# Cutaneous Manifestations of Inflammatory Bowel Disease

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Manifestations cutanées des maladies inflammatoires chroniques de l'intestin

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**RÉSUMÉ**

**Prérequis :** Quoiqu'elles varient largement, les manifestations cutanées sont des complications communes des maladies inflammatoires chroniques de l'intestin. Au moment du diagnostic de la maladie inflammatoire chronique de l'intestin, l'incidence moyenne de ces manifestations est d'environ 10%.

**Le but** de cet article est une analyse critique des lésions cutanées fréquemment associées aux maladies inflammatoires chroniques de l'intestin.

**Méthodes:** une recherche électronique dans la littérature médicale a été effectuée sur les sites "PubMed", "ScienceDirect" et "Interscience Wiley".

**Résultats:** Les manifestations cutanées associées aux maladies inflammatoires chroniques de l'intestin étaient divisées en 3 groupes basés sur la nature de cette association : lésions granulomateuses cutanées, éruptions cutanées réactionnelles et autres dermatoses associées. Dans cette revue de la littérature, nous avons focalisé sur les lésions granulomateuses cutanées et les éruptions cutanées réactionnelles

**Conclusion:** Les manifestations cutanées doivent être recherchées systématiquement chez les patients ayant une maladie inflammatoire chronique de l'intestin. Pour la plupart de ces manifestations, la cible thérapeutique demeure l'intestin.

**Mots-clés**

lésions granulomateuses cutanées – éruption cutanée réactionnelle – maladies inflammatoires chroniques de l'intestin - maladie de crohn – rectocolite ulcéro-hémorragique.

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**SUMMARY**

**Background :** Cutaneous manifestations are relatively common complications of inflammatory bowel disease, although they vary widely. At the time of inflammatory bowel disease diagnosis, the mean incidence of these manifestations is around 10%.

**The aim** of this article was to review some of the noteworthy skin disorders associated with inflammatory bowel disease.

**Methods:** An electronic research of the medical literature was carried out on the web sites "PubMed", "ScienceDirect" and "Interscience Wiley".

**Results:** The cutaneous manifestations associated with inflammatory bowel disease were divided into 3 groups based on the nature of the association: granulomatous cutaneous disease, reactive skin eruptions and other associated dermatoses. In this review, focus has been given on granulomatous cutaneous disease and reactive skin eruptions.

**Conclusion:** Patients presenting with inflammatory bowel disease should be examined for cutaneous manifestations. For most of these cutaneous manifestations, the primary therapeutic target remains the bowel.

**Key-words**

Granulomatous cutaneous lesions - Reactive skin eruptions – inflammatory bowel disease - Crohn's disease - Ulcerative colitis.

Cutaneous manifestations are relatively common complications of inflammatory bowel disease, although they vary widely. At the time of inflammatory bowel disease diagnosis, the mean incidence of these manifestations is around 10% (1). However, a great variety of skin lesions may develop during the course of the disease (2).The cutaneous manifestations may be specific lesions such as ulcers and fistulas, oral crohn's disease and metastatic crohn's disease where there is direct involvement of mucous membranes or skin by the same disease process. However, many patients develop reactive skin eruptions such as erythema nodosum, pyoderma gangrenosum, and sweet's syndrome which are non-specific reaction patterns. The third type of cutaneous manifestations observed includes manifestations related to hypercoagulability, to nutritional deficiency, to treatments used for inflammatory bowel disease, or associated diseases.

The aim of this article was to review some of the noteworthy skin disorders associated with inflammatory bowel disease. In this review, focus has been given on granulomatous cutaneous disease and reactive skin eruptions.

