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Pseudomembranous colitis with presence of signet – ring cells: report of two cases and review of the literature

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Abstract

We describe two cases with pseudomembranous colitis: the first case concerns a 73-year-old male patient with clinical history of cardiovascular disease and pulmonary insufficiency, admitted to the hospital for urinary tract infection and was treated with broad-spectrum antibiotics for a long period of time. During his hospitalization he developed abdominal pain and haematochezia. The second case concerns a 64-year-old woman treated with antibiotics for community-acquired pneumonia. After the treatment she developed abdominal pain and diarrhea. In both cases the colonic biopsy showed pseudomembranous colitis with presence of signet-ring cells within dilated crypts of the colonic mucosa. The presence of signet–ring cells is a rare finding in pseudomembranous colitis and may lead to misdiagnosis of signet-ring carcinoma of the colon.

Keywords pseudomembranous colitis, signet – ring cells, immunoprofile

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Introduction

The diagnostic histologic criteria for pseudomebranous colitis (PMC) are well documented. It has also been documented however in the literature that pathologists should be aware of the possibility that along with the classic features of PMC the presence of signet-ring cells (SRCs) on the surface epithelium and crypts of the lesion should be assessed with caution in order to avoid a misdiagnosis of carcinoma [1-6], especially since SRCs are most commonly associated with mucus-producing malignant epithelial tumors. They may also be found however in thyroid lesions (i.e., nodular goiter), nonepithelial neoplasms (i.e. signet-ring lymphoma) and in reactive conditions in a variety of organs (i.e., degenerated lymphocytes and vacuolated smooth-muscle cells in transurethral prostatectomy specimens) [1,3].

In the literature there are only 20 cases of PMC associated with signet-ring cells without any evidence of carcinoma of the colon or carcinoma in another organ [1-6]. With the aim of increasing awareness of this rare potential pitfall and to avoid misdiagnosis we report two cases of PMC with the presence of signet-ring cells within dilated crypts of the colonic mucosa.

Case series

A 73-year-old male patient with clinical history of cardiovascular disease and pulmonary insufficiency was admitted to the hospital for urinary tract infection and was treated with broad-spectrum antibiotics for a long period of time. During his hospitalization he developed abdominal pain and hematochezia. The clinical and endoscopic impression was compatible with ischemic colitis and colonic biopsy was performed.

The second case is a 64-year-old woman treated with antibiotics for community-acquired pneumonia. After the treatment she developed abdominal pain and diarrhea. A colonoscopy and biopsy was performed with the probable diagnosis of PMC.

Colonic biopsies were fixed in 10% neutral-buffered aqueous solution of formalin and processed for light microscopy. In addition, the two cases were stained immunohistochemically for p53, Ki-67, cytokeratin 7 and cytokeratin 20.

The colonic biopsies revealed foci of ulceration, cystic dilatation of crypts covered by exudate composed of mucus and fibrin containing polymorphonuclear leukocytes. In some areas the crypts were replaced by signet-ring cells, confined above the basement membrane of the crypts and did not infiltrate the lamina propria (Fig. 1). A small number of SRCs were

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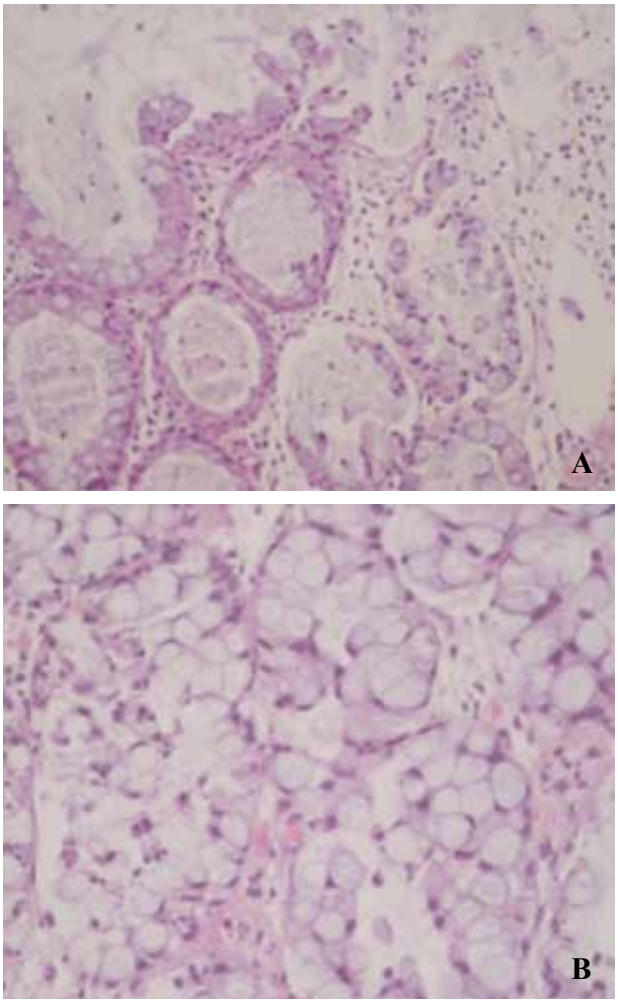

