Fibroblastic Rheumatism in a Female of Systemic Lupus Erythematosus

Yu-Ju Shen  Gwo-Shing Chen  Jin-Yuang Chen  Chieh-Shan Wu

Fibroblastic rheumatism is a relative rare syndrome characterized by polyarthralgia and joint stiffness associated with multiple cutaneous papules and nodules ranging from 2 to 20 mm in diameter. The skin nodules usually regress spontaneously, but there are often sequels of deformed joint. We described the occurrence of fibroblastic rheumatism in a female patient with systemic lupus erythematosus. Her skin nodules and arthralgia resolved after combination therapy of daily prednisone and hydroxychloroquine. In conclusion, fibroblastic rheumatism is a rare rheumatologic entity of unknown etiology. This diagnosis should be considered when patient present with sudden onset of symmetric polyarthritis and multiple cutaneous nodules. (Dermatol Sinica 24: 135-139, 2006)

Key words: Fibroblastic rheumatism, Systemic lupus erythematosus

From the Department of Dermatology, Kaohsiung Medical University Hospital,1 and Kaohsiung Municipal Min-Sheng Hospital2
Accepted for Publication: November 24, 2005
Reprint requests: Chieh-Shan Wu, M.D., Department of Dermatology, Kaohsiung Medical University, No. 100, Shih-Chuan 1st Rd., Kaohsiung, Taiwan, R.O.C.
TEL: 07-3208214  FAX: 07-3216580
INTRODUCTION

Fibroblastic rheumatism (FR) was first described in French literature in 1980. It is a relatively rare syndrome featured by polyarthralgia, joint stiffness with or without joint destruction, and multiple cutaneous nodules. The nodules showed characteristic histological pictures of prominent proliferation of fibroblasts in the dermis, and increased collagen fibers with a whorl-like pattern. The skin nodules usually regress, but there are often sequelae of deformed joint. Here we describe the occurrence of FR in a patient of systemic lupus erythematosus.

CASE REPORT

A 25-year-old female patient suffered from hair loss, bilateral symmetric arthralgia, since June 1999. Laboratory tests showed mild leukopenia, proteinuria and elevated titer of antinuclear antibodies (ANA) and anti-Sm antibodies. She was diagnosed as SLE and was treated with prednisone in another institute. She discontinued regular medical control after her symptoms resolved 6 months later. In December 2002, multiple reddish, non-tender lesions developed on her dorsal hands within one month. During the course, the patient also experienced morning stiffness, Raynaud’s phenomenon and symmetric polyarthralgia involving the hands, metacarpophalangeal and proximal interphalangeal joints. She was not taking any medication, nor was there a history of allergy to medication. On physical examination, she was afebrile and in a good general condition. She was unable to fully extend her fingers because of partial restriction of the interphalangeal joints. Several papules and nodules were located over the knuckle areas of the fingers. These papules and nodules were asymptomatic, firm, erythematous or flesh-colored and measured 3 to 7 mm (Fig. 1). Telangiectasia, calcinosis and digital sclerodermic change were not present.

The laboratory data showed an elevated erythrocyte sedimentation rate (22 mm/hr). High titer of ANA (>1:5000) and positive of anti-Sm and anti-RNP antibodies with decreased of complement profile (C3/C4: 58.8/7.52 mg/dl) were noted. Full blood count revealed mild leukopenia (3220/µl). The following investigations were normal or negative: rheumatoid factor, biochemical profile and radiography of chest. Mild proteinuria appeared in urinalysis. Joint radiography showed periarticular soft tissue swelling and osteoporosis around bilateral metacarpophalangeal joints and proximal interphalangeal joints. Nail fold capillary microscopy revealed a decreased in the number of capillaries and tortuous capillary loops.

Fig. 1
Multiple erythematous, non-tender nodules developed over the knuckle areas of the fingers

Fig. 2
(a) (b). Histopathology revealed hyperplasia of spindle cells in the mid and lower ermis with sparse inflammatory infiltrate. The collagen fiber were increased and disorganized in a whorl-like pattern (H&E, a. 40X, b. 200X). (c). High power field of the plump spindle cells (H&E, x400)
Histopathology of the skin biopsy from the cutaneous papules and nodules revealed hyperplasia of spindle cells in the mid and lower dermis with sparse inflammatory infiltrate (Fig. 2). The special stains for these spindle cells showed negative for S-100 and CD68, and positive for vimentin and SMA focally, indicating that these cells possessed feature of myofibroblast (Fig. 3). The collagen fibers were increased and disorganized in a whorl-like pattern. The periodic acid-Schiff and alcian blue stain disclosed no abnormal accumulation of mucopolysaccharides. There was continuous granular deposition of IgM and C3 along the dermal-epidermal junction in direct immunofluorescence study.

Prednisone 15 mg and hydroxychloroquine 400mg was prescribed daily. The skin nodules resolved markedly and did her arthritis about ten months later (Fig. 4). The titer of ANA decreased to 1:1280 and the value of C3/C4 increased to 75.8/15 mg/dl. She was still on low dose of steroid treatment (prednisone, 10 mg/day) without recurrence.

