Acral Acquired Cutis Laxa Associated with IgA Multiple Myeloma, Joint Hyper laxity and Urticarial Neutrophilic Dermatosis

Kluger, Nicolas

2014


http://hdl.handle.net/10138/161814
https://doi.org/10.2340/00015555-1846

Downloaded from Helda, University of Helsinki institutional repository.
This is an electronic reprint of the original article.
This reprint may differ from the original in pagination and typographic detail.
Please cite the original version.
Acral localised acquired cutis laxa (ALACL) is a very rare form of acquired cutis laxa characterised by loose redundant skin folds confined to the hands and feet, giving the appearance of premature aging, and histological loss of dermal elastic tissue (1–9). We report here a new case of ALACL associated with IgA multiple myeloma and also, for the first time, with joint hyperlaxity and recurrent neutrophilic urticarial dermatosis.

CASE REPORT (for detailed methods see Appendix S11)

A 40-year-old man presented in 2007 for the management of ALACL and monoclonal IgA gammopathy. He had chronic urticarial dermatosis of the extremities, mostly involving the hands, which had manifested in 1996 and progressively worsened, with repeated swelling of the fingers. ALACL was diagnosed at that time in association with an unusual hyperlaxity of the distal interphalangeal joints. Over the past several years, he has received multiple treatments including methotrexate, colchicine, hydroxychloroquine, intravenous gammaglobulins and dapsone. All have either been ineffective or had debilitating side effects. Oral prednisone resulted in complete remission of the urticarial dermatosis. Amyloid Congo red staining was negative in all biopsy specimens. Between 2007 and 2012, the following treatments were ineffective: plasmapheresis (6 sessions), anakinra (3 months), infliximab (4 months), rituximab (4 sessions) and alkeran (2 sessions). Unfortunately, the patient chose not to follow-up.

Direct immunofluorescence investigation of lesional skin revealed abundant IgA deposits that decorated the dermoeidermal junction (DEJ) and the capillary network of the dermal papillae (Fig. 3A). A control specimen from non-lesional forearm skin showed only faint staining in the DEJ (data not shown). Electron microscopy showed conspicuous diminution of the elastic fibres with normal-appearing collagen fibres; macrophages were observed phagocytising the elastic fibres. Direct immunoelectron microscopy further localised the IgA deposits at the anchoring fibres located underneath the DEJ (Fig. 3B). Additional gold-staining was observed in the papillary dermis but no association with a defined structure was determined (data not shown).

Molecular analysis of the $FBLN5$ gene and exon 4 and the last 7 exons of the $ELN$ gene revealed no mutations. In addition, the western blot of extracellular matrix proteins (ECM) secreted by isolated lesional ALACL fibroblasts was probed with anti-fibulin-5 antibody. The detected proteins had the same apparent molecular weight as in the ECM extracts produced by control fibroblasts. Last, the same ECM blots were probed with patient’s antibodies (concentrated sera obtained after plasmapheresis) and no specific reaction against ALACL ECM extracts was revealed (data not shown).

**DISCUSSION**

The acral localisation of cutis laxa is very rare. To the best of our knowledge, only 12 cases (including the present case) have been described (see Table S11). Our patient developed striking spontaneous joint hyperlaxity after...
several years of disease progression in the absence of any underlying rheumatologic disease. This feature has not been reported thus far in any of the prior cases of ALACL. A history of local swelling and chronic urticaria at the location of the cutis laxa was reported in 3 cases of ALACL (1, 5) with variable delay, the maximum thus far being 14 years (1). Only one biopsy specimen from an urticarial lesion associated with ALACL has been documented and it showed the same pattern of neutrophilic urticarial dermatosis (NUD) (11) as observed in our case. NUD is considered as one of the clinical and histological expressions of skin autoinflammation and a sign of autoinflammatory syndromes or suspected disorders of the innate immunity, including adult-onset Still’s disease and Schnitzler syndrome. Schnitzler syndrome is classically characterised by a constant recurrent urticarial rash and monoclonal IgM gammopathy, and deposition of IgM in the epidermis, the dermoeipidermal junction and the papillary dermal vessels is a suspected trigger for the urticarial lesions (12). In our observation, the results of direct immunofluorescence and immunoelectron microscopy of the IgA deposits in skin sections along the basement membrane zone or around the superficial dermal vessels were strikingly similar, suggesting a common pathogenic mechanism of inflammatory dermal lesions induced by monoclonal Ig in these 2 diseases.

ACKNOWLEDGEMENT

The authors are grateful to Chantal Cazevieille and Cécile Sanchez for their technical assistance and data interpretation concerning the ultrastructural microscopy (Centre de Ressources en Imagerie Cellulaire de Montpellier, France) and to Anne Tesniere for protein analysis.

REFERENCES