Neoadjuvant Biologic Therapy in the Surgical Management of Patients with Hidradenitis Suppurativa: A Cohort Study

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Hidradenitis suppurativa (HS) is a chronic skin disease characterized by recurrent flares of nodules, abscesses and fistulae, predominantly in the apocrine gland-bearing areas. These symptoms progress to scarring if not adequately treated, leading to functional limitations (1). Disease management is challenging, the 2 mainstays of treatment being biologic drugs and surgery. However, scientific evidence regarding the combined use of both therapies is scarce and is limited to a few studies (2–4). A clinical trial (SHARPS Study) is in progress on the safety and efficacy of peri-surgically administered adalimumab, but the results are not yet available (5).

The objectives of this study were: to assess the clinical features of patients with HS undergoing surgery with neoadjuvant biologic treatment; to explore the complications of this combined approach; and to compare recurrence rates at 24 weeks after surgery between patients on concomitant biologic treatment and those who are not on biologic treatment.

MATERIALS AND METHODS (see Appendix S1[1])

RESULTS

The study included 59 patients: 21 in the biologic cohort (17 patients on adalimumab 40 mg weekly, 2 patients on ustekinumab 90 mg every 12 weeks and 2 patients on infliximab 5 mg/kg every 8 weeks) and 38 patients in the non-biologic cohort. Baseline characteristics of the groups prior to surgery are shown in Table SI[1]. Structural and inflammatory disease features were more severe and there was a longer history of the disease and higher proportion of males in the biologic vs non-biologic cohort. Antibiotic use was more frequent among the non-biologic cohort.

Data on post-surgical complications are shown in Table SII[1]. Only one case of post-surgical infection was detected in the biological cohort and none in the surgery-only cohort, and there was no between-group difference in post-surgical pain score. The risk of a bleeding emergency was higher and the time to complete healing was longer in the biologic cohort. Multivariate logistic regression analysis found no increased risk of bleeding due to the presence of the biological drug, but showed an association with younger age, Hurley stage III, and a trend toward statistical significance of male sex. Biologic treatment and the size of the excised area were both associated with a longer time to complete healing.

Although a lower surgical recurrence rate was observed in the biologic cohort, the difference did not reach statistical significance, as shown in Table SII[1]. However, a difference was found in recurrences, which were mainly abscesses and inflammatory nodules in the biologic cohort vs abscesses and draining tunnels in the non-biologic cohort.

DISCUSSION

This prospective study compared outcomes and adverse effects between HS treatment by a combination of surgery with neoadjuvant biologic treatment and by surgery alone. Only one case of post-surgical wound infection was observed in the biologic cohort, and there was no difference between the 2 groups in post-surgical pain or bad odour episodes. The patients receiving both surgery and biologic treatment showed a longer time to healing and more frequent bleeding emergencies, although multivariate analysis revealed that the latter were probably not influenced by the biologic treatment. Recurrences involved less severe lesions in the combined therapy cohort, and the recurrence rate at 24 weeks was lower, although this difference did not reach statistical significance.

The patients assigned to the biologic cohort had a longer history of the disease, which was more severe, with greater structural damage and increased inflammatory load. They were also predominantly male, which is associated with greater disease severity (6). In addition, the surface area excised was larger than in the cohort receiving surgery alone, and although the difference was not statistically significant, a similar finding has been reported previously (3, 4) and reflects the more extensive surgery required for Hurley stage III disease. Patients with Hurley stage III have more severe disease and are more likely to receive biologic treatment.

This study found a statistically significant difference in the pre-surgical antibiotic treatment between the 2 cohorts, with a higher prevalence in the non-biological cohort. This is due to the fact that this antibiotic therapy represents the main systemic anti-inflammatory treatment for these patients. No differences in the post-surgical use of antibiotics were found between the 2 groups.

Only one case of post-surgical wound infection was observed among both cohorts, similar to previous findings of virtually no cases of infection after surgery and with no increased risk in patients receiving adjuvant biologic

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treatment (4). The more frequent bleeding emergencies in those receiving adjuvant biologic therapy may be attributable to various factors: the higher prevalence of Hurley stage III, which requires more extensive surgery; their younger age, implying less rigorous adherence to resting recommendations; and the predominance of the male sex, associated with more severe forms of the disease needing more complex surgery.

A longer time to complete healing in the biologic cohort was reported previously by Prens et al., who also observed a significant association between healing time and the surface area of the wound (3). Besides their larger wounds, the majority of patients in the present biologic cohort and that studied by Prens et al. were treated with tumour necrosis factor (TNF) inhibitors. TNF alpha is one of the cytokines involved in stimulating connective tissue production (7, 8), and its inhibition would contribute to a delay in wound closure.

Despite the more severe disease in patients in the biologic cohort, recurrences were milder (abscesses, inflammatory nodules) than in those receiving surgery alone (abscesses, draining tunnels), and the rate of recurrence tended to be lower in the biologic cohort. These results are in line with the findings of DeFazio et al. (4) on the synergistic effect of surgery and biologic therapy in the control of HS.

The limitations of this study include the small sample size and the aforementioned differences between groups inherent to the observational nature of the study. Based on the results of previous studies, sample size was calculated to detect a larger difference in the proportion of recurrences (4). Despite this limitation, we believe that the results of the current study show a clear trend towards statistical significance and are clinically meaningful. They are applicable in the daily clinical practice of patients with HS and could serve as a basis to design future studies on this field. The follow-up period was also limited, although the median time to recurrence has been reported to be 6 months (9), and our objective was to compare differences in the proportion of recurrences between the cohorts, not to assess their incidence.

Study strengths include the protocolized treatment procedure and the application in all patients of excision with secondary intention healing, which is associated with a lower recurrence rate, improved functionality, and greater patient satisfaction (10, 11). All patients in the biologic cohort were in the maintenance phase of their treatment, which was not interrupted (12–14). DeFazio et al. (4) closed wounds after the presence of infection had been ruled out, delaying the biologic therapy until 2 weeks post-surgery, while Prens et al. (3) discontinued the biologic treatment one week before surgery. Finally, this observational study was carried out in a real-life clinical setting, including patients with very severe disease and/or comorbidities who might be excluded from a clinical trial.

In conclusion, surgery in combination with biologic treatment appears to be a safe approach to the management of patients with moderate-to-severe HS, with a similarly low rate and severity of adverse effects to those observed with surgery alone. There is no need to discontinue drug treatment before the procedure, and there is no increase in the frequency of recurrences, which are less severe than in surgery alone. However, surgery in combination with biologic treatment may be associated with a longer time to complete wound healing compared with surgery alone.

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The authors have no conflicts of interest to declare.

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