DISCUSSION

FR is a rare disease characterized by symmetric polyarthralgia with joint stiffness, cutaneous nodules and sclerodactyly. At least 18 cases of FR have been reported in the literature. This disease has a female predominance (2:1), and principally affects young adults, but may occur in the elderly. The onset is often sudden and consists of polyarthralgia, which is predominantly distal, involving the hands, wrists and feet, but may also affect the elbows, shoulders, knees or hip. The radiographic finding of FR is variable, from no destruction or erosions with demineralization to rapidly progressive bony and cartilage destruction. Raynauld's phenomenon may be present.

Cutaneous manifestations include sclerodactyly and several to numerous papules and nodules.
nodules. They are firm, flesh-colored to erythematous, and various in size from 2 to 20 mm in diameter. Although the nodules occur mainly on the dorsal aspects of the fingers in para-articular area, they can also appear on wrists, elbows, and knees. There is no telangiectasia, calcinosis or digital ulceration. Nail fold capillary microscopy may show a decrease in the number of capillaries, but no megacapillaries. Systemic manifestations are uncommon, except pulmonary restrictive syndrome without alveolar-capillary diffusion abnormality has been reported in three patients, and associated with malignancy (undifferentiated bronchial adenocarcinoma) has been reported in one patient. Laboratory investigations are usually normal, except for increased ESR. An elevation of urine hydroxyproline has been detected in four cases. Histology of the skin nodules shows fibrosis in the deep dermis and subcutaneous tissue, usually associated with loss of elastic fibers, and an increased number of dermal fibroblasts. The increased collagen may be disorganized in a whorl-like pattern. The vessels and adnexae are usually not destroyed by the fibrosis. There is no, or only a moderate, inflammatory cell infiltrate.

In order to establish the diagnosis of FR in our patient, other entities associated with fibrotic skin nodules and rheumatologic symptoms should be considered. Rheumatoid arthritis (RA) may be associated with rheumatoid nodules, but they often located on extensor surfaces, especially the elbows, the ulnar border of the forearm and the pressure sites. The palisaded granulomatous pattern in rheumatoid nodules and serological features of RA allow an easy distinction from FR. Multicentric reticulohistiocytosis is also characterized by a polyarthritis with stiffness of the hands and associated papulonodules mainly on fingers and hands. Histology of the nodules revealed lipid-laden histiocytes and multinucleate giant cells. Multiple dermatofibromas may suddenly develop in immunosuppressed patients under long term prednisone treatment. However, the location of dermatofibroma are not distal prominent. The histological features including absence of entrapment of collagen at the periphery, immunohistochemical findings, and treatment response helped us to make the differential diagnosis. In nodular scleroderma, the nodules develop mainly on the trunk and histology shows thickened collagen bundles without fibroblast proliferation. Tophi as numerous cutaneous nodules may appear in patients of gouty arthritis, but they have totally different histological findings.

The pathogenesis of FR is unknown. Several immunohistochemical and ultrastructural studies suggest that FR is associated with proliferation of fibroblasts in skin nodules. These proliferating fibroblasts express morphological features of myofibroblast differentiation, which could be involved in the pathogenesis of FR. The study of collagen metabolism in cell culture, demonstrated that the secretion of collagen by FR fibroblasts from involved skin is decreased. The reduction of collagen synthesis in FR is in complete contrast with scleroderma, where increase in collagen synthesis has been demonstrated both by biochemical methods and in-situ hybridization studies. The increased deposition of these dermal components is probably secondary to the fibroblast proliferation. Therefore, FR is considered to be an acquired intrinsic abnormality of fibroblasts which leads to an increase in their proliferation rate, and features of myofibroblastic differentiation, with a reduction in collagen synthesis. The cause of this increased proliferation rate is unknown, and could be either endogenous, such as secretion of growth factors or exogenous infectious or toxic agents. No association with SLE and FR has been described before, and there is no report of FR-like manifestation in a patient of SLE in the literature. The autoantibodies and immune-complex may play a role of endogenous origin for stimulating fibroblast proliferation that is helpful to explain the occurrence of FR in our patient with SLE. But further investigations are needed for demonstration the hypothesis.

The course of FR is variable. The cuta-
neous nodules in some patients undergo spontaneous remission, but some patients develop varying degrees of permanent loss of joint movements and disabling finger flexion deformities. Recognition of the disease in its early active phases may allow potentially beneficial treatment, including resolution of the skin lesions and improvement in arthritis using non-steroidal anti-inflammatory drugs (NSAID) and prednisone before progression to irreversible joint sequelae. Low dose MTX in an individual with favorable response was reported. Other therapies have been tried in FR, including colchicines, interferon, penicillamine but the proof of their efficacy is lacking. With prednisone 15 mg and hydroxychloroquine 400mg for 10 months, our patient has great improvement in skin nodules without any disabling joint sequelae. The remission of skin nodules is correlated with the diseases activity of SLE in our patient with decreased ANA titer to 1:1280 and increased C3/C4 to 75.8/15 mg/dl after 10 months treatment. This clinical finding may point some kind of association between FR and SLE.

In summary, FR is a rare rheumatologic entity of unknown etiology. This diagnosis should be considered when patient present with sudden onset of symmetric polyarthritis and multiple cutaneous nodules. The occurrence of FR in this SLE patient may suggest some connection between FR and other autoimmune disease. More experience about FR is needed to prove the hypothesis.

REFERENCES