Scleromyxedema Without Monoclonal Gammopathy in HIV Association Presenting with Leonine Facies and Madarosis: A Case Report

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โรคผิวหนังชนิด scleromyxedema ที่ไม่พบ monoclonal gammopathy ในผู้ป่วยติดเชื้อเอชไอวี ที่มีหน้าสิงโตและขนคิ้วร่วง: รายงานผู้ป่วย

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Introduction

Scleromyxedema is a rare disease characterized by skin eruption from mucin accumulation in the dermis. It presents with symmetrical distribution of yellowish or erythematous papules that commonly involves the face, neck, and arms. The papules may coalesce into plaques, especially on the face, creating leonine-like facies. Histologically, the tissues present mucin accumulation in upper dermis, fibroblast proliferation and fibrosis. The association of scleromyxedema with other systemic diseases including human immunodeficiency virus (HIV) infection, has already been documented. Leonine facies and madarosis as found in this case are rarely stated in routine differential diagnosis of scleromyxedema. We report a case of HIV-associated scleromyxedema without monoclonal gammopathy presenting with papular mucinosis and other two clinical clues: leonine facies and bilateral madarosis which may be helpful in reminding a physician of the diagnosis of scleromyxedema before confirmation by further laboratory investigation.

Case report

A 54-year-old obese male who was HIV-positive last year and on highly active antiretroviral therapy (HAART). The patient presented with a 2 - month history of swelling erythematous patches, papules and plaques with intense pruritus at the face, neck, chest and upper back. The papular skin lesions started at scalp one year earlier, and subsequently developed on the neck, chest and upper back together with facial swelling. His family history was unremarkable. He did not have difficulty in swallowing, tightening face or fingers, nor other neurological deficits. He appeared alert, oriented and well-cooperative without clinical signs of hypothyroidism.The skin examination revealed multiple edematous erythematous patches, papules at the face (Figure 1). The indurated coarsening skin at forehead, particularly above the glabella area, and around the orbital area looks similar to lion-like appearance (leonine facies, leontiasis). Superciliary madarosis was also noted at both eyebrows. Scattering mild erythematous, waxy firm papules and plaques in a centimetric diameter were seen in the nuchal region, chest and upper back (Figure 2 and 3).

