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Overview

IBD and ostomies are associated with a number of varying skin complications. These skin complications can arise as a result of inflammation from disease activity, trauma from disease/surgeries, associated medication use and other proposed mechanisms. There is wide variability in the presentation of different skin conditions associated with IBD and ostomies, which are listed (in part) below:



• Erythema nodosum presents as painful, tender bumps (nodules) that can occur anywhere on the body but most frequently appear on the shins. The bumps may appear sore and hot at first and become more bruise-like as they disappear (which takes about six weeks). Approximately 4-15% of Crohn's disease patients and 3-10% of

ulcerative colitis patients will experience erythema nodosum.

- Pyoderma gangrenosum is a condition in which non-infectious nodules form and later develop into deep and painful ulcers. Pyoderma gangrenosum is more common in individuals with ulcerative colitis (5-12%) as opposed to individuals with Crohn's disease (1-2%). It commonly presents on the legs or on skin surrounding a stoma (Huang).
- Acrodermatitis enteropathica is a skin condition which presents with a flaky rash and blisters on the hands, feet, face, or genitals. Acrodermatitis enteropathica is caused by low zinc levels and can be either congenital or acquired (acquired, in the case of IBD and ostomy patients).
- Sweet's syndrome can appear similar to erythema nodosum (when impacting the lower limbs) with the development of painful, tender bumps on the skin. In addition to nodule-formation, Sweet's syndrome also causes fever and is more common in women though overall is rare in occurrence.
- Bowel-associated dermatosis-arthritis syndrome (BADAS) is a rare skin complication of IBD in which flat, discolored lesions of the skin develop and later evolve into purple, raised pustules. In addition to dermatological complications, BADAS also presents with joint pain, fever, and chills.

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Overview (continued...)

- Fistulae are abnormal passageways between an organ and another structure caused by inflammation or injury. Crohn's disease patients are more likely to experience fistulae as opposed to ulcerative colitis patients. There are several types of fistulae defined on the basis of the passageway between the organ and subsequent structure. These include:
 - **Perianal fistulae** are the most common type of fistulae in Crohn's patients. This type of fistula generally originates from infected anal glands which then open onto the skin surrounding the anus.
 - Enterocutaneous fistulae form between the intestine and the skin. They can form as a result of disease activity or as a complication of surgery.
 - Enteroenteric or enterocolic fistulae form between the small and large intestine.
 - Enterovaginal fistulae form between the intestine and the vaginal wall.
 - Enterovesical fistulae from between the intestine and the bladder.
 - **Ilio-anal pouch fistulae** occur when an abnormal connection is developed between the pouch and the bowel, bladder, vagina or outer skin. This is a rare complication and generally treatable with medication (although certain cases may require surgery) (Crohn's and Colitis UK).
 - Fissures are small tears in the lining of the anus which can cause pain and bleeding when passing stool. Anal fissures are more common in individuals with Crohn's than individuals with ulcerative colitis.
 - Skin tags are small, flap-like growths of the skin that commonly present in Crohn's patients. Skin tags associated with IBD generally develop around the anus and can become irritated if fecal matter attaches to them.
 - Psoriasis is an autoimmune skin condition in which red, itchy, scaly patches present on the knees, elbows, torso, and scalp (most commonly). IBD and psoriasis have been linked as possible co-occurring conditions and can uncommonly occur as a medication side effect.
 - Secondary amyloidosis is a condition in which irregular protein deposits accumulate onto the skin and is thought to be associated with IBD as result of chronic inflammation (Real de Asúa).
 - Vitiligo is an autoimmune disease in which patches of unpigmented skin develop on varying locations of the body. The connection between vitiligo and IBD is thought to be due to overlap of underlying autoimmune mechanisms.

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Causes and Risk Factors in IBD/Ostomy Patients

Although the cause of certain skin conditions associated with IBD and/or ostomy are not entirely known, there are certain conditions with known pathogenesis and/or proposed mechanisms of causation. Please note the term proposed – there is a high likelihood we will see development in this area of study in the near future, and changes in our understanding of IBD and ostomies are inevitable. Theories proposed at this time may or may not stand in the future.





