A case of unusual histiocytic colitis in a chronic alcoholic obese patient with ankylosing spondylitis

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Short Abstract

A 64 year-old Caucasian man was first investigated 21 years ago for persistent diarrhoea. A colonoscopy revealed an erosive pancolitis with unusual vacuolated macrophages. Characteristics of ulcerative colitis or Crohn's disease were absent. Similar findings were observed consistently over the following years. A treatment with Sulfasalazine, Methotrexate or Budesonide was efficient. Histiocytic colitis is rare, and the various causes and different diagnoses are reviewed. The cause for the chronic pancolitis in this obese chronic alcoholic remains unknown at the time of writing. Links to the dyslipidaemia and chronic ankylosing spondylitis presented by the patient are possible hypotheses worth investigating further. (Acta gastroenterol. belg., **2018**, 81, **327-329**).

Keywords : chronic colitis, histiocytes, ankylosing spondylitis, dyslipidaemia.

Introduction

Chronic colitis has a rising incidence globally and it is most usually diagnosed as ulcerative colitis (UC), Crohn's disease (CD) or microscopic colitis (MC), with prevalences in Europe of 0.5%, 0.3% and 0.015% respectively (1-2). Other causes include infectious, drug-induced, vascular, idiopathic or eosinophilic colitis, a new entity described in the past decade (3). In this paper we present a case of chronic histiocytic pancolitis of unknown origin, responsive to Sulfasalazine, Methotrexate and Budesonide.

The case history

The patient, a chronic alcoholic obese non-smoker Caucasian man aged 64 at the time of writing, presented at the Hospital of Saint-Joseph (Gilly, Belgium) 21 years ago. He was complaining of diarrhoea and abdominal pain without fever. His medical history included ankylosing spondylitis, dyslipidaemia and gouty arthritis. Clinical abdominal examination revealed sensitivity in the left inferior quadrant of the abdomen. His lipase level was almost double their maximum normal values and following ultrasound confirmation he was treated for acute pancreatitis. However, whilst his pancreatitis subsided, his diarrhoea persisted, negative for Salmonella, Shigella, *Yersinia enterocolitica*, Campylobacter, *Escherichia Coli* and common parasites (*Giardia lamblia, Enterobius vermicularis,…*).

Following a CT-scan indicating a thickened hepatic flexure of the colon, the patient underwent an upper and lower endoscopy. The gastric and ileal mucosa were normal but erosions were observed involving the whole colonic mucosa. Lesions were particularly florid in the sigmoid and right colon.

Pathological examination of the colonic biopsies could neither confirm the initial hypothesis of ulcerative colitis nor conclude to a Crohn's disease. The colonic glandular crypts' architecture was preserved, the chorion was oedematous and congestive, with a mild excess of lymphocytes and plasma cells. There were focal neutrophils and eosinophils, but mainly numerous vacuolated macrophages arranged in clumps in superficial and deep parts of the mucosa, but not in the submucosa (Figure 1). Duodenal biopsies revealed moderate

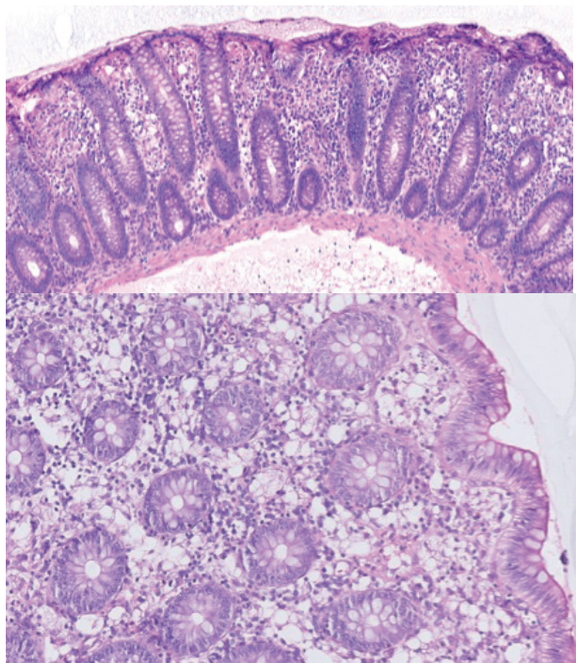

Fig. 1.

