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New entities in dermatopathology

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Superficial pyoderma gangrenosum;
Acute generalized exanthematous pustulosis;
Granuloma faciale

Summary This article discusses some recently described entities in dermatopathology that are uncommon but important to recognize. The interstitial granulomatous drug reaction was described in 1998 and shares some differential diagnoses with palisaded neutrophilic and granulomatous dermatitis, an entity that has been given many different names. Nephrogenic fibrosing dermatopathy and calciphylaxis are rare but important conditions occurring in patients with renal failure. The seriousness of a diagnosis of calciphylaxis and of cholesterol embolization syndrome must be communicated to clinicans as a matter of urgency. Cutaneous Rosai Dorfman disease and acute generalized pustulosis are important in that their prognosis is excellent and good news for the patient. Superficial pyoderma gangrenosum and granuloma faciale are included as not-so-new entities whose features are not commonly known and which may be underdiagnosed.

Interstitial granulomatous drug reaction

Interstitial granulomatous drug reaction (IGDR) was first described in 1998 by Magro et al. They described 20 patients with a characteristic rash that histopathologically had both granulomatous and lichenoid features. IGDR has a number of important pathological differential diagnoses including granulomatous mycosis fungoides (MF).[1]

Patients presented with non-pruritic plaques that were often annular, on the inner aspects of the

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arms, medial thighs and intertriginous areas. The clinical differential diagnoses included cutaneous T-cell lymphoma, erythema annulare centrifugum, granuloma annulare (GA), drug eruptions and subacute cutaneous lupus.[1] All patients were on drug treatment for other conditions.

Histopathological features[1]

- Diffuse granulomatous dermatitis with lymphocytes and histiocytes.
- Fragmentation of collagen and elastin fibres but no central necrobiosis.
- Interface dermatitis with vacuolar changes, dyskeratosis and lymphocytes along the dermoepidermal junction.
- Atypical lymphocytes are described in half of cases, most often in the dermal infiltrate although some cases show epidermotropism.
- No true vasculitis although lymphocytes may infiltrate vessel walls.

The differential diagnosis includes GA, GA associated with systemic disease, interstitial granulomatous dermatitis with arthritis (IGDA), and granulomatous MF. GA is more patchy than IGDR with discrete collections of histiocytes with central mucin. There is also no interface change in GA. A GA-like pattern has been described in association with some systemic diseases.[2] The clinical location is often atypical and histopathologically there is a vasculitis, sometimes with interstitial neutrophils. An interface change is described specifically in the reaction pattern associated with infectious disease.[3] In contrast to this GA-like pattern, IGDR does not have vasculitis or extravascular neutrophils.

IGDA was first described by Ackerman et al.[4] It is associated with seronegative arthritis in women, and presents with large plaques producing a rope-like configuration from the axillae down the flanks. This 'rope sign' was thought to be pathognomonic of the condition, but cases with papules and annular plaques have also been described.[5] There are interstitial and palisading granulomas with collagen and elastin damage. In contrast to IGDR, the process is pandermal and sometimes bottom-heavy with neutrophils. There is no lichenoid inflammation and increased mucin is not characteristic. More acute cases with lots of neutrophils may overlap with palisaded neutrophilic and granulomatous dermatitis (PNGD, see below).

Granulomatous MF can present in a very similar way to IGDR. In the granulomatous variant of MF, there are dermal tuberculoid granulomas with numerous atypical lymphocytes. Giant cells are prominent, and epidermotropism may be present but is not always obvious. Since lymphocyte atypia can be pronounced in IGDR, it is recommended that cases not responding to drug withdrawal should be reviewed and clonality analysis should be considered.[1]

All cases of IGDR that discontinued the suspect drugs resolved, although more slowly than usual drug reactions, in a period of weeks to months. It took 40 weeks for one case to resolve fully. A wide range of drugs was implicated including calcium-channel blockers, beta-blockers, lipid-lowering agents, diuretics, anti-inflammatories, antidepressants and anticonvulsants.[1]

Palisaded neutrophilic and granulomatous dermatitis

The term 'PNGD' was proposed in 1994 by LeBoit et al.[6] for an entity that was first termed 'Churg Strauss granuloma' or 'cutaneous extravascular necrotizing granuloma' in 1983.[7] Other terms include 'rheumatoid papules', 'superficial ulcerating rheumatoid necrobiosis' and maybe even 'IGDA'. The relatively small number of case series reported may be a reflection of the multiple possible terms used for this entity.

Patients with lupus, rheumatoid and other diseases with immune complex deposition develop a symmetrical papular eruption on the extremities. More women than men are affected.

Histopathological features[6]

- In early stages, a diffuse pandermal infiltrate of polymorphs, nuclear dust and amorphous basophilic material are seen.
- Degeneration of collagen.
- Leucocytoclastic vasculitis with prominent fibrin around vessels.
- Palisaded granulomas form around the polymorphs, fibrin and altered fibrin (Fig. 1).
- Mucin can be demonstrated.
- In late stages, much less inflammation is seen and the features look like IGDA (Fig. 2).

The differential diagnosis of very early lesions is of a leukocytoclastic vasculitis. PNGD has more polymorphs, denser nuclear dust and more fibrin than ordinary leukocytoclastic vasculitis with a palisaded appearance to the perivascular infiltrate.[6] The differential diagnosis of later lesions includes rheumatoid nodules which occur in the subcutis rather than dermis, rheumatoid