening and inscribed calcification. No lymphadenopathy was documented along the main abdominal and pelvic stations. Intra-abdominal effusions were not present.
In consideration of the clinical-instrumental findings and the patient's family history, it was decided to perform video laparoscopic sigmoidectomy.
Grossly, the surgical specimen of sigmoid colon measured 15 cm in length with perivisceral adipose tissue. At the opening of the surgical resection, along the antimesenteric side, the bowel's wall was thickened and narrowed and, at 2 cm from the distal margin, a polypoid lesion was found. On its cutting surface, the lesion showed a mucinous appearance, with areas of increased consistency similar to calcifications; numerous diverticula were detected in the remaining mucosa.
The histological analyses of the polypoid lesion showed mucin-filled cysts in the bowel wall beneath the mucosal layer (Fig. 1). The diagnosis of colitis cystic profunda associated with diverticulosis and focal diverticulitis was rendered (Fig. 2).
The post-surgical course was uneventful and the patient was discharged 4 days after surgery.

Discussion

CCP is a rare, uncommon and nonneoplastic condition. There are a few cases reported in the medical literature [1-4] and it is well described since the 18th century when Stark identified this lesion for the first time during an autopsy; later in 1863, Virchow introduced the term colitis cystic polyposa [5-6].
This benign entity can occur anywhere in gastrointestinal tract (gastritis cystica profunda in stomach, enteritis cystica profunda in small intestine) and may diffusely involve the entire large bowel but mainly occurs in the rectum and sigmoid colon [7]. The etiology is unknown and remains controversial; due to the frequent association with inflammatory bowel disease, diverticulosis or ischemia, the cystic formations are thought to arise after mucosal ulceration or inflammatory damage to the submucosa that stimulate outgrowth of epithelial elements into deeper layers of the bowel wall [8]; a congenital origin was also proposed [9] but since CCP is almost always associated with inflammation, its congenital origin seems unrealistic.
Usually CCP occurs in the third and fourth decades of life with a male predilection, but rare cases have been also described in pediatric age [9,10].
CCP is characterized by the presence of mucin filled cysts lined by benign epithelium, surrounded by lamina propria, beneath the muscularis mucosae; although usually confined to submucosa, involvement of the muscularis propria and serosa have been reported [11].
CCP can have diffuse or localized distribution: the localized form, predominantly polypoid, can clinically and histological mimic an adenoma or a malignant lesion, it has been described in association with conditions such as rectal prolapse and solitary rectal ulcer. The diffuse form, involving a variable length of the mucosa, has been described in conditions such as inflammatory bowel disease, radiation and infectious colitis; moreover, an association with adenocarcinoma [8,12] or diverticulosis/diverticulitis [13], like in our case, has been reported.
The nonspecific and variable signs and symptoms (from asymptomatic to rectal bleeding, mucus discharge, abdominal or perineal pain, tenesmus, intestinal obstruction, altered bowel habits) are all compatible with colorectal adenocarcinoma, so an endoscopic examination and simultaneous biopsy is mandatory.
Endoscopic features are not specific: usually CCP presents as a nodular or polypoid lesion, with or without ulcerated mucosa.
Transrectal ultrasonography, when available, can help and usually shows hypoechoic and anechoic cysts in the submucosa layer without deeper infiltration and without associated lymphadenopathies.
CT and/or MRI show non-infiltrating submucosal cyst lesion with some loss of perirectal fatty tissue and thickening of elevator ani muscle, without local or regional lymphadenopathies [14].
In our case, CT showed widespread diverticulosis of the sigma, with wall thickening and inscribed calcification; no local or regional lymphadenopathies
Small endoscopic biopsies are usually unrevealing, if not including the submucosal layer, as in our case, in which, the biopsies revealed only the presence of fragments of granulation tissue.
The histological findings that allow a definitive diagnosis are better appreciable in resected surgical specimens.

