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The histological and pathogenetic spectrum of cutaneous disease in monoclonal gammopathies

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ABSTRACT

The dermatological disorders associated with monoclonal gammopathies are clinically heterogeneous and may be divided into four groups with distinctive pathogenetic mechanisms (a) specific (infiltrative) disorders including primary and secondary cutaneous plasmacytoma and cutaneous lymphoplasmacytic infiltration of Waldenström's disease (b) skin disorders because of the deposition of monoclonal immunoglobulin (M protein), including amyloidoisis macroglobulinemia cutis, light chain deposition of Randall's disease, follicular spicules of the nose, and cryoglobulinemia (c) skin disorders associated with monoclonal gammopathies, including highly associated (>50%), weakly associated (<50%) or anecdotal and (d) miscellaneous (non specific). In most cases, histopathology is crucial to confirm or to diagnose those skin conditions and is also very useful to understand their pathogenetic mechanisms.

Article Text

The monoclonal gammopathies (paraproteinemias or dysproteinemias) include all the clonal proliferations of plasma cells that produce a monoclonal immunoglobulin protein. They are associated with a wide variety of skin conditions that may be important clues to the correct diagnosis of the underlying plasma cell disorder.[1,2] In most cases, histopathology is crucial to confirm or to diagnose those skin conditions and is also very useful to understand their pathogenetic mechanisms. This review will focus on the histological spectrum and the possible pathogenesis of those dermatologic disorders associated with monoclonal gammopathies. They can be divided into four groups: (a) specific (infiltrative) disorders, including primary cutaneous plasmacytoma and cutaneous lymphoplasmacytic infiltration of Waldenström's macroglobulinemia; (b) skin disorders because of the deposition of monoclonal immunoglobulin (M protein) or of its fragments, including amyloidosis, macroglobulinemia cutis immunoglobulin (Ig)M storage papules, light chain deposition of Randall's disease, follicular spicules of the nose, and cryoglobulinemia; (c) skin disorders associated with monoclonal gammopathies to varying degrees, including highly associated (> 50%, i.e. scleromyxedema), weakly associated (< 50%, i.e. neutrophilic dermatoses), or anecdotal; and (d) miscellaneous skin conditions, symptoms, or complications related to monoclonal gammopathy but not specific for the diagnosis, such as pruritus, xerosis, drug reactions and infections (Table 1).

Table 1. **Skin disorders associated with monoclonal gammopathy**

Specific (infiltrative)
Cutaneous plasmacytoma
Primary
Secondary (Metastatic)
Cutaneous lymphoplasma cell infiltration of Waldenström's macroglobulinemia
Because of deposition of M protein
Amyloidosis (AL)
Macroglobulinemia cutis (IgM storage papules)
Follicular spicules of the nose
Light chain deposition of Randall's disease
Cryoglobulinemia
Associated
Strong association
Scleromyxedema
Scleredema
Diffuse normolipemic plane xanthomas
Necrobiotic xanthogranuloma

Schnitzler syndrome

Glomeruloid hemangioma

Waldenström's macroglobulinemia-induced bullous dermatosis

Weak association

Neutrophilic dermatoses (i.e. pyoderma gangrenosum, Sweet syndrome, subcorneal pustular dermatosis, erythema elevatum diutinum)

Leucocytoclastic vasculitis

Capillary leak syndrome

Angioedema with acquired C1-inhibitor deficiency

Anecdotal

With particular significance (Xanthoma disseminatum, Acquired cutis laxa, Cutaneous mucinous angiomatosis in AESOP)

Miscellaneous (non-specific) including pruritus, xerosis, drug reactions, infections

Specific (infiltrative) disorders

This group includes those diseases due to a specific skin infiltration of the monoclonal proliferating cells (Table 2).

Table 2. Specific infiltrative disorders associated with monoclonal gammopathies

Specific infiltrative disorders	Infiltrate		Infiltrating cells	Maturation	Inclusions	Immunoreactivity
	Location	Distribution				
Primary and secondary plasmacytomas	Mainly dermis	Nodular, Diffuse or interstitial	Plasma cells	Variable (also immunoblasts)	Dutcher and Russell bodies	CD 79A, CD 38, and CD 138

Waldenström	Reticular dermis (grenz zone)	Perivascular, periadnexial and interstitial	Lymphoplasmacytoid B cells	Binucleate cells	PAS+ inclusions	IgM κ

Ig, immunoglobulin; PAS, periodic acid schiff