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CASE REPORT

Erythema Nodosum as a Manifestation of HIV Infection

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SUMMARY **Various musculoskeletal syndromes have been well described in patients infected with the human immunodeficiency virus (HIV). Surprisingly, erythema nodosum, an inflammation of the adipose tissue of the skin, has rarely been described. We report a 24-year-old known case of HIV infection, who developed fever and multiple tender subcutaneous nodules that were proven to be erythema nodosum. The patient also had polymyositis. She responded well to a high dose of corticosteroids. Erythema nodosum should be listed as possible the rheumatic manifestation of HIV infection.**

Various musculoskeletal and connective tissue disease syndromes have been well documented in association with human immunodeficiency virus (HIV) infection. These include infectious arthritis, seronegative spondyloarthropathies, arthralgia syndrome, diffuse infiltrative lymphocyte syndrome (Sjögren's-like syndrome), the lupus-like syndrome, hypertrophic osteoarthropathy, poly/dermatomyositis, Behcet's disease and various vasculitides.[1-7] Surprisingly, erythema nodosum, an inflammation of subcutaneous fat, which is a common rheumatic disease, has rarely been described in these patients.[8-9] We, herein, report an HIV-infected patient who presented with polymyositis and erythema nodosum during the course of her disease.

CASE REPORT

A 24-year-old woman was readmitted to the Chiang Mai University Hospital because of generalized muscle ache, pain and weakness, which had developed over the last 2 weeks. Two months ago she was found to have HIV infection when first admitted for acute severe headache, vomiting and blurred vision. A cranial computed tomography (CT) showed multiple irregular hyperdense lesions at the left parieto-posterior and right frontal lobes. A serological test for toxoplasmosis was negative. Cerebrospinal fluid examination was normal. Daily intravenous dexamethasone at 20 mg, oral pyrimethamine at 25 mg and sulfadiazine at 2.0 gm were given to cover possible cerebral toxoplasmosis. The patient showed a partial improvement of the headache. As a follow up cranial CT, performed one month later, showed no improvement in the size of the lesions, a stereotactic brain biopsy was done. The pathological results showed necrotic brain tissue, but without a definite diagnosis. Corticosteroids, pyrimethamine and sulfadiazine were discontinued. The patient received no anti-retroviral treatment, because of economic problems.

Two weeks before this admission, she began to have generalized muscle ache and pain. One-week later, high spiking fever and multiple tender subcutaneous nodules on both upper and lower extremities developed. There was no history of red eyes, skin rashes, oral or genital ulcers, diarrhea, Raynaud's phenomenon or joint pains. The patient did not take other medications. Her vital signs were normal except for a temperature of 39.5°C. She was slightly pallor. Generalized tenderness of the muscle and slight edema of both upper and lower extremities were noted. The power of the proximal muscle group was grade III and the distal group was grade IV. Multiple tender subcutaneous nodules, 0.5-3.0 cm in size, were noted on the calves

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shins, buttocks and arms. The skin over these nodules was slightly red, on which some had turned into reddish-purple color. There was no definite joint swelling. Other physical examinations were unremarkable.

A complete blood count showed a hematocrit of 28%, and a white blood cell count of 11,900 cells/mm^3 with normal differential counts. A hemoglobin typing showed AH. The CD4 count was 240 cells/mm^3 with a CD4/CD8 ratio of 0.1. Serum muscle enzymes showed SGOT 90 U/l (normal 3-35), LDH 780 U/l (normal 113-246) and CPK 726 U/l (normal 0-195). Other investigations including urine analysis, blood and urine cultures, renal and liver functions, serum amylase,

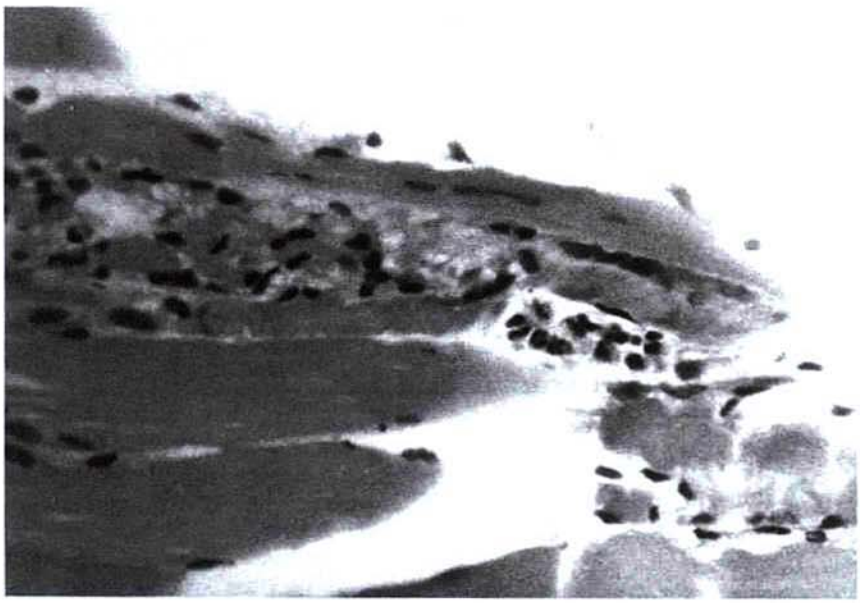

Fig. 1 Muscle fiber destruction with inflammatory cell infiltration (H & E stain, x400).