Colon without inflammation = reduced risk of skin conditions



Colon with active disease = increased risk of skin conditions

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Active disease: Many of the dermatological

manifestations of IBD and ostomy have been shown to ease during times of remission. This leads researchers and healthcare professionals to believe active disease states are connected to development of associated skin conditions – extraintestinal manifestations of IBD and ostomy are shown to be more prevalent during active disease. Although there are numerous theories as to the exact cause of this, it seems inflammation associated with active disease likely disrupts the gut mucosa, which in turn leads to immune dysregulation (Huang). This immune dysregulation can then present as certain extraintestinal manifestations (including dermatological conditions).

- Chronic inflammation: As described above, chronic inflammation of the digestive tract is thought to alter the gut mucosa leading to immune dysregulation and associated dermatological conditions.
- Malabsorption issues: Certain skin conditions associated with IBD and ostomies are a result of poor vitamin/mineral intake. This can be caused by intestinal damage or inflammation leading to malabsorption of nutrients, as well as chronic diarrhea or vomiting causing nutrient loss. For example, acrodermatitis enteropathica can be induced by low zinc levels caused by significant loss of zinc from dietary sources during periods of excessive diarrhea.

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Causes and Risk Factors in IBD/Ostomy Patients (continued...)

- Certain medication options: Some medications have been associated with development of skin conditions. Use of sulfasalazine may produce an allergy-type skin rash in individuals allergic to the sulfa component of the medication. Long-term steroid use has been connected with thinning of the skin, development of stretch marks, aggravation of acne, facial and ankle swelling, and impaired wound healing (Crohn's and Colitis Foundation). While anti-TNF agents can be used for the treatment of both IBD and psoriasis, they have actually been associated with development of spontaneous psoriatic plaques in patients utilizing the medication solely for IBD treatment. Resolution of mild plaques typically occurs with mild to moderate medical involvement such as topical steroids, while more severe plaques, not responding to topical treatment, may require cessation of the responsible anti-TNF agent (Huang).
- Genetics: Although this is an area still requiring much research, certain genetic dispositions that put an individual at increased susceptibility of IBD or ostomy development may also predispose an individual to particular dermatological manifestations, such as vitiligo or psoriasis (Chi) (Lee).

Signs and Symptoms

Signs and symptoms of dermatological conditions associated with IBD and ostomies will vary widely depending upon the specific type of skin manifestation. Visual identification of the skin condition through rashes, plaques, pustules, bumps, etc., will frequently notify an individual of a possible skin manifestation. Dermatological conditions such as fistulae, fissures, or skin tags (particularly anal ones) may be less visible with the first signs and symptoms being pain or discomfort. It is recommended to consult with your gastroenterologist, primary care physician, or dermatologist in order to get the care you need (whether that be direct care or referral to a specialist).



Diagnosis

Diagnosis and treatment of skin conditions associated with IBD and ostomies will be dependent upon the specific dermatological manifestation.

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Diagnosis (continued...)

Many conditions can be diagnosed upon physical examination and patient history (e.g. erythema nodosum and pyoderma gangrenosum). Specifically, a rectal examination can be used to identify anal fissures, anal skin tags, and fistulae dependent upon their location. In certain cases, a biopsy of the skin tissue may be taken to identify underlying disease processes as observed under microscope. Skin biopsies can be taken to confirm a diagnosis (as with erythema nodosum and pyoderma gangrenosum) or may be required for initial identification of the condition (such as Sweet's syndrome, BADAS, psoriasis, secondary amyloidosis, or vitiligo).

Bloodwork may also be a useful tool in identification of certain skin conditions. For example, acrodermatitis enteropathica can be identified by low plasma zinc levels (Jagadeesan). Elevated markers of inflammation, such as C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), may also aid in diagnosis of certain skin conditions.

Diagnosis of particular conditions can be difficult due to a lack of a key diagnostic sign. For example, lesions of Sweet's syndrome and BADAS appear similar under a microscope and present with comparable blood test results, making differentiation difficult (Hassold).



Negative blue dye test = no enterovaginal fistula



Positive blue dye test = enterovaginal fistula present Fistulae can involve a specific regimen of testing in order to diagnose - especially dependent upon the type and location of the fistula. Possible testing options for fistulae include:

- Blue dye test: This test is utilized to identify an enterovaginal fistula. A tampon is inserted into the vagina followed by injection of a blue dye into the rectum.
 Presence of the blue dye on the tampon upon removal indicates the presence of an enterovaginal fistula.
- Computed tomography (CT) scan: A CT scan can be used to visualize soft tissue structures and thus identify the presence of fistulae. CT scans utilize multiple x-ray scans to produce an image. While this does require radiation, risk can be decreased by targeting imaging on only certain areas of the body and using CT scans in appropriate clinical scenarios.
- Magnetic resonance imaging (MRI): A MRI can be utilized to visualize soft tissue structures and thus identify the presence of fistulae. MRIs do not utilize radiation.

