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The Course of Fistulizing Crohn's Disease Excluding Ano-Perinéal Lésions (Apl) On Biotherapy.

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ABSTRACT

Castelman's disease is a rare clinicopathological entity characterized by a united or pluricentric lymph node enlargement. The diagnosis is usually made by anatomopathological examination after surgery. We report the case of unicentric abdominal Castelman disease revealed by upper gastrointestinal bleeding.

Introduction

Crohn's disease is a chronic disabling inflammatory disease affecting the entire digestive tract. The development of biotherapy, in the forefront of which are the anti-TNF alpha drugs, has led to changes in the management of this disease, particularly in terms of improving fistulising forms of the disease outside the anoperineal lesions. We report on the evolution of fistulising Crohn's disease excluding APL under biotherapy.

Materials and methods

This is a retrospective descriptive study including all patients with fistulizing Crohn's disease phenotype put on biotherapy, conducted over a period from January 2015 to January 2021 at the department of "Medecine B" of CHU Ibn Sina. We studied the following data: age, gender, patient history, disease phenotype, and type and duration of treatment. We excluded patients with ano-perineal involvement alone. All our patients underwent endoscopic (FOGD and colonoscopy) and radiological (Entero-MRI) assessment.

Results

We collected 28 patients (62%) with Crohn's disease of fistulizing phenotype: 25 patients (90%) had digestive fistulas with ano-perineal lesions and 03 patients (10%) had digestive fistulas without LAP. The average age at diagnosis was 40 years (extremes ranging from 20 to 60 years). There were 19 men (64%) and 9 women (36%) with a sex ratio of M/F=2. The average age of the disease was 11 years (6-20 years). 16 patients (60%) initially had glairo-bloody diarrhoea and 12 patients (40%) had König's syndrome. A biological inflammatory syndrome was present in all patients. 16 patients (60%) were active smokers. 6 patients (21%) had a history of appendectomy. 12 patients (42%) had an ileo-caecal resection and 2 cases (7%) had familial CD.

Table 1. Montreal classification, Crohn's disease phenotype and location of digestive fistulas in our patients

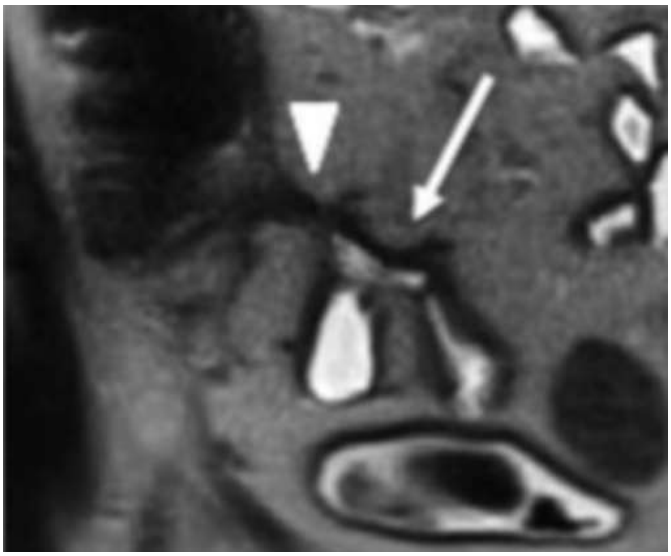
	Number of cases n(%)
Montreal Classification :	
Colic (L2)	n=8 (46%)
Ileo-caecal (L3)	n=20 (71%)
Crohn's disease phenotype :	
Fistulising	n=22 (29%)
Stenosing and fistulising	n=6 (21%)
Location of digestive fistulas	
Enterocutaneous fistula	n=8 (28%) de
Greco-colic fistula	n=9 (32%)
Greco-Greek Fistula	n=11 cas (39%)

21 patients (78%) were on Infliximab and 7 patients (22%) on Adalimumab. 22 patients (80%) had clinical remission with a return to normal bowel function, biological remission with CRP<5, endoscopic remission with mucosal and radiological remission with closure of digestive and enterocutaneous fistulae after one year of treatment. We noted a loss of primary response in 5 patients (17%) and 1 patient worsened and died of malnutrition. None of our patients required surgery.