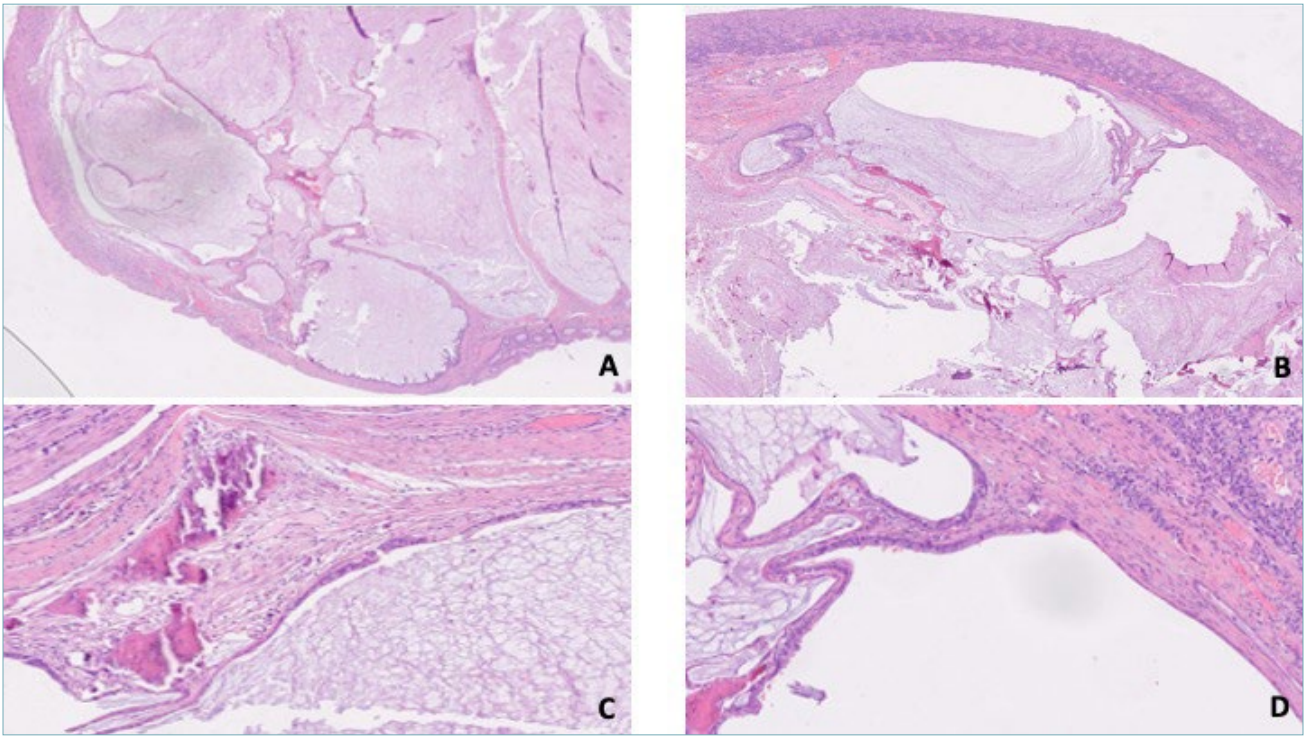

Figure 1. Mucin filled cysts of variable size, below the muscularis mucosae (a,b,c,d) with osseous metaplasia (c).