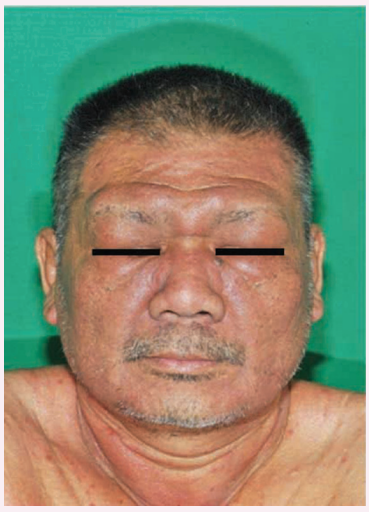

Fig. 1 swelling erythematous plaque on the face

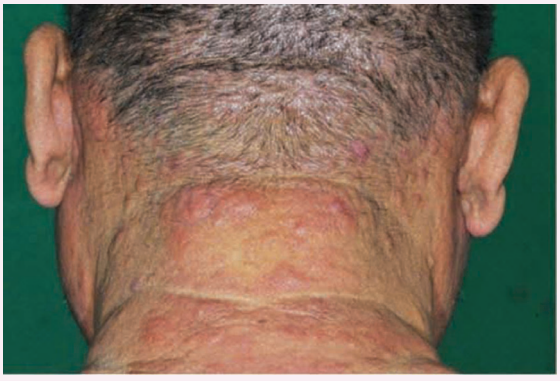

Fig. 2 multiple erythematous papules and plaques on the nape of neck

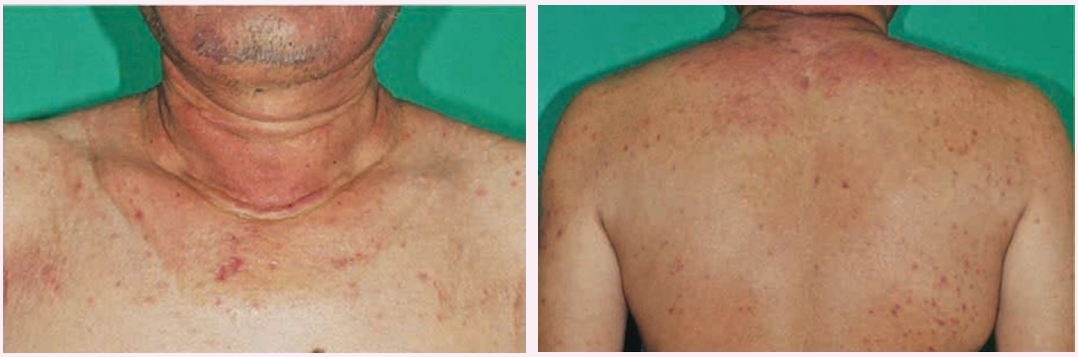

Fig. 3 **multiple erythematous papules on the chest and upper back**

A skin biopsy that has been taken from the nape of neck demonstrated irregular acanthosis and hyperkeratosis of epidermis. The extensive interstitial deposition of bluish fibrillary material throughout reticular dermis as well as sclerosis were noted. The dermis showed a mild superficial perivascular infiltration of lymphocytes. The proliferation of irregularly arranged fibroblasts was presented. The deposition of basophilic substance between collagen bundles was seen within the papillary dermis and reticular dermis. Neither basophilic substance nor an increase in collagen bundle is observed in subcutaneous septa and subjacent tissue. Alcian blue staining has confirmed an increase of mucin deposition (Figure 4 and 5). Direct immunofluorescence was negative. From the above histopathologic findings, the skin lesion was mostly compatible with scleromyxedema.

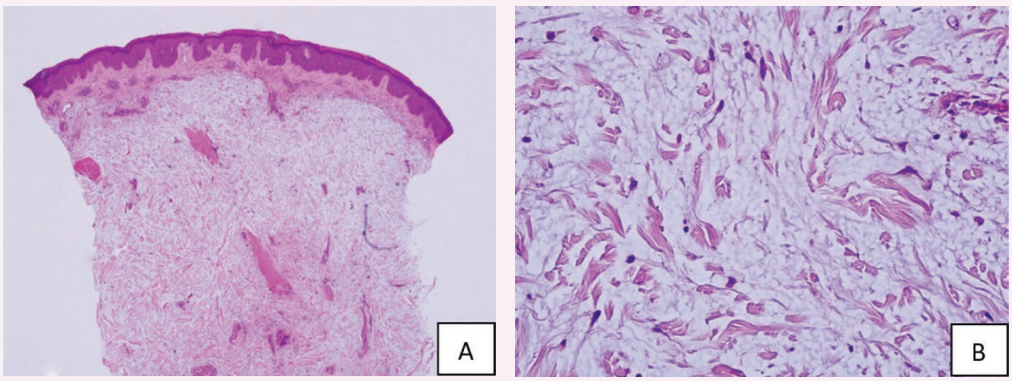

Fig. 4 **Histologic features of skin biopsy from nape of neck; the dermis shows a mild superficial perivascular infiltration of lymphocytes. Marked interstitial deposition of bluish fibrillary material is noted throughout reticular dermis with fibrosis. (H&E; original magnification: A x4, B x40)**