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chronic inflammation with excessive intra-epithelial and chorionic lymphocytes and plasma cells, and included again numerous clumps of vacuolated macrophages. The villous architecture was slightly altered. The histiocytes' vacuoles did not contain glycogen nor mucus, and were not characteristic of either Whipple's disease or malakoplakia.

Assuming the patient was suffering from chronic inflammatory bowel disease (IBD), treatment of Sulfasalazine 2g three times a day was begun.

One month later, the patient's symptoms were improved, and his rectosigmoidoscopy appeared normal. However, numerous macrophages were still observed throughout the colonic mucosa.

One year thereafter, the chronic alcoholic patient suffering a recurrent bout of pancreatitis, Sulfasalazine was discontinued, considered a possible aggravating factor. He remained asymptomatic two years. Sulfasalazine was then re-introduced though less effectively than the first time.

At electron microscopy, the macrophages' mitochondria appeared normal, the rough endoplasmic reticulum was slightly dilated, nuclei had irregular outlines without macronucleoli. The cytoplasmic vacuoles, irregular in shape and number, containing finely granular or lamellar material, were neither characteristic of lipids, glycogen, microorganisms or virus-like particles. A hypothesis of lysosomial drug toxicity was then formulated.

Two years later, following an exacerbation of the patient's ankylosing spondylitis, Sulfasalazine was exchanged for Methotrexate and the patient remained asymptomatic for eight years. When his symptoms recurred, histological lesions were found to be identical to those first described. A trial of Budesonide of 9 mg per day led to rapid improvements, and to this day, the patient has remained asymptomatic when kept on this dose, with diarrhoea recurring only with decreasing dosage, as clinically tried 2 years ago and just recently (Figure 2).

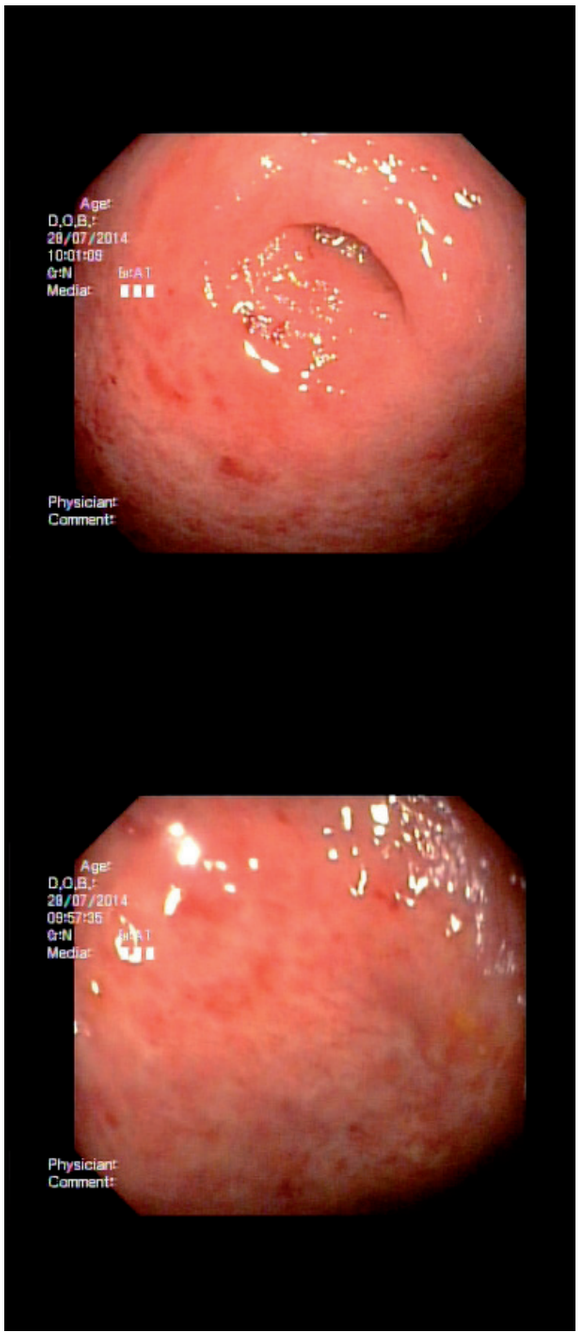

Fig. 2.

Discussion

This 64 year-old chronic alcoholic man with ankylosing spondylitis suffering from symptomatic chronic histiocytic colitis responsive to Sulfasalazine, Methothrexate and Budesonide led to many differential diagnostic hypotheses.

