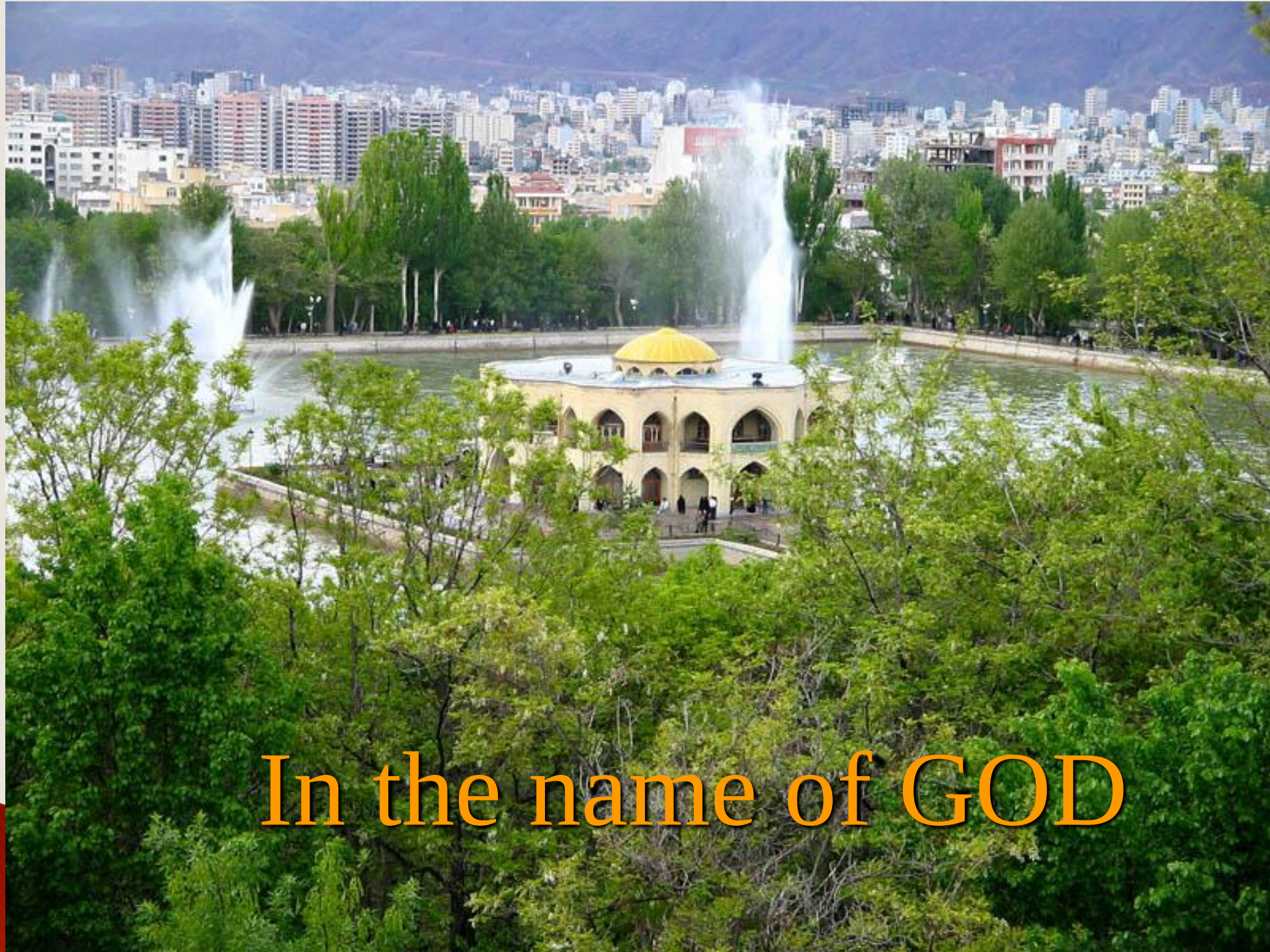

In the name of GOD

Dermatitis Herpetiformis
and
Linear IgA Bullous Dermatosis

Dr. Mohammadreza Ranjkesh

Associated professor of Dermatology, Tabriz University of Medical Sciences

Dermatitis Herpetiformis

Introduction

- Inflammatory disease of skin
- Specific cutaneous manifestation of Celiac Disease (CD)
- Symmetrical polymorphic pruritic lesions on extensors

History

- 135 years ago
- Luis Duhring firstly reports
- 1950 dapsone was found to be effective
- 50 years ago, IgA deposits at the papillary dermis described

DERMATITIS HERPETIFORMIS – HISTORIC LANDMARKS	
1884	Louis Adolphus Duhring of Philadelphia described in detail "dermatitis herpetiformis" (DH)
1888	Jean Louis Brocq of Paris renamed the condition "dermatite polymorphe prurigineuse"
1890	T Caspar Gilchrist outlined the histologic changes of DH, which were included in the 1897 edition of Duhring's textbook *Cutaneous Medicine: A Systemic Treatise on Diseases of the Skin*
1940	Sulfapyridine was reported to be an effective treatment for DH. The clinical response to sulfapyridine became a diagnostic test
1950	Dicke, a Dutch pediatrician, observed that patients with celiac disease (CD) improved during World War II when bread was in short supply, and their disease worsened when grain supplies were restored
1953	Diamino-diphenyl sulfone (dapsone), the parent compound of sulfapyridine, also proved to be effective in DH
1969	JB van der Meer demonstrated IgA deposits in the papillae of uninvolved skin in DH
1967	Independent accounts connected DH with CD
1972	Stephen Katz linked DH to the HLA-B8 antigen. This strengthened the association between CD and DH
1986	IgA class anti-endomysial antibodies discovered to be highly specific for DH and CD
1997	DH and CD found to have a common immunogenetic background with strict association with HLA alleles DQ A1*0501 and B1*02, which encode HLA-DQ2 heterodimers
2003	Epidermal transglutaminase was identified as an autoantigen in DH
2012	Zone and colleagues demonstrated that transfer of DH sera or goat anti-human epidermal transglutaminase antibodies to human skin-grafted mice mimics DH immunopathology

Table 31.1 Dermatitis herpetiformis – historic landmarks.

Epidemiology

- Rare
- Caucasian
- From 11.2 to 75.3 per 100.000
- Highest in Finland
- Extremely rare in Asian and African
- Any age, but typically adulthood 3-4 decade
- Male/female 2:1 to 1:1

Associated Diseases

- Several autoimmune disorders
  - Type I diabetes mellitus
  - Thyroid diseases
  - Connective tissue diseases, Sjögren
  - Bullous pemphigoid (BP)
- Non-Hodgkin lymphomas
- Gastrointestinal malignancies
- Less hypercholesterolemia
- Fewer smoker compared general
  - Smoking have protective
  - Suppresses natural killer lymphocyte

AUTOIMMUNE DISORDERS ASSOCIATED WITH DERMATITIS HERPETIFORMIS	
Common	
• Autoimmune thyroid disease (Hashimoto thyroiditis) • Insulin-dependent diabetes mellitus	
Uncommon	
• Pernicious anemia	
Rare	
• Addison disease • Autoimmune chronic active hepatitis • Alopecia areata • Myasthenia gravis • Sarcoidosis	• Systemic sclerosis (scleroderma) • Sjögren syndrome • Systemic lupus erythematosus • Vitiligo

Table 31.2 Autoimmune disorders associated with dermatitis herpetiformis.

Clinical Manifestations

- **polymorphism**
  - Erythematous papule
  - Urticarial plaque
  - Overwhelming vesicle
  - Small tense blisters with serohemorrhagic content
  - Centrifugal growth pattern
  - Erosion, excoriation, and crust

Clinical Manifestations...

- **Symmetrical**
  - Extensor surfaces of upper and lower limb
  - Elbow, knees, buttocks, and sacral
- **mucosal involvement sporadically**
  - pain and burning
- **Pruritus is the leading symptom**
  - Along with stinging &burning is presenting sign
  - 12–24 h before the cutaneous lesions

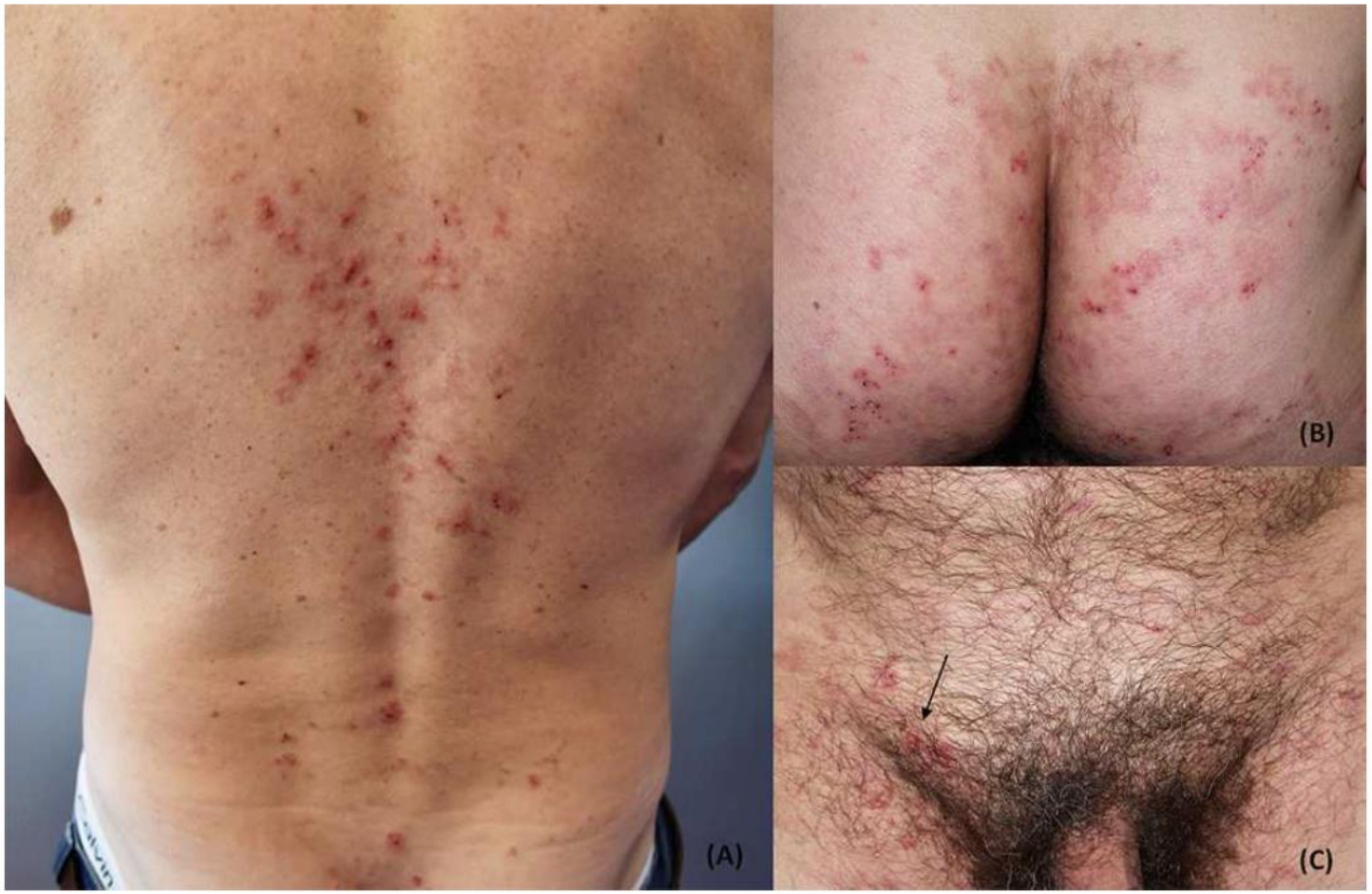


FIGURE 1 | Clinical presentation of dermatitis herpetiformis (DH): erythematous grouped papules and vesicles associated with excoriations and crusts at the back **(A)**, sacral region and buttocks **(B)**. Rarely, DH may also affect the groin and pubis (arrow) **(C)**. The patient gave written informed consent for the publication of these pictures.

