Case Report of Papular Mucinosis in Systemic Lupus Erythematosus

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ABSTRACT:

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Papulonodular mucinosis, a rare cutaneous manifestation of autoimmune connective tissue diseases, mainly lupus erythematosus (LE). The characterized histologic findings include papillary and mid-reticular dermal mucin without any typical epidermal inflammatory changes. We describe a patient with systemic LE who subsequently developed papular mucinosis. At the time of this report she achieved significant improvement of her papular mucinosis with intralesional steroids in addition to methotrexate and prednisolone.

Key words: Systemic lupus erythematosus, lupus erythematosus, papulonodular mucinosis

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Introduction

Skin disease is a frequent complaint of patients with systemic lupus erythematosus (LE). The most commonly recognized mucocutaneous manifestations are a malar rash (40%), alopecia (24%), and oral ulcer (19%)[1]. A wide spectrum of other cutaneous manifestations of LE also have been reported including papulonodular mucinosis (PNM).

PNM also called papular and nodular mucinosis of Gold or cutaneous lupus mucinosis, was first recognized as early as 1954[2]. PNM can occur in up to 1.5% of patients with LE in the fourth and fifth decades of life[3]. A review reported that about 75% of the PNM cases were associated with systemic LE, 20% were associated with discoid LE and 5% were associated with subacute cutaneous LE[4]. Cases of secondary cutaneous mucinosis have also been described in systemic sclerosis, dermatomyositis, mixed connective tissue disease and unclassified autoimmune connective tissue disease, albeit infrequently[5-8]. We describe a patient who experienced papular mucinosis associated with malar rash, photosensitivity and non-scarring alopecia in systemic LE.

Case report

A 41-year-old woman presented with a 2-months history of several erythematous to skin-colored papules on both sides of the groin. During this time, several new lesions developed on the left submammary region as well. The physical examination showed multiple dome-shaped waxy erythematous to skin-colored papules scattered on both sides of the groin and on the left submammary region. (Figure 1)

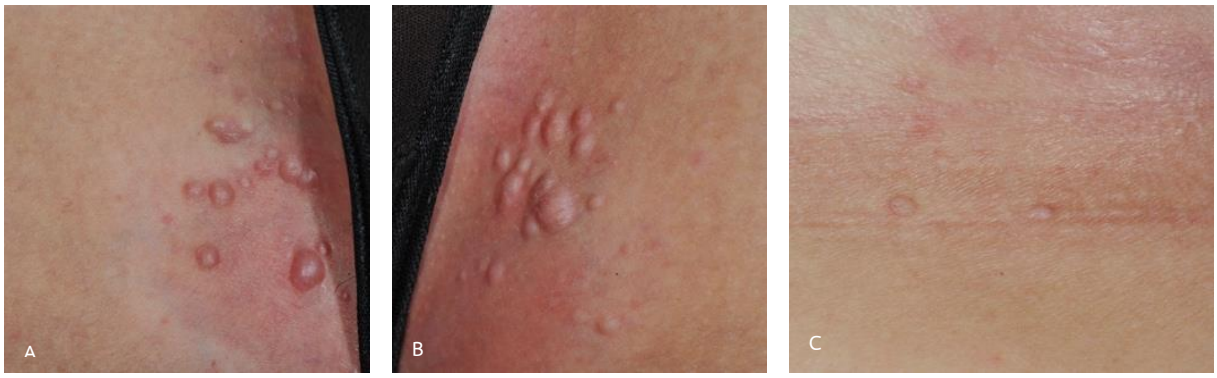

Figure 1 Multiple dome-shaped waxy erythematous to skin-colored papules on both sides of the groin (A and B) and on the left submammary region (C).

Two years earlier, she had been diagnosed with systemic LE. Malar rash, photosensitivity and non-scarring alopecia were presented. Other history and physical examination were unremarkable. The significant laboratory values included an antinuclear antibody titer of 1:640 in a homogeneous pattern, leukopenia (3,500/mm^3). However, the hemoglobin level, platelet count, thyroid function tests, liver function tests, renal function tests and urinalysis were all within normal limits.

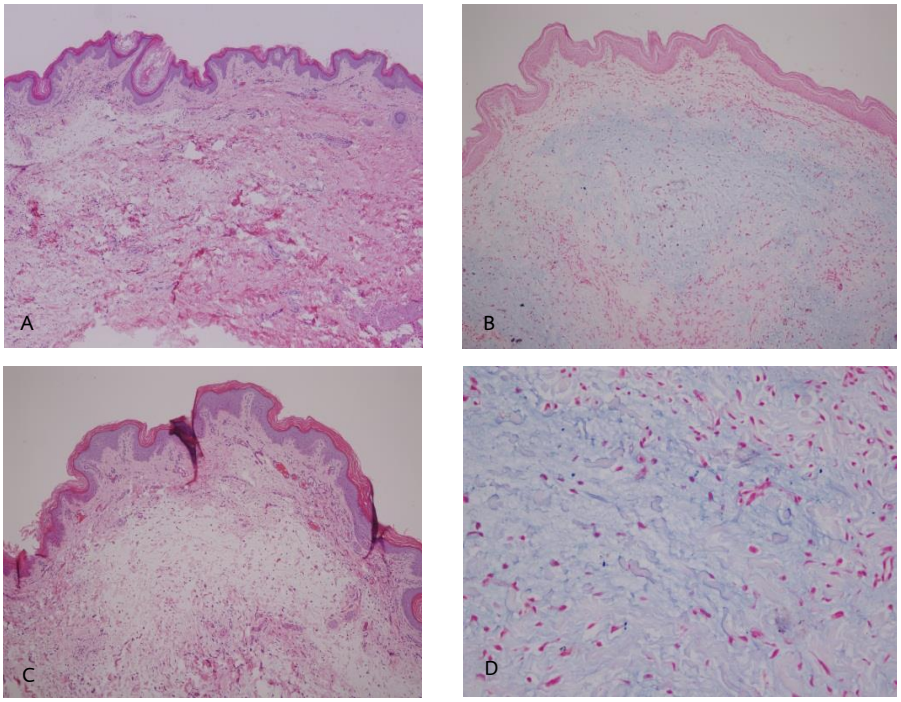

Figure 2 Cutaneous histopathological findings showing mucinous change in the upper dermis
(A) H&E staining; X20, (B) H&E staining; X20 Alcian blue staining (pH 2.5) revealed deposits of acid mucopolysaccharides between collagen bundles in the upper dermis, (C); X20 (D); X40

She was treated with hydroxychloroquine (subsequently withdrawn because of drug eruption), azathioprine (subsequently withdrawn due to transaminitis) and prednisolone (10-30 mg/day) for two years, which resulted in trivial improvement, meaning that almost all cutaneous findings (malar rash, photosensitivity and non-scarring alopecia) remained the same.

An excisional biopsy from a papule on the left side of the groin was performed and showed unremarkable epidermis with hyperkeratosis with increased mucin deposition in the upper dermis (Figure 2).

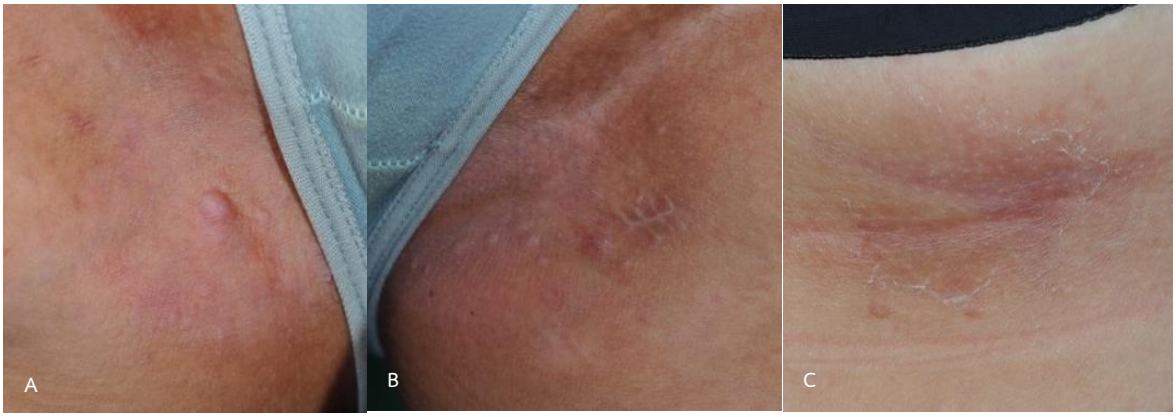

Figure 3 After treatment, the sizes of papules were decreased on both sides of the groin (A and B) (postsurgical scar due to excisional biopsy on the left groin) and on the left submammary region (C)