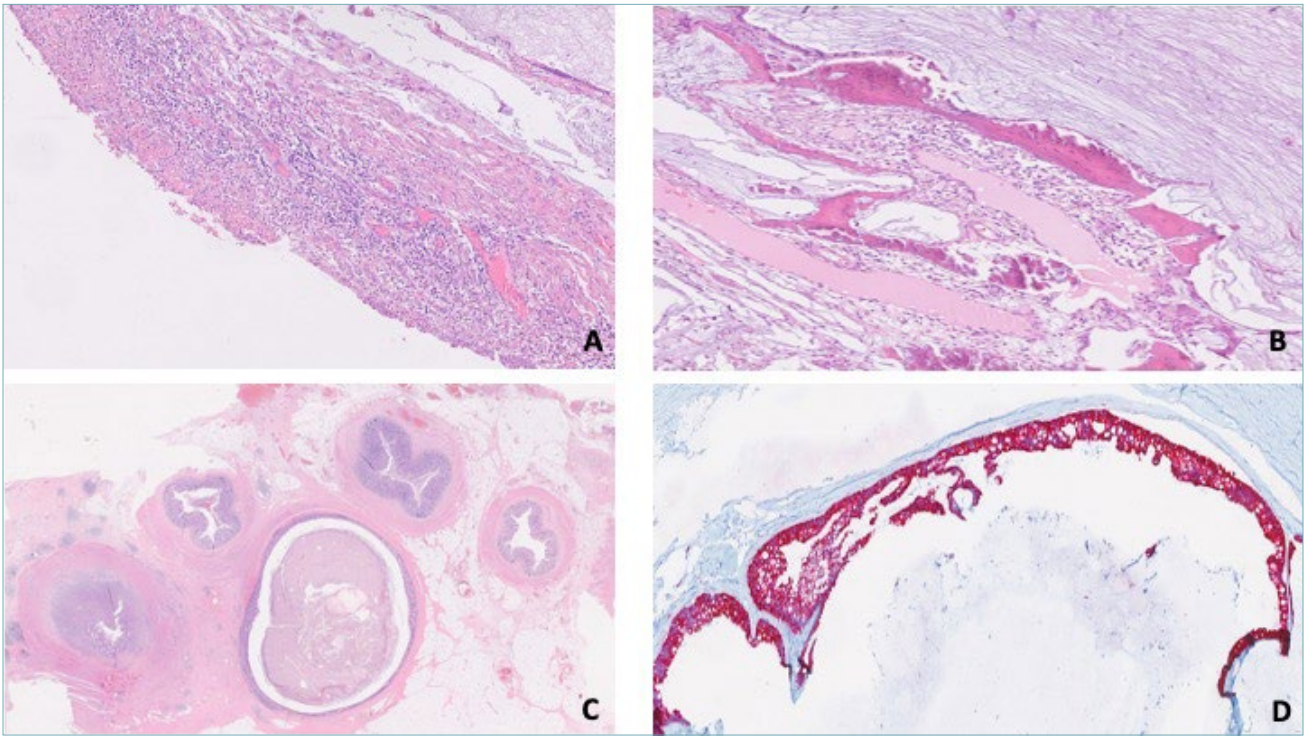

Figure 2. The superficial mucosa is diffusely eroded (A), with osseous metaplasia (B). The cysts are lined by CK20+ epithelial cells (D) with adjacent diverticulosis (C).

Microscopically CCP shows, in the localized form, a polypoid lesion with atrophic overlying mucosa; in our case the mucosa was diffusely eroded, covered by fibrin-leukocytic exudate and replaced by granulation tissue. CCP is typically characterized by misplaced colonic mucinous epithelium, without cellular atypia, forming mucin filled cysts of variable size below the muscularis mucosae, usually in the submucosa, but that can intrude into the muscularis propria of the colonic wall, like in our case, up to the serosa [11]. In our case the lining of the cysts was focally disrupted and discontinuous and often assumed a pseudopapillary morphology

The surrounding peri-tumoral connective tissue, usually, shows fibrosis, chronic inflammation and, as in the present case, the presence of granulation tissue, extravasated mucin from ruptured cysts with inspissated mucin and dystrophic calcification up to osseus metaplasia with bony trabeculae.

Mesenchymal metaplasia, in particular osseus metaplasia, in the gastrointestinal tract is exceedingly rare and has been documented in many benign and malignant lesions such as adenomatous or non-adenomatous polyps, gastric carcinoid, rectal adenocarcinoma, appendiceal mucinous neoplasm [15]. The pathogenetic mechanism is unclear and many theories have been proposed, such as inflammatory process as one of the factors causing osteogenic stimulation, extravasation of mucin as a stimulatory role in ossification; fibroblast transformation into osteoblast along with persistent chronic inflammation; epithelial elements may prompt the ossification of mesenchymal tissue [16]. To our knowledge, there are few cases described with calcifications, fibrosis and ossified deposits within the mucin lakes [15,16].

The most important differential diagnosis of CCP includes the mucinous adenocarcinoma (a subtype of colorectal carcinoma with mucin lakes, comprising at least 50% of tumor mass, according to WHO), especially in localized, polypoid form [17], but the absence of histological features of malignancy such as infiltrating morphology, stromal desmoplasia, atypical epithelium floating in mucin, glandular atypia and dysplasia of overlying mucosa, confirmed our diagnosis of CCP. In some challenging cases, immunohistochemistry with Ki-67, p53 and E-cadherin can aid in the differential diagnosis with adenocarcinoma.

Any other polypoid and intramural masses of the colon and rectum (adenomatous polyps and its inverted or pseudo invasion aspect, polypoid inflammatory granulomas, mucosal prolapse syndromes, leiomyoma, lipoma, carcinoid tumor, pancreatic heterotopia, sarcoma), inflammatory bowel disease and endometriosis should all be considered in the differential diagnosis [8,10].

Treatment of CCP is mostly conservative and a surgical approach is only indicated in patients with severe and persistent symptoms such as intestinal obstruction, significant rectal prolapse or for persistent bleeding, like in our case.

Our case emphasizes that histology, especially on the surgical specimen and not on the superficial bioptic samples, remains prominent for a correct diagnosis of CCP and that radiological and endoscopic diagnosis are not always specific.

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Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Ethical consideration

Ethical review and approval were not required for the study on human participants in accordance with the local legislation and institutional requirements. The patient provided her written informed consent to participate in this study.

Authors contribution

All listed authors contributed to the production of this manuscript and are listed in the appropriate order.

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