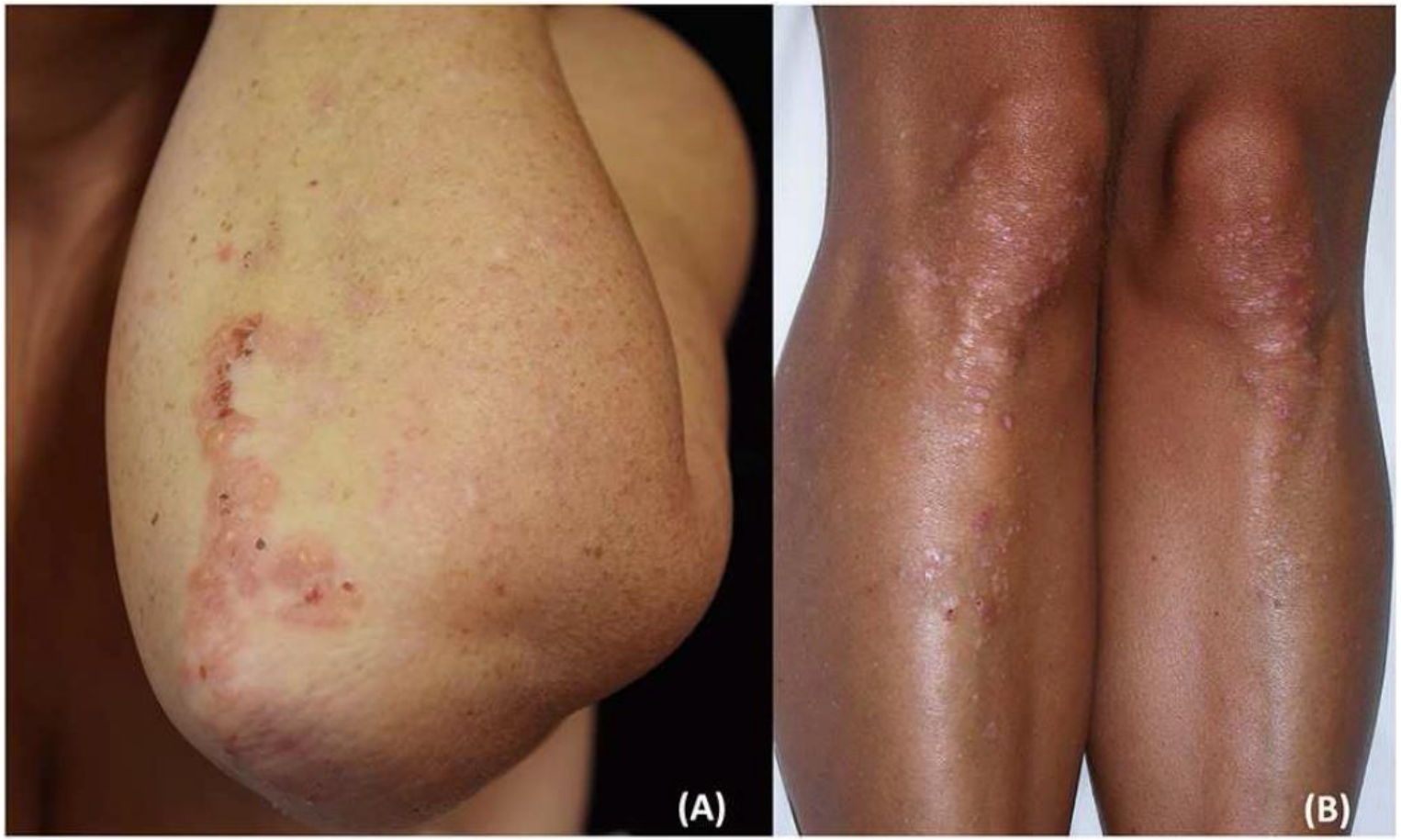
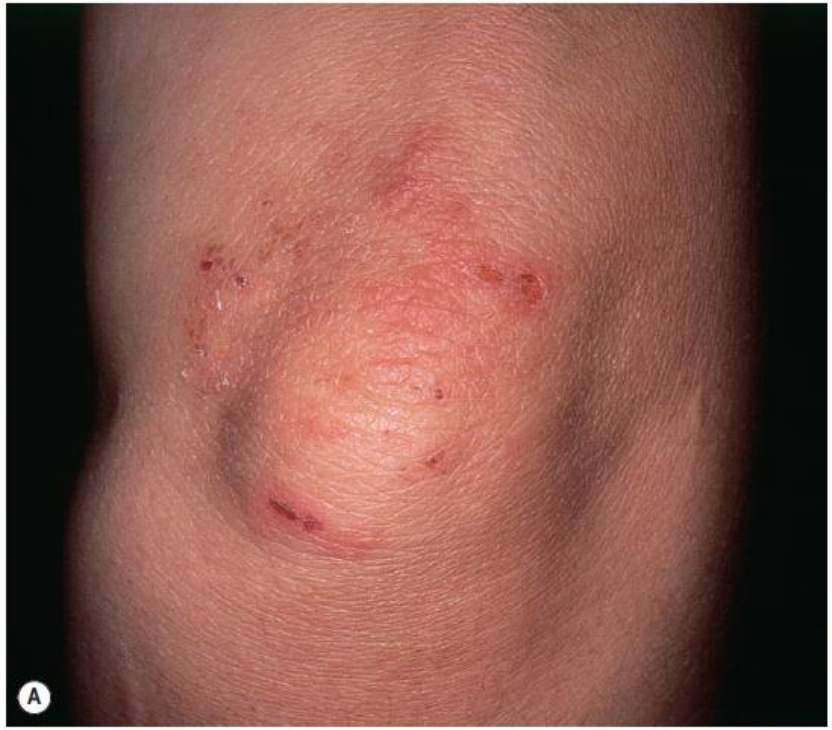
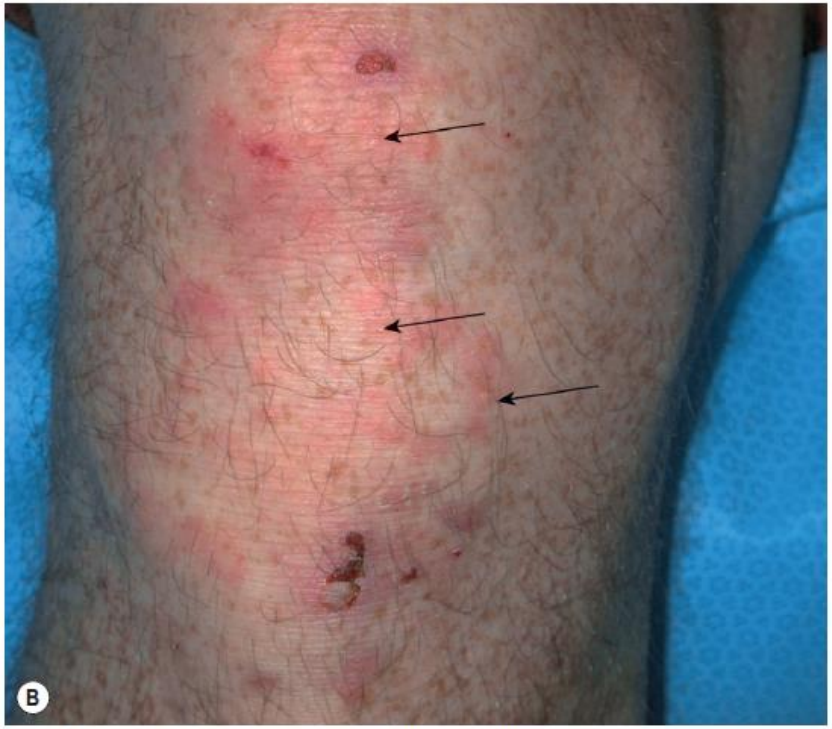


FIGURE 2 | Clinical presentation of dermatitis herpetiformis: grouped papules and vesicles associated with excoriations and crusts at the elbows **(A)** and lower limbs **(B)**. Post-inflammatory pigmentary changes such as hypo-pigmentation could be also appreciated **(B)**. The patient gave written informed consent for the publication of these pictures.





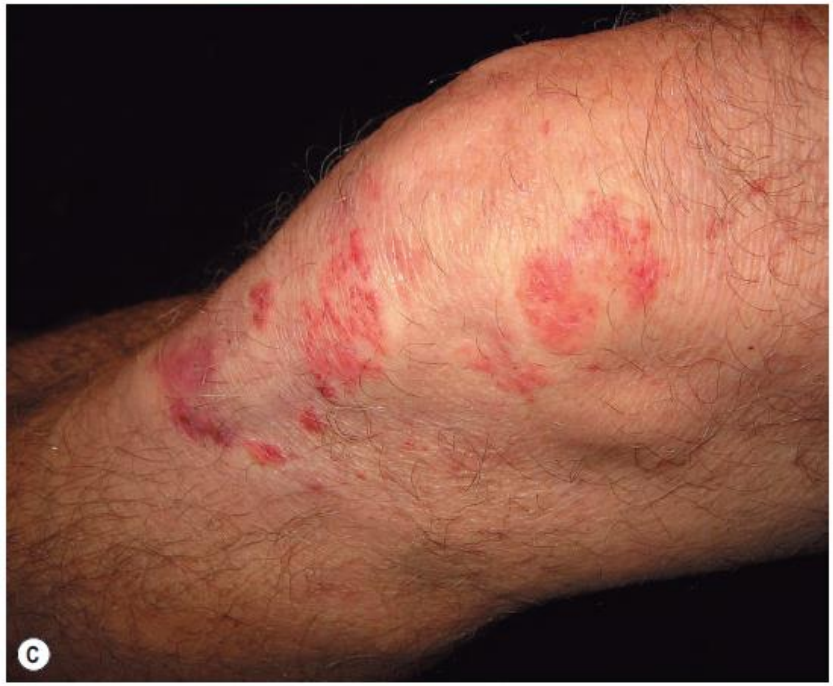
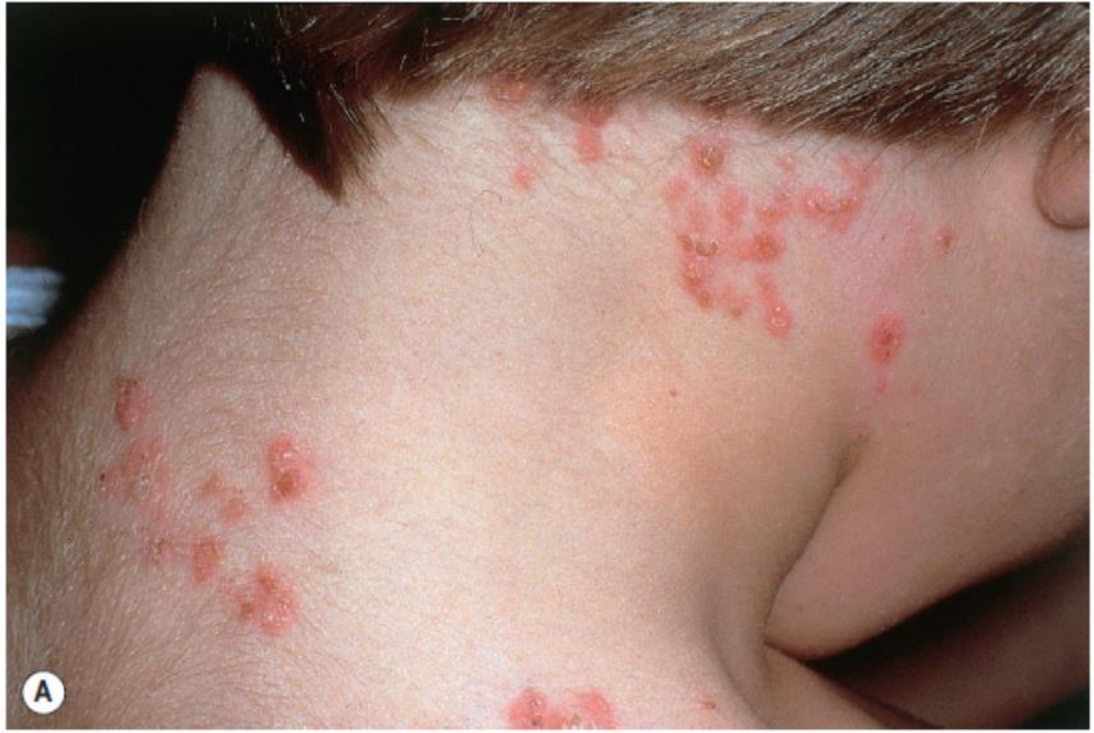


