Chapter 15
Inflammatory Bowel-Associated Spondyloarthropathy

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Inflammatory bowel disease is relatively common with a prevalence of 100–200/100,000 for Crohn's disease and 150–250/100,000 in ulcerative colitis. There is an equal sex distribution and a bimodal age distribution, with the greatest incidence in adolescence and young adults. Between 4 % and 11 % of patients with inflammatory bowel disease can develop spondyloarthropathy (SpA). Once again, males are more commonly affected than females, and patients have a higher prevalence of HLA-B27. In general, up to 36 % of patients with inflammatory bowel disease, with or without SpA, will develop extra-intestinal manifestations, many of which are mucocutaneous. These include erythema nodosum, pyoderma gangrenosum, pyoderma vegetans, vesiculopustular eruption of ulcerative colitis, cutaneous polyarteritis nodosa, metastatic Crohn's disease, Sweet's syndrome, linear IgA bullous dermatosis, psoriasis, perianal skin tags, and epidermolysis bullosa acquisita. Ocular manifestations include episcleritis and uveitis, retinal artery and vein occlusion, neuroretinitis, and ischemic optic neuropathy [1].

Erythema nodosum (EN) is a delayed hypersensitivity response to an as of yet unidentified antigen. It is clinically characterized by the acute eruption of tender, subcutaneous, erythematous nodules usually overlying the shins bilaterally. Rarely, it can localize to other surfaces of the body as well. Oftentimes there are also systemic symptoms, such as fever, chills, malaise, myalgias, and arthralgias. It can either accompany or precede the inflammatory bowel-associated SpA and usually

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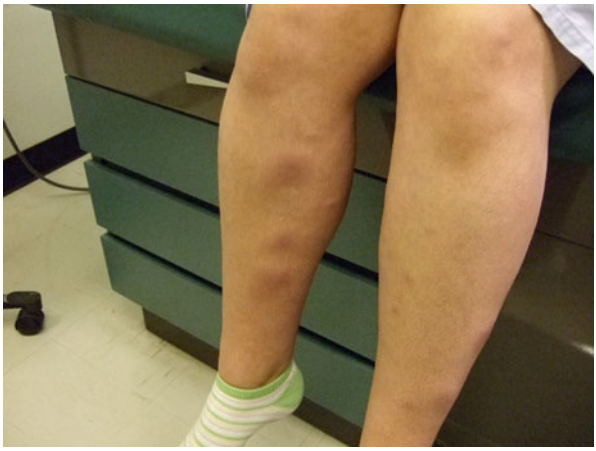

Fig. 15.1 Typical presentation of erythema nodosum with tender nodules on the shins

has a self-limited course, although recurrences can occur. The diagnosis is based on the clinical presentation and can be confirmed with an incisional wedge biopsy that includes the subcutaneous fat (Fig. 15.1) [2].

Pyoderma gangrenosum (PG) is a rare, inflammatory disorder thought to be due to abnormal immune reactivity and/or cross-reacting autoantibodies. Clinically, it can arise over a few days on any part of the skin or mucosa. It may present in one of four distinct forms: ulcerative, bullous, pustular, or vegetative. The ulcerative form presents as a large, painful, purulent, undermined ulceration. Bullous lesions present as painful, rapidly expanding superficial bullae that erode and ulcerate. Pustular lesions present as an acute, widespread eruption of painful pustules over any part of the body. This is the most characteristic presentation of PG in patients with inflammatory bowel disease. Vegetative lesions are rare and present as hypertrophic, mildly painful nodules, or abscesses. Patients can also have systemic symptoms of fever, chills, and malaise and internal organ involvement of the liver, kidney, and spleen. This is a diagnosis of exclusion on biopsy, and frequently other conditions, such as cutaneous infections, need to be ruled out [3] (Fig. 15.2a, b).

