Interstitial Granulomatous Dermatitis
-A Case Report Associated with Rheumatoid Arthritis

Wen-Yu Chang   Gwo-Shing Chen

Interstitial granulomatous dermatitis is a rare entity first described by Ackerman et al. in 1993. We described a 57-year-old female, with a long-standing history of rheumatoid arthritis, presenting with symmetric violaceous to erythematous indurated papules and nodules on her buttock and medial thighs arranging in an arciform fashion for more than three months. Pathologically, it showed palisaded granulomas containing degenerated collagen, predominantly lymphohistiocytic infiltration with scattered eosinophils leading to dermal fibrosis. Some atypical histiocytes were also present. Combining the clinical and pathological pictures, interstitial granulomatous dermatitis was diagnosed.(Dermatol Sinica 23: 91-95, 2005)

Key words: Interstitial granulomatous dermatitis, Rheumatoid arthritis

From the Department of Dermatology, Kaohsiung Medical University Hospital
Accepted for publication: December 31, 2004
Reprint requests: Gwo-Shing Chen, Ph.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

Interstitial granulomatous dermatitis with arthritis is a rare disorder first described by Ackerman et al. in 1993. The clinical features of the cutaneous lesions include linear inflammatory indurations (the “rope sign”), erythematous to violaceous annular plaques on the extremities and buttocks, or erythematous papular eruptions and plaques on hands. Histologic features show diffuse “bottom-heavy” granulomatous dermal infiltrates composed mainly of histiocytes, scattered neutrophils and eosinophils, and foci of central degenerated collagen. We herein report a case of interstitial granulomatous dermatitis associated with rheumatoid arthritis, which hopefully reminds us a variable clinical and histologic spectrum of cutaneous lesions in rheumatoid arthritis, and also possibly other collagen vascular diseases associated with preceding arthritis.

CASE REPORT

A 57-year-old female complained of multiple symmetric indurated nodules and plaques on her buttock and medial thighs for 3 months. The symmetric erythematous lesions extended from her buttock to medial thighs in arciform. She noticed the skin lesions progressed in recent 3 months. The nodules and plaques were asymptomatic without discharge, erosion, or ulceration. No history of insect bite, Raynaud’s phenomenon, photosensitivity, fever, or trauma was elicited. She was treated with topical anti-fungal agents at local dermatologic clinics previously but the condition did not show any improvement.

She was diagnosed to have rheumatoid arthritis (RA)16 years ago. She also had history of hypertension and proteinuria under control with Irbesartan 150 mg per day. Her RA was controlled with sulfasalazine 1000 mg, and rofecoxib 37.5 mg per day. Methotrexate 5 mg per week has been started 5 years ago and gradually added up to 25 mg due to intractable arthralgia. The level of rheumatoid factor was around 600 — 700 IU/ml for about 2 years. However, the patient refused methotrexate treatment and her rheumatoid arthritis was controlled only by sulfasalazine and refecoxib in recent half year. The conditions of polyarthralgia and problems with gait worsened. Trace back her level of rheumatoid factor, it started to elevate from 600 — 700 IU/ml to 1280 IU/ml 5 months ago, 2280 IU/ml 3 months ago, and high up to 2560 IU/ml at the time of her visit.

Physical examination revealed multiple 5 to 15 mm erythematous to violaceous indurated nodules and plaques extending from her buttock to medial thighs in arciform fashion. The lesion distributed more than 10 cm in length (Fig. 1 Left). Palpation of inguinal area did not reveal lymphadenopathy. The lesions were asymptomatic. There was no surface erosion, vesiculation, or ulceration. The body skin elsewhere did not show any abnormality. Skin scraping for fungus identification was negative.

Incisional biopsy was taken from a papule on right buttock. Under the microscope, the epidermis was unremarkable. However, the reticular dermis showed diffuse infiltrates composed mainly of histiocytes (Fig. 2). Some appeared with atypical features with large hyperchromatic nuclei, prominent nucleoli, and occasionally mitotic figures (Fig. 3a, 3b). Scattered eosinophils, neutrophils, and nuclear dusts were
noted. The infiltrate surrounded the degenerated collagen ranging from focal fibrillar change to fractured necrobiosis (Fig. 3c). Vasculitis was not present.

Results of the following laboratory examinations were normal or negative: blood cell count, liver function, creatinine, blood urea nitrogen, uric acid, sugar level, C3, C4, and anti-ENA antibodies. Erythrocyte sedimentation rate and C-reactive protein were slightly elevated up to 134 mm/hr and 12.7 mg/L respectively. Proteinuria was noticed with daily protein loss of 6.5 g per day, composing 100% albumin in protein electrophoresis. An abdominal echogram, chest X-ray of the chest were both normal.

The patient was treated with topical fluocinonide and received 3 J/cm² local infrared irradiation three times a week for 1 month. The lesions became regressed, and we performed the second biopsy ten days after the first time. A significant fibrosis was demonstrated by thickening and hypereosinophilic change of collagen bundles replacing the original granulomatous infiltrates. Interstitial infiltration still contained some atypical histiocytes, but perivascular plasma cells infiltrates appeared to be predominant in the latter (Fig 3d). Direct immunofluorescence study was negative.

During this period, sulfasalazine was added up to 1000 mg twice daily due to uncontrollable arthralgia. After 1 month of treatment, the indurated lesions all subsided with post-inflammatory hyperpigmentation (Fig. 1 Right). There was moderate improvement of arthralgia. The serial serologic survey was demonstrated as table 1. No more indurated papules and plaques were palpated on buttock and medial thighs until the last visit, and the patient was kept followed-up at our out-patient department.

