Case No.12

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Patient: A 57-year-old Thai woman, from Bangkok

Chief complaint: Multiple skin-colored papules on back and extremities for 1 year

Present illness:
The 57-year-old woman presented with multiple skin-colored papules with mild pruritus on upper back for 1 year. Two months ago lesions slowly progressed to upper and lower extremities without systemic symptoms. She has not had any treatment.

Past history: She had history of spinal stenosis but now the symptoms relieve. Sometimes she takes analgesic drugs when she feels painful. She has no history of drug or food allergy. No history of trauma

Family history: No family member experienced the same condition as the patient.

Physical examination:
General appearance: Active female, good consciousness
HEENT: not pale, anicteric sclera
Lymph node: no lymphadenopathy
Lung: clear, equal breath sound
Abdomen: soft, not tender. No mass is palpated.

Dermatological examination:
Skin: multiple confluent 2 to 4 mm dome-shaped waxy skin-colored papules on back, upper and lower extremities in symmetrical pattern
Nail: Normal
Oral cavity: Normal

Investigation:
CBC: Hb 12.2 g/dL, Hct 37.2%, WBC 8.6×10³/µL, neutrophil 44%, lymphocyte 47%, monocyte 5%, basophil 1%, eosinophil 3%, platelet 354×10³/µL
ESR 22 mm/hr
BUN 10.4 mg/dL, creatinine 1.0 mg/dL
LFT: albumin 4.8 g/dL, total protein 8.3 g/dL, total bilirubin 0.45 g/dL, direct bilirubin 0.15 g/dL, AST 18 U/L, ALT 16 U/L, ALP 75 U/L
Urinalysis: clear, specific gravity 1.025, epithelium 1-2, RBC 0-1, WBC 2-3, protein negative, glucose negative, ketone negative
FT3 2.7 pg/mL, FT4 1.3 ng/dL, TSH 1.804 uIU/mL, antithyroglobulin Ab 1.078 IU/mL, antithyroperoxidase 7.34 IU/mL
Anti HIV: negative
HBs Ag: negative
Anti HCV: negative
Serum protein electrophoresis: normal

Histopathology: Slide No.60/1145 (Right forearm)
Sections show unremarkable epidermis. Neither spongiosis nor interface change is noted. The dermis shows a minimal superficial perivascular lymphocytic infiltration. Fontana-Masson stain shows focal loss of melanin pigment. Mucin deposit component is demonstrated by alcian blue stain in the upper dermis. The overall features suggest lichen myxedematosus.
Diagnosis: *Discrete papular lichen myxedematosus*

**Treatment:** She had been treated with topical 0.1% triamcinolone acetonide and emollient. After treatment for 1 month, there is a nearly complete resolution of lesions on both forearms and lower legs.

**Discussion:**

Lichen myxedematosus is a subtype of primary cutaneous mucinoses. It is thought to be a reactive process but the etiology remains unknown. It was first described in 1906. The classification was revised and classified into three main clinicopathological subsets as generalized, localized and atypical types. Scleromyxedema, also called generalized lichen myxedematosus, is characterized by sclerodermoid plaques or generalized lichenoid papules. It usually affects middle-aged men and female equally. Diagnostic criteria are 1) generalized papular and sclerodermoid eruption 2) mucin deposition, fibroblast proliferation and fibrosis in histopathology 3) paraproteinemia i.e. monoclonal gammopathy, which is typically IgG λ, and 4) the absence of thyroid dysfunction. Monoclonal gammopathy with IgG λ light chain elevation is a common finding and can be found in more than 80% of patients but progression to multiple myeloma occurred only 10% of cases. Scleromyxedema may be associated with many systemic disorders. Common extracutaneous involvement includes dysphagia, upper gastrointestinal tract dysmotility, carpal tunnel syndrome, restrictive obstructive lung disease, cardiovascular abnormalities, nephropathy and dermato-neuro syndrome, characterized by fever, encephalopathy, seizure and coma. An association between lichen myxedematosus and paraneoplastic syndrome is rare. Squamous cell carcinoma of lip, thymoma, adenocarcinoma of stomach, hepatocellular carcinoma and ovarian cancer were reported. Natural history is chronic and progressive with morbidity and mortality. Spontaneous regression can occur but very rare. Systemic involvement is quite refractory to treatment.

