

Predictive Factors of a New Episode of Suppuration after Remission of Fistulizing Ano Perineal Crohn's Disease: A Moroccan Series

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Abstract

Original Research Article

Fistulizing ano-perineal lesions occur in more than 20% of patients with Crohn's disease (CD). Although many medical and surgical treatments are now available, the relapse rate of such lesions remains high at nearly 30%. The objective of this study was to identify factors predictive of a new episode of anal suppuration in patients with fistulizing ano-perineal CD initially put into remission. This was a retrospective single-center study that included between 2018 and 2022 all patients with CD complicated by ano-perineal fistula put into remission. Achievement of remission was defined by the absence of new suppuration within 3 months of the last drainage surgery. Fifty-seven patients (57% female; median age at drainage 31 years) with multiple episodes of suppuration were included consecutively during the period. The rate of new ano-perineal suppuration was 22%, which occurred within a median of 1.8 years. Actuarially, survival without new suppuration was 96.7% at 1 year, 78.4% at 3 years, and 74.4% at 5 years. In the 38 (66.6%) patients receiving anti-TNF therapy after drainage, colonic (OR 1.25, $p = 0.015$) or ileocolic (OR 5.16, $p = 0.015$) location of CD, stenosing luminal phenotype (OR 5.32, $p = 0.013$) and discontinuation of anti-TNF therapy during follow-up (OR 3.37, $p = 0.049$) were associated with an increased risk of a new supplicative episode in multivariate analysis. Conversely, discontinuation of conventional immunosuppressive therapy was associated with a reduced risk of a new episode of suppuration (OR 0.22, $p = 0.29$).

Keywords: Crohn's disease (CD), surgery, ano-perineal lesions, anti-TNF therapy.

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INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disease of the intestine characterized by typically segmental and granulomatous transmural lesions. It evolves in relapses and is clinically manifested by abdominal pain, diarrhea, and weight loss. This disease can affect the entire digestive tract, from the mouth to the anus. The localization of CD is divided between ileal, colonic, ileocolic or upper gastrointestinal tract involvement, but it can also reach the ano-perineal region. The prevalence of PABs in the Crohn's disease population is highly variable, estimated to be between 20 and 80% depending on the study. Such a disparity can be explained by the lability of the descriptive, evolutionary and recruitment criteria. fistulizing ano-perineal lesions of CD therefore constitute a separate entity of CD with an occurrence and evolution that seems different from luminal disease. Fistulizing ano-perineal lesions occur in more than 20% of patients with Crohn's disease (CD). Although many

medical and surgical treatments are now available, the relapse rate of such lesions remains high at nearly 30%.

MATERIAL AND METHODS

Study Setting: The study was conducted in the gastroenterology department of the Mohamed VI University Hospital of Marrakech.

Type of Study: We conducted a retrospective descriptive study, including 50 cases of anoperineal lesions during a period of 15 years and a half, from June 2004 to December 2019.

Patients Included: We included in the study all patients with CD complicated by an anoperineal fistula put in remission at the Gastroenterology Department of the Mohamed VI University Hospital Center, whose diagnosis was retained on a bundle of clinical, endoscopic, histological and radiological arguments.

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Excluded Patients: We excluded patients with PABs outside of Crohn's disease, and patients with Crohn's PABs who were lost to follow-up.

Classification of Ano-Perineal Lesions: PABs were classified according to the Cardiff classification.

Data Collection and Statistical Analysis: Data were collected through the patients' files on a data processing form. We used Microsoft Excel 2016 software for statistical analysis of the data. The data were converted into percentages, averages or medians.

Ethical Approval: Verbal informed consent was obtained from patients before enrolling them in the study. No ethical approval was sought for analysis of the data set because it contained no personally identifiable information.

RESULTS

Epidemiologic Characteristics of Patients: The median age of the population at drainage was 31 years with a slight female predominance.

Patient History: 46% of our patients were smokers, and 16% had undergone an appendectomy.

Clinical Manifestations: Proctological symptoms were predominantly proctalgia in 36% of cases, purulent discharge in 42% of cases. Abdominal pain was present in 29 patients (58% of cases) and diarrhea in 37 patients (74% of cases).

Classification of Ano-Perineal Lesions: We used the Cardiff score to classify the ano-perineal lesions. 11% of the patients had an associated anal or rectal stenosis, 12% had an associated superficial fissure and 26% had a hollow anal or rectal ulcer.

In our study, the luminal localization of CD was ileocolic in 43% of cases, colonic in 27%, ileal in 24% and upper GI involvement in 6%. The phenotype of luminal CD was inflammatory in 75% of cases, stenosing in 17%, fistulizing in 8%.

Treatment: For the management of PABs; a suture was placed during drainage in 60% of patients and this for a median duration of 36 weeks. The pathway was flattened in 39% of patients and 21% had only a simple removal of the nipple(s). The median time to remission was 9 months.

