Lichen Planus in Association with Adult-onset Still's Disease Successfully Treated with Mycophenolate Mofetil

To the Editor:

A 55-year-old woman presented with acute onset of spiking fever, symmetric polyarthritis with intense myalgia, and sore throat. Onset was associated with diffusely itchy purple papules involving the trunk, anterior chest wall, and upper and lower limbs. Initial laboratory investigation showed elevated erythrocyte sedimentation rate (90 mm/h), elevated C-reactive protein (17.8 mg/dl), negative rheumatoid factor (RF), negative anti-citrullinated protein antibody, and negative antinuclear antibody (ANA). Complete blood count showed leukocytosis with white blood cell count $14.7 \times 10^3/\mu$l, anemia with hemoglobin 9.6 g/dl, thrombocytosis with platelet count $802 \times 10^3/\mu$l, and 2-fold increase in serum ferritin levels (350 ng/ml, normal values up to 150 ng/ml). Other laboratory investigations showed elevated liver enzymes [aspartate transaminase 69 IU/l, alanine transaminase 125 IU/l, and elevated creatine phosphokinase (CPK) levels 320 IU/l, normal 40–120 IU/l] with negative virology screening for viral hepatitis. Skin biopsy showed focal thinning of the epidermis with focal destruction of basal layers and focal dermal mononuclear infiltrate, features consistent with the diagnosis of lichen planus (LP; Figure 1). No history of medications known to induce LP was given by the patient.

The case fulfilled the Yamaguchi criteria for classification of adult-onset Still's disease (AOSD)[1], with the presence of 3 major criteria (spiking fever, arthritis, and leukocytosis) and 3 minor criteria (sore throat, liver dysfunction, and negative ANA and RF).

However, the patient was generally ill, with severe constitutional manifestations and marked weight loss. We requested a technetium dual-phase bone scan to exclude underlying malignancy; the early phase showed symmetrical hyperemia of the skeletal muscles, and the late osseous phase showed symmetric hot uptake at different joints (Figure 2). The patient received methotrexate (MTX) 15 mg/week intramuscularly and oral steroid 15 mg/day. Further clinical assessment 1 month after initial treatment showed she still had active synovitis in the joints noted above, with intense myositis with no improvement of the skin disease. Repeated liver enzyme tests showed persistently elevated liver enzymes and CPK. MTX was stopped and mycophenolate mofetil (MMF) 1500 mg/day was started and the dose of oral steroids was increased to 30 mg/day. On this regime she showed much improvement of the arthritis, myositis, and other constitutional disease manifestations, with partial improvement of LP lesions. Importantly, CPK and liver enzymes returned to normal values 1 month after treatment and remained normal after 6 months of followup with gradual improvement of LP skin lesions.

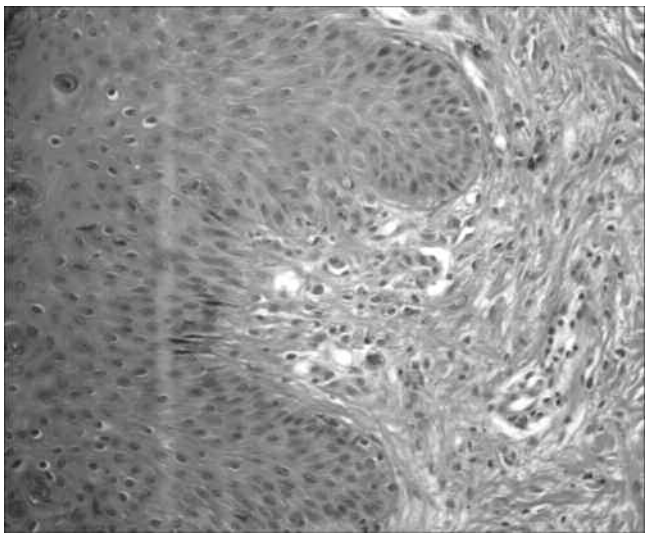

Figure 1. Histopathological examination of skin biopsy, showing focal thinning of the epidermis with focal destruction of the basal layers and minimal exocytosis, with focal dermal mononuclear and macrophage infiltrates.

