Bowel-Associated Dermatosis–Arthritis Syndrome

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Clinical signs and features include:

- Seen in up to 20% of patients with jejunal-ileal bypass 3 months to 5 years following surgery; also associated with biliopancreatic diversion, Billroth II gastrectomy, occasionally inflammatory bowel disease (IBD), and rarely after laparoscopic gastric bypass surgery [1-3]
- Presents with flu-like symptoms of fevers, myalgia, and tenosynovitis with symmetrical small joint polyarthritis without deformities [1]
- Painful skin rash develops 12–36 h after flu-like symptoms with crops of small erythematous purpuric macules often on the upper trunk and extremities that progress to indurated, urticarial purpuric papules and then vesiculopustular lesions over the next 24–48 h (see Fig. 22.1). The lesions heal without scarring over the next 2 weeks [1].
- Symptoms tend to recur every 4–6 weeks [1]
- Erythema nodosum-like nodules may be present on the legs [1]

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The differential diagnosis should include other neutrophil mediated skin disorders, such as:

- Pyoderma gangrenosum
- Sweet's syndrome
- Pustular vasculitis of the hands
- Leukocytoclastic vasculitis
- Septic vasculitis
- Behçet's syndrome
- Rheumatoid neutrophilic dermatosis
- Acute generalized exanthematous pustulosis
- Erythema nodosum
- Henoch-Schönlein purpura

Pathogenesis of this disease involves:

- Bacterial overgrowth in blind loops of bowel leads to immune complexes containing peptidoglycans that circulate in the bloodstream and deposit in the skin and joints leading to the joint and skin pathology [3]

Histopathological features include:

- Neutrophilic dermatosis similar to Sweet's syndrome with leukocytoclasis and perivascular inflammation, usually without vasculitis or vessel wall destruction (see Fig. 22.2)
- Early: perivascular lymphocytic infiltrate with neutrophils, leukocytoclasis, extravasated red blood cells without fibrin depositions
- Mature: papillary dermal edema results in subepidermal blister, papillary and reticular dermal edema, and nodular neutrophilic infiltrate with nuclear dust that may include some lymphocytes and histiocytes

The diagnosis is made using a combination of:

- Clinical symptoms in a patient with appropriate clinical history
- Biopsy can help distinguish from other skin processes associated with gut pathology
- No radiographic joint changes with negative rheumatoid factor, antinuclear antibodies (ANA), immunoglobulins, uric acid

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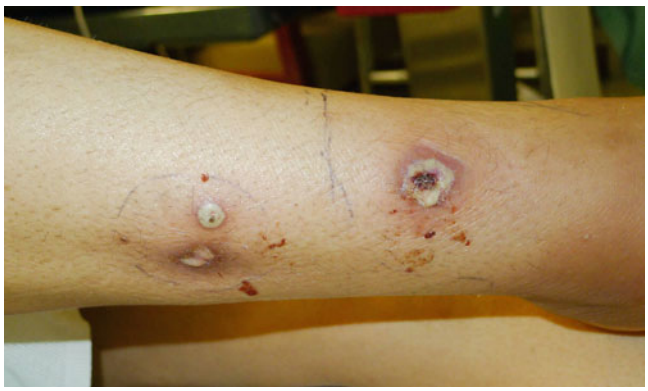

Fig. 22.1 Bowel-associated dermatosis–arthritis syndrome. Purulent nodules and ulcers