The medical treatments at drainage were as follows: IS in 44 patients (88%), including 35 on thiopurines and 9 on methotrexate, Anti-TNF in 6 patients (12%), including 4 on IFX and 2 on ADA.

Medical treatments at remission were as follows: IS in 12 patients (24%), including 9 on thiopurines and 3 on methotrexate, Anti-TNF in 18

patients (36%), including 10 on IFX and 8 on ADA, 15 patients treated in combination therapy (30%). During their follow-up, 17 patients stopped treatment and 6 switched from IFX to ADA.

Progression: The rate of new ano-perineal suppuration was 22%, which occurred within a median of 1.8 years. In multivariate analysis, 4 factors emerged as statistically significant predictors: luminal location of CD, stenosing phenotype was associated with an increased risk of recurrence compared to inflammatory phenotype (OR 5.32 [CI95 1.79-15.80], p 0.013), discontinuation of anti-TNF therapy during follow-up was associated with an increased risk of recurrence compared with its continuation (OR 3.37 [CI95 1.01-11.26], p 0.049), discontinuation of IS therapy during follow-up was associated with a decreased risk of recurrence compared with its continuation (OR 0.22 [CI95 0.05-0.85], p 0.029).

DISCUSSION

This is a retrospective study that included 50 patients over 4 years, who were followed up with a median duration of 3.6 years. The crude relapse rate was 22%, with a median time to relapse of 94.1 weeks. The proctectomy rate was 2.5%. In multivariate analysis, 4 factors appeared to be statistically significantly predictive of fistulizing ano-perineal relapse: luminal location of CD, luminal phenotype of CD, discontinuation of anti-TNF therapy during follow-up and discontinuation of IS therapy during follow-up.

New suppurative episode: In our study, the number of new episodes of ano-perineal suppuration was low with a crude relapse rate of 22%. Suppuration-free survival was 96.7% at 1 year, 78.4% at 3 years and 74.4% at 5 years. In the historical cohorts of Stockholm County (1955-1974) and Olmsted County (1970-1995), the relapse rate of perineal fistulas was higher, at 35% in 2.5 years.

We found a total of 10 factors predictive of a new episode of ano-perineal suppuration (4 in multivariate analysis and 6 in univariate analysis only).

Predictive Factors for Relapse in Multivariate Analysis:

Luminal location of CD: Colonic and ileocolic locations were associated with an increased risk of ano-perineal relapse; this association was much higher for ileocolic location with an OR of 5.16. In the literature, the Stockholm County cohort found a recurrence rate of 10% in case of ileal luminal involvement but more than 80% in case of rectal involvement. **The luminal phenotype:** The stenosing phenotype was very strongly associated with an increased risk of relapse with an OR of 5.32. **Discontinuation of anti-TNF therapy during follow-up:** Discontinuation of anti-TNF therapy was associated with an increased risk of relapse with an OR of 3.37. In the Löffler and JB Lee studies, the efficacy

of medical treatment was not analyzed because of the very low number of patients receiving immunosuppressants or biotherapy (9% in the German study and 5.8% in the Korean study). In the Bouguen study, the influence of medical treatment on the recurrence of anoperineal fistula was observed but none of the factors analyzed was significant: neither the duration of IFX treatment, nor the discontinuation of IFX treatment, nor the combination therapy.

Predictive Factors for Relapse in Univariate Analysis

Age at diagnosis of CD: There was a trend towards an increased risk of relapse for CD diagnosed before 17 years of age and a decreased risk for CD diagnosed after 40 years of age. Type of ano-perineal fistula: An upper trans-sphincter fistula was associated with a trend toward increased risk of relapse compared with a superficial fistula, whereas an inferior trans-sphincter fistula was associated with a trend toward decreased risk. Presence of anal ulceration at drainage: Paradoxically, the presence of a superficial fissure was associated with a tendency to increase the risk of relapse, whereas the presence of a deepening ulcer was associated with a tendency to decrease the risk. Fistulotomy treatment: This factor was associated with a tendency to decrease the risk of relapse. Placement of a nipple at drainage: This factor was associated with a tendency to increase the risk of relapse. Conservative treatment: This factor was associated with a trend toward increased risk.

CONCLUSION

After effective drainage, survival without new ano-perineal suppuration related to CD is high, about 75% at 5 years. Associated colonic involvement, stenosing phenotype, and discontinuation of anti-TNF therapy are associated with a new suppurative episode. For medical practice, we can recommend treating all patients drained for fistulizing ano-perineal Crohn's disease with anti-TNF and not discontinuing therapy during follow-up. As the efficacy of IFX and ADA appears to be equivalent, the choice between the two molecules will depend on the patient's therapeutic history and the desired mode of administration.

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