Fig. 31.2 Dermatitis herpetiformis. A Pink papulovesicles, erosions, and hemorrhagic crusts on the elbow. **B** Multiple urticarial pink papules on the knee, in addition to a few erosions and small subtle intact vesicles (arrows and circles). **C** Pink plaques on the knee composed of grouped papules and papulovesicles, admixed with tiny hemorrhagic crusts. *C, Courtesy, Thomas Horn, MD.*



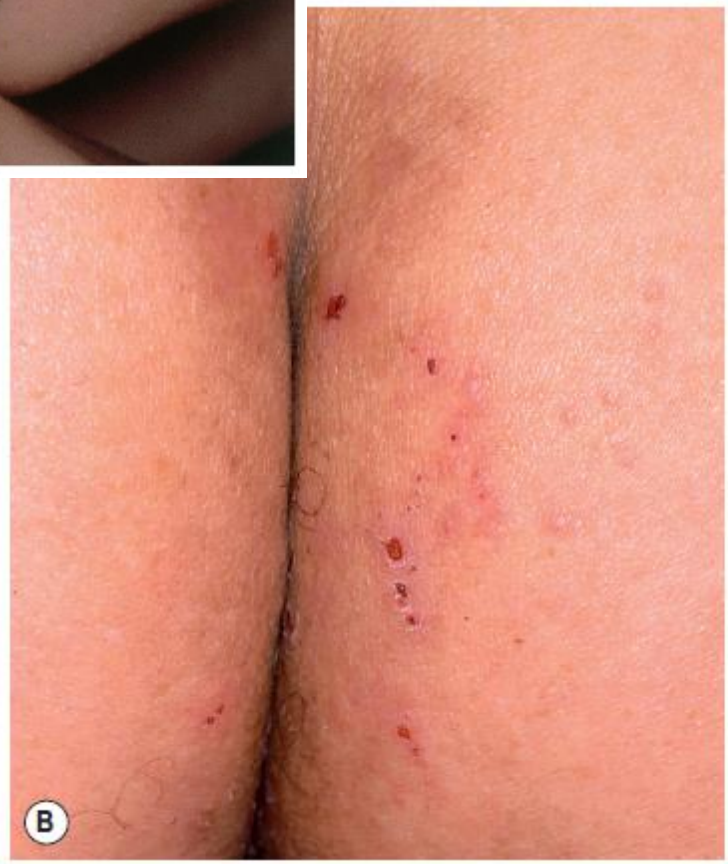


Fig. 31.3 Dermatitis herpetiformis.
A Grouped pink papulovesicles on the upper back, neck and scalp in a child. **B** Pruritic pink papules on the buttocks, some of which have central hemorrhagic crusts. *B, Courtesy, Louis A Fragola, Jr, MD.*

Atypical Cases

- Asymptomatic palmoplantar petechiae
- Diffuse petechial rush
  - Perivascular IgA immune complexes explain small vessel inflammation
- Palmoplantar keratosis
- Chronic urticaria with purpuric lesion

TABLE 1 | Different characteristics between Caucasian and Japanese patients with dermatitis herpetiformis.

Characteristics	Caucasian DH	Japanese DH
HLA	HLA-DQ2 (DQB1*02:01)–85% HLA-DQ8 (DQB1*03:02)–15%	HLA-DQ2 (DQB1*02:01)–0% HLA-DQ8 (DQB1*03:02)–37%*
Sites of involvement	Elbow, buttock, knee, face, ear, neck, scalp, groin	Elbow, buttock, knee, face, ear, neck, scalp, groin Non-predilection sites, including the extremities and trunk. Whole body
Villous atrophy	Most of the patients	Not known**
Circulating anti-tTG IgA	50–95%	38%
Circulating anti-eTG IgA	50–95%	43%
DIF	Granular IgA deposits	Granular and fibrillar IgA deposits
Response to the GFD	Most of the patients	Lack of consistent data
Association with autoimmune diseases	Frequent	Rare

HLA, Human Leucocyte Antigen; DIF, Direct Immunofluorescent; GFD, gluten-free diet.

**The frequency of HLA-DQ8 refers to the study by Ohata et al. (18), where the allele was found in six (37%) out of 16 Japanese patients with DH (19).*

***Found in three out of six patients in the study by Ohata et al. (79), including a total of 91 patients in 2012.*

Pathogenesis

- **External trigger:** Gluten
- Complex inflammatory network along gut-skin axis
- 5–10% of DH patients have first-degree relative affected
- Genetic factor:
  - HLA-DQ2 and DQ8 in 85% and 15%
  - On chromosome 6
  - Involved in processing gluten antigen gliadin
  - Same as coeliac disease
- All DH patients show evidence of a potential or mild, CD.

Pathogenesis…

- **Other trigger**
  - KI (potassium iodide)
  - Mini-gastric bypass surgery
  - Hormonal: hypothalamic pituitary gonadal Axis, leuprolide, OCP
  - Anti TNF
  - Adenocarcinoma of lung
  - Gastrointestinal infection
    - Rota-virus
    - Epstein Bar Virus
    - Cytomegalovirus

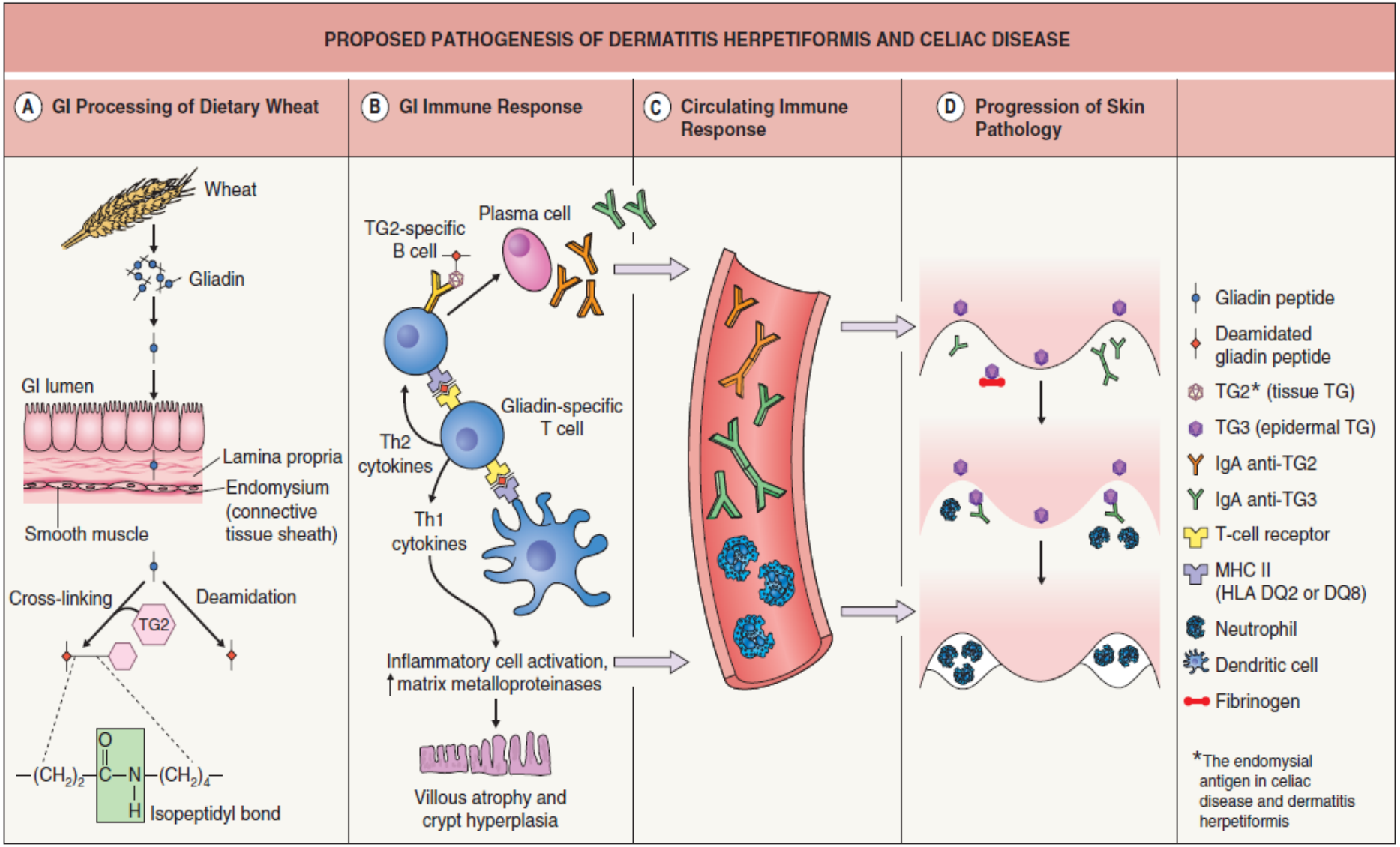


Fig. 31.1 Proposed pathogenesis of dermatitis herpetiformis and celiac disease. A Dietary wheat, barley or rye is processed by digestive enzymes into antigenic gliadin peptides, which are transported intact across the mucosal epithelium. Within the lamina propria, tissue transglutaminase (TG2): (1) deamidates glutamine residues within gliadin peptides to glutamic acid; and (2) becomes covalently cross-linked to gliadin peptides via isopeptidyl bonds (formed between gliadin and TG2 lysine residues). B CD4+ T cells in the lamina propria recognize deamidated gliadin peptides presented by HLA-DQ2 or -DQ8 molecules on antigen-presenting cells, resulting in the production of Th1 cytokines and matrix metalloproteinases that cause mucosal epithelial cell damage and tissue remodeling. In addition, TG2-specific B cells take up TG2-gliadin complexes and present gliadin peptides to gliadin-specific helper T cells, which stimulate the B cells to produce IgA anti-TG2. C Over time, IgA directed against TG3 (IgA anti-TG3) forms as a result of epitope spreading [illegible] both IgA anti-TG2 and IgA anti-TG3 circulate in the bloodstream. D When IgA anti-TG3 antibodies reach the dermis, they complex with TG3 antigens which have been produced [illegible] keratinocytes (epidermal TG) and then have diffused into the dermis. That is, IgA/TG3 immune complexes are formed locally within the papillary dermis. This leads to neutr[illegible]motaxis (with formation of neutrophilic abscesses), proteolytic cleavage of the lamina lucida, and subepidermal blister formation.