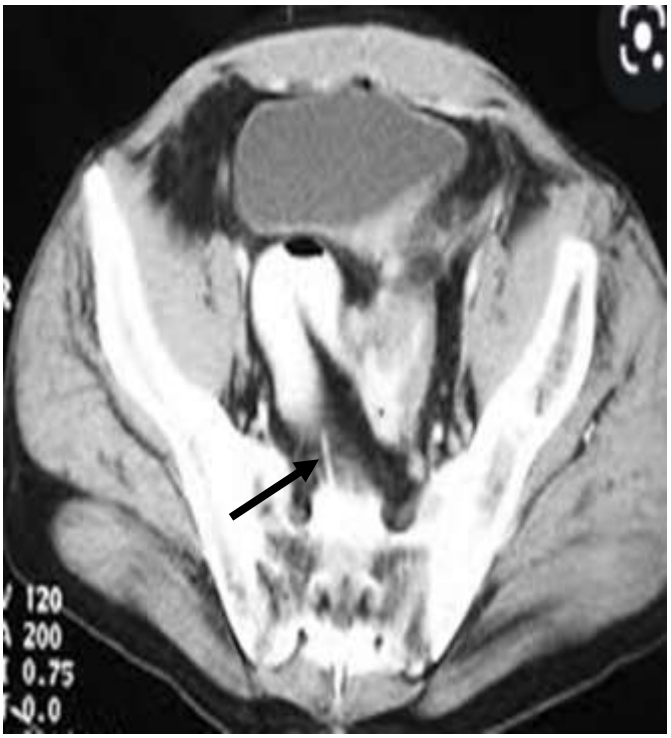
Discussion

The severity of crohn's disease lies in the occurrence of complications such as strictures, abscesses and internal or external intestinal fistulas. These fistulas may be entero-enteric, entero-vesical or enterocutaneous fistulas.

The risk of developing enteral fistulas in patients with Crohn's disease varies between studies but is estimated to be between 20% and 40%. (1) In a population-based study, 35% of patients with Crohn's disease developed internal fistulas. These fistulas were entero-enteric in 27%, entero-cutaneous in 6% and entero-vesical in 3%. (2)



Appearance of an MRI scan showing Ileo-ileal fistula



Appearance of an MRI scan showing Entero-vesical Fistula

The data from our study are similar to those in the literature, since the predominant location of the fistulas was enteroenteric.

In a study investigating the risk factors associated with the progression to intestinal complications of Crohn's disease, 14% of patients will develop internal fistula complications. (3) A recent study investigated factors associated with progression to penetrating complications: male gender, active smoking, extradigestive manifestations and ano-perineal involvement were significantly associated with the occurrence of intestinal complications, particularly digestive fistulas (4)

The risk of developing an intestinal fistula was also significantly higher in the case of ileal involvement than in the case of pure colonic involvement (3), which has been shown to protect against the appearance of digestive fistulas. (4)

The results of our study are consistent with those of the literature, since the population studied was made up of a majority of rather young male patients with an average age of 40 years, 60% were active smokers and 90% had ano perineal lesions.

Clinical symptoms differ according to the type of fistula (5): an enterocolonic fistula may cause severe diarrhoea whereas an entero-enteric fistula may be completely asymptomatic and therefore clinically difficult to diagnose, which explains why it is often discovered incidentally during surgery or on radiological imaging (entero CT or MRI). (6) In our study, the majority of patients consulted for bloody diarrhoea.

Fistulising Crohn's disease excluding ano-perineal fistula poses a problem of medical and surgical management. Surgical treatment was indicated in the majority of cases of fistulising Crohn's disease (7). Currently, the advent of biotherapies, led by infliximab and adalimumab, has revolutionised the management of this condition.

Biotherapies, in particular anti-TNFα, have an important place in the therapeutic arsenal for Crohn's disease. The first molecule was infliximab, which has been used in the treatment of Crohn's disease since the late 1990s. Other biotherapies have also been shown to be effective in Crohn's disease: adalimumab, certolizumab pegol, anti-integrins such as Vedolizumab and the anti-interleukin IL12/IL23, namely Ustékunimab. (8)

Several studies have been conducted to evaluate the efficacy of anti TNF agents such as Infliximab and Adalimumab in the closure of GI fistulae in Crohn's disease.

The ACCENT II trial studied the efficacy of infliximab in 306 patients with fistulising Crohn's disease with one or more GI or perianal fistulas. Infliximab was administered as a loading dose of 5mg/kg at S0, S2 and S6 and then infused every 8 weeks with 54 weeks of follow-up. The results were as follows: Closure of more than 50% fistulae was 23% on placebo versus 46% on Infiximab and closure of all fistulae on placebo was 19% versus 36% on Infiximab (9).

The study by Present et al. included 94 patients with crohn's disease with drained GI or perineal fistula. These patients received infliximab at doses of 5 and 10mg/kg at weeks 0, 2 and 4. 55% of patients assigned to 5mg/kg infliximab and 38% of those assigned to 10mg/kg had closure of all fistulae compared to 13% of patients assigned to placebo (10).

The study by Daniel H et al. also demonstrated the efficacy of infliximab in fistulising crohn's disease as 46% of patients treated with infliximab 5mg/kg achieved closure of enterocutaneous fistulae, compared with 13% of the placebo group (11)

In two larger cohorts, almost half of the patients eventually underwent surgery. (12,13). A recent study of 156 patients with CD with internal fistula of whom 117 patients (75%) were put on Infliximab, the results of this study suggest that surgery was often necessary despite anti-TNFtreatment in more than half of the cases. (14) Factors associated with the risk of surgery were the association with intestinal stenosis, low albumin levels and the number and complexity of internal fistulas.

Conclusion

Anti TNF drugs have an important place in the therapeutic arsenal of Crohn's disease. They have allowed better management of our patients, mucosal healing and a

reduction in fistulas. They are an alternative to surgery but must be discussed on a case-by-case basis depending on the patient's condition, the severity of his Crohn's disease and its complications.

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