## METHODS

An electronic research of the medical literature was carried out on the web sites "PubMed", "ScienceDirect" and "Interscience Wiley". The key words "cutaneous manifestations", "skin disorders", "fissures", fistulas", "oral manifestations", "pyostomatitis vegetans", "metastatic crohn's disease", "erythema nodosum", "pyoderma gangrenosum" and "psoriasis" were used in various association with "inflammatory bowel disease", "ulcerative colitis" and "crohn's disease". The articles available in English (review articles, case reports, and original articles) and who highlight an association between cutaneous diseases and inflammatory bowel disease were retained.

## RESULTS

The cutaneous manifestations associated with inflammatory bowel disease were divided into 3 groups based on the nature of the association.

**Granulomatous cutaneous lesions**

The cutaneous manifestations of inflammatory bowel disease may be specific lesions such as ulcers and fistulas, oral crohn's disease and metastatic crohn's disease where there is direct involvement of mucous membranes or skin by the same disease process.

**1. Ulcers and fistulas**

Fissures and fistulas are the most common cutaneous manifestations of inflammatory bowel disease, and may even be the presenting complaint in crohn's disease. The most commonly affected site is the perineum, especially the perianal area, although peristomal skin and the abdominal wall may also be affected. Perianal disease was found in 36% of patients with crohn's disease (3). The clinical spectrum of perianal lesions is variable, with the most common early lesions being perianal erythema, aphthous ulcers in the anal canal and perianal fissures. Linear ulcers and pseudotumour-like lesions resembling oedematous marisques or condylomata are common manifestations. More aggressive forms include profound ulcers that destroy the anal sphincter, abscesses complicating anoperianal or rectovaginal fistulas and scarring leading to deformations (1). Skin biopsy taken from affected areas may reveal granulomatis inflammation with non-caseating granulomas. Examination under anesthesia in combination with either anorectal endoscopic ultrasound or pelvic magnetic resonance imaging constitutes the best approach for evaluating and classifying perianal fistulas (4). Treatment for complex fistulas includes antibiotics, azathioprine/ mercaptopurine, infliximab and surgery (5).

**2. Oral manifestations**

Oral lesions occur in 9% of patients with crohn's disease and may represent the initial manifestation of disease (6).

**• Aphthous stomatitis**

Aphthous ulcers are common in patients with inflammatory bowel disease. They have been reported to have an incidence of 4,1% in crohn's disease and 1,5% in ulcerative colitis (7). They often occur during flares in patients with ulcerative colitis. Aphthae associated with inflammatory bowel disease cannot be differentiated clinically from common aphthae. Histologic examination often reveals non-caseating granulomas and granulomatous inflammation similar to that seen in the bowel wall (8). Treatment of the underlying condition may be curative (9). Symptomatic treatment, including topical anesthetics such as viscous xylocaine, can be helpful in alleviating the pain of aphthous ulcers.

**• Mucosal nodularity (cobblestoning)**

Mucosal nodularity, although infrequent, is specific for crohn's disease. It appears as mucosal coloured papules forming firm plaques on the buccal mucosa and palate. Cobblestoning may be painful and interferes with speaking and eating. Treatment of the underlying disease is necessary. Corticosteroids are generally effective. However, severe or refractory cases may require infliximab therapy (10).

**• Pyostomatitis vegetans**

Pyostomatitis vegetans is a rare specific marker of inflammatory bowel disease. Lesions appear as yellowish flat ulcerations on the buccal and gingival mucosa, typically in the shape of "snail tracks". Generally, inflammatory bowel disease precedes the onset of pyostomatitis vegetans and mimics the activity of the bowel disease (11). Treatment of the underlying disorder may result in resolution of oral lesions (12). Topical and systemic therapy with corticosteroids is the approach of choice. Dapsone and azathioprine are considered second-line agents. Oral cyclosporine A has been reported to be beneficial for pyostomatitis vegetans (13).