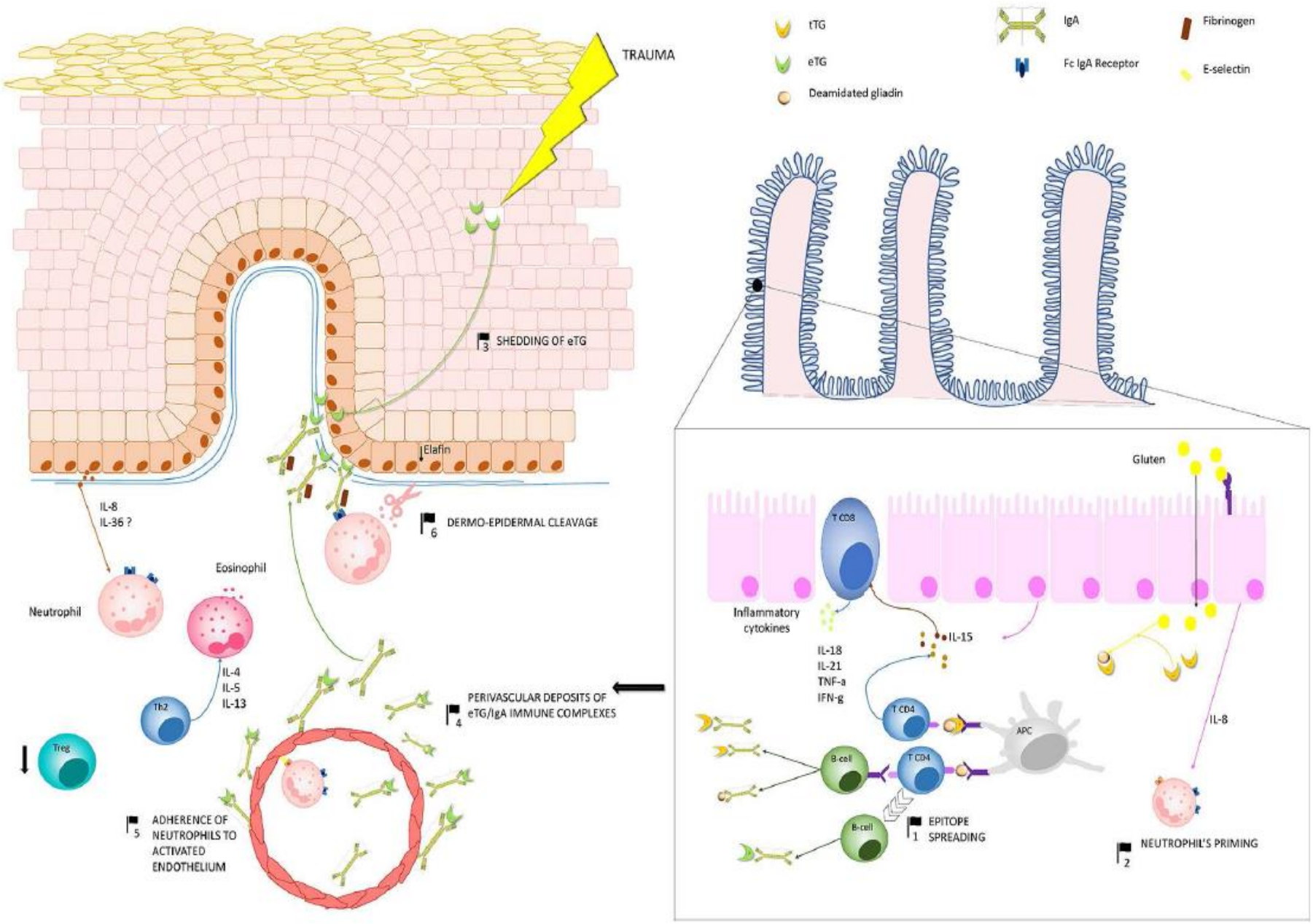


FIGURE 3 | Pathogenesis of dermatitis herpetiformis (DH)

Pathogenesis…

- **Epidermal Transglutaminase**
  - In spinous layer of the epidermis
  - Is the main auto antigen in DH
  - In CD, tissue transglutaminase is main
  - IgA autoantibody binding to eTG and deposits in papillary tips in granular pattern
  - Major controversy in role of eTG/IgA aggregates in DH

TABLE 2 | Evidence which seem to support or point against the pathogenic relevance of eTG/IgA deposits which are typically found in the perilesional skin of patients with DH.

Evidence supporting the pathogenic role of eTG/IgA aggregates in DH

1) Circulating eTG IgA correlate with disease activity and disappear after a GFD
2) eTG/IgA complexes are enzimatically active, and activate fibrinogen at the tips of the papillary dermis
3) Circulating and skin resident neutrophils express Fc IgA receptor (CD89), suggesting a direct interaction between neutrophils and IgA.

Evidence against the pathogenic role of eTG/IgA aggregates in DH

1) eTG/IgA complexes can be found in the healthy skin of patients with DH
2) eTG/IgA complexes can be detected in the skin of coealic patients without DH
3) eTG/IgA complexes disappears even years after the introduction of the GFD and the resolution of the skin rash
4) Passive transfer of goat anti-eTG IgG or human DH sera in mice with human skin grafts reproduces DH-like granular deposits in the engrafted skin, but not DH lesions

DH, dermatitis herpetiformis; eTG, epidermal transglutaminase; IgA, immunoglobulin A; GFD, gluten free diet.

Pathogenesis…

Epidermal Transglutaminase…

- eTG/IgA aggregates activate fibrinogen in papillary dermis
- Fibrinolysis directly contributes in blister formation
- Chemoattractant for neutrophil, T-cell and macrophage
- Neutrophil express Fc IgA receptors, suggesting interaction with eTG/IgA
- KI increases capacity of eTG/IgA complex binding the cadaverin in skin of DH on dapsone and GFD.

Pathogenesis…

- **Cytokine Network**
  - Neutrophil accumulation
  - Responsive to dapsone support
  - Show the role of neutrophils in DH inflammationan
  - CD11b increase and Fc IgA increase
  - Show priming of neutrophil
  - IL-8 mRNA and Circulating IL-8 increased
  - Local production of IL-8 and GM-CSF
    - Neutrophil elastase and granzyme B
  - Induce subepidermal split
  - Activation of coagulation cascade is additional mechanism

Pathogenesis…

- **Pathogenesis of Pruritus**
  - Far less clear
  - Neurogenic inflammation:
    - Neuropeptides:
      - Receptor for endotelin B
      - Corticotropin releasing
  - Mechanical itch dysesthesias
  - Release of inflammatory cytokines:
    - IL-31 has gained a major interest
    - Interact IL-31 receptor A
    - Oncostatin M receptor
      - On T cell, keratinocyte, dendritic cell, eosinophil and macrophage
    - Implicated in pruritic of dermatoses related to prevalent Th2 type inflammation
      - Like BP, AB

Gluten and the Skin

- **Skin in Celiac Patients**
  - Psoriasis, Atopic dermatitis, Urticaria, Aphtous Stomatitis, and Rosacea more common than general
  - In psoriasis 3-fold increased risk of CD
  - Testing for CD is not advisable
- **Skin in Non-celiac Gluten Sensitivity (NGS)**
  - New entity
  - Affects the bowel
  - Located on extensor surfaces of limbs
  - Erythema, papule, crust, and vesicle
  - DIF show DH-like granular C3 deposits but no IgA

Diagnosis

- Delay from occurrence of the first symptom

Biopsy

- Subepidermal vesicles and blisters, accumulation of neutrophil at the
- Papillary tips, in $^{1}/_{3}$ non-specific
- DIF from perilesional gold standard
  - Granular IgA deposits dermal papillae and/or junction
  - Some C3 granular deposition without IgA
- Umbrella concept including different diseases (DH, cutaneous gluten sensitivity, non-DH dermatoses in CD)

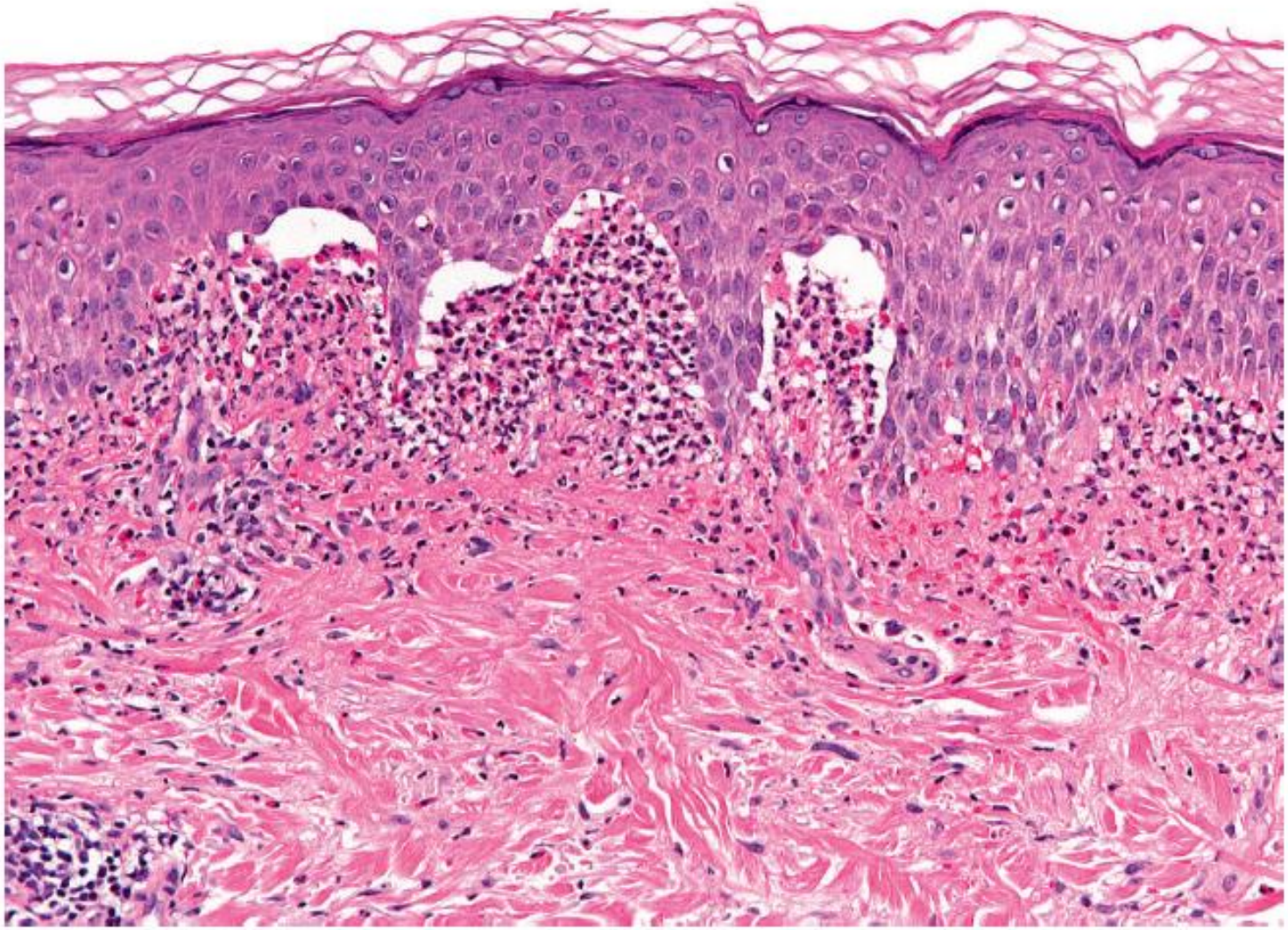


Fig. 31.4 Dermatitis herpetiformis – histopathologic features. Subepidermal clefts beneath which are collections of neutrophils within dermal papillae. Scattered eosinophils are also present. *Courtesy, Lorenzo Cerroni, MD.*