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Diagnosis (continued...)

- Vaginogram/barium enema: This test is utilized to identify a rectovaginal fistula. A contrast material is inserted into the vagina or rectum and can be seen on x-ray imaging. If there is a rectovaginal fistula present, the dye will be seen (to a degree) in both the vaginal and rectal structures.
- Exam under anesthesia (EUA): A physician may perform a manual exam under anesthesia to either identify the location of the fistula or further exam the fistula for treatment/surgery.
- Rectal ultrasound: This test is utilized to identify a perianal fistula. A rectal ultrasound probe (termed a "transducer") is passed through the anus into the rectum which allows visualization of the rectum and subsequent identification of a perianal fistula (Gecse).



Treatment

Treatment of skin manifestations associated with IBD and ostomies will depend on the condition and can fall within a wide range, from vitamin/mineral supplementation to surgery.

Because many of the dermatological conditions associated with IBD and ostomy are influenced by active disease, control of gastrointestinal symptoms is key to prevention and treatment of skin manifestations. Control of underlying disease has been shown to decrease prevalence of conditions such as erythema nodosum and pyoderma gangrenosum and can prevent development of conditions such as anal fissures, fistulae and anal skin tags.

Dermatological conditions associated with inflammation can generally be treated with antiinflammatory medication options such as oral or topical low dose steroids (such as erythema nodosum, Sweet's syndrome and BADAS). More aggressive disease processes (such as pyoderma gangrenosum, secondary amyloidosis or conditions failing the first line of low-dose anti-inflammatories) may require high dose steroids or immunosuppressives.

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Treatment (continued...)

Skin manifestations resulting from poor vitamin/mineral intake can be resolved by supplementation, injections or infusions dependent upon the vitamin/mineral in deficit. For example, zinc supplementation can be utilized in treatment of acrodermatitis enteropathica for IBD or ostomy patients suffering from low zinc levels from chronic diarrhea or vomiting (Jagadeesan). As with most dermatological conditions associated with IBD and ostomy, treatment of the underlying gastrointestinal symptomology is also crucial to treatment.





Treatment of psoriasis-associated with IBD can be resolved through use of medications that concurrently treat both IBD and psoriasis. For psoriasis caused by anti-TNF agents, transition from an anti-TNF agent to a different treatment modality has been shown to resolve certain cases of IBD-induced psoriasis; however, this is not always necessary as mild and moderate cases are easily treated with topical steroids. Vitiligo has also been shown to be exacerbated by anti-TNF agent use, so treatment transition may be necessary in these cases as well. In addition, vitiligo may require repigmentation, depigmentation or light therapy to treat. When switching treatment modalities, it is important to weigh the benefits and risks of transition with a healthcare provider.

Multiple modalities can be utilized in treatment of fistulae and depend on the type and location of the fistula. A combination of medications may be used to ease inflammation in addition to nonoperative and operative treatments. Fibrin glue can be utilized as a nonoperative treatment modality in which a medicinal adhesive is used to seal the fistula. Operative treatments include fistula plug repair, surgical mesh, seton drains, advanced flap repair and graciloplasty. Fistula plug repair involves a surgeon placing a cone-shaped graft into the fistula tract where it can cover the opening and close the passageway. A surgical graft for a fistula functions similarly to that of mesh repair for a hernia and can be used to block the fistula. Seton drains allow air and stool to drain from fistulae helping to prevent abscess formation. This can help to close the tract (or shrink it in the case of enterovaginal fistulae) and prevent infection. In an advanced flap repair, a surgeon removes the fistula and stitches the tract back down. In graciloplasty, a section of the gracilis (a thigh muscle) is removed and placed between the bowel and vagina to create a wall (Sanders).

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Prevention

Management of gastrointestinal disease activity is key to prevention of dermatological manifestations. By controlling inflammation, one can aim to avoid skin conditions associated with IBD and ostomy. In addition, maintenance of a well-balanced diet can also help in prevention of vitamin/mineral deficiencies which can then lead to development of certain dermatological conditions. As always, regular use of sunscreen is recommended. Coordination with a multidisciplinary healthcare team is critical in managing IBD and ostomy, while also ensuring quick treatment with any skin manifestations that may arise.



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