

Cutaneous and ocular manifestations of IBD

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SUMMARY

Cutaneous and ocular manifestations reflect the systemic nature of the inflammation seen in inflammatory bowel disease (IBD). These manifestations occur more commonly in association with active IBD. Thus, they may respond to therapy for bowel disease, but may require this at an intensity out of proportion to that needed for the bowel. Corticosteroids are considered to be the first line treatment, whereas in cases refractory to steroids or with, the presence of side-effects, immunosuppressive drugs offer an alternative option. Recently, anti-TNF has been proposed as an effective treatment for extraintestinal manifestations of IBD refractory to conventional therapies, especially for pyoderma gangrenosum. However, the optimal form of treatment of extraintestinal manifestations has yet to be established. Cutaneous and ocular manifestations are well recognized complications of inflammatory bowel disease (IBD) and reflect the systemic nature of the inflammation seen in these conditions (1). Although the reported prevalence of these complications in IBD varies, it is well known that extra-intestinal manifestations occur preferentially in patients with disease of the colon and they may rarely complicate disease confined to the small bowel. Cutaneous complications are reported in 6-15% of Crohn's disease patients,¹⁻³ and in 1-9% of ulcerative colitis (UC) patients,⁴ while acute ocular inflammation in up to 10% of Crohn's and 5% of UC patients.^{1,2} Both cutaneous and ocular complications are said to occur more commonly in association with active IBD, and often coexist with other extra-intestinal manifestations.⁵ Erythema nodosum (EN) is the most common form of cutaneous manifestations followed by pyoderma gangrenosum

and Sweet's syndrome. Ocular inflammation of IBD is predominantly anterior in contrast to other systemic inflammatory disorders; uveitis, iritis, episcleritis are the commonest forms of ocular complications in patients with IBD.

CUTANEOUS MANIFESTATIONS

Erythema Nodosum

Erythema nodosum is the most common skin lesion and appears clinically in conjunction with symptoms of active bowel disease. The prevalence of EN in IBD patients is 4-10%, and it appears more often in women. The manifestation tends to occur, for the first time, during the first 2 years of the clinical course of the disease and may recur in approximately 50% of cases.³ EN presents as painful, raised red lesions typically on the shins. Although EN may recur with further exacerbations of the intestinal disease, it is rarely recurs after proctocolectomy.

The aim of therapy is to relieve pain of cutaneous eruptions and to restore cutaneous integrity. Standard therapy of EN consists of administration of pain-killers such as acetaminophen or NSAIDs/COX-2 inhibitors, bandage, and elevation of affected limbs. EN is normally self-limited, runs a broadly parallel to active disease course that does not normally require specific therapy, and typically responds to treatment of active IBD. On the basis of uncontrolled data, EN lesions usually respond to treatment with oral corticosteroids (prednisolone 1mg/kg of body weight), although occasionally immunosuppressive therapy may be required.³ Severe or refractory cases have been treated effectively with Infliximab.⁶⁻⁷ Oral potassium iodide⁸ and extracorporeal monocyte granulocytapheresis⁹ have been suggested as an alternative treatment for resistant cases.

Pyoderma gangrenosum

Pyoderma gangrenosum (PG) affects 2% of IBD patients. It is more common in long-standing disease, is usu-

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ally associated with active colitis, and occurs in concomitance with other extraintestinal manifestations (arthritis, erythema nodosum). The lesions are single and on the lower limb in just over half of all cases. They characteristically develop into deep ulcers with necrotic base, undermined purple edges, and a purulent sterile discharge, but there are many exceptions.³ PG may respond to therapy for inflammatory bowel disease, but may require this at an intensity out of proportion to that needed for the bowel. Moreover, it may be very troublesome to treat because it tends to run a course that is independent to that of IBD. PG seems to benefit less than EN from proctocolectomy in IBD patients.¹⁰

The optimal form of treatment of PG has yet to be established. The prevailing management strategy for PG includes wound care in conjunction with systemic treatment with immunomodulating agents to control the inflammation. Topical management is aimed at prevention of secondary contamination and includes dressings, application of potent steroid preparations beneath an impermeable dressing, and intralesion injection of corticosteroids or cyclosporine. Surgical debridement should be avoided because the lesions exhibit pathergy.¹¹ Oral corticosteroids (prednisolone 1-2 mg/kg BW per day) in addition to wound care is advocated as the treatment of choice. Other immunosuppressive agents, such as cyclosporine, tacrolimus and azathioprine are additional options for difficult lesions. Cyclosporine (5mg/kg BW, divided in two doses daily) given orally or intravenously has been shown to be beneficial.¹² Azathioprine has been suggested as a suitable agent, but there are no data to support its superiority over other immunosuppressants. In patients who fail to respond or develop severe side effects, oral (0.1mg/kg BW, divided in two doses) or topical tacrolimus has been successfully used.¹³⁻¹⁵ Dapsone (initial dose: 100mg/day, maximal dose: 300mg/day), and mycophenolate mofetil have also been suggested.^{11,16} Use of Infliximab in PG has been reported in a number of case reports and small series.¹⁷⁻¹⁹ Patients treated with infliximab have shown rapid healing of their lesions; infliximab appeared to be effective as a single infusion but PG often recurred, necessitating repeat infusions.¹⁹ Infliximab has become the first choice in the treatment of PG due to its high efficacy and safe profile. For extreme intractable cases of PG, surgical intervention may be required.²⁰

Sweet's syndrome

Sweet's syndrome is a neutrophilic dermatosis probably related to pyoderma gangrenosum consistent with painful erythematous plaques often associated with fe-

ver and leukocytosis.²¹ This rare cutaneous manifestation usually responds rapidly to corticosteroids therapy,^{21,22} whereas Infliximab is effective in patients with persisting symptom.²³

OCULAR MANIFESTATIONS

Episcleritis

Episcleritis is the most common complication of IBD, it characteristically flares during increases of intestinal IBD activity, and manifests as acute redness, irritation, burning, and tenderness to palpation.^{3,24,25} Treatment is tailored to the severity of eye symptoms and associated bowel complaints. Application of cool compresses or topical steroids may be sufficient in conjunction with appropriate treatment of underlying bowel disease.²⁴ Oral NSAID's are effective in selected cases, but should be used with caution since these medications may be associated with a flare of IBD. Episcleritis can benefit first of all by the appropriate treatment of active disease. A recent report highlighted the successful use of infliximab in a refractory case of episcleritis associated with active Crohn's disease.²⁶

Scleritis

Scleritis is a more severe ocular disorder than episcleritis because it may impair vision. In this case, a referral to an ophthalmologist is mandatory for risk of vision loss. Patients often complain of severe eye pain, associated with tenderness to palpation.²⁷ Scleritis must be treated aggressively with systemic steroids, NSAID's, or immunosuppressants to prevent significant visual loss. Recurrences are common, but with control of the underlying bowel disease, the prognosis remains good.²⁷

Uveitis

Uveitis can be anterior and posterior and is often associated with joints and skin manifestations. Anterior uveitis is the most common and presents painful eye, visual blurring, and photophobia. A seriously affected eye will be miotic and may have an abnormal pupillary response to light.^{24,25} Uveitis can occur during active bowel disease, during quiescent periods, and sometimes may precede the diagnosis of IBD.²⁸ Treatment of uveitis includes cycloplegics and topical steroids, and will often require systemic steroids and immunosuppressant medications. Uveitis has responded favorably to colectomy in a few cases.²⁷ Sulfasalazine/mesalazine seems to prevent anterior uveitis recurrence, whereas infliximab has recently shown efficacy in treating acute uveitis.²⁹

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