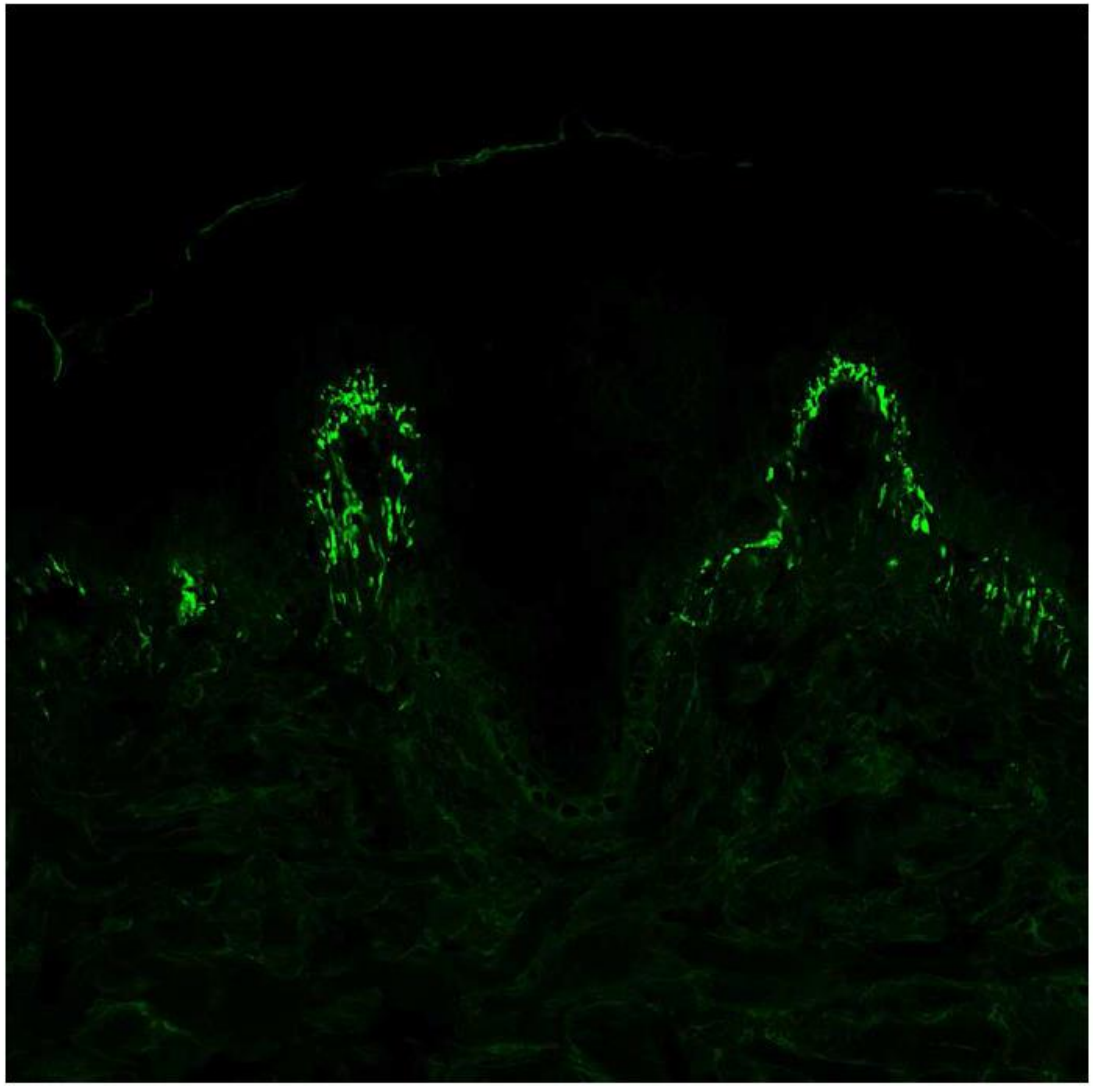


FIGURE 4 | Direct immunofluorescence of perilesional skin specimens from patients with dermatitis herpetiformis (DH). Granular IgA deposits at the dermal papillary tips are considered a pathognomonic finding of DH (magnification 400×).

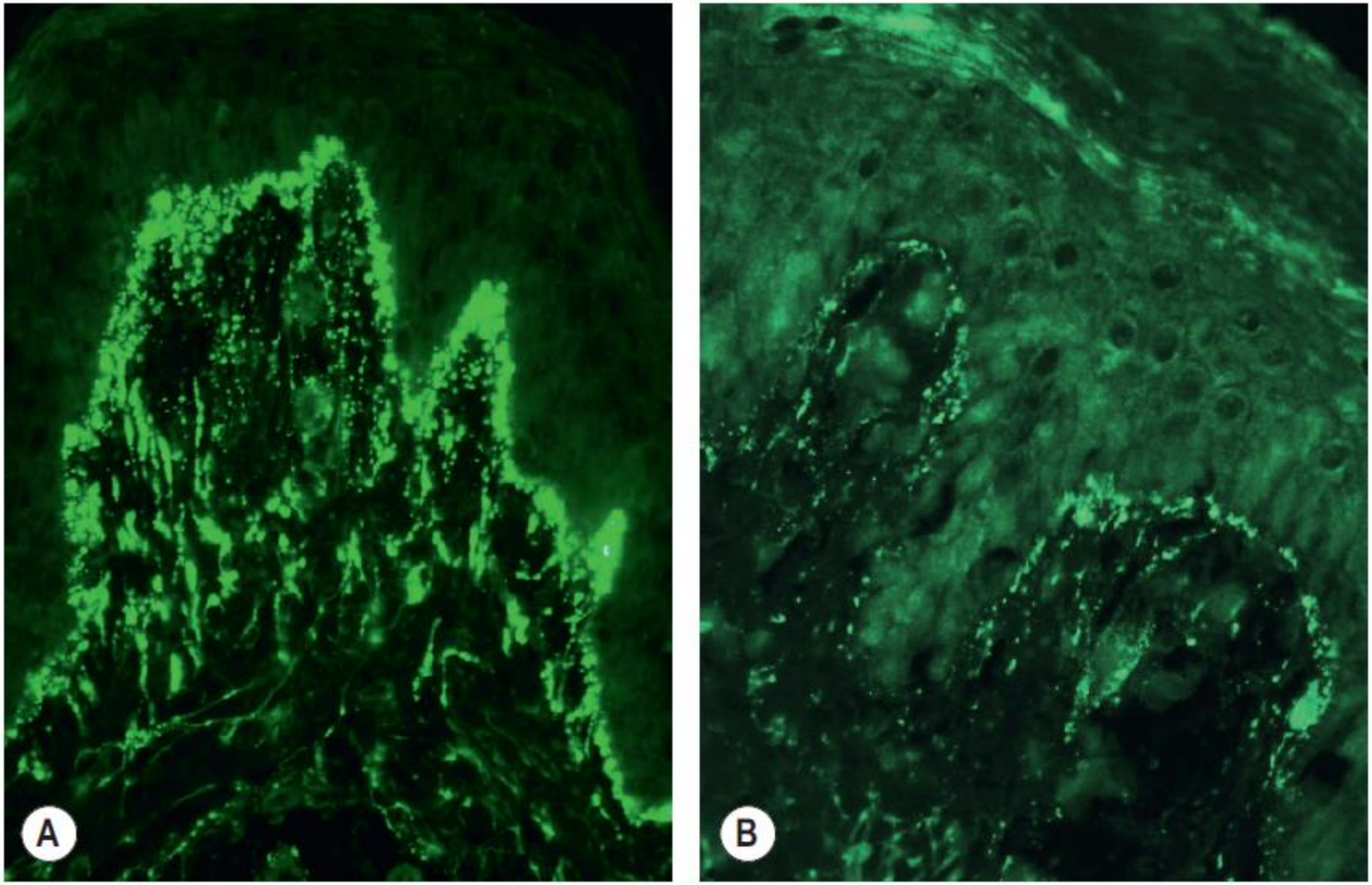


Fig. 31.5 Dermatitis herpetiformis – direct immunofluorescence. A Granular IgA deposition along the dermal–epidermal junction of normal-appearing skin adjacent to a lesion. **B** Granular deposition of epidermal transglutaminase (TG3) within the dermal papillae, which co-localizes with the IgA. *A, Courtesy, Kristin Leiferman, MD.*

Diagnosis…

Serology

- Anti eTG, anti-tTG, anti-EMA and anti-deamidated synthetic gliadin-derived peptides
- 50 - 95% sensitivity, and 95% specificity

HLA-DQ2 , DQ8

Dermoscopy

- Absence of yellow scales

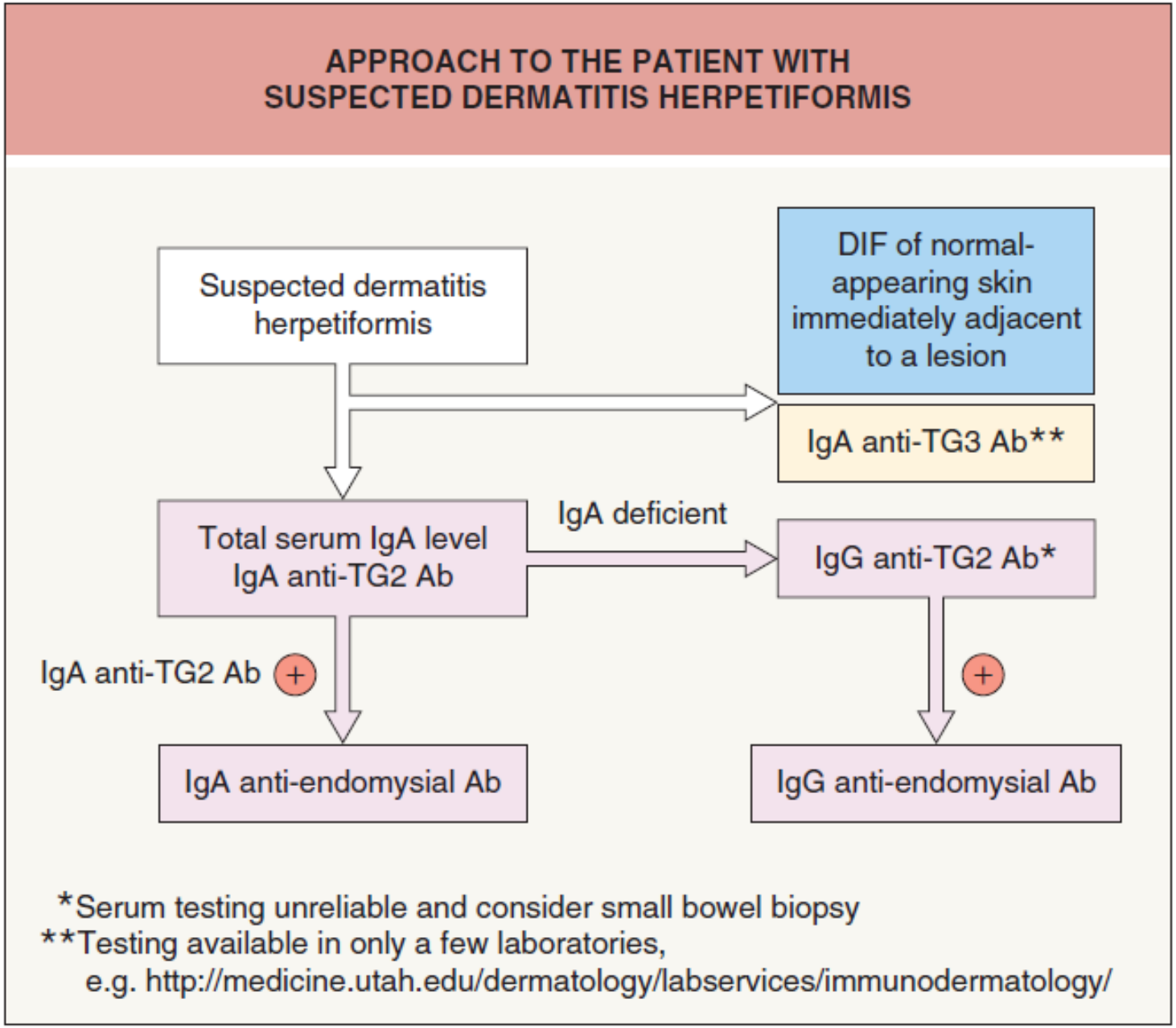


Fig. 31.6 Approach to the patient with suspected dermatitis herpetiformis.

CHARACTERISTICS THAT DIFFERENTIATE DH, LABD, AND BP			
	DH	LABD	BP
Cutaneous lesion	Grouped papules and small vesicles, often excoriated	Small vesicles and/or large bullae	Large tense bullae
Distribution pattern	Extensor surfaces, symmetrical	Similar to DH or BP	Trunk, extremities, occasionally mucosal surfaces
Routine histology	Subepidermal bullae with neutrophilic infiltrate	Subepidermal bullae with neutrophilic infiltrate (sometimes eosinophils predominate)	Subepidermal bullae with eosinophilic infiltrate
Direct IF	Granular IgA in dermal papillae	Linear IgA at BMZ, possibly also IgG	Linear IgG and C3 at BMZ
Site to biopsy for direct IF	Adjacent normal-appearing skin	Perilesional	Perilesional
Routine indirect IF	Negative	Linear IgA at BMZ (70%)	Linear IgG at BMZ (70%)
Enteropathy	>90%	Rare	None
HLA-DQ2	>90%	30%	Normal (20%)
Dapsone responsiveness	Excellent	Good, may also require systemic corticosteroids	Minimal to moderate

Table 31.3 Characteristics that differentiate dermatitis herpetiformis (DH), linear IgA bullous dermatosis (LABD), and bullous pemphigoid (BP). BMZ, basement membrane zone; IF, immunofluorescence.