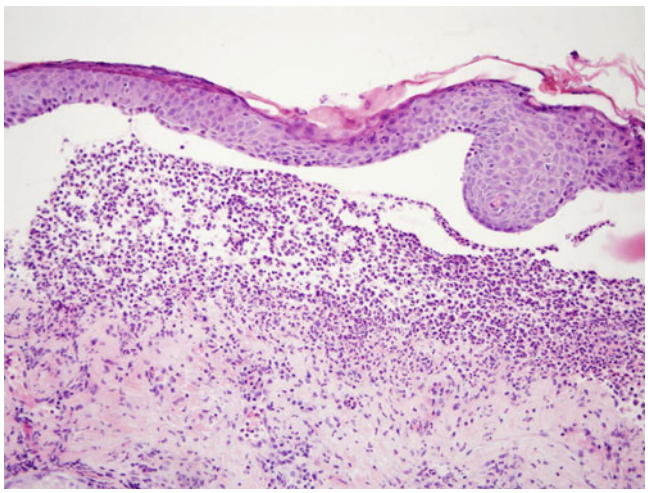

Fig. 22.2 Bowel-associated dermatosis–arthritis syndrome. Dense neutrophilic infiltrate in the superficial and mid-dermis (40×)

Treatment options include [1]:

- Systemic corticosteroids antibiotics such as tetracycline, minocycline, sulfapyridine, erythromycin, metronidazole, rifaximin although response is inconsistent
- Colchicine
- In refractory cases may need to remove blind loops surgically

Acrodermatitis Enteropathica

Clinical signs and features include:

- Acrodermatitis enteropathica can be genetic or acquired [4, 5] Zinc (Zn) deficiency
- Acrodermatitis enteropathica [4, 5]
  - Classic clinical triad of diarrhea, alopecia, and a periorificial, acral cutaneous eruption (see Fig. 22.3)
  - Genetic disease presents soon after weaning off the breast (breast milk has its own zinc binding factor) or between fourth and tenth week in formula-fed infants
  - Begins as symmetric, eczematous plaques that evolve into vesiculobullous, pustular, desquamative, and erosive plaques
  - Often periorificial with classic sparing of the upper lip: "horseshoe-shaped" or "U-shaped" configuration
  - Risk of superinfection with *Staphylococcus aureus* and *Candida albicans*
  - Alopecia with brittle and dry hair
  - Other signs: hypopigmentation, impaired wound healing, stomatitis, angular cheilitis, paronychia, photophobia, conjunctivitis, and irritability
  - Infants can be listless and apathetic; can be fatal in infants
  - Mild deficiency can lead to growth retardation in children, hypogonadism in men, dysgeusia, abnormal dark adaptation, and psoriasiform dermatitis of the hands, feet, and occasionally knees

The differential diagnosis should include:

- Other forms of deficiency dermatitis due to deficiency in amino acids (*e.g.*, Hartnup disease), fatty acids, biotin (multiple carboxylase deficiency), niacin (pellagra) [6]
- Necrolytic migratory erythema
- Necrolytic acral erythema: zinc deficiency and/or improvement of rash with zinc supplementation is observed in patients with hepatitis C and necrolytic acral erythema [7]

Pathogenesis of this disease involves:

- Genetic: autosomal recessive due to mutations SLC39A4 intestinal zinc transporter on chromosome 8q24.3 that encodes ZIP4-transporter on chromosome 8q24.3 that encodes ZIP4-transporter on enterocytes with resultant impaired zinc absorption [5]
- Acquired: decreased dietary intake; alcoholics; vegetarians and vegans; anorexia nervosa; total parenteral nutrition; diets high in cereal grain and low in animal protein; increased usage and decreased stores in premature infants; decreased absorption secondary to cystic fibrosis, gastric bypass, IBD, celiac disease, short bowel syndrome, chronic diarrhea, premature gut epithelium; increased elimination related to alcoholism, burns, malignancy, infections, pregnancy, renal disease (nephrotic syndrome), and stress; medications: penicillamine, diuretics, antimetabolites, valproate [4]

Histopathological features include:

- Psoriasiform epidermal hyperplasia with prominent confluent parakeratosis occasionally with neutrophils, pallor of keratinocytes due to intracellular edema in the superficial epidermis, leading to intraepidermal blisters, hypergranulosis, occasional acantholysis, focal dyskeratosis, edema of papillary dermis, and dilated tortuous capillaries (see Fig. 22.4)