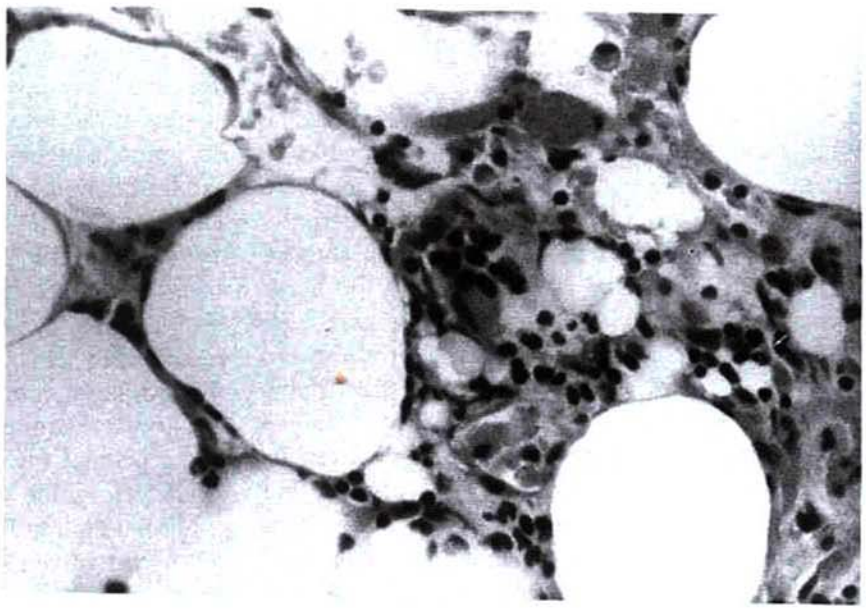

Fig. 2 Dense inflammatory cell infiltration in the septa of the fat lobules (H & E stain, x400).

blood electrolytes, stool examination for parasites, anti-streptolysin O, anti-nuclear antibodies, complement levels, Coomb's test and a chest radiograph and tuberculin skin test were all normal or negative. Alpha-one antitrypsin was not determined, as it was not available at our institution.

A muscle biopsy showed variable degrees of muscle fiber destruction and infiltration of inflammatory cells (Fig. 1). The necrotic muscle fibers were ingested by macrophages and neutrophils. Perivascular neutrophilic infiltration and areas of muscle fiber regeneration were noted. Granulomatous inflammation, stainable specific microbes, fungus or mycobacterium were not identified. A skin biopsy showed dense inflammatory infiltration in the septa of the fat lobules with destroyed adjacent fat cells (Fig. 2).

Prednisolone at 1 mg/kg/day was given resulting in a rapid resolution of the fever and muscle pain. At the end of the second week, the patient's serum muscle enzymes and muscle strength returned to normal, and the subcutaneous nodules disappeared. Unfortunately, she did not return for follow up after being discharged from the hospital.

DISCUSSION

Erythema nodosum (septal panniculitis) is the term used to describe the disorder, in which an inflammation occurs in the subcutaneous fat. It is characterized as erythematous or violaceous nodules, symmetrically distributed over the skin, with the thighs and lower legs most commonly affected.[10] Erythema nodosum can be associated with drugs (sulfonamide, bromide and oral contraceptives), malignancies (leukemia and lymphoma), inflammatory bowel diseases (ulcerative colitis and Crohn's disease) and many bacterial, fungal and viral infections, e.g. tuberculosis, leprosy, histoplasmosis, blastomycosis, hepatitis B, and infectious mononucleosis.[10]

Although the non-inflammatory disease of the adipose tissue, lipodystrophy (both lipoatrophy and lipohypertrophy), which is a complication of protease inhibitor therapy in patients with HIV infection, has been well recognized and reviewed,[11] inflammatory disease of the adipose tissue in these patients has rarely been reported. Martinez *et al.*[12] described a case of acute pancreatic panniculits in a patient with primary HIV infection and haemophagocytic syndrome. The painful erythematous subcutaneous nodules involved both legs. The skin lesion responded well to high dose intravenous corticosteroids. Venkataramani *et al.*[13] reported an HIV-infected patient who had recurrent abdominal pain, which was proven to be sclerosing mesenteritis by laparoscopic biopsy. The patient responded well to tamoxifen. Fegueux *et al.*[8] reported erythema nodosum in 4 HIV-infected patients. Three of these patients were immunodeficient. All of the patients had positive tuberculin skin tests. One was found to have tuberculous lung infection and another had tuberculous lymphadenitis 2 years later. Narzaez *et al.*[9] reported additional cases of erythema nodosum in relation to tuberculosis. Recently, a case of necrotizing lobular panniculitis caused by infiltration of *Acanthamoeba* species was described.[14]

Our patient had erythema nodosum, which was proven by the presence of septal panniculitis in biopsies. We believed that erythema nodosum in this case was a manifestation of HIV infection. Although the patient had been given sulfadiazine treatment for possible cerebral toxoplasmosis, it was discontinued approximately one month prior to developing this illness. Searches for other possible causes of erythema nodosum including bacterial and fungal infections, pancreatic diseases and autoimmune diseases were all negative. Recurrent panniculitis has been described recently in a patient who received protease inhibitor therapy,[15] but our patient had never received such treatment. The presence of polymyositis in this case was not surprising as polymyositis is a well recognized manifestation of HIV infection.[1] Unfortunately, we did not have the chance to follow-up this patient.

Although the pathogenesis of erythema nodosum is not cleary understood, the presence of mononuclear cell infiltrations, deposition of immunoglobulins and complements in the lesions and the good response to corticosteroids, support the belief that an immunologic reaction that had been triggered by a wide range of antigenic stimuli was a cause of the inflammation.[10] We did not perform special staining for HIV antigen for this patient. The good response to corticosteroids supported the speculation that the clinical features were from the immunopathogenicty.

Erythema nodosum should be listed as possible rheumatic manifestation of patients with HIV infection.

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