Treatment

- **Central Role of Gluten**
  - Gluten-Free Diet (GFD)
    - Rice, corn, potato
    - Been/ Soya
    - Supplents
  - GFD not only symptomatic treatment can decreases risk of associated diseases (like NHL) is DH.
- **Pharmacologic Treatment**
  - Dapsone 50 - 100 mg /day
  - side effect is these doses are rare
  - Hemolytic anemia and methemoglobinemia
  - glucose-6-posphate dehydrogenase (G6PD) level
  - Frequent testing of CBC and reticulocytes
  - topical dapsone 5% gel as an adjuvant

SIDE EFFECTS OF DAPSONE		
Red blood cell toxicity	• Hemolytic anemia • Methemoglobinemia^	
White blood cell toxicity	• Leukopenia • Agranulocytosis	
Dapsone hypersensitivity syndrome	• Fever, fatigue, anorexia, hepatitis, lymphadenopathy	
Cutaneous reactions	• Morbilliform eruption • Urticaria • Fixed drug eruption • Erythema nodosum • Exfoliative dermatitis	• SJS/TEN • Phototoxicity • Drug-induced cutaneous lupus erythematosus
Gastrointestinal manifestations*	• Anorexia, nausea • Hepatitis • Cholestatic jaundice • Severe hypoalbuminemia	
Neurologic associations*	• Headache, dizziness • Peripheral neuropathy • Blurred vision, tinnitus • Insomnia • Psychosis	
Miscellaneous	• Fever • Nephrotic syndrome	

^Patients should be warned that arterial desaturation may be noted by pulse oximetry, even with relatively low levels of methemoglobinemia.
*In decreasing order of frequency.

Table 31.4 Side effects of dapsone. SJS, Stevens–Johnson syndrome; TEN, toxic epidermal necrolysis.

Treatment …

- Alternative:
  - Sulfonamides
  - Sulfasalazine
  - Sulfapyridine
  - Sulfamethoxypyridazine
- Others:
  - Cyclosporin
  - Azathioprine
  - Colchicine: second choice after dapsone
  - Heparin
  - Tetracycline
  - Nicotinamide
  - Mycophenolate
- Biologics:
  - Rituximab

Linear IgA Bullous Dermatosis

Introduction

- Autoimmune Cutaneous disease
- In adult linear IgA bullous dermatosis
- Children known as "chronic bullous disease of childhood"

Epidemiology

- **all age spectrums**
  - Adults:
    - Teenage
    - Sixth decade
  - In children:
    - Pre-school age (average age of 4.5 years old)
- **Rare disease**
  - 0.2 to 2.3 per 1,000,000

Etiology

- Circulating IgA anti-basement membrane zone antibody
- Against 97 kDa portion of BPAG2 (BP180) in the lamina lucida
- Some against LAD-1 (120 kDa truncated domain of BPAG2)
- Drugs is a frequent underlying cause in adults
  - Vancomycin 50% of drug-induced cases
  - Penicillins, cephalosporins, and rarely, sulfonamides
  - Angiotensin-converting enzyme (ACE)
  - NSAIDs
  - Phenytoin
  - Starts within the first month of drug

DRUG-INDUCED LINEAR IgA BULLOUS DERMATOSIS

Common

- Vancomycin*

Less common

- Penicillins
- Cephalosporins
- Captopril > other ACE inhibitors
- NSAIDs: diclofenac, naproxen, oxaprozin, piroxicam

Uncommon

- Phenytoin
- Sulfonamide antibiotics: sulfamethoxazole, sulfisoxazole

Rare

- Allopurinol
- Amiodarone
- Angiotensin receptor blockers: candesartan, eprosartan
- Atorvastatin
- Carbamazepine
- Cyclosporine
- Furosemide
- Gemcitabine
- Glyburide
- Granulocyte colony-stimulating factor
- Infliximab
- Influenza vaccination
- Interferon-α and interferon-γ
- Interleukin-2
- Lithium carbonate
- PUVA
- Rifampin
- Somatostatin
- Verapamil
- Vigabatrin

*Unusual variants include toxic epidermal necrolysis-like and morbilliform.

Table 31.5 Drug-induced linear IgA bullous dermatosis. ACE, angiotensin-converting enzyme; NSAIDs, nonsteroidal anti-inflammatory drugs.

Etiology…

- Genetic predisposition
  - Several human leukocyte antigen (HLA) types have been implicated
  - HLA-B8, HLA-DR3, HLA-DQ2, and HLA-cw7
  - Association with childhood and adult

Pathophysiology

- Potential causative factors
  - Varicella-zoster virus (VZV) infections
  - Autoimmune disease:
    - Dermatomyositis, Rheumatoid Arthritis, Systemic Lupus Erythematosus, Ulcerative Colitis
  - Malignancy:
    - Is weak
    - Lymphoproliferative disorders
    - Thyroid
    - Bladder
    - Colon
    - Renal
    - Esophageal
  - GT disease:
    - Loose associations
    - Celiac
    - Crohn
    - Ulcerative colitis

Clinical Manifestations

- **Adult:**
  - Varied presentation in adult
  - Scattered, tense bullae on non-inflamed skin
  - More herpetiform vesicles with erythema at base
  - Widespread distribution in trunk, extremities, scalp, genital, and face.
  - Expanding annular vesiculobullous plaque or TEN like lesion

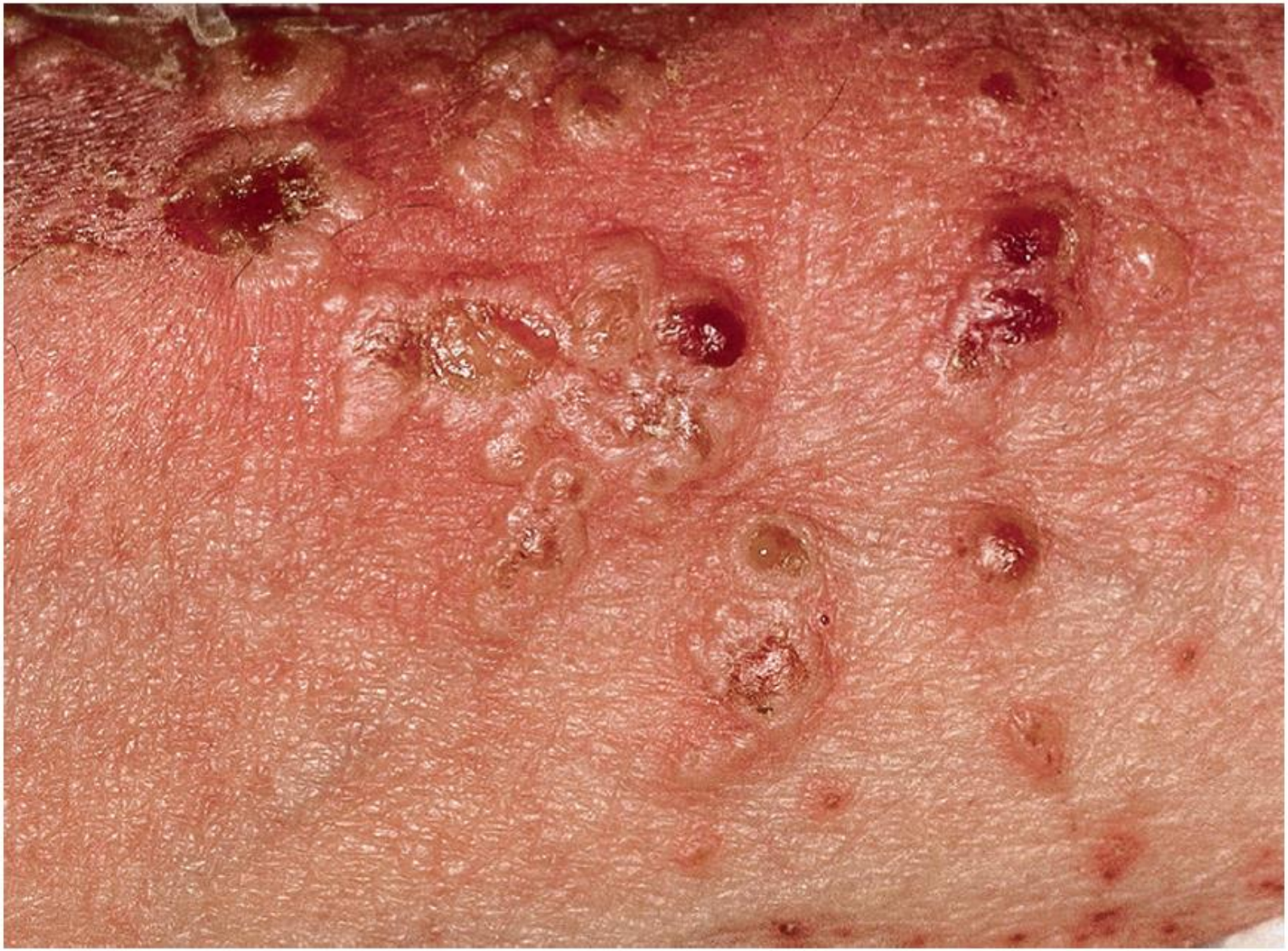


Fig. 31.10 Drug-induced linear IgA bullous dermatosis. Annular vesicopustules and central crusting are seen in this patient receiving vancomycin.

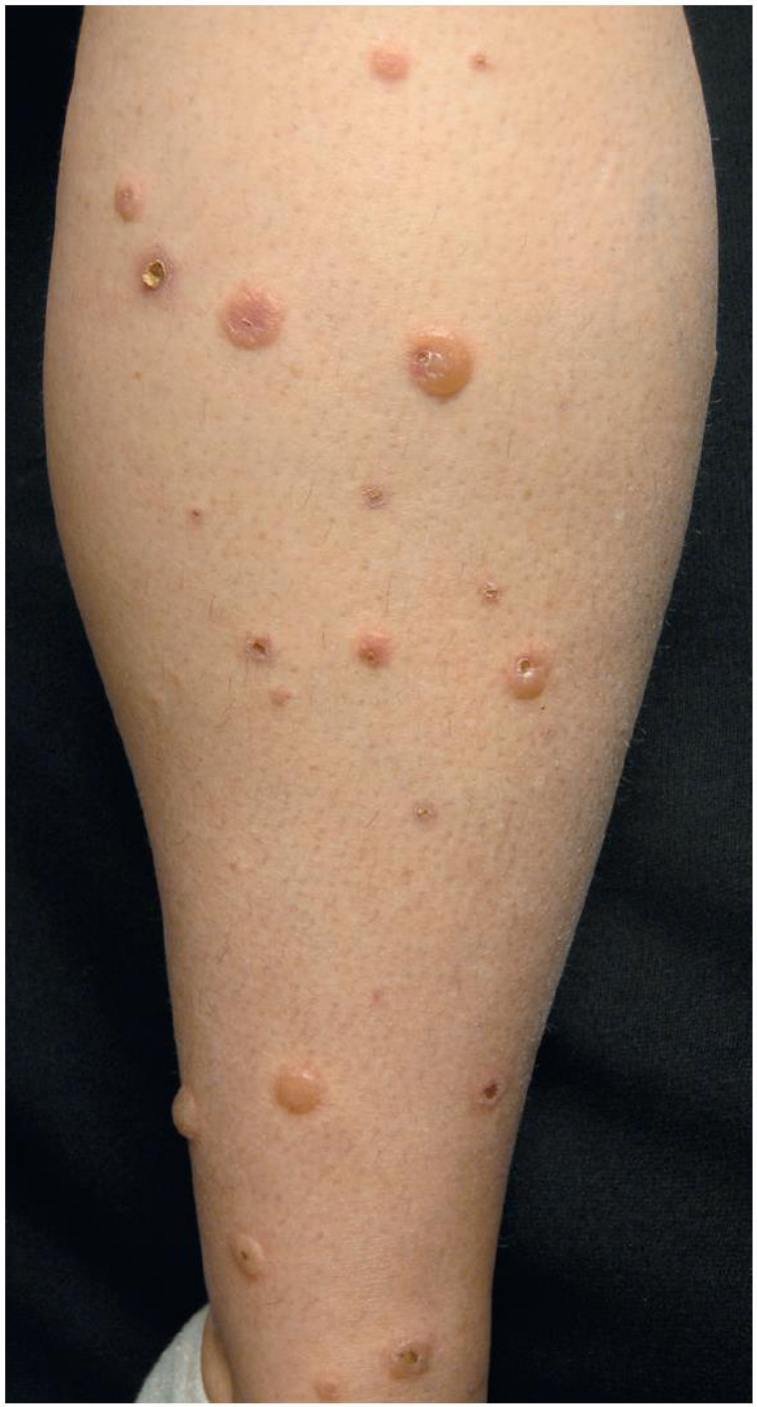


Fig. 31.11 Linear IgA bullous dermatosis. Vesicles and bullae arising within normal-appearing skin as well as scattered annular lesions. The former can also be seen in bullous pemphigoid. *Courtesy, Jeffrey P Callen, MD.*

