A 62-year-old man presented with an erythematous flaky rash associated with burning pain on the right medial second toe that persisted for several months. Prior treatment with econazole, ciclopirox, and oral amoxicillin had failed. A shave biopsy was performed.

THE BEST DIAGNOSIS IS:

a. drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome
b. lichen simplex chronicus
c. necrotic migratory erythema
d. psoriasis
e. subacute cutaneous lupus erythematosus

H&E, original magnifications ×20.
The Diagnosis: Necrolytic Migratory Erythema

Necrolytic migratory erythema (NME) is a waxing and waning rash associated with rare pancreatic neuroendocrine tumors called glucagonomas. It is characterized by pruritic and painful, well-demarcated, erythematous plaques that manifest in the intertriginous areas and on the perineum and buttocks. Due to the evolving nature of the rash, the histopathologic findings in NME vary depending on the stage of the cutaneous lesions at the time of biopsy. Multiple dyskeratotic keratinocytes spanning all epidermal layers may be a diagnostic clue in early lesions of NME. Typical features of long-standing lesions include confluent parakeratosis, psoriasiform hyperplasia with mild or absent spongiosis, and upper epidermal necrosis with keratinocyte vacuolization and pallor. Morphologic features that are present prior to the development of epidermal vacuolation and necrosis frequently are misattributed to psoriasis or eczema. Long-standing lesions also may develop a neutrophilic infiltrate with subcorneal and intraepidermal pustules. Other common features include a discrete perivascular lymphocytic infiltrate and an erosive or crusted epidermis. Although direct immunofluorescence typically is negative, nonspecific findings can be seen, including apoptotic keratinocytes labeling with fibrinogen and C3, as well as scattered, clumped, IgM-positive cytoid bodies present at the dermal–epidermal junction (DEJ). Biopsies also have shown scattered, clumped, IgM-positive cytoid bodies present at the DEJ.

Psoriasis is a chronic relapsing papulosquamous disorder characterized by scaly erythematous plaques often overlying the extensor surfaces of the extremities. Histopathology shows a psoriasiform pattern of inflammation with thinning of the suprapapillary plates and elongation of the rete ridges. Further diagnostic clues of psoriasis include regular acanthosis, characteristic Munro microabcesses with neutrophils in a hyperkeratotic stratum corneum (Figure 1), hypogranulosis, and neutrophilic spongiform pustules of Kogoj in the stratum spinosum. Generally, there is a lack of the epidermal necrosis seen with NME.

Lichen simplex chronicus manifests as pruritic, often hyperpigmented, well-defined, lichenified plaques with excoriation following repetitive mechanical trauma, commonly on the lower lateral legs, posterior neck, and flexural areas. The histologic landscape is marked by well-developed lesions evolving to show compact orthokeratosis, hypergranulosis, irregularly elongated rete ridges (ie, irregular acanthosis), and papillary dermal fibrosis with vertical streaking of collagen (Figure 2).

Subacute cutaneous lupus erythematosus (S克莱) is recognized clinically by scaly/psoriasiform and annular lesions with mild or absent systemic involvement. Common histopathologic findings include epidermal atrophy, vacuolar interface dermatitis with hydropic degeneration of the basal layer, a subepidermal lymphocytic infiltrate, and a periadnexal and perivascular infiltrate (Figure 3). Upper dermal edema, spotty necrosis of individual cells in the epidermis, dermal–epidermal separation caused by prominent basal cell degeneration, and accumulation of acid mucopolysaccharides (mucin) are other histologic features associated with S克莱.
The immunofluorescence pattern in SCLE features dust-like particles of IgG deposition in the epidermis, subepidermal region, and dermal cellular infiltrate. Lesions also may have granular deposition of immunoreactions at the DEJ.\(^9,12,13\)

The manifestation of drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome (also known as drug-induced hypersensitivity syndrome) is variable, with a morbilliform rash that spreads from the face to the entire body, urticaria, atypical target lesions, purpuriform lesions, lymphadenopathy, and exfoliative dermatitis.\(^{14}\) The nonspecific morphologic features of DRESS syndrome lesions are associated with variable histologic features, which include focal interface changes with vacuolar alteration of the basal layer; atypical lymphocytes with hyperchromic nuclei; and a superficial, inconsistently dense, perivascular lymphocytic infiltrate. Other relatively common histopathologic patterns include an upper dermis with dilated blood vessels, spongiosis with exocytosis of lymphocytes (Figure 4), and necrotic keratinocytes. Although peripheral eosinophilia is an important diagnostic criterion and is observed consistently, eosinophils are variably present on skin biopsy.\(^{15,16}\)

Given the histopathologic variability and nonspecific findings, clinical correlation is required when diagnosing DRESS syndrome.

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**REFERENCES**


15. Borroni G, Torri S, Pezzini C, et al. Histopathologic spectrum of drug reaction with eosinophilia and systemic symptoms (DRESS): a diagnostic criterion and is observed consistently, eosinophils are variably present on skin biopsy.\(^{15,16}\) Given the histopathologic variability and nonspecific findings, clinical correlation is required when diagnosing DRESS syndrome.