***no patient handout*

Dermatitis herpetiformis

Synopsis

Dermatitis herpetiformis (DH) is a chronic pruritic autoimmune blistering disorder associated with gluten-sensitive enteropathy. DH most commonly affects patients of Northern European descent and occurs more frequently in men than women. While more than 90% of patients have associated gluten-sensitive enteropathy on small bowel biopsy, only 20% exhibit symptoms of intestinal disease. The pathogenesis involves the deposition of IgA immune complexes in the papillary dermis. The associated autoantigen is an epidermal transglutaminase. There is a genetic predisposition to the disease, as certain human leukocyte antigen (HLA) haplotypes, HLA class II DQ2, demonstrate increased expression.

The disease manifests as an intermittent pruritic papulovesicular eruption over the extensor surfaces of the extremities. Many patients who adhere to a strict gluten-free diet experience complete remission of their disease. Patients with DH are at an increased risk of developing **Hashimoto thyroiditis**, **insulin-dependent diabetes mellitus**, and enteropathy-associated T-cell lymphoma, and therefore warrant close surveillance.

For more information, see **OMIM**.

Codes

ICD10CM:
L13.0 – Dermatitis herpetiformis

SNOMEDCT:
111196000 – Dermatitis herpetiformis

Look For

Small, fragile, clustered vesicles on an urticarial base located symmetrically over the elbows, knees, shoulders, scalp, and buttocks. The face and soles may also be involved. Due to the severe pruritus resulting in secondary excoriation, intact vesicles are rare, and so cutaneous findings are usually limited to pinpoint erosions and excoriations.

Diagnostic Pearls

Symmetrically grouped, extremely pruritic urticarial plaques with pinpoint vesicles over extensor arms, legs, scalp, and buttocks.

History of bloating and diarrhea associated with gluten-containing foods.

DH may be worsened by iodides and certain nonsteroidal anti-inflammatory drugs (NSAIDs).

Differential Diagnosis & Pitfalls

- **Scabies** manifests with interdigital burrows and involvement of the hands, wrists, and genital region, sparing the head.
- **Papular urticaria** may be associated with arthropod bites and is distributed over exposed areas.
- **Bullous pemphigoid** presents with urticarial erythematous plaques and intact, tense bullae in older patients.
- **Linear IgA bullous dermatosis** presents with grouped vesicles and bullae, classically in an annular configuration.
- **Atopic dermatitis** is also pruritic, with ill-defined, weeping erythematous plaques.
- **Herpes simplex virus** has nonsymmetric, localized, clustered vesicles with more pain and less pruritus.
- **Epidermolysis bullosa acquisita** may have associated milia.
- **Transient acantholytic dermatosis** (Grover disease) is a pruritic papular eruption in the seborrheic regions of older men.
- **Neurotic excoriations** are distributed in areas within reach for the patient to scratch, and no primary lesions are appreciated on exam.
- **Pemphigoid gestationis** is characterized by tense bullae over the abdomen in pregnant women.
- Chronic **prurigo** consists of lichenified excoriated papules or nodules.
- Evaluate for other causes of pruritus.

Best Tests

Skin biopsy of the edge of a lesion for histology and perilesional skin for direct immunofluorescence is diagnostic.

Serological testing includes total serum IgA level, anti-tissue transglutaminase, anti-epidermal transglutaminase, and anti-endomysial IgA antibodies. Obtaining a total serum IgA level is important as some patients with celiac disease exhibit a selective IgA deficiency resulting in false negative serologies.

Histopathology Findings:
Common features

- Aggregates of neutrophils and some eosinophils at the tips of dermal papillae (early stage)

- Subepidermal vesicles rich in neutrophils and eosinophils (later stage)
- Papillary dermal edema
- Fibrin deposition at the tips of dermal papillae
- Perivascular lymphohistiocytic infiltrate with some neutrophils and eosinophils
- Granular deposition of IgA in the papillary dermis on direct immunofluorescence

Occasional features

- Leukocytoclasia
- Intraepidermal microabscesses

Management Pearls

A strict gluten-free diet alone can greatly ameliorate symptoms. Patients should be referred to gastroenterologist to evaluate for intestinal disease. Consultation with a dietician may be helpful. DH should be managed by a dermatologist.

Therapy

A gluten-free diet and dapsone are considered first-line therapy.

- Dapsone can be started at 25 mg p.o. daily with gradual increase to an average maintenance dose of 0.5-1.0 mg/kg p.o. daily. Dapsone will improve cutaneous disease but has no effect on intestinal involvement. **Caution:** Dapsone may produce hemolysis, methemoglobinemia, a hypersensitivity syndrome, and a peripheral neuropathy (motor neuropathy more frequently seen than sensory neuropathy). Idiopathic leukopenia / aplasia is another potential complication (typically early). It is not dose related. Obtain the following baseline studies: CBC, liver function tests, and glucose-6-dehyrdrogenase levels. After the initiation of therapy, monitor patients with a CBC every week for the first month, and then follow the CBC monthly for 6 months and liver function tests every 6 months.
- Sulfapyridine 500 mg p.o. 3 times daily (slowly up-titrate to maximum dose of 2 gm p.o. 3 times daily) may be substituted in cases of dapsone intolerance.
- High-potency topical steroids can help alleviate symptoms such as pruritus.
- Other therapies that have demonstrated some benefit in case reports and series include cyclosporine, colchicine, heparin, sulfasalazine, systemic corticosteroids, and tetracycline in combination with nicotinamide.

Drug Reaction Data

Below is a list of drugs with literature evidence indicating an adverse association with this diagnosis. The list is continually updated through ongoing research and new medication approvals. Click on Citations to sort by number of citations or click on Medication to sort the medications alphabetically.

Medication	Citations
Estrogen	1
flurbiprofen	1
Gonadotropin releasing hormone agonist	2
ibuprofen	1
infliximab	1
iodide	2
leuprolide	2
NSAID	1
Oral contraceptives	2
potassium iodide	2
progesterone	2