Hidradenitis Suppurativa and Crohn's Disease: Response to Treatment with Infliximab

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Received March 7, 2001; accepted July 24, 2001.

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Cutaneous manifestations occur frequently in inflammatory bowel disease. The association between hidradenitis suppurativa (HS) and Crohn's disease (CD) has been reported. We present a new case supporting this association. A dramatic improvement after treatment with infliximab was achieved for both refractory fistulizing CD and axillary HS.

INTRODUCTION

The most frequent extraintestinal manifestations in inflammatory bowel disease include the joints, skin, and eyes (1). The most common cutaneous complications are aphthous stomatitis, pyoderma gangrenosum, and erythema nodosum (2), although there are several cutaneous manifestations related to both Crohn's disease (CD) and ulcerative colitis (3).

The association between CD and hidradenitis suppurativa (HS) has been suggested in previous reports (4-11). The precise meaning of this association remains unclear. We present yet another patient with CD who developed HS.

CASE REPORT

A 30-year-old woman with history of factor XII deficiency, pilonidal sinus, and gallstones was diagnosed with CD in 1993 after recurrent episodes of abdominal pain and cramp and diarrhea, based on clinical, radiologic, endoscopic, and histologic criteria. The disease affected the distal ileum, cecum, and ascendant and transverse colon. For 6 years, the evolutive pattern had been neither obstructive nor fistulizing, with less than one relapse per year, and remission-maintaining treatment consisted of 3 g daily of 5-aminosalicylic acid, requiring methylprednisolone during relapses.

In February 1999, during pregnancy, the patient developed perianal abscesses (which required surgical drainage) and rectovaginal fistulas. No inflammatory intestinal activity was detected. In the last month of pregnancy, the perianal disease was severe; therefore, a cesarean section was performed. After delivery, medical treatment with metronidazole and ciprofloxacin was started, with improvement of the perianal disease.

In December 1999, two erythematous and painful nodules appeared in both axillae. The left one drained spontaneously. With the clinical diagnosis of hidradenitis suppurativa, surgical drainage was performed, and therapy with topic antibiotics and local applications of antisepsics was given, with only limited success (Fig. 1).
In February 2000, the perianal disease relapsed again, in spite of the antibiotics (metronidazole and ciprofloxacin). Endoanal ultrasonography was performed, demonstrating the presence of rectovaginal and anovulvar fistulas, and the absence of abscesses. Therapy with anti-tumor necrosis factor (TNF) (infliximab) in a dosage of 5 mg/kg/d i.v. (three doses) was started. After the first dose, both perianal and axillary lesions improved significantly, with complete disappearance of the left axillary nodules and clear amelioration of the right axillary lesions. Simultaneously, treatment with azathioprine (2.5 mg/kg/d) was initiated. During the administration of the second dose of infliximab, the patient had an adverse reaction consisting of generalized erythematous eruption and dyspnea, which abated after discontinuing the infusion of infliximab. Obviously, the third dose was not administered.

After the second dose, the axillary lesions disappeared (Fig. 2), and rectovaginal fistulas closed almost completely (only a mild and well-tolerated vaginal drainage persisted).

Six months later, the patient is in remission both from skin lesions and fistulizing disease, and continues remission-maintaining treatment with azathioprine.

DISCUSSION

Associated cutaneous manifestations are frequent in CD, as in other forms of inflammatory bowel disease (12).

HS is a chronic inflammatory disease of the apocrine glands that can involve axillae, groin, chest, perineal region, and genitalia (13). It is characterized by follicular obstruction and secondary bacterial infection. Hormonal and genetic factors are suspected to play a role in the physiopathology of the disease, but the initial events remain unknown. A wide range of medical treatments have been used: estrogens, systemic corticosteroids, isotretinoin, etretinate, antibiotics (minocycline, metronidazole, clindamycin, erythromycin), and finasteride. Surgical drainage, excision, or even radiotherapy are often required.

The association between HS and CD has been suggested by six reports (4-11). Church et al. (9) report 24 patients with CD of 61 with HS, most of them with colonic disease (only one case of ileal involvement alone). The diagnosis of CD predated that of HS by an average of 3.5 years. The majority of these patients had more than
one apocrine territory affected, basically groin and perineal region. Biopsies demonstrated the presence of granulomas in only six patients. In the case we present, the large bowel was involved, and CD had been diagnosed 6 years before HS (shortly after the perianal fistulizing disease) as well.

In the first report of the association between HS and CD (4), three cases of hidradenitis with perineal and genital involvement were presented. They pointed out the clinical similarities with the perianal lesions of the CD. In our patient, perianal fistulizing CD coexisted with axillary HS, and the clinical appearance was very similar. Perianal CD, noncontiguous with the involvement of the gastrointestinal tract, is regarded by some as metastatic CD. There is a report of one case of refractory perineal cutaneous CD treated successfully with anti-TNF (14).

Anti-TNF is a chimeric monoclonal IgG1 antibody directed against the TNF (15). TNF-\(\Delta\) is the most important proinflammatory cytokine in the Th1 response, which is increased in CD. The efficacy of anti-TNF has been proven in fistulizing and refractory CD (16,17). Whether immunomodulators (such as azathioprine) should be added or not is a controversial issue (18,19).

The treatment of cutaneous manifestations of CD is basically the same as that for bowel disease, in some regard. Because pyoderma gangrenosum may develop slowly, independent of the course of intestinal disease, it has been suggested that immunosuppressive agents such as cyclosporine and azathioprine could be the first treatment of choice in such cases (20,21).

Apart from the case of metastatic CD mentioned above, there are two reports of Fournier gangrene (22) and psoriasis (23) (both associated with CD) treated with anti-TNF with good results.

In our patient, therapy with anti-TNF was initiated because of the lack of response to treatment with antibiotics (metronidazole and ciprofloxacin) and surgical drainage. Both perianal and axillary lesions recovered quickly after anti-TNF administration, remaining inactive with maintaining treatment with azathioprine.

CONCLUSION

In conclusion, the increasing number of articles reporting the association between HS and CD strengthen the likelihood of the association. The cause of both entities remains elusive, as well as the hypothetical link between them. It has been suggested that the damaged gut mucosal barrier may result in the absorption of toxins from the bowel (4), leading to an immune response that is responsible for the extraintestinal manifestations. These responses could be modulated with immunosuppressive agents.
The initial good results obtained with anti-TNF and immunomodulators in cutaneous manifestations of CD suggest the usefulness of these agents in this indication. Further evaluation is needed to clarify the precise meaning of this association and other skin manifestations of CD, as well as the role of anti-TNF as a therapeutic choice for them.

REFERENCES TOP


Keywords:
Hidradenitis suppurativa; Crohn's disease; Anti-tumor necrosis factor; Infliximab

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