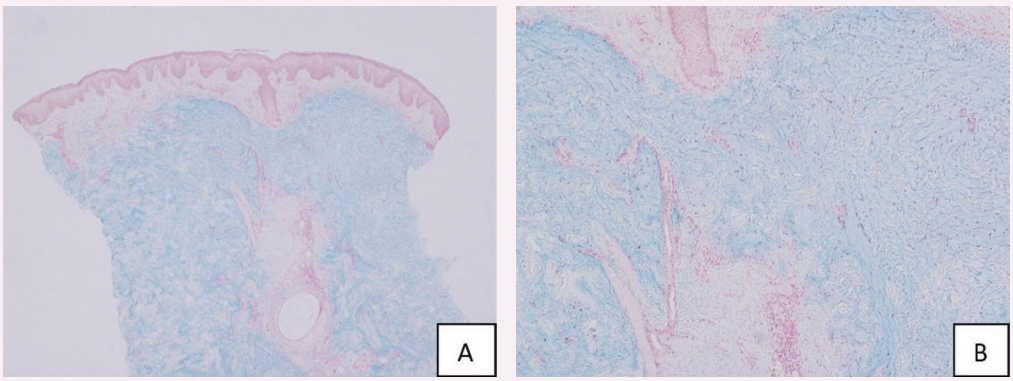

Fig. 5 **Alcian blue staining demonstrates deposition of mucin in the dermis. (A x4, B x10)**

A complete blood count was in normal range. No pathologic cells were determined in peripheral blood smear. Fluorescent antinuclear antibody (FANA) was negative. The complement C1 and C4 levels were normal. Serum protein electrophoresis was performed and the result was within normal limit. Unfortunately, after establishing the diagnosis of scleromyxedema, the patient denied to have additional blood check for biochemistry, erythrocyte sedimentation rate, C-reactive protein, hepatitis B and C serology and thyroid function tests. So far no organ involvement was determined by physical examinations and aforementioned laboratory investigations. From the all of data, atypical form of scleromyxedema is still included in the differential diagnosis of this case.

Discussion

The classification of mucin accumulation (papular mucinosis or lichen myxedematosus) in connective tissue producing lichenoid papules or scleroderma-like skin lesion has been updated recently.[1] This skin disorder has been divided into three main clinicopathological subsets including generalized, local and atypical/intermediate varieties.[1] Scleromyxedema is a generalized form of lichen myxedematosus, presenting with 1) generalized papular and sclerodermoid eruption, 2) mucin deposition, fibroblast proliferation and the presence of fibrosis histopathologically, 3) paraproteinemia, i.e. monoclonal gammopathy (typically IgGλ), and 4) the absence of thyroid function disorder. The generalized form may also have variable extracutaneous involvement. Actually, both the skin and the other organs are prone to be involved extensively in generalized form, leading significant morbidity.[2] If visceral organs are involved, the disease will be fatal. Moreover, the prognosis of scleromyxedema is highly associated with paraproteinemia and it is believed that paraproteins and other factors in the blood probably cause fibroblast proliferation and increase mucin production.[3-4] Most cases of scleromyxedema have an IgG monoclonal paraprotein. However, the association between paraprotein and mucin deposition is not clear. The majority of cases with monoclonal gammopathy of undetermined significance (MGUS) rarely progress to multiple myeloma and if it happens to be present, a patient has a poor prognosis.[5] Causes of death in scleromyxedema depend on not only concomitant malignancy (multiple myeloma in particular), but also systemic involvement and complications of systemic treatments.[6]

The localized form (localized lichen myxedematosus) presents with small, firm, waxy papules limited only in a few sites (commonly on the upper and lower extremities and trunk). This form is subdivided into 5 subtypes including 1) a discrete form, 2) acral persistent papular mucinosis, 3) self-healing papular mucinosis, 4) papular mucinosis of infancy and 5) a pure nodular form. Its histopathologic finding demonstrates mucin deposition with variable fibroblast but lacks of fibrosis by which makes it different from the generalized subset. The localized lichen myxedematosus runs benign course and may not require therapy or even can regress spontaneously contrary to the generalized form which is quite refractory to treatment.

Atypical/ intermediate form includes those are not fit to the criteria for generalized nor the localized form of lichen myxedematosus. For example, scleromyxedema without monoclonal gammopathy, localized forms with monoclonal gammopathy and/or with systemic symptoms (other than HIV infection), localized forms with mixed featured of the 5 different subtypes of the localized form and other non-specified cases.

Based on the underlying HIV positive, generalized lesion, the histopathologic finding shows mucin deposition, fibroblast proliferation, fibrosis and the serum protein electrophoresis is normal, this case is most fit to the atypical form of lichen myxedematosus.

According to the literature reviews, approximately 115 cases of scleromyxedema have been reported.[3] The etiopathogenesis of scleromyxedema is unknown. This condition is chronic progressive and equally affects both men and women during mid to late life.[7] It is characterized by the formation of numerous lichenoid papules which coalesce to form generalized plaques then result in extensive thickening and hardening of skin. The skin lesions usually present on the dorsal aspect of the hands, face, elbows, and extensor surface of the extremities. Mucosal lesions are absent. Associated myopathy, seronegative polyarthritis, bizarre neurological findings including psychosis, accelerated coronary disease, hepatomegaly and lymphadenopathy have been reported in a few patients.[8] Moreover, intense pruritus, scalp involvement, associated eosinophilia without paraproteinemia and morbidity may occur. The most important form of central nervous system involvement is the dermato-neuro syndrome, which may have a fatal outcome.[9]

The pathogenesis of an association between HIV and abnormal mucin deposition is not clear. It is believed that abnormal mucin deposition in the skin is activated by autoantibodies, paraproteins, cytokines or defective pathways of mucin degradation[1,10] and HIV infection might induce abnormal cytokine-secretion and B-cell hyperactivation resulting in paraproteinemia.[4] To the best of our knowledge, only 16 cases of localized lichen myxedematosus associated with HIV infection had been reported.[11] Most of them were homosexual men and their CD4 counts were less than 100/uL.[11] A few cases of localized lichen myxedematosus had been successfully treated with zidovudine by which the lesion gradually regressed over a period of 4-years.[12-13] Additionally, the skin lesion of one case whose CD4 count was 58/uL and HIV RNA level was 100,000 copies/mL, has been improved with antiretroviral regimen comprising lopinavir and ritonavir plus zidovudine and lamivudine about 4 months.[11]

The coexistence of HIV and scleromyxedema is rare.[1] The antiretroviral therapy partially improved the skin lesion in one case, and isotretinoin cleared the skin lesion in another case.[4,14] The following young male who had skin lesion and histopathologic finding similar to our case also responded to antiretroviral

therapy. He presented with CD4 count of 258/uL, HIV viral load of 61,300 copies/mL and widespread indurated skin color papules about 1 year. The histopathologic study of the lesional skin revealed mucin deposition and irregularly arrangement of proliferative fibroblasts in papillary and reticular dermis. On the contrary to our case, he had polyclonal hypergammaglobulinemia.

There is no curative treatment for scleromyxedema. Various treatments have been used, including systemic corticosteroids, topical or oral or intralesional corticosteroids, intralesional hyaluronidase, psoralen ultraviolet A (PUVA), grenz irradiation, electron-beam therapy, retinoids, plasmapheresis, intravenous immunoglobulin (IVIG), extracorporeal photochemotherapy and dermabrasion. Chemotherapeutic agents, particularly low-dose melphalan, have induced some improvement. Minipulse of oral corticosteroid and methotrexate has been tried with some success in scleromyxedema patients presenting with leonine facies.[15] However, the data that related to the efficacy of these agents are insufficient, in fact, most agents are considered to be inefficient.

Concerning on treatments in our case, he was scheduled to complete 3-month PUVA phototherapy together with daily topical steroid and isotretinoin was an alternative choice of treatment for him.

Finally, long term follow up is necessary for monitoring treatment response and his prognosis but unfortunately, the patient was loss to follow up.

Conclusion

We report a rare case of scleromyxedema without monoclonal gammopathy in HIV association who presented with leonine facies and bilateral superciliary madarosis with typical histologic pattern. This case demonstrated two importance of initial skin manifestation namely leonine facies and superciliary madarosis which led to further investigation to get the definitive diagnosis.

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