A Case Report of Papulonodular Mucinosis Associated with Unclassified Autoimmune Connective Tissue Disease

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ABSTRACT:

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Papulonodular mucinosis (PNM) is an uncommon but distinctive cutaneous manifestation of autoimmune connective tissue disease mainly associated with lupus erythematosus. Mucin deposition in the dermis is a common histologic finding. The pathogenesis is still uncertain but it is thought to be due to increased glycosaminoglycans production by dermal fibroblast stimulated by some cytokines or immunoglobulins. In terms of treatment, PNM is usually unsatisfactory. Many modalities have been suggested including glucocorticosteroids (topical, intralesional or systemic), antimalarial agents, retinoids, cyclophosphamide, methotrexate, plasmapheresis or surgical procedures such as laser and excision may have benefits.

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We report a case of 45-year-old female presented with a 5-years history of multiple erythematous hyperpigmented papules, nodules on trunk and skin colored papules coalescing to plaques on both forearms and knuckles. The patient denied systemic symptoms and the physical examination showed only Raynaud phenomenon. The histopathology and special staining were compatible with dermal mucinosis. Laboratory investigation showed high titer antinuclear antibodies and weakly positive anti-Jo1 while other serological tests for autoimmune disease were normal. The final diagnosis of papulonodular mucinosis associated with unclassified autoimmune connective tissue disease (AI-CTDs) was made as there was neither symptom nor laboratory result of definite AI-CTDs. Clinical improvement was seen after 3 months of oral methotrexate and topical glucocorticoids.

Key words: Papulonodular mucinosis, autoimmune connective tissue diseases

Case report

A 45-year-old Thai female with a past medical history for hypertension presented with a 5-years history cutaneous eruption on trunk and extremities. The patient had denied photosensitivity rash, fever, weight loss, mucous membrane lesions, arthritis and neuropsychiatric symptoms. The physical examination showed multiple erythematous hyperpigmented papules, nodules on trunk and skin colored papules with coalescing to plaques on both forearms and knuckles (Figure 1) and Raynaud phenomenon. Laboratory investigation revealed positive antinuclear antibodies titer (1:1280) in homogenous pattern and (1:160) nucleolar pattern. Anti-Smith, anti RNP antibodies, anti-dsDNA antibodies, anti Scl-70 and anti-centromere were also negative. Myositis 16 profiles showed only weakly positive anti-Jo1. Complete blood count, thyroid function test, creatinine phosphokinase and lactate dehydrogenase were within normal limits. Human immunodeficiency virus and hepatitis profile were negative. The serum protein electrophoresis and immunofixation electrophoresis were all negative.

Histologic examination of a punch biopsies from the trunk and dorsum of the left hand demonstrated markedly diffuse deposition of mucin throughout the reticular dermis. Neither spongiosis nor interface change was noted. The dermis showed mild superficial perivascular infiltration of lymphocytes (Figure 2A). Immunohistochemical staining with Alcian blue showed diffuse bluish material in reticular dermis (Figure2B). Direct immunofluorescence examination of lesion skin was negative. The aforementioned clinical and histopathologic results were compatible with papulonodular mucinosis (PNM), yet there were no specific signs and symptoms that fulfilled the criteria for the diagnosis of any autoimmune connective tissue disease (AI-CTDs). Hence, the final diagnosis of

PNM associated with unclassified AI-CTDs was made. After 3 months of treatment with oral methotrexate and topical glucocorticoids, clinical improvement was observed (Figure 3).

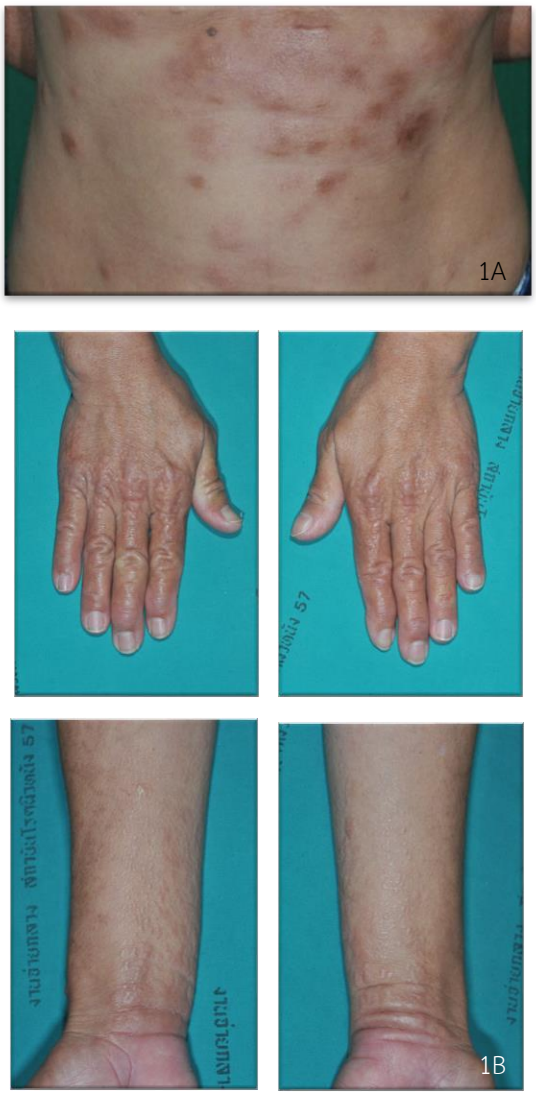

Figure 1 (A) Multiple erythematous hyperpigmented papules, nodules on trunk **(B)** Skin-colored, firm papules with coalescing to plaques on both forearms and knuckles

