Cutaneous manifestations and gastrointestinal disorders: Report of two emblematic cases

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Abstract

Gastrointestinal (GI) diseases, such as inflammatory bowel diseases (IBD), can manifest themselves with intestinal and extra-intestinal symptoms. Among the latter, cutaneous manifestations, such as pyoderma gangraenosum (PG) and metastatic Crohn’s disease (MCD), represent a possible onset of IBD, with or without simultaneous bowel alterations. In such cases, intestinal and skin lesions are supported by the same immune-mediated mechanism. We hereby report two cases of patients with skin manifestations together with signs and symptoms suggestive of IBD. IBD and some skin lesions arise from the same immune-mediated mechanism. A multidisciplinary approach to these immune-mediated diseases is needed for an early and correct diagnosis, which in turn may lead to the use of the right drug avoiding useless treatment. Clin Ter 2015; 166(4):e269-272. doi: 10.7417/CT.2015.1872

Key words: cutaneous manifestations, immune-mediated mechanism, inflammatory bowel disease

Introduction

The skin represents a common site for the extraintestinal manifestations of inflammatory bowel diseases (IBD), i.e., Crohn’s disease (CD) and ulcerative colitis (UC). Cutaneous alterations are classified as followed: i) reactive skin findings (erythema nodosum, pyoderma gangrenosum (PG), psoriasis, secondary amyloidosis, polyarteritis nodosa, vasculitis allergica, systemic lupus erythematos, Sweet’s syndrome, sarcoidosis); ii) specific skin lesions (distant cutaneous metastatic CD (MCD), contiguous perianal CD, oral CD); iii) nutritional skin changes (acrodermatitis enteropathica, pellagra, disorders in nail and/or hair growth) (1). Among the aforementioned lesions, the most common are the non-specific reactive skin findings, while specific skin lesions and in particular the MCD are rare, with less than 100 cases described in literature (2). We here report two cases of patients with cutaneous lesions and a positive anamnesis for gastrointestinal (GI) symptoms: a 50-year-old woman affected by MCD and a 32-year-old woman with PG. The aforementioned skin lesions belong to the granulomatous skin disorders’ group and have similar clinical features but different histological characteristics, incidence and correlation with GI diseases. PG is one of the most common skin manifestation in patients with IBD and is usually related to the disease activity; MCD is instead a very rare skin manifestation of CD and its occurrence and severity are not necessarily related to the disease activity.

Case reports

Case 1

A 50-year-old woman was admitted to our dermatology department with an extensive inflammatory erythematous plaque of the medial side of the thigh with multiple small ulcers and polipoid lesions. Her clinical history began in 1996 with bloody diarrhoea, mild fever and abdominal pain together with nodular erythematous lesions on the anterior left leg, diagnosed as erythema nodosum. An incomplete colonoscopy showed erosions of the rectal mucosa and the histological samples described a rectal CD. The patient was then treated with a short cycle of intravenous steroids and antibiotics, with a fast improvement of both the intestinal symptoms and the cutaneous manifestations. After this first acute episode, Mesalazine (800 b.i.d.) was administered to the patient with a stable remission. In May 2010, without any intestinal symptoms, a new skin lesion on the anterior left leg appeared and it quickly turned into an infiltrated ulcerated plaque with a florid inflammation (Fig. 1 a-b). A biopsy showed the histological features of a cutaneous localization of CD. A colonoscopy was performed with the evidence of erosions of the caecum and erythema of the rectal mucosa; the histological findings demonstrated a recurrence of CD in the caecum and rectal mucosa. The patient was treated with infliximab (anti-TNF-alpha monoclonal antibody) 5 mg/kg at weeks 0, 2 and 6 for induction followed by a scheduled q8 week for one year for remission.
maintenance. Right after the induction cycle, cutaneous ulcers disappeared (Fig. 1c) and after the first maintenance infusion the skin was completely restored.

Case 2

A 32-year-old woman presented to our dermatology department with the presence of a 10 centimetres (cm) large, flat and sharp margins ulcer, with a swollen necrotic base and raised, dusky, undermined borders, surrounded by an erythematous area, located on the distal part of her right leg (Fig. 2). Cutaneous examination revealed a 5 cm ulcerated plaque, clearly demarcated, with an irregular and violaceous border, surrounded by an erythematous area. The patient reported that the aforementioned lesion appeared fifteen years before, immediately after a leg trauma. A first skin biopsy suggested an exuberant granulation tissue with vasculitic features. Moreover, the patient’s anamnesis was positive for GI symptoms, in particular abdominal pain and recurrent episodes of diarrhoea (3-5 bowel movements a day for 7-10 days in a month). Therefore a colonoscopy was performed and biopsies were taken from all colonic segments. The histology showed an increased chronic inflammatory infiltrate without specific IBD features. The patient was then treated with immunosuppressive therapy for 8 months (cyclosporin 100 mg/day and mesalazine 800 mg 3 times/day), with improvement of both the skin ulcerative lesion and the abdominal symptoms (2-3). Later on, a new skin biopsy of the ulcer’s border was taken and it was suggestive for acanthosis, parakeratotic hyperkeratosis, epidermal papillomatosis with spongiotic foci, and for the presence of junctional small areas of fibrinoid necrosis and full-thickness epidermal necrosis. A marked vascularization with a hemorrhagic extravasation, haemosiderin deposits and a chronic lympho-mononuclear infiltrate were described in the dermis. Granulomatous le-
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The contribution of the skin to the natural history of immune-mediated inflammatory bowel diseases (IBD) is increasingly recognized. Although the onset of GI symptoms are poorly described in literature (12-14), moreover, the severity of cutaneous manifestations is not necessarily related to the CD's activity (3). The case of the 50-year-old woman showed an intestinal CD of the caecum and rectal mucosa, associated with a mild clinical activity together with severe skin lesions. These features have been poorly described (11) in literature and MCD is often associated with a concomitant intestinal active CD (15). There are no treatment guidelines for MCD and, because of its rarity, no clinical trials have been led yet (12). However, different therapeutic strategies have been used, including drugs such as metronidazole, topical and oral steroids, azathioprine, sulfasalazine and infliximab, with different clinical responses (11-13, 16).

In conclusion, we now know that IBD and some skin lesions arise from the same immune-mediated mechanism. In the past years, the increased use of immunomodulatory drugs, such as anti-TNF alpha antibodies, have determined a deep impact on the natural history of immune-mediated diseases.

Therefore, a proper evaluation of these clinical conditions is needed, with a close surveillance and a longer follow-up. Moreover, since CD and the aforementioned skin lesions have the same therapeutic target (TNF alpha), an early and correct diagnosis is of main importance. Indeed, such a diagnosis would allow the use of the right drug, with the improvement of both cutaneous and intestinal symptoms, while avoiding unnecessary treatments.

References

12. Delgado J, Delgado B, Sztarkier I, et al. Presentation of