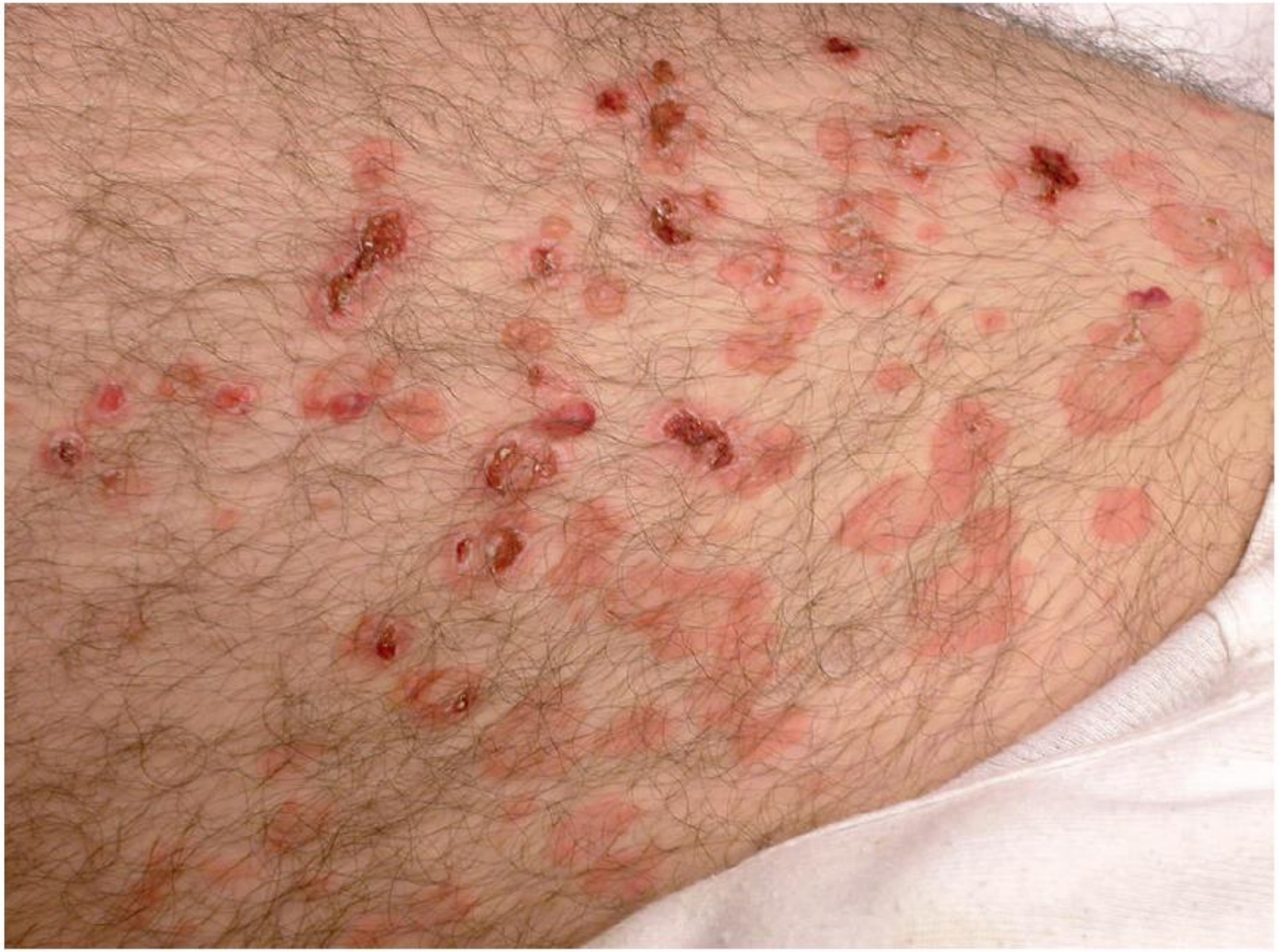


Fig. 31.12 Linear IgA bullous dermatosis. Annular and herpetiform vesicles arising on an inflammatory base. Annular pink plaques are also present. *Courtesy, Jeffrey P Callen, MD.*

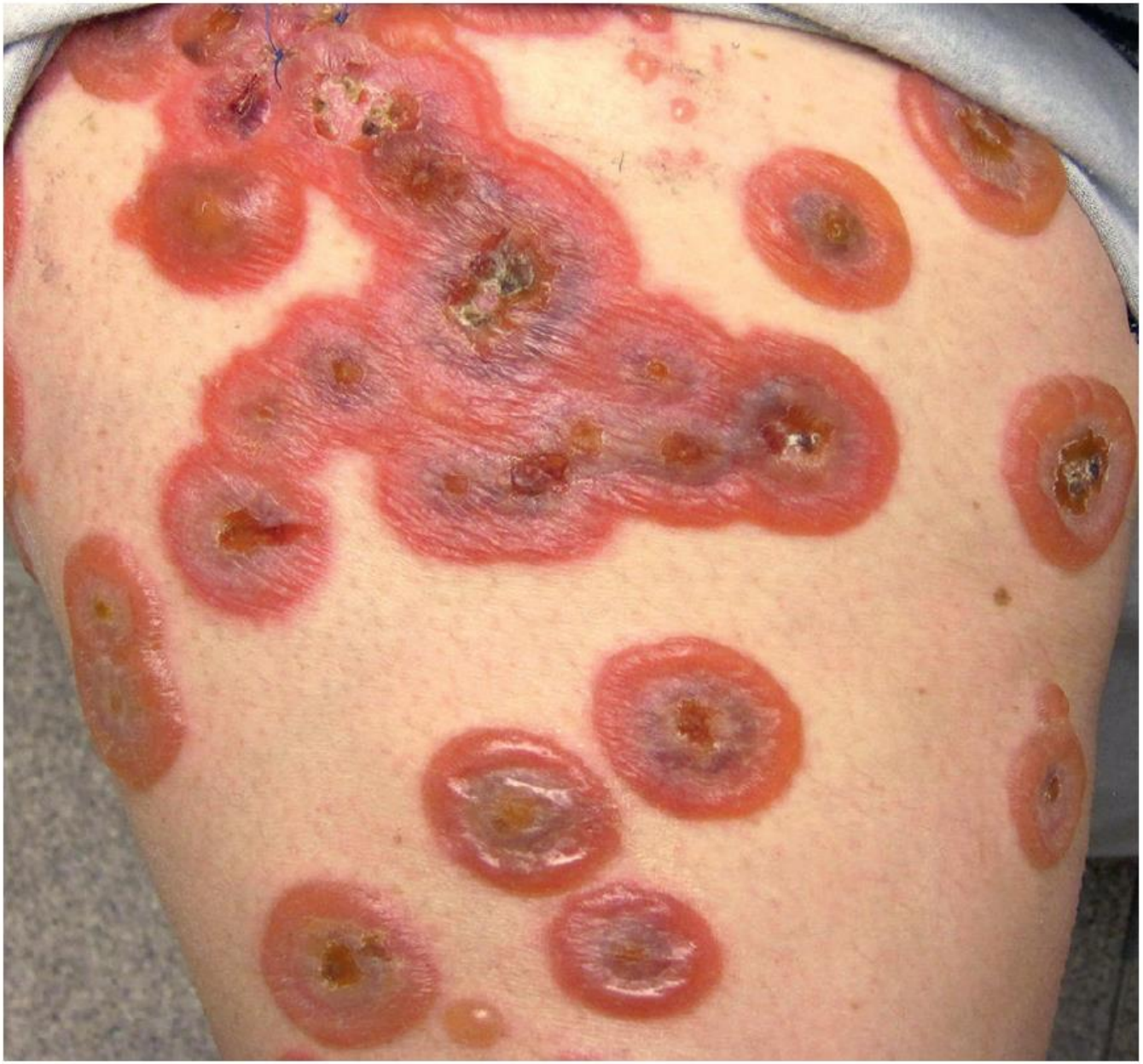


Fig. 31.13 Linear IgA bullous dermatosis. Striking annular vesiculobullous lesions on the thigh with central erosions and crusting. A figurate outline is seen in the area of

Clinical Significant …

- **Childhood**
  - Classic:
    - Annular erythematous lesions with a ring of vesicles "crown of jewels"
    - On abdomen, lower back, thighs, groin area, eyes and mouth
  - Mucous membrane involvement in 50% of patients:
    - Firstly oral, conjunctivae and then nares and genital
    - Significant scarring
    - In drug-induced , involvement is more severe
  - Atypical variants:
    - Eczematous
    - Prurigo nodularis-like
    - Urticarial
    - Morbilliform
    - Seborrheic dermatitis

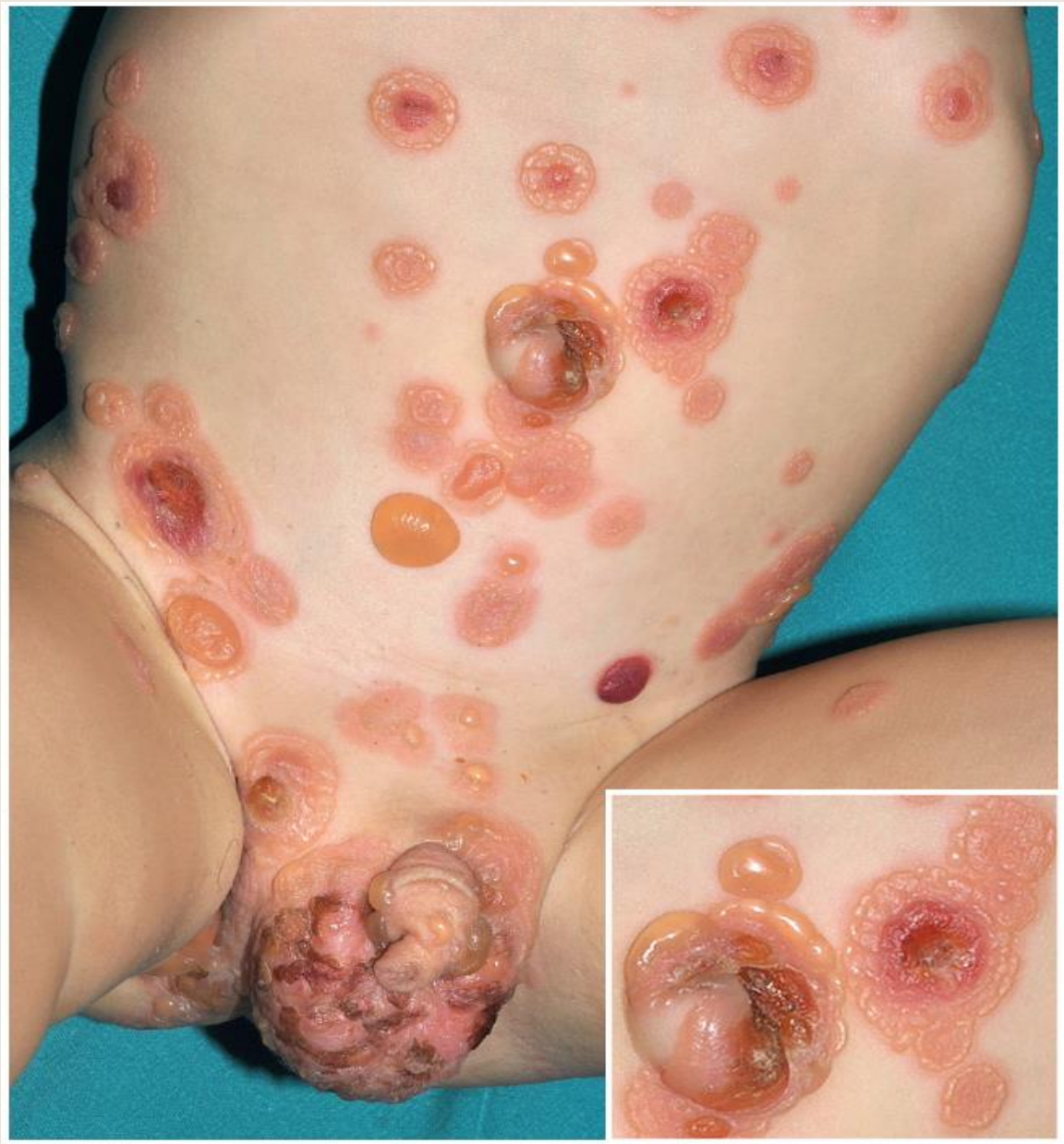


Fig. 31.7 Linear IgA bullous dermatosis. Characteristic findings in this child include the annular array of bullae (inset) and involvement of the genital region. There are also tense bullae arising on normal-appearing skin with either clear or hemorrhagic fluid and annular bullae with central crusting. *Courtesy, Antonio Torello, MD.*

Histopathology

- H and E:
  - Subepidermal Blistering with neutrophil
  - In early neutrophil is dermal papillae and be confused with dermatitis herpetiformis (DH)
  - In later after split, eosinophil intermix in dermis confuse with BP
  - Neutrophil appear "line up" at basement membrane (BM)
- DIF
  - Gold standard
  - linear deposition of IgA at the basement membrane
    - In lamina lucida
    - In sub-lamina densa
  - Sometimes IgG can be seen

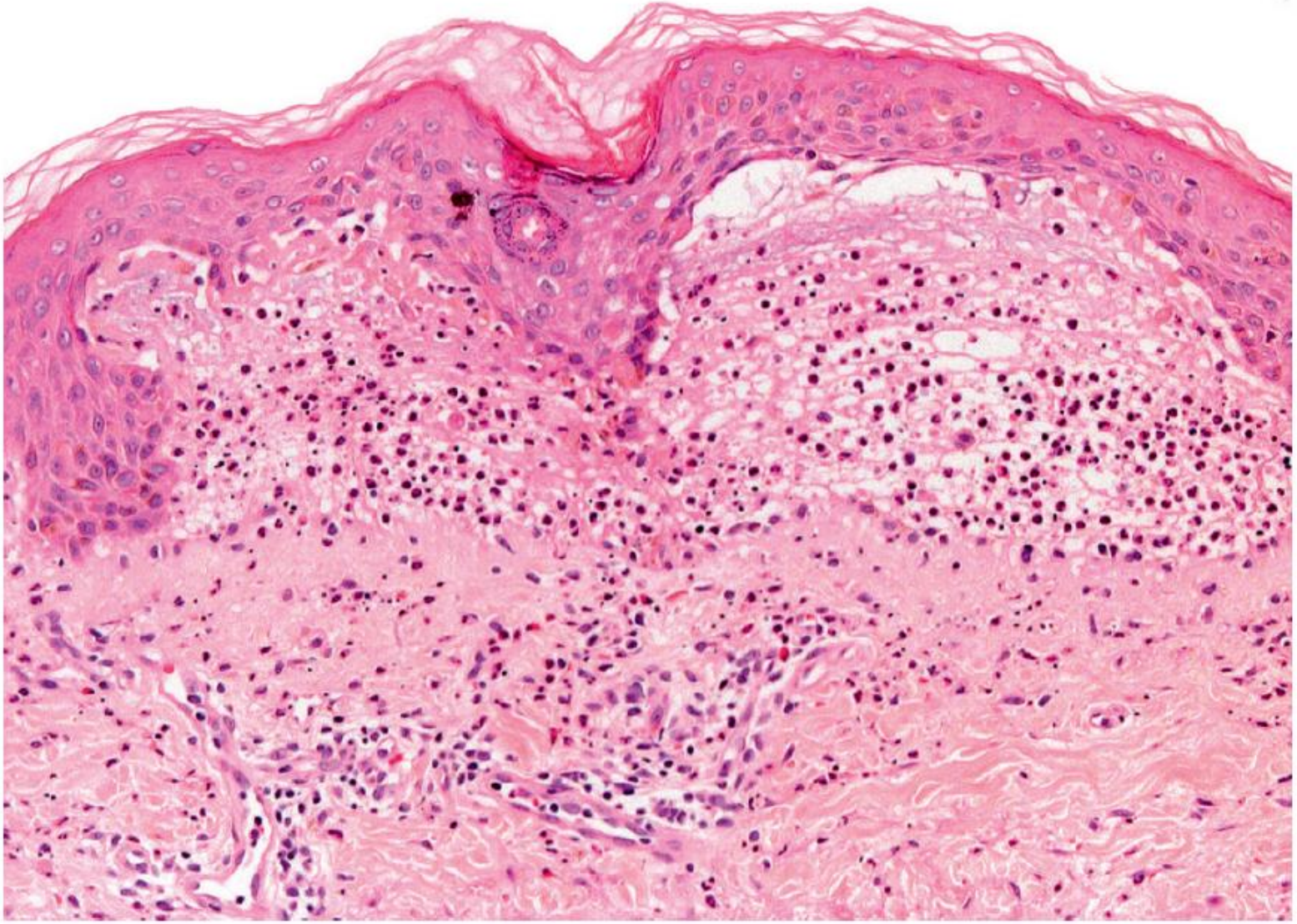


Fig. 31.14 Linear IgA bullous dermatosis – histopathologic features. Subepidermal blister filled with neutrophils. Neutrophils and a few eosinophils are also present within the underlying dermis. *Courtesy, Lorenzo Cerroni, MD.*

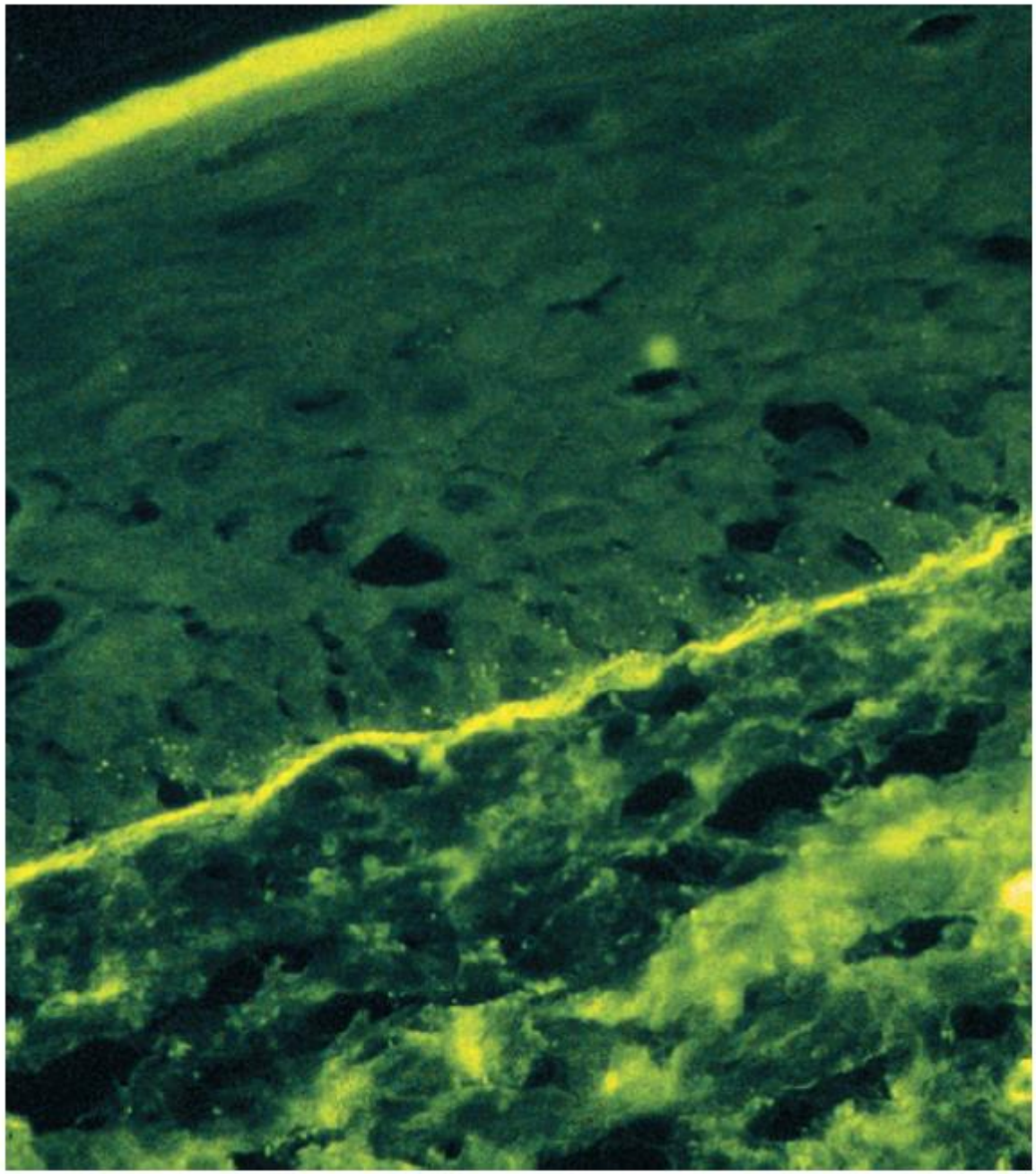


Fig. 31.8 Linear IgA bullous dermatosis – direct immunofluorescence. A linear pattern of IgA deposition is present within perilesional

Evaluation

- Biopsy:
  - As mentioned above
- IIF
  - test circulating IgA against BMZ Auto-antibody
  - In 70% of patients
  - In lamina lucida type
    - ✓ adhere to the roof of salt-split skin (epidermal)
  - In sub-lamina densa type
    - ✓ adhere to the floor (dermal)

Differential Diagnosis

- Dermatitis herpetiformis
- Bullous pemphigoid
- Epidermolysis bullosa acquisita
- Bullous impetigo
- Pemphigus vulgaris
- Erythema multiforme
- Toxic epidermal necrolysis (TEN)

Treatment

- Oral Dapsone:
  - In 2 to 3 days
  - Low dose 100 mg/day (1 - 2 mg/kg per day)
  - Monitored for:
    - Hemolytic anemia
    - Agranulocytosis
    - Hypersensitivity
    - Nephropathy
    - Neuropathy
    - Jaundice

Treatment…

- Antibiotic:
  - Tetracycline class
  - Dicloxacillin and Amoxicillin
  - Trimethoprim-sulfamethoxazole
  - Discontinuation of drug
- Nicotinamide: 0.5- 1.5 g/day inhibitor inflammatory patching
- MTX
- Systemic Steroid: 0.5-1 mg/kg/day

Treatment…

- Biologics:
  - Rituximab
    - anti-CD20 antibody
    - 1 g/day-2 weeks apart for two cycle
    - 375 mg/m^2/weekly for a month
    - In resistant cases
  - IVIG
    - 2 g/kg over few days
    - Sever and resistant cases
  - Topical steroid population in pediatric

Prognosis

- Generally promising
- Spontaneous remission in 30% - 60% of patients, in 2-3 years, in adult and children
- In drug-induced remit 2 -6 weeks after discontinuing
- Wax and wane in severity
- Mucous membrane lesions leave scar and cause morbidity


Thank You