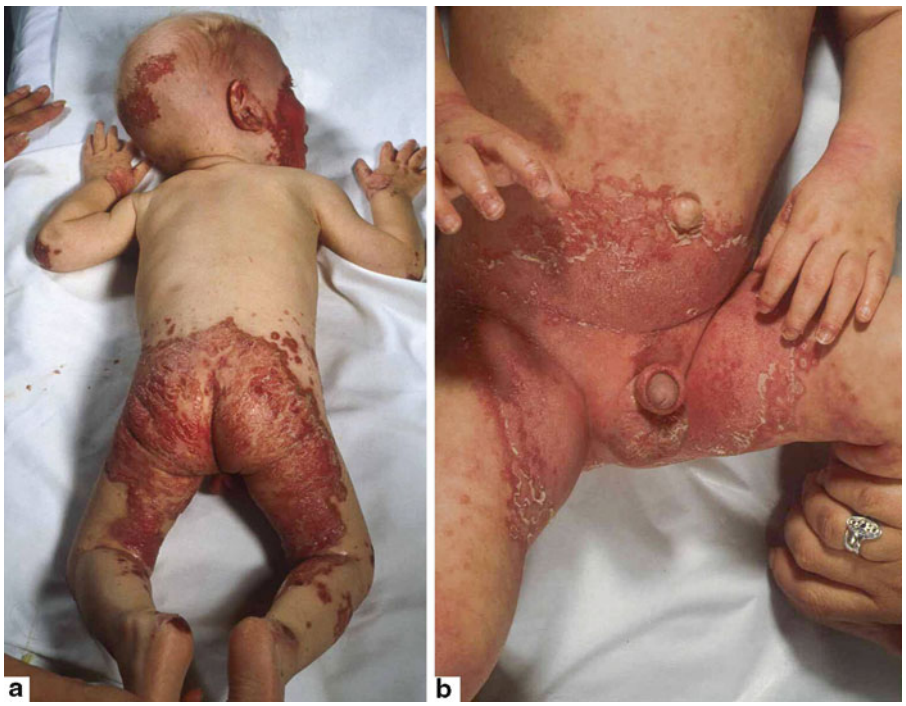

Fig. 22.3 Acrodermatitis enteropathica. Alopecia and confluent erythematous, scaly, eroded plaques involving the periorificial and diaper regions (Image courtesy of Howard Pride, MD)

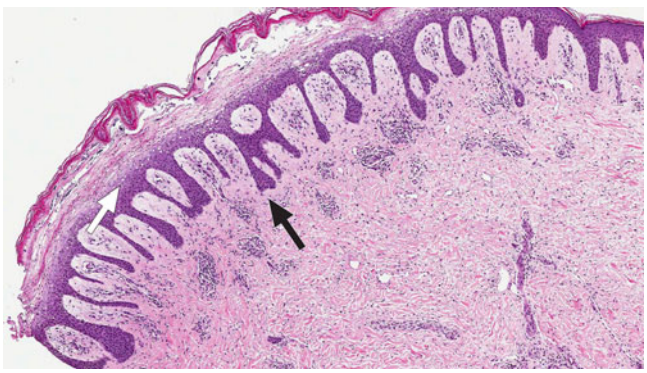

Fig. 22.4 Acrodermatitis enteropathica. Epidermal acanthosis (*black arrow*), with spongiosis, pallor, and ballooning degeneration of the upper epidermis (*white arrow*) (Image courtesy of Rajendra Singh, MD)

- Bullous form: intraepidermal vacuolar changes leading to intraepidermal blisters and vesiculation with prominent necrosis
- Candida and staph superinfection not uncommon

The diagnosis is made using a combination of [5]:

- Measuring zinc levels: need to draw in AM (diurnal variation with lower levels later in the day due to meals); watch for fluctuation with inflammation, increased with hemolysis
- Measuring zinc-dependent enzymes: alkaline phosphatase, which is low in zinc deficiency
- Hypoalbuminemia will decrease zinc levels

Treatment options include [8]:

- Zinc-sulfate: enteral supplementation; zinc-chloride: parenteral supplementation (need to monitor copper levels, which can be severely decreased with elevated Zn levels)
- Clinical improvement in 2–7 days and healing in 2–4 weeks

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