Figure 1 Colonic mucosa with dilated crypts and presence of signet-ring cells (H.E. x100) A, Signet-ring cells in dilated crypts (H.E.x200) B

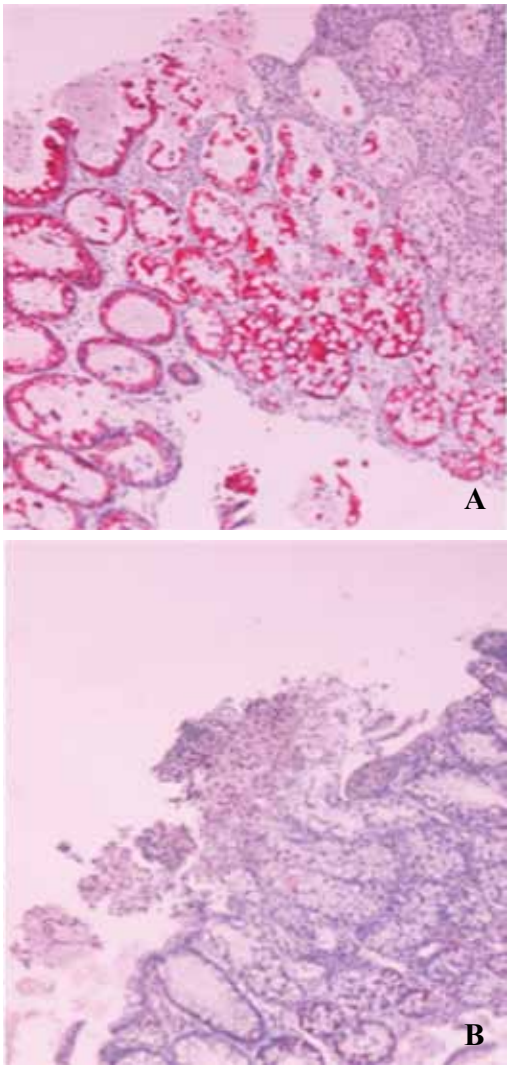

Figure 2 Signet-ring cells cytokeratin 20 positive (x40) A, Signet-ring cells MIB-1 negative (x40) B

seen in the pseudomembranes. The SRCs had peripherally placed nuclei and intracytoplasmic vacuoles. The nuclei were not enlarged, displayed uniform chromatin distribution and no nucleoli or mitoses were observed.

The signet-ring cells were positive for cytokeratin 20 and negative for cytokeratin 7, MIB-1 and p53 (Fig. 2).

Discussion

In 1996 Schiffman [1] first described a case of PMC associated with signet-ring cells. The incidence of the presence of signet-ring cells in PMC has not been fully evaluated. Five of the cases in the literature were associated with toxic megacolon [1,2,4,5]. However, in a more recent study, of 14 cases with PMC with signet-ring cells, none of the patients had associated toxic megacolon [6], comparably to our cases. In the same study by Wang et al, the incidence of PMC with signet-ring cells was 28% whereas in our series of 56 cases with PMC in the last ten years the incidence is 4%. The differential diagnosis between PMC with signet-ring cells and signet-ring cell carcinoma in cases where the basement membrane of the crypts is not fully preserved, can be made using immunohistochemical stains against p53 and Ki-67. In PMC the signet-ring cells are negative where as in signet-ring cell carcinoma they are positive for both antigens [6]. On occasions where the basal lamina is preserved one can demonstrate the benign nature of these SRCs by using anti-collagen IV and anti-laminin antibodies where it can be clearly demonstrated that these cells are confined entirely within the basal lamina surrounding the crypts [4]. These cells can also be seen, as in our cases, within the exudates constituting the pseudomembranes.

Regarding the biologic mechanism by which SRCs are formed many hypotheses have been put forward, none of which however can adequately explain the process of SRC formation under different circumstances. It has been proposed

that SRCs in PMC might be associated with the fatal form of PMC [2], however neither our cases nor the fourteen cases of other investigators were fatal [6].

Chen [9] suggested that the signet-ring appearance in Peutz-Jeghers polyps could be mechanically induced by the torsion or stretching of the polyp, maybe this can give an explanation for the formation of SRCs in PMC as well. Others [3] have suggested that signet-ring cell formation in PMC could be related somehow to inflammation. However, as previously stated, these hypotheses still remain to be proven and in general SRC morphology in tissues benign or malignant is an issue that requires further research so that the whole array of events that lead to this morphologically distinct entity can be elucidated.

If anything, these cases indicate the importance of paying particular attention to the history, endoscopic findings, and microscopic features of the SRCs which are confined to the crypts and the surface epithelium without infiltration of the lamina propria thus avoiding a misdiagnosis [8].

The occurrence of benign signet-ring cells in the colon may greatly increase the risk of a diagnostic mistake, especially in small, endoscopic biopsies [7]. The use of immunohistochemistry can be helpful in difficult cases but the most important parameter in the correct diagnosis is awareness of the issue and efficient co-operation between clinicians and pathologists.

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