In the few case reports, LP can be associated with various rheumatic disorders, e.g., rheumatoid arthritis (RA)[2], Sjögren's syndrome[3], and systemic lupus erythematosus (SLE)[4]. On the other hand, LP can develop as a reaction to disease-modifying antirheumatic drugs[5]. We observed LP in a case with AOSD, which seems to be a rare association, with no previous reports addressing such a relation.

The choice to use MMF in our case was considered for many reasons: recent reports documented both efficacy and safety of MMF in treatment of resistant LP lesions[6,7]; MMF can control other elements of the disease, notably arthritis and myositis; and MMF seems useful in patients with autoimmune hepatitis and overlap syndromes[8].

MMF inhibits T and B cell proliferation by blocking the production of guanosine nucleotides required for DNA synthesis, and acts as a selective, reversible noncompetitive inhibitor of inosine monophosphate dehydrogenase, which is a critical enzyme for *de novo* synthesis of guanosine nucleotides.

Relative to AOSD, Chen, *et al*[9] suggested that dysregulation of Th17 cells may be a common pathogenic mechanism that underlies development of AOSD. Moreover, the frequencies of circulating Th17 cells were positively and significantly correlated with serum levels of interleukin 17 (IL-17). Specifically, IL-17-producing Th17 cells have crucial functions in host defense, and dysregulated Th17 cell responses mediate a variety of autoimmune and inflammatory conditions such as RA and inflammatory bowel disease[10].

In a recent study, Abadja, *et al*[11] showed that MMF and tacrolimus had a comparable influence on T cell response. However, MMF exerted a stronger inhibitory effect on IL-17 production than tacrolimus. A simple link between the first study[9] and the second[11] would explain the beneficial effect of MMF in our case, together with the increased dose of steroids.

Recently, a number of uncommon and clinically diverse inflammatory skin diseases were linked by the presence of a set of histopathological elements that have traditionally been referred to as lichenoid tissue reaction/interface dermatitis (LTR/IFD). The latter can also be seen in skin disorders associated with systemic illnesses (e.g., SLE, dermatomyositis)[12], and this may also explain the myositic element observed in our case.

To our knowledge, this is the first English-language case report in which LP is associated with AOSD.

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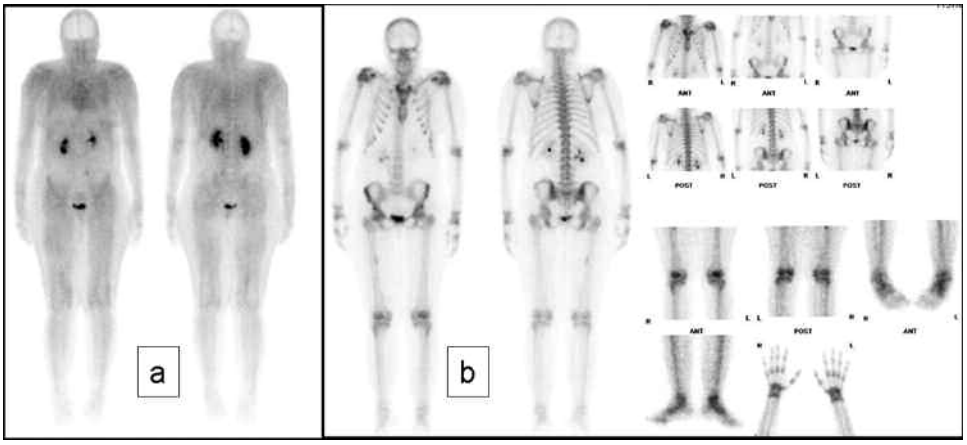

Figure 2. Technetium dual-phase bone scans: (a) early phase shows symmetrical hyperemia of skeletal muscles of the gluteal regions, shoulder girdle, arm, back, and pectoral muscles; (b) late osseous phase shows bilateral and symmetric hot uptake in metacarpophalangeal, proximal interphalangeal, wrists, elbows, knees, shoulders, and ankle joints.

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