**DISCUSSION**

Interstitial granulomatous dermatitis with arthritis, which may presents with variable appearance of eruption, is considered as a distinct entity by Ackerman et al. It may consist of the characteristic linear or arciform, elongated, dermal bands without epidermal changes on trunk and extremities (the “rope sign”), or erythematous to violaceous, indurated and annular plaques on the extremities and buttocks, and erythematous papular eruptions and plaques on hands. To our knowledge, 42 cases of IGD were reported and 26 of the reported cases presented with plaques, so as our patient. Pathologically,
it shows multiple granulomas with central small foci of degenerated collagen, prominent palisaded histiocytic infiltration, which may have atypical features such as a large nucleus, mitotic figures, or prominent nucleoli. There are also infiltrates of neutrophils or eosinophils but usually without vasculitis. Results of direct immunofluorescence studies were all negative in the 17 cases reported by Tomasini and Pippione. Differentiating interstitial granulomatous dermatitis from interstitial form of granuloma annulare (GA) needs to be cautious. Histopathologic examination of GA shows giant cells and a lympho-histiocytic infiltrate without atypical histiocytes. Neutrophils and eosinophils sometimes but not usually present in granuloma annulare, particularly in areas of necrobiotic collagen. Plasma cell-rich infiltrates, which predominant in the late stage of our patient, is not a feature of GA either. Rheumatoid nodules, which often occur in the subcutis and deep dermis of joints and exhibit eosinophilic fibrinoid degeneration in the center of granuloma, are clearly differentiated from dermal granulomatous infiltrates in interstitial granulomatous dermatitis.

Drug-induced interstitial granulomatous dermatitis need to be differentiated from interstitial granulomatous dermatitis with arthritis. The drug classes cited are calcium channel blockers, angiotensin-converting enzyme inhibitors, \( \beta \)-blockers, and lipid-lowering agents. Serologic immune abnormalities were not reported. The histology shows a diffuse lymphohistiocytic infiltrate, piecemeal fragmentation of collagen, and moreover, vacuolar interface dermatitis, which is absent in our patient. Pathologically, the differential diagnoses include other palisaded granulomatous dermatides. Churg-Strauss disease shows abundant eosinophils in the center of granuloma and leukocytoclastic vasculitis. Wegener’s granulomatosis often presents with many foci of active vasculitis.

Chu et al. categorized IGD with arthritis into the continuous spectrum of palisaded neutrophilic and granulomatous dermatitis (PNGD) of immune complex disease, which also includes Churg-Strauss granuloma, cutaneous extravascular necrotizing granuloma (Winkelmann granuloma), rheumatoid papules, and superficial ulcerating rheumatoid necrobiosis. His concept was based on similar histologic evidences of damage to collagen. The authors described a spectrum of clinical and histopathologic changes according to the stage of the lesion, especially ulceration and vasculitis in early lesions. However, our patient had never developed ulceration before and there was no evidence of vasculitis in the biopsies. We consider our case is not a PNGD, and regard that the two entities are different.

Table I. Serologic findings

<table>
<thead>
<tr>
<th></th>
<th>RF (IU/ml)</th>
<th>ANA</th>
<th>Anti-dsDNA</th>
<th>IgG (mg/dl)</th>
<th>IgA (mg/dl)</th>
<th>IgM (mg/dl)</th>
<th>IgE (IU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal range</td>
<td>&lt;60</td>
<td>+</td>
<td></td>
<td>917.2-1871.2</td>
<td>183.9-322.3</td>
<td>102.6-200.2</td>
<td>66.4-109.0</td>
</tr>
<tr>
<td>Initial survey</td>
<td>2560</td>
<td>1:640</td>
<td>+</td>
<td>2130</td>
<td>764</td>
<td>229</td>
<td>1188</td>
</tr>
<tr>
<td>(Indurated skin lesions)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month later</td>
<td>1060</td>
<td>1:2560</td>
<td>-</td>
<td>1450</td>
<td>637</td>
<td>137</td>
<td>869</td>
</tr>
<tr>
<td>(Hyperpigmentation)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RF: rheumatoid factor, ANA: anti-nuclear antibody
terized by flares and remissions with variable prognosis. Most of the reported cases under immunosuppressive therapy including topical steroid, hydroxychloroquine, NSAID, dapsone, and doxycycline were ineffective, and failed to remit completely. The best result from Tomasini and Pippione showed 11 spontaneous resolution in 17 plaque type IGD ranging from 3 to 34 months. Two other patients remit, one’s presentation was considered as paraneoplastic phenomenon, and the other remitted under the treatment of cyclosporin A. Our patient remitted and remained symptom free until present.

Interstitial granulomatous dermatitis with arthritis is a distinctive disease with clinical and pathological features. Previous debates with different names may be due to a spectrum of reactions to autoimmune disorders. Our case illustrates that interstitial granulomatous dermatitis is associated with the clinical course of the underlying rheumatoid arthritis, evolves with stages, and remits with combination of topical steroid, topical infrared irradiation, and increase dosage of sulfasalazine. This report demonstrated the importance of the parallel relationships between the flare-up of IGD lesions and the deterioration of underlying autoimmune disease. It also reminds us when evaluating variable cutaneous manifestations in patients with underlying autoimmune diseases, the concept of taking different clinical and pathological morphologic evolution into consideration at different stages, may be valuable.

REFERENCES