Atypical Lichen Myxedematosus: A Case with Remarkable Response to Low Dose Melphalan

Abstract
A 41-year-old man was referred to our outpatient department as a case of urticaria with angioedema of 3 months duration. On examination, he had generalized coalescent waxy papules and plaques causing extensive thickening and hardening of the skin secondary to mucin deposition and variable dermal fibrosis in the absence of thyroid dysfunction. The exact etiology of this rare disorder is still not known. 

Case Report
A 41-year-old man was referred to our outpatient department with a diagnosis of urticaria with angioedema of 3 months duration. On examination, he had generalized coalescent waxy papules and plaques causing extensive thickening and hardening of the skin secondary to mucin deposition and variable dermal fibrosis in the absence of thyroid dysfunction. The exact etiology of this rare disorder is still not known. 

Keywords: Atypical type, melphalan, lichen myxedematosus

Introduction
Lichen myxedematous (LM) or papular mucinosis (PM) is a rare cutaneous myxedematous condition characterized by the formation of numerous closely-set lichenoid monomorphous waxy papules and plaques causing extensive thickening and hardening of the skin secondary to mucin deposition and variable dermal fibrosis in the absence of thyroid dysfunction. The exact etiology of this rare disorder is still not known. In an updated classification, Rongioletti and Rebora described in detail about the generalized papular and sclerodermoid form or scleromyxedema (SM), the localized papular form which includes discrete papular, acral persistent papular mucinosis, self healing papular mucinosis (juvenile and adult variant), papular mucinosis of infancy and nodular LM, and a third atypical or intermediate form. More than 80% cases of SM show an association with monoclonal gammopathy particularly of the immunoglobulin G lambda type. PM runs a chronic and nonlethal course. The course of the atypical form is unpredictable. No standard therapeutic regimen exists for any of the different clinical types of LM. Different therapeutic agents or therapies tried in different clinical types showed varying responses. In the present study, we report a case of an atypical LM with remarkable response to low dose melphalan for a short period.

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were normal. Urine Bence–Jones protein was negative. ANA (Anti-nuclear antibody), RA (Rheumatoid factor), and ELISA (Enzyme linked immunosorbent assay) for HIV (Human immunodeficiency virus) were negative. Chest X-ray, skeletal radiological survey, and ultrasonogram of the abdomen were normal. Histopathological examination of a representative lesion from the thigh stained with hematoxylin and eosin showed normal epidermis and separation of collagen fibres in the upper and mid reticular dermis [Figure 4a and b]. Alcian blue staining demonstrated intradermal mucin deposition [Figure 5]. The diagnosis of LM was confirmed. There were no marked increase in dermal fibroblasts. However, a significant number of stellate fibroblasts were present. Because he had generalized eruption with absence of sclerodactyly and leonine facies (usually seen in scleromyxedema, but not in LM), normal thyroid function, absence of monoclonal gammopathy, and typical histological findings, a final diagnosis of atypical LM was made.

The patient did not respond to oral antihistamines and topical steroids. Because the lesions were progressing, we started him on melphalan tablet at a dose of 2 mg per day. There was remarkable improvement with clearing of the lesions within 2 weeks [Figure 6a and b]. There was no recurrence in the 1 year follow-up period, after which the case was lost to follow up.

Discussion

First authentic classification of LM was conducted by Montgomery and Underwood in 1953. Rongioletti and

![Figure 1: (a) Monomorphous papules with linear arrangement on the forehead; (b) monomorphous papules with linear arrangement on the trunk](image)

![Figure 2: Glabella showing exaggerated facial folds with horizontal and longitudinal furrows and upper eyelid edema](image)

![Figure 3: (a) Coalescent papules on the trunk showing the “doughnut sign”; (b) coalescent papules on the thigh showing the “doughnut sign”](image)

![Figure 4: (a) Dermis showing separation of the collagen fibres, hematoxylin and eosin (H and E, ×40); (b) dermis showing separation of the collagen fibres, (H and E, ×400)](image)

![Figure 5: Intradermal mucin deposition and separation of collagen fibres, Alcian blue ×400](image)

![Figure 6: (a) Clearing of the lesions on the face, 2 weeks after melphalan treatment; (b) clearing of the lesions on the trunk, 2 weeks after melphalan treatment](image)
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Rebora had updated the diagnostic criteria in 2001 and classified LM into two clinicopathologic subsets and a third group of atypical or intermediate forms based on the clinicopathological findings and presence or absence of monoclonal gammopathy in the absence of thyroid dysfunction. The subsets include a generalized papular and sclerodermoid form or SM and the localized papular form (PM). The atypical type of LM include SM without monoclonal gammopathy, localized LM with monoclonal gammopathy and/or systemic symptoms other than HIV infection, localized LM with mixed features of different subtypes, and other nonspecified cases. Our case had generalized papular eruption, absence of monoclonal gammopathy, typical histological findings, and normal thyroid function, justifying the final diagnosis of atypical LM.

Multiple inciting stimuli have been suggested as the cause for the over production of mucin by the fibroblasts. The precise mechanism is still unknown. Serum from LM patients even after separation of the paraprotein, stimulated DNA synthesis and cell proliferation in cultured fibroblasts, suggesting the role of certain circulating factor or factors other than paraprotein. Indirect mechanisms of development appear to include circulating cytokines, inflammatory mediators, and fibroblast precursor cell lineages that migrate from the blood, take up residence in the dermis as well as in other tissues and synthesis mucin. Approximately 10% cases of the SM form associated with IgG paraprotein show progression to multiple myeloma. Cardiovascular system abnormality may occur in another 10%. Other systemic features include neurologic involvement, carpal tunnel syndrome, the dermatoneuro syndrome, seronegative polyarthritis, Raynaud’s phenomenon, esophageal dysmotility, dyspnoea, restrictive or obstructive pulmonary defects, pneumonia, hematologic malignancies, scleroderma-like renal disease, corneal opacities, thickened eyebrow or eyelid skin, lagophthalmos, ectropion, and rarely laryngeal involvement. Autopsy studies have shown mucin deposition in multiple organs suggesting the systemic nature of the disease.

The prognosis of SM is poor even after treatment with cyclophosphamide and melphalan. Other treatment options include intravenous immunoglobulin, glucocorticoids, other immunosuppressants, thalidomide, oral isoretinoin, PUVA, electron beam radiation, plasmapheresis combined with pulsed corticosteroids, extracorporeal photopheresis, and autologous peripheral blood stem cell transplantation. The prognosis and course of atypical LM is unpredictable because of the limited data from the low number of reported cases.

In the updated classification, Rongioletti and Rebora had suggested that whenever cases of LM are dealt with, an indication of the subset should always be given. The subtype involved should be then added in cases of the localized forms. Moreover, PM and LM may be used synonymously, however, the term SM should be preferred for the generalized sclerodermoid form.

Our case was of the atypical type with widespread cutaneous eruption, absence of monoclonal gammopathy, and showed remarkable response to low dose melphalan for a short period. Other features such as accentuation of facial lesions and bilateral peri orbital angioedema had indeed misled the physician. An additional finding in our case was the “doughnut sign” at unusual sites (trunk and thigh). Because there are many reports of melphalan-induced hematological malignancies, our case warrants further follow up even though he received melphalan only for a short period.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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