



Alimentary Tract

Anal ulcerations in Crohn's disease: Natural history in the era of biological therapy



Timothée Wallenhorst^a, Charlène Brochard^{a,b,c,d,*}, Eric Le Balch^a, Anaïs Bodere^a, Aurélien Garros^a, Alexandre Merlini-l'Heritier^a, Guillaume Bouguen^{a,c,d}, Laurent Siproudhis^{a,c,d}

^a Department of Gastroenterology, University Hospital of Rennes, Rennes, France

^b Department of Digestive Physiology, University Hospital of Rennes, Rennes, France

^c INSERM U991, University of Rennes, Rennes, France

^d CIC-1414, University of Rennes, Rennes, France

ARTICLE INFO

Article history:

Received 13 March 2017

Received in revised form 22 July 2017

Accepted 24 July 2017

Available online 4 August 2017

Keywords:

Crohn's disease

Fissure

Perianal Crohn's disease

Ulceration

ABSTRACT

Background: The natural history of anal ulcerations in Crohn's disease remains unknown.

Aims: To assess the long-term outcomes of anorectal ulcerations.

Methods: Data from consecutive patients with perineal Crohn's disease were prospectively recorded. The data of patients with anal ulceration were extracted.

Results: Anal ulcerations were observed in 154 of 282 patients (54.6%), and 77 cases involved cavitating ulcerations. The cumulative healing rates were 47%, 70% and 82% at 1, 2 and 3 years, respectively. Patients with a primary fistula phenotype had a shorter median time to healing of their anal ulceration (28 [13–83] weeks) than those with a stricture (81 [28–135] weeks) or those with isolated ulceration (74 [31–181] weeks) ($p=0.004$). Among patients with ulcerations but no fistula at referral ($n=67$), only 4 (6%) developed *de novo* abscesses and/or fistula during follow-up. There was no benefit associated with introducing or optimising biologics, nor with combining immunosuppressants and biologics.

Conclusion: Anal ulceration in Crohn's disease usually requires a long time to achieve sustained healing. Determining the impact of biologics on healing rates will require dedicated randomised trials although it does not show a significant healing benefit in the present study.

© 2017 Editrice Gastroenterologica Italiana S.r.l. Published by Elsevier Ltd. All rights reserved.

1. Introduction

Perianal involvement was first documented as a possible manifestation of Crohn's disease (CD) in 1965 [1]. Perianal Crohn's disease (PCD) includes fistulising lesions (fistulas and abscesses) and non-fistulising lesions (fissures, ulcerations and strictures). A large body of literature and many guidelines about fistulising lesions have been published [2,3]. In contrast, data on non-fistulising PCD, especially ulcerations, remain scarce [4]. Anal ulcerations are common in CD, with a reported incidence of 5%–43%. Superficial fissures account for one-third of anal lesions, and cavitating ulcerations occur in the anus and rectum in 5–10% of cases [4]. Current knowledge of the outcomes of ulceration is poor and remains difficult to interpret due to frequent confusion between

superficial fissures and deep ulcerations [5]. Moreover, the majority of reports published before the era of biologic drugs were retrospective [6,7].

The aim of this study was to identify and describe the factors associated with the healing of ulcerations in a prospective cohort of patients with anal ulcerations in the era of anti-tumor necrosis factor alpha (TNF alpha) therapeutics.

2. Patients and methods

2.1. Study population

Between 2007 and 2012, a tertiary referral centre database prospectively recorded the following key data from consecutive cases of PCD: sex, age at diagnosis, height, weight, smoking habits, luminal CD phenotype according to the Montreal classification at diagnosis [8], treatments (including steroids, 5-ASA, immunosuppressants, TNF antagonists) and surgery (including ileal and/or colonic resection, anal fistula surgery/dilatation, stoma,

* Corresponding author at: Service des Maladies de l'Appareil Digestif, 2 rue Henri le Guillou, 35033 Rennes Cedex, France. Fax: +33 2 99 28 24 04.

E-mail address: charlene.brochard@chu-rennes.fr (C. Brochard).

and proctectomy). At each visit, CD activity was assessed using the Harvey-Bradshaw score [9]; the anatomic classification of PCD was described according to the Cardiff-Hughes classification (including a digital examination) [5], and PCD activity was assessed with the Perianal Disease Activity Index (PDAI) [10]. Data for patients with evidence of anorectal ulceration and a CD diagnosis (on at least one visit) were extracted. The questions specifically focused on Crohn's disease characteristics.

2.2. Definitions and follow-up

Ulceration was defined according to the Cardiff classification, distinguishing superficial fissures (U1) from cavitating ulcerations (U2) [5]. Using the Harvey-Bradshaw score (HBS), CD was considered to be in clinical remission when the HBS was less than 4, mild to moderately active when the HBS ranged from 4 to 12 and severely active with an HBS greater than 12 [9]. Although elementary PCD lesions are usually described separately, they are often associated at an individual level. The main anal phenotype was defined by the predominant type of anal lesion at referral (fistula, stricture or isolated ulceration). Anal strictures were mostly associated with other PCD lesions (e.g., ulcerations and/or fistula). Because clinical evaluations are more sensitive than imaging techniques [11], anal ulcerations were assessed by physical examination at each follow-up visit. Follow-up was determined by the duration between the diagnosis of ulceration and the last physical examination. Healing of ulceration was defined by the sustained disappearance of the ulceration during the follow-up period.