Ulcerative colitis (UC) was the first diagnostic hypothesis, in view of the widespread superficial continuous lesions throughout the colon and given the absence of small bowel lesions (except microscopic duodenal lesions). However, the architecture of the glands was preserved, unlike the typical UC characteristics of severe architectural crypt distortions and crypt abscesses (4). Moreover, histiocyte accumulation is not a classic characteristic of UC although it has been described (5).

The hypothesis of Crohn's disease (CD) was discarded early on, as the lesions were continuous, never transmural with no sign of typical ulceration nor granuloma, and the patient never developed any of CD's complications (stenosis, fistula, abscess,...) over 21 years (4). In addition, the presence of vacuolated histiocytes has not been described in the literature.

However, Orlando et al. reported in 2009 that up to two-thirds of patients with ankylosing spondylitis presented asymptomatic bowel inflammation, which in 5% to 10% of cases was overt IBD (6).

Macroscopically, the mucosa usually looks normal in collagenous and lymphocytic colitis (7). This was not

the case in the present patient. However, histologically, the number of intraepithelial lymphocytes was increased, and the vacuolated macrophages within the lamina propria could simply be linked to local inflammation, as for UC and CD (6-7).

Iatrogenic colitis is important to bear in mind, as removal of the causing agent will lead to rapid improvement of the disease. Although electron microscopy was suggestive of lysosomial drug toxicity, this was never confirmed, and stopping the patient's homeopathic drugs of unknown composition tried 15 years ago had shown neither clinical nor histological improvement. Furthermore, the presence of vacuolated histiocytes has not been described in iatrogenic colitis.

The presence of eosinophils in the mucosa led the medical team to look for a parasitic cause, which can have varying endoscopic and histologic features (8). However, the patient had not travelled abroad, he had not been in contact with endemic sources of parasites in Belgium, his blood levels of eosinophils were never high, and stool samples and biopsies were always negative for *Ascaris spp*, *Fasciola hepatica*, bilharziosis and Trichinella spp. An infectious aetiology was carefully excluded over the past 21 years, and research for mycobacteria always came back negative. Again, the presence of vacuolated histiocytes has not been described in parasitic or infectious colitis.

The diagnosis of eosinophilic colitis is a challenge as eosinophils can be observed in several pathologies (drug-induced colitis, parasites, cancer,…). Histologically, there is no consensus: eosinophil infiltration can be patchy or diffuse, from mucosa to serosa, with in addition varying normal values between <10 to >30 eosinophils per high-power field (HPF) in the rectum and caecum respectively. It is therefore important to specify and accurately localise the biopsies for histological interpretation (9). In the present case, only 4-5 eosinophils per HPF were observed. Moreover, the presence of vacuolated histiocytes has not been described in association with eosinophilic colitis.

Xanthomas of the gastro-intestinal tract are characterized by the accumulation of "foamy" histiocytes in the lamina propria, submucosa, muscularis propria, and/or subserosa. Although this phenomenon is much more common in the stomach, xanthomas can be observed in the colon in association with hyperlipidaemia (10-11). Diffuse colonic lesions such as the ones observed in this patient have been reported in a young 16-year old patient with febrile ileocolitis complicated by a megacolon of unknown origin (12).

Several arguments support this hypothesis: 28% of patients have elevated triglycerides, they are generally male, suffering from obesity, and presence of *Helicobacter Pylori* (positive 2 and 4 years ago in the present case) is known as a promoting factor (10).

Histiocytic disorders of the gastrointestinal tract have recently been reviewed as being of unknown, neoplastic or reactive origin (12). This raises the question of two distinct mechanisms in the present patient: ankylosing spondylitis is reportedly associated with IBD, and our patient's bowel inflammation does indeed respond to classic IBD treatment. However, numbers of vacuolated macrophages remained unaffected, their continuous presence over the past 21 years is therefore likely to be linked to another phenomenon, maybe the patient's dyslipidaemia and xanthomatosis.

In conclusion, this unusual case of chronic histiocytic colitis responding to Sulfasalazine, Methothrexate and Budesonide in a chronic obese alcoholic patient with ankylosing spondylitis has for 21 years puzzled clinicians and pathologists alike. It would be interesting to compare various similar cases to understand the underlying causes and possibly separate mechanisms involved, in view of both ankylosing spondylitis and hyperlipidaemia.

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