**3. Metastatic crohn's disease**

Metastatic crohn's disease is characterized by cutaneous granuloma formation distant from the gastrointestinal tract in patients with crohn's disease. It is a specific lesion representing a non-caseating granulomatous histology identical to the

underlying disease (14). It should be pointed out that the disease is not considered contagious nor is it capable of metastases in the manner we associate with malignancies. Lesions can occur anywhere on the body, but are found mainly in the lower extremities and intertriginous areas. The clinical appearance of metastatic crohn's disease is variable. The lesions may manifest as subcutaneous nodules or erythematous plaques and secondary ulcers (1). This disorder is more commonly seen in patients with colonic or rectal involvement rather than the terminal ileum alone (15). Treatment of the underlying inflammatory bowel disorder may cause resolution of the skin lesions in some patients. Some of these lesions may respond to treatment with corticosteroids (16). Azathioprine and infliximab have been used successfully in some cases (17).

**Reactive skin eruptions**

Reactive skin eruptions include a variety of cutaneous manifestations that are strongly associated with inflammatory bowel disease such as erythema nodosum, pyoderma gangrenosum and sweet's syndrome (1).

**1. Erythema nodosum**

Erythema nodosum is characterized by raised, tender, red or violet subcutaneous nodules of 1 to 5 cm in diameter. It affects 3 - 8% of patients with inflammatory bowel disease (2) and occurs primarily on the anterior portion of the lower extremities. Histopathologically, the nodules represent a septal panniculitis. In patients with inflammatory bowel disease, eruptions of erythema nodosum often are associated with exacerbations of the bowel disease (15) but not with the severity or extent (18). In most cases, erythema nodosum is self-limiting and will resolve in three to six weeks without scar formation (19). Nevertheless, treatment consists of controlling the underlying flare of bowel disease by administration of oral non steroidal anti-inflammatory medications. However, severe or refractory cases may require infliximab therapy (20).

**2. Pyoderma gangrenosum**

Pyoderma gangrenosum has been reported in 1% to 10% of patients with ulcerative colitis and in 0,5% to 20% of patients with crohn's disease (15). Lesions often begin as pustules that rapidly ulcerate and form crater-like holes overlying pus-filled fistulous tracts. Pyoderma gangrenosum can occur anywhere on the body but the commonest sites are the legs and peristomal sites. The correlation of pyoderma gangrenosum with the activity of the inflamed bowel is controversial, but sometimes coincides with an exacerbation of the underlying intestinal disease (1). Treatment of pyoderma gangrenosum has relied on topical and systemic steroids, with cyclosporine or tacrolimus reserved for refractory cases (21). Infliximab is highly effective in healing refractory lesions (22).

**3. Sweet's syndrome**

Sweet's syndrome is characterized by tender, red inflammatory nodules or papules, usually affecting the upper limbs, face or neck. It is part of the group of acute neutrophilic dermatoses that includes pyoderma gangrenosum. The rash is associated with active disease in 67% - 80%, but may precede the onset of intestinal symptoms in 21% and has been reported 3 months after proctocolectomy for ulcerative colitis (23). This rare extraintestinal manifestation of inflammatory bowel disease usually responds rapidly to corticosteroid therapy (1).

**Associated diseases**

An increased association between inflammatory bowel disease and psoriasis has been reported (24). Psoriasis occurs in 9,6% of patients with crohn's disease compared to 2,2% of the controls (25). Vitiligo occurs with greater frequency amongst patients with inflammatory bowel disease compared with the general population. Polymyositis, lupus erythematosus and scleroderma have also been reported in association with inflammatory bowel disease (1). Other cutaneous manifestations are related to hypercoagulability, to nutritional deficiency, or to treatments used for inflammatory bowel disease. The spectrum of cutaneous manifestations associated with inflammatory bowel disease is broad and varied even though some of the skin lesions is distinctive and easily diagnosed. When the aetiologies of inflammatory bowel disease are better understood, the occurrence of particular cutaneous lesions will be clearer. Patients presenting with inflammatory bowel disease should be examined for cutaneous manifestations. Treatment should be directed both at the cutaneous lesions and at the underlying gastrointestinal disease.

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