2.3. Statistical analysis

Quantitative variables are presented as the mean and standard deviation. Categorical variables are presented as the number and percentage of the cohort. Healing of the ulceration was the main endpoint for the analyses.

The cumulative probabilities of ulceration healing were estimated using the Kaplan–Meier method, from the time of diagnosis of the ulceration to the occurrence of healing. To identify factors associated with each event, univariate analysis was first performed using the log-rank test. To identify independent predictors of healing using multivariate analysis, baseline variables with p values <0.2 in the log-rank test were retained in the model and included in a Cox proportional hazards regression model. The results are shown as hazard ratios (HRs) with 95% confidence intervals [CIs].

Statistical analyses were performed using JMP[®] Pro software, version 10.0.2 (© SAS Institute Inc., USA).

2.4. Ethical considerations

The study was approved by the Hospital Ethics Committee of Rennes and the “Commission Nationale Informatique et Liberté” (CNIL no. 1412467).

3. Results

3.1. Study population

Data from 282 consecutive CD patients (M/F: 108/174, aged 35 [27–47] years old) were prospectively recorded during the study period: 154 patients (54.6%) had anal ulcers, 118 patients (41.8%) had fistula, 49 patients (17.4%) had strictures and 94 patients had no anal lesion (33.3%). Anal ulcerations were associated with fistulas (N=87/154) in more than half of the cases (56.5%) and were isolated (N=55/154) in one-third (35.7%) of patients. Strictures were most often (94%) associated with other lesions (N=46/49). The mean duration of CD was 364 [108–630] months, and the mean

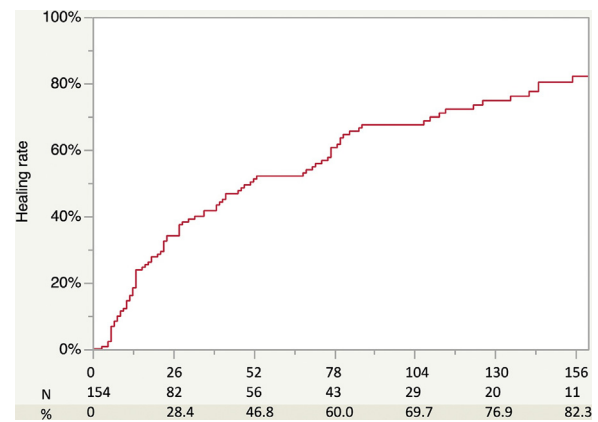


Fig. 1. Cumulative probabilities of healing for anal ulcerations in Crohn's disease.

duration of anal symptoms was 6 [2–24] months. Previous anal surgery for fistula was performed in 110 patients (39%). Previous ileal resection (N=21; 7.5%), ileocollectomy (N=38; 13.5%), partial colectomy (N=5; 2.5%) and total colectomy (N=12; 4.3%) were reported by 76 patients (26.6%). Anti-TNF treatment was prescribed in 183 patients (64.9%), for a mean duration of 12 [0–48] months: 122 (43.3%), 43 (15.2%) and 18 (6.3%) subjects received anti-TNF treatment before, during and after referral, respectively. Infliximab was the most commonly used biologic (N=109; 59.6%), followed by adalimumab (N=44; 24%). Thiopurines and methotrexate were used in 148 (52.4%) and 34 (12.1%) patients, respectively. Regarding luminal CD, 127 patients (45%) were in remission according to the HBS (<4), 118 patients (41.9%) had mild to moderate disease activity (HBS score from 4 to 12), and 37 patients (13.1%) suffered from severe active disease (HBS >12).

Anal ulcerations were observed in 154 cases (M/F=55/99; aged 33 [25–45] years). The characteristics of the 154 patients are depicted in Table 1. Cavitating ulcerations (U2) and superficial (U1) fissures were reported in 77 and 77 patients, respectively. Overall, the median follow-up duration was 65 weeks [20–134]. The healing rate was 63%. More than one-third ($n=57/154$, U1=24/77 and U2=33/77) of patients never healed within this period of time. The mean healing time was 29 weeks [14–77]. The cumulative healing rates for anal ulcerations were 28%, 47%, 70% and 82% at 0.5, 1, 2 and 3 years, respectively (Fig. 1).

Among patients with ulcerations but no fistula at referral ($n=67$), only 4 (6%) developed *de novo* abscesses and/or fistula during follow-up.

3.2. Follow-up

A single examination was performed in 10 cases. The characteristics of patients who healed and those who did not heal are shown in Table 1. Luminal phenotype, sex ratio, mean age and BMI at referral were not different between patients who healed and those who did not heal. Fig. 2 shows the cumulative probabilities of healing according to the severity of ulceration and association with a fistula. The anal lesion phenotype at referral also appeared to determine the healing rate of anal ulcerations. Patients with a fistula phenotype had a shorter median time to healing of their anal ulceration (28 [13–83] weeks) than those with a stricture (81 [28–135] weeks) or those with isolated ulcerations 74 [31–181] weeks) ($p=0.004$).

Fig. 3 shows the cumulative probabilities of healing according to therapeutic approach. There was no apparent benefit to introducing or optimising biologics. Moreover, patients who received both immunosuppressants and biologics did not heal more quickly.

Multivariate analysis considered pertinent baseline characteristics that might impact ulceration healing rates: age, gender,

Download English Version:

<https://daneshyari.com/en/article/5655241>

Download Persian Version:

<https://daneshyari.com/article/5655241>

[Daneshyari.com](https://daneshyari.com)