Pyostomatitis vegetans is thought to be a variant of pyoderma gangrenosum that occurs mainly in the oral or genital mucosa. It is characterized by an acute-onset, painful, pustular or erosive eruption alongside vegetating plaques. The vesiculopustular eruption of ulcerative colitis also presents very similarly with an acute eruption of vesicles and pustules on the skin that heal with residual hyperpigmentation.

Cutaneous polyarteritis nodosa is a medium vessel vasculitis that presents as painful, erythematous, purpuric, or ulcerated nodules on the lower extremities bilaterally.

Metastatic Crohn's is a non-caseating, granulomatous inflammatory disorder that appears clinically as erythematous or ulcerated nodules or plaques on the skin.

Sweet's syndrome, also known as acute febrile neutrophilic dermatosis, is characterized by fever, malaise, and an explosive eruption of dozens of erythematous, indurated, occasionally vesicular papules and plaques (Fig. 15.3).

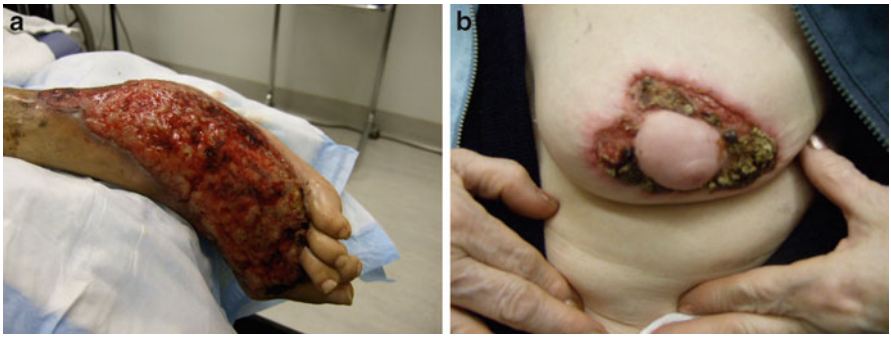

Fig. 15.2 (**a**, **b**): Two images of different patients with severe, necrotizing, ulcerating pyoderma gangrenosum

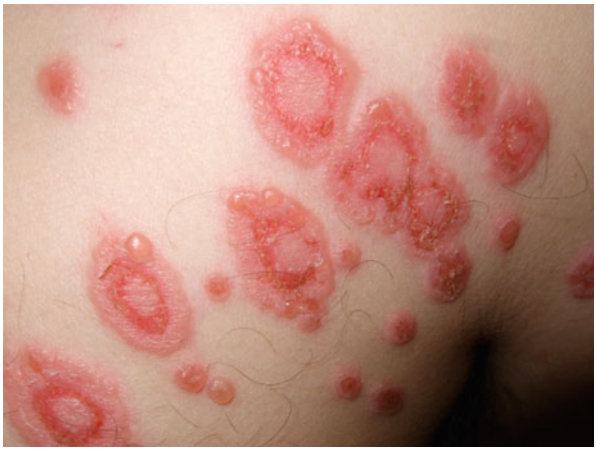

Fig. 15.3 The annularly arranged, "string of pearls," blistering seen in typical linear IgA bullous dermatosis

Linear IgA bullous dermatosis is an autoimmune blistering condition characterized by the eruption of multiple bullae in polycyclic or annular configurations.

Epidermolysis bullosa acquisita is an acquired autoimmune disorder of type VII collagen. Patients often complain of fragile skin that blisters at sites of friction or trauma and heals with residual scar formation and milia (tiny epidermoid inclusion cysts).

Psoriasis is a manifestation of inflammatory bowel-associated SpA that shares genetic features with both SpA and Crohn's disease as defined by genetic markers at the interleukin-23 locus.

Perianal skin tags, flesh-colored, well-defined, 1–10 mm, pedunculated papules, can also be found and are considered to be related to constant friction and trauma [1].

Differential Diagnosis

The differential diagnosis of erythema nodosum includes all other causes of panniculitis – morphea/scleroderma, alpha1-antitrypsin deficiency, pancreatic panniculitis, lupus panniculitis, lipodystrophic panniculitis, cold panniculitis, lipodermatosclerosis, and malignancy-related panniculitis. One also needs to rule out vasculitis, such as erythema induratum, nodular vasculitis, and polyarteritis nodosa [4]. The differential diagnosis for pyoderma gangrenosum, pyostomatitis vegetans, vesiculopustular eruption of ulcerative colitis, and metastatic Crohn's disease includes bacterial, viral, or fungal infections, vasculitis, neutrophilic disorders (Sweet's syndrome, Behcet's disease, bowel-associated arthritis dermatosis), drug eruptions, malignancy, and dermatitis artefacta. Polyarteritis nodosa also needs to be differentiated from other forms of vasculitis, panniculitis, drug eruptions, and infections. Perianal skin tags can often be confused with hemorrhoids and condylomata acuminata. Finally, epidermolysis bullosa acquisita needs to be differentiated from other autoimmune blistering conditions (such as pemphigus vulgaris, bullous pemphigoid, porphyria cutanea tarda, bullous lupus erythematosus), drug eruptions, and infections [5].

Biopsy

Histologically, erythema nodosum is a prototypical septal panniculitis of lymphocytes, histiocytes, neutrophils, and/or eosinophils. Occasionally, multinucleate giant cells and fibrosis can be seen as well. Pyoderma gangrenosum, pyostomatitis vegetans, and vesiculopustular eruption of ulcerative colitis can all appear as a bullous, pustular, necrotic, or ulcerative lesion with a predominant neutrophilic infiltrate. Pseudoepitheliomatous hyperplasia of the ulcer edge can also be seen. Metastatic Crohn's disease is often seen under the microscope as non-caseating, granulomatous inflammation with a predominance of histiocytes and lymphocytes. Polyarteritis nodosa has the prototypical leukocytoclastic vasculitis of small- and medium-sized blood vessels with intimal proliferation and/or thrombus. Sweet's syndrome shows a diffuse dermal neutrophilic infiltrate with prominent dermal edema and no evidence of true vasculitis. Psoriasis appears as regular acanthosis of the rete ridges with neutrophils on the stratum corneum and overlying hyperkeratosis or parakeratosis. Perianal skin tags are papillomatous and acanthotic with dilated blood vessels. Epidermolysis bullosa acquisita is characterized by a subepidermal blister with limited cellular infiltrate that will stain IgG and complement linearly along the dermal-epidermal junction on direct immunofluorescence [6].

Patient has confirmed diagosis of inflammatbory bowel disease.
Purpura, petechiae, ecchymoses, bruising and/or ulcerations and/or scarring
Erythematous, painful, 1cm or larger, swollen nodules
Erythematous, scaly white, well demarcated plaques
Bullae / Vesicles / Blisters / Pustules
Likely Polyarteritis nodosa
Likley Erythema Nodosum
Likely Psoriasis
Possible Pyostomatis Vegetans, Metastatic Crohns, Pyoderma gangrenosum, Epidermolysis bullosa acquisita, Linear IgA Bullous Dermatosis or Sweets Syndrome
Confirm diagnosis with biopsy
Confirm diagnosis with biopsy: Follow diagnostic algorithm in Erythema Nodosum chapter.
Clinical diagnosis, biopsy not needed. If there is uncertainty, you can do a biopsy to confirm. Follow diagnostic algorithm in Psoriasis chapter.
Confirm Diagonsis: History, Physical exam, biopsies (histology, immunofluorescence and tissue culture for bacteria and myocobacteria), cultures (to rule out bacterial, fungal and viral disease), routine bloodwork
Note – Pyoderma Gangrenosum, Linear IgA Bullous Dermatosis and Metasttic Crohns disease can occur anywhere on the skin
Pyostomatitis vegetans
Classic Plaque Psoriasis
Sweets Syndrome
Epidermolysis Bullosa Acquisita
Polyarteritis Nodosa
Erythema nodosum

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