These clinical and histopathological findings were consistent with PNM associated with systemic LE. She was treated with intralesional triamcinolone acetonide 10 mg/mL monthly together with methotrexate (5-7.5 mg/week) and prednisolone (10-15 mg/day). The lesions regressed after a period of four months. (Figure 3)

Discussion

PNM, a rare cutaneous manifestation of autoimmune connective tissue diseases, mainly LE. It is clinically characterized by asymptomatic flesh-colored papules and nodules, which occur in the presence or absence of the typical cutaneous lesions of LE. PNM can develop before or after being diagnosed with autoimmune connective tissue diseases. In our patient, PNM occurred after the clinical manifestations of systemic LE same as reported by Dallo C, et al.[9]

PNM has a predilection for the trunk and upper extremities, but the face and other areas of the body such as the neck and thighs may also be affected[10]. In our patient, apart from on the left submammary region, PNM lesions also appeared on both sides of the groins. PNM is histopathologically characterized by mucin deposition in the superficial and mid dermis associated with a slight to moderately dense perivascular lymphocytic infiltration and the absence of the typical epidermal and interface changes of LE,[11] which were similar to our patient. Histopathologically, tumid LE can be very similar to PNM. However, the tumid LE is distinguished by abundant dermal mucin deposition and a superficial and deep perivascular and periadnexal infiltration. In addition, tumid LE is seldom related to systemic LE.

The pathogenesis of PNM is not well elucidated. The most accepted theory is the

overproduction of glycosaminoglycans by dermal fibroblasts stimulated by circulating autoantibodies and cytokines such as interleukin-1, tumor necrosis factor-α and transforming growth factor-β[12]. Another possible contributing factor may be ultraviolet light, as exposure to sunlight reduces catabolic degradation of mucin, induce or exacerbate the skin lesions[4]. However, all PNM in our patient occurred on the sun-protected areas. Despite a higher incidence of systemic LE in women (female-male ratio of 9:1), PNM occurs more frequently in men (male-female ratio of 18:13), indicating a possible role of sex-related factors, such as androgenic hormones, in the pathogenesis of this disease[13].

Rongioletti F, et al. have reviewed 14 cases of PNM and stated that 57% of patients with PNM have associated renal disease and 50% have arthritis[14]. This high frequency urges that clinicians should have a high index of suspicion for kidney and joint involvement. Fortunately, our patient had neither symptoms of renal nor articular involvement, and she had normal renal function tests and urinalysis.

Since there is no standardized treatment for PNM and some variants of cutaneous mucinoses, many therapeutic modalities have been proposed to treat this condition including glucocorticoids, methotrexate, antimalarial agents, retinoids and cyclophosphamide; intralesional hyaluronidase; plasmapheresis and surgical options such as dermabrasion, laser and excision, but the results of treatment are variable[4,15]. Antimalarial drugs and topical or systemic corticosteroids are the most frequently used. On the basis of previous reports, approximately 20% of cases respond well to antimalarial drugs. The remaining cases often require additional treatment with oral corticosteroids. In rare instances, the papulonodular eruptions is refractory to both antimalarial drugs and topical or systemic corticosteroid therapy[14,16,17]. Nonetheless, spontaneous resolution has been reported as well[18-20].

Fortunately, our patient demonstrated nearly complete resolution with medication comprised of intralesional glucocorticoids in combination with methotrexate and prednisolone after a period of four months.

Conclusion

In summary, the PNM is a rare cutaneous manifestation of autoimmune connective tissue diseases, mainly LE. We describe a patient with systemic LE who subsequently developed papular mucinosis. Intralesional, systemic glucocorticoids and methotrexate have been used with favorable outcomes in this patient.

As of today, no clinical guidelines have been published for the treatment of PNM and the responses to current available treatment are variable, there is a great need for further clinical

studies to elucidate the pathogenesis and identify an effective treatment with a positive long-term safety and risk profile.

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