Localized lichen myxedematosus (localized LM) has limited cutaneous involvement. The diagnostic criteria for localized LM are 1) papular or nodular eruption 2) mucin deposition with variable fibroblast proliferation and 3) absence of both monoclonal gammopathy and thyroid disease. The localized form is subdivided into 5 subtypes, including 1) discrete papular lichen myxedematosus (DPLM) 2) acral persistent papular mucinosis (APPM) 3) cutaneous mucinosis of infancy 4) self-healing papular mucinosis (SHPM) and 5) nodular LM. Discrete papular lichen myxedematosus is most common subtypes of localized LM, which affects both gender equally. It is characterized by reddish, violaceous or skin-colored papules on trunk or extremities in symmetrical pattern. Most of them commonly appear at proximal site of extremities, in contrast to acral persistent papular mucinosis which appears at distal sites. The lesions progress slowly to involve extensive area and progression to scleromyxedema has not yet been reported. Acral persistent papular mucinosis is much more commonly seen in women, characterized by multiple shiny papules on dorsum of hands and wrists, and extensor of forearms. Papular mucinosis of infancy typically occur at elbows and upper arms. And self-healing papular mucinosis is a subtype that mostly involves extremities and have spontaneous resolution in 7 to 14 months from the previous reports. Nodular LM is characterized by nodules on trunk and extremities. This subtype is rare and appears at younger age as compared to discrete LM. Some cases of localized LM were associated with HIV infection. After starting antiretroviral therapy, the lesions subsided. The
improvement of lesions associated with an increase of CD4 count by 100 cell/mm$^3$ and a two-log reduction in HIV viral load$^{14}$. Moreover there was association between chronic hepatitis C infection and localized LM, which had been mostly reported in Japan. Only two cases were reported in non-Japanese$^{15-16}$. Natural history of localized LM is benign course and lesions can regress spontaneously.

Atypical subtype of lichen myxedematosus includes scleromyxedema without monoclonal gammopathy, localized lichen myxedematosus with monoclonal gammopathy and/or systemic symptoms other than HIV infection, localized lichen myxedematosus with mixed features of different subtype and other not well-specified cases$^4$. The course is unpredictable.

Histopathology of all forms of lichen myxedematosus is characterized by dermal mucin deposition in papillary and upper reticular dermis. In scleromyxedema, mucin is diffuse and number of fibroblasts is also more increased as compared to localized subtype$^4$. In localised subtype, fibroblast proliferation is varying and rarely seen sclerosis. Thickened collagen bundles are irregularly arranged. Mild superficial perivascular infiltration of lymphocyte and plasma cell may be present. Alcian blue staining shows focal or diffuse mucin deposition in upper and mid reticular dermis$^{17-18}$.

Now there is still no effective and standard treatment for lichen myxedematosus. Many treatments have been tried with variable results. Localized LM is usually limited to skin. Systemic involvement and morbidity are rarely occur. So treatment may not be necessary in patient with asymptomatic localized LM and closed observation is recommended. However, treatment may be useful in pruritic eruption, cosmetic concern or generalized LM. Topical therapy includes topical steroid and calcineurin inhibitor. Topical steroid was a first line of treatment but success was still variable$^2$. Tacrolimus 0.1% ointment, which was an alternative treatment, was reported a few cases of disease regression in 1 to 3 months$^{19}$. Intralesional injection of hyaluronidase or triamcinolone, dermabrasion, CO2 laser and PUVA also had variable outcomes. In patient with extracutaneous involvement, systemic treatments have a role. The systemic treatments include systemic steroids, retinoids, immunosuppressive drugs i.e. methotrexate, cyclosporine and cyclophosphamide, thalidomide, intravenous immunoglobulin and chemotherapeutic agents$^{10,17}$. Systemic steroids showed partial and complete response in a few cases. The relapse occurred after steroid tapering$^{20-21}$. Systemic retinoids showed favorable results in some patients with systemic involvement and HIV infection$^{22-23}$. Clinical improvement was reported in cyclosporine$^{24}$ and oral cyclophosphamide administration$^{25}$. Intravenous immunoglobulin showed good results with no recurrence in a few reports but some had recurrence in 5 months to 3 years$^{26}$. Plasmapheresis is showed dramatic response in patients with neurological symptoms$^{27}$. Biologic therapy i.e. Bortezomib was also effective with rapid response but more data is still required$^{28}$.

Our case presented with slowly progressive multiple symmetrical 2 to 4 mm dome-shaped waxy skin-colored papules on back and extremities for 1 year without systemic symptoms. Histopathology of tissue from right forearm reveals normal epidermis with mucin deposition in upper dermis. With alcian blue staining at 2.5 pH shows focal dermal mucin
deposition. Laboratory investigation including complete blood count, liver function test, renal function and urinary analysis were normal. Serology tests for human immunodeficiency virus (HIV), hepatitis B and C viruses (HBV, HCV) were all negative. Thyroid hormones, antithyroglobulin and antithyroperoxidase are normal. Serum protein electrophoresis is unremarkable. Our patient’s findings meet the criteria diagnosis of discrete papular lichen myxedematosus without systemic involvement. Clinical differential diagnosis include eruptive collagennoma or lichenoid eruption.

The patient was treated with topical corticosteroid and emollient. After treatment, there is a dramatic response on both forearms and back within 1 month.

References: