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Successful treatment of therapy-resistant metastatic Crohn's disease with infliximab

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Sir, Metastatic Crohn's disease is a rare dermatological manifestation of Crohn's disease in which there is prominent granulomatous inflammation involving a skin area that can be distant from the affected gastrointestinal tract.[1] The cutaneous lesions (papules that may enlarge, ulcerate and/or drain pus) can occur at various locations, although they are most frequent in the perineal region, particularly in patients with fistulizing perianal disease or previous proctectomy.[2]

In contrast to other cutaneous manifestations of Crohn's disease, such as erythema nodosum or pyoderma gangrenosum, metastatic Crohn's disease usually has an unsatisfactory response to medical and/or surgical therapy. A complete healing of the lesions is rarely obtained by medical treatment, although some partial benefit has been reported following treatment with azathioprine,[3] steroids,[4] mycophenolate mofetil,[5] surgery and hyperbaric oxygen therapy.[6]

Infliximab, an antitumour necrosis factor (TNF)-α chimeric monoclonal antibody, has been used successfully in fistulizing perianal Crohn's disease,[7] and its potential efficacy in the treatment of cutaneous metastatic complications of Crohn's disease has recently been suggested.[2,8,9] We report a patient with metastatic Crohn's disease that was treated successfully with infliximab.

A 31-year-old woman was initially diagnosed as having ulcerative colitis in 1984, when she underwent a subtotal colectomy with ileorectal anastomosis because of a toxic megacolon. In 1986 she developed a perianal fistula and a small perianal ulcer which gradually enlarged. Rectoscopy and rectal biopsies revealed a morphological picture of Crohn's disease. In 1987 she underwent fistulectomy that resolved the fistula but not the perianal ulceration. For about 10 years she had no intestinal or fistulous manifestation of disease but the skin lesion persisted.

In 2002 the patient presented with a 12-cm cutaneous ulcer located in the perianal area and extending to the gluteal fold (Fig. 1a). No perineal fistula or mucosal alterations were found on rectoscopy. Transrectal sonography and pelvic magnetic resonance imaging excluded a perianal fistulizing complication. The lesion was unresponsive to several medical therapies (oral mesalamine; topical and systemic steroids; a course of therapy with azathioprine for about 1 year; metronidazole plus ciprofloxacin for 3 months). There was local pain and bleeding, but no intestinal symptoms were present. A biopsy of the skin ulcer revealed a noncaseating granulomatous inflammation and the diagnosis of metastatic Crohn's disease was made. We proposed a course of infliximab at the dosing schedule used for fistulizing Crohn's disease (5 mg kg^{-1} intravenously at 0, 2 and 6 weeks).[7] Two weeks after the third infusion of infliximab, the perianal ulcer was completely healed (Fig. 1b) and no side-effects were observed. There was a recurrence of the ulcer 4 months later. A further dose of infliximab was given, initially with clinical benefit. However, at the time of the second administration, the patient experienced a severe immediate adverse reaction (laryngospasm, hypotension and cutaneous rash). The adverse reaction was effectively treated with intravenous betamethasone 4 mg and the treatment with infliximab was discontinued.

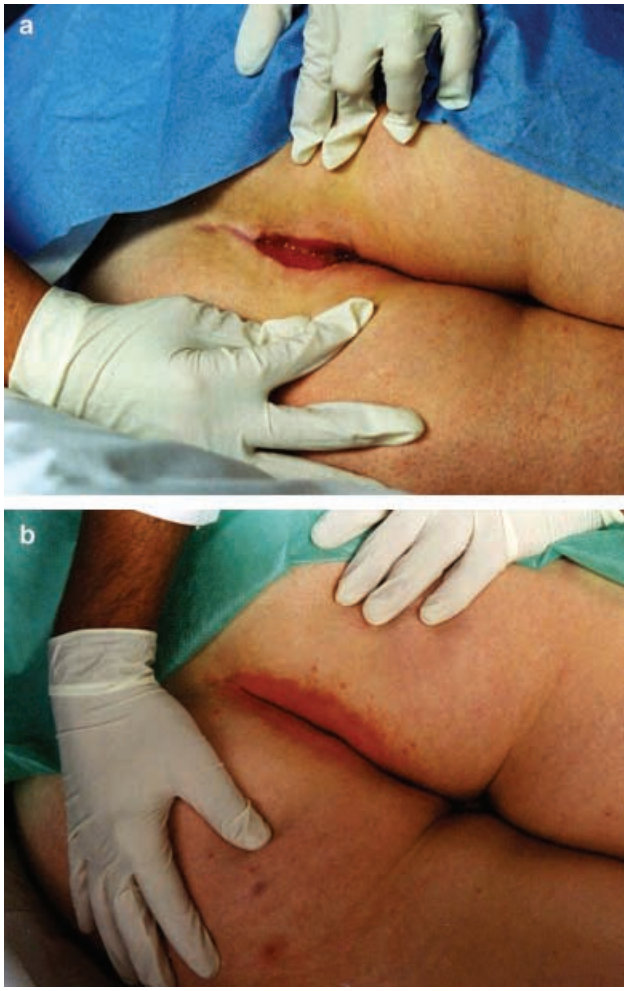

Figure 1. (a) The gluteal fold lesion before the first infusion of infliximab. (b) Appearance of the lesion 2 weeks after the third infusion of infliximab. Complete healing is evident.

Metastatic Crohn's disease, although a rare complication of Crohn's disease, represents a difficult problem for the clinician because of unsatisfactory response to conventional therapy. This condition significantly affects the patient's quality of life, thus justifying the search for alternative treatments. Forty-five cases of variously localized metastatic Crohn's disease are reported in the literature. The therapeutic approach is well documented in 39 of these 45 cases.[10] An improvement of metastatic lesions was obtained in 15 of 18 patients treated with systemic or topical steroids,[3,4] in two of four patients treated with azathioprine,[3] in two patients treated with metronidazole, in one patient treated with mycophenolate mofetil,[5] in two patients who had undergone hyperbaric oxygen therapy,[6] in four of five patients treated surgically and in four patients treated with infliximab infusion.[2,8,9] Our case represents the fifth report of metastatic Crohn's disease effectively treated with anti-TNF antibodies that has been reported in the literature. In contrast to the two cases described by van Dullemen *et al.*,[2] the case described by Miller *et al.*[8] and the paediatric case described by Escher *et al.*[9], in which anti-TNF induced only a partial healing of the lesions, in our patient the treatment brought about complete resolution of the metastatic disease. Furthermore, a re-treatment upon recurrence appeared to be effective, even though the therapy was not completed due to an adverse reaction.

Our experience confirms that infliximab is an effective and well-tolerated option for the treatment of therapy-resistant metastatic Crohn's disease, indirectly suggesting the TNF-α-dependent nature of this cutaneous complication.

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Eczema-like lesions and disruption of therapy in patients treated with interferon-alfa and ribavirin for chronic hepatitis C: the value of an interdisciplinary assessment

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SIR, '*I would urge upon you in your own practice, to care more particularly for the individual patient than for the special features of the disease*' (William Osler).

We read with interest the controversy in the *BJD*[1,2] regarding the premature withdrawal from therapy with interferon-alfa and ribavirin in patients treated for chronic hepatitis C (CHC), due to eczema-like lesions. In the study of Dereure *et al.*[1] this combined treatment had to be interrupted in half of their patients presenting with diffuse eczema-like lesions (10 of 20). On the other hand, Kerl *et al.*[2] followed 52 patients undergoing combination treatment with peginterferon alfa and ribavirin, of whom 12 (23%) developed eczema-like lesions but, in contrast to Dereure *et al.* none had to interrupt the antiviral treatment, as the lesions were well controlled with topical corticosteroids and emollients.

We consider it to be of interest to add our experience to this controversy.[3] We evaluated 210 patients with CHC undergoing a 1-year treatment with recombinant interferon-alfa 2b and ribavirin, between June 1998 and September 2000. Not taking into account local reactions to injections, we observed *de novo* skin lesions in 27 patients (13%). Among patients with skin lesions, 16 patients (59%) presented eczema-like lesions, mostly localized on the legs, arms or trunk. Only two of them had generalized eczematous lesions with very severe pruritus. We also observed disseminated prurigo-like lesions (four patients, 2%); lichenoid eruptions (two patients, 1%); seborrhoeic dermatitis (two patients, 1%); maculopapular exanthema (two patients, 1%) and herpes zoster (one patient, 0·5%).

We treated those patients presenting with diffuse, eczema-like lesions and pruritus with oral hydroxyzine, moderately potent topical steroids and emollients. Most of them were well