Sarcoidosis Presenting as Papulonecrotic Tuberculid-like Lesions: Report of a Case

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A 50-year-old Thai woman presented with papulonecrotic tuberculid-like eruptions on her back and inframammary area with fever, nonproductive cough and weight loss. Chest radiograph showed diffuse bilateral reticulonodular opacities in both lungs with bilateral hilar lymph node enlargement. High resolution computed tomography (HRCT) of the lungs showed peribronchovascular interstitial thickening with multiple lymph nodes enlargement. Sputum for AFB was negative. Monotest (PPD) was negative. Skin biopsy revealed multiple naked granuloma compatible with sarcoidosis. She was treated with isoniazid, 300mg/d, rifamipicin, 600 mg/d, ethambutal, 800, mg/d and pyrazinamide, 1000 mg/d for 2 months without improvement of skin and lung lesions. Prednisolone 45 mg/d was then administered adjunctive with isoniazid and rifampicin. After two weeks of treatment with prednisolone, the cutaneous and pulmonary lesions markedly improved. Prednisolone was tapered in 6 months. Skin lesions, fever, dry cough disappeared and chest radiograph, HRCT of the chest were markedly improved.

Keywords : *Systemic sarcoidosis, Papulonecrotic tuberculid, Cutaneous manifestation*

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Sarcoidosis is a systemic granulomatous disease of undetermined etiology. Many internal organs including skin are involved in this disease. The first case of sarcoidosis was reported by Jonathan Hutchinson, a surgeon-dermatologist at King's College Hospital in London more than a century ago[1]. Diagnosis of sarcoidosis is often delayed or missed because of its resemblance to tuberculosis, leprosy, blastomycosis and other granulomas. Skin manifestations of sarcoidosis include maculopapular eruptions, plaques, nodules, subcutaneous nodules, annular, infiltrative scars and lupus pernio[2]. However, skin lesions resembling papulonecrotic tuberculid are rare; only one such case has been reported in the literature[3]. The authors report a case of systemic sarcoidosis which initially presented with skin lesions that looked like papulonecrotic tuberculid.

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Case Report

A 50-year-old married Thai woman from Pathumtanee province presented with a 6-month history of asymptomatic multiple brownish papules on her back and inframammary area. She also had low grade fever, non productive cough and progressive weight loss for one year. There was no dyspnea. She had taken systemic corticosteroid for many years for myalgia and discontinued corticosteroid 6 months before her attendance. At the time of presentation she had adrenal insufficiency secondary to steroid withdrawal. She had neither history of contact tuberculosis nor drug allergy.

Physical examination revealed a thin, middle-aged woman. Body temperature was 37.1 degree Celsius. She had multiple discrete brownish papules, ranging from 0.5 to 0.7 cm in size, on her back and inframammary area (Fig. 1). Some of the papules had central necrosis (Fig. 2). Lymph nodes were not palpable. Liver was not enlarged but spleen was just palpable. The physical examination otherwise was

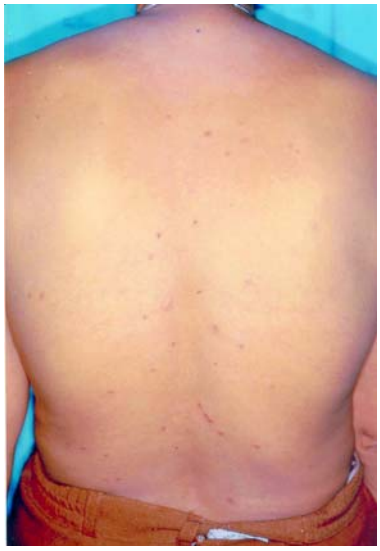

Fig. 1 Multiple discrete brownish papules on the back and inframammary area