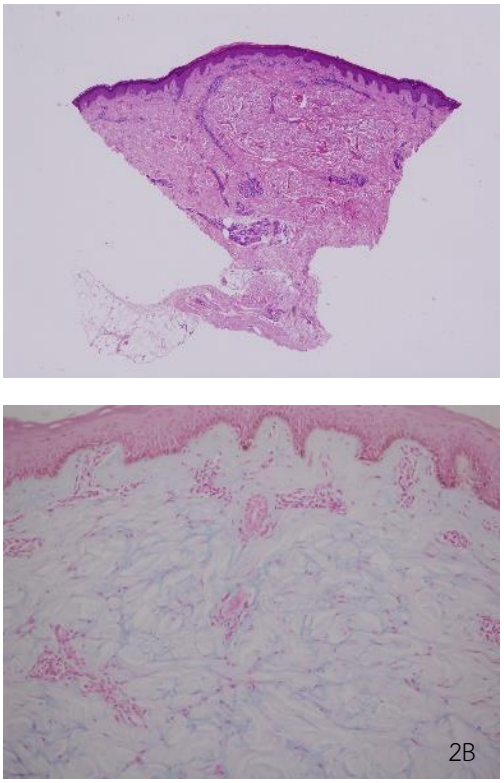

Figure 2 (A) Histopathology shows increased dermal mucin deposit in reticular dermis with mild superficial perivascular lymphocyte infiltration in dermis (Hematoxylin and Eosin stain; original magnification X4.) **(B)** The abundant deposition of mucin in the dermis (Alcian blue stain at pH2.5; original magnification X40)

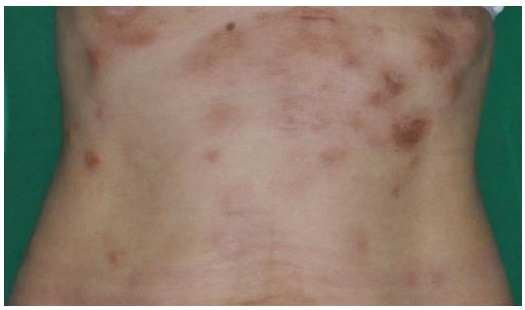

Figure 3 3 months after oral methotrexate and topical glucocorticoids treatments

Discussion

Cutaneous mucinosis are connective tissue disorders characterized by an abnormal mucin deposition in the dermis and within the hair follicle, which can be classified into primary and secondary mucinoses[1]. Primary mucinosis is termed when the mucin deposition is the main histopathological finding resulting in clinically distinctive manifestation, whereas secondary mucinosis occurs as a result of other skin disorders. Papulonodular mucinosis (PNM) was first described in 1954 as an uncommon but distinctive cutaneous manifestation of dermal inflammatory degenerative primary mucinosis[2-5]. Since the lesion is uncommon, among all lupus erythematosus (LE) cases only 1.5% of patients reported with PNM[1]. Sonntag et al. reported a review of 41 cases of PNM associated with LE, 31 cases had systemic lupus erythematosus (SLE), 8 had discoid LE and 2 with subacute cutaneous LE[6]. Other associations include dermatomyositis and systemic sclerosis[7]. There has been a report of PNM presenting with multiple asymptomatic skin colored papules on the face, trunk and arm which was similar to our case. Further investigation was done with the final diagnosis of PNM associated with SLE, confirmed by laboratory investigation and histologic findings[8].

The pathogenesis of PNM remains unclear. Overproduction of glycosaminoglycans by dermal fibroblasts, stimulated by immunoglobulins and cytokines has been described[9]. Other possible triggering factors are androgenic hormones and ultraviolet light[10]. Clinically, typical PNM is characterized by asymptomatic skin-colored papules and nodules on back, V of the chest and upper extremities. Lesions may also appear on the face and other areas of the body[6]. The onset of the cutaneous mucinosis may precede, during or after the presentation of connective tissue disease. Histopathologic examination demonstrated marked deposition of mucin interspersed among collagen bundles in the upper and mid dermis and may be extended into the subcutaneous layer. There may be mild perivascular lymphocytic infiltration[11]. Other histological features of LE are usually absent. However, Direct immunofluorescence examination may reveal linear or granular deposition of IgG, IgM, and C3 at the basement-membrane zone[12]. Serological testing for autoimmunity is suggested if autoimmune disease is suspected. In our patient, the serology testing for autoimmune connective tissue disease (AI-CTDs) has been investigated. Due to lack of the fulfilled criteria for the diagnosis of any specific AI-CTDs. The diagnosis PNM associated with unclassified AI-CTDs was made. To date, there has been no report on PNM associated with unclassified AI-CTDs. Anyway, PNM may highlight as an unusual presentation of AI-CTDs and the condition may precede the clinical onset of the

disease. The physicians should be aware and acknowledge such lesions with a mandatory clinical follow-up to observe the clinical.

In terms of treatment, PNM is usually unsatisfactory. Many treatment modalities have been proposed to treat this condition including glucocorticoids, antimalarial agents, retinoids, cyclophosphamide and methotrexate. Surgical procedures such as dermabrasion, laser and excision have been reported[13]. Effective treatment with intralesional hyaluronidase has also been reported[7,14].

In our case, the patient presented with a 5-years history of multiple erythematous hyperpigmented papules and nodules on trunk skin colored papules coalescing to plaques on both forearms and knuckles. The examination showed only Raynaud phenomenon. The histology and immunohistochemical were compatible with dermal mucinosis. Laboratory investigation revealed high titer antinuclear antibodies, while other serological tests for autoimmune disease showed only weakly positive anti-Jo1. The final diagnosis of PNM associated with unclassified AI-CTDs was made until other specific presentations of AI-CTDs could be found. Clinical improvement was seen after 3 months of oral methotrexate and topical glucocorticoids. The possibility of the patient to develop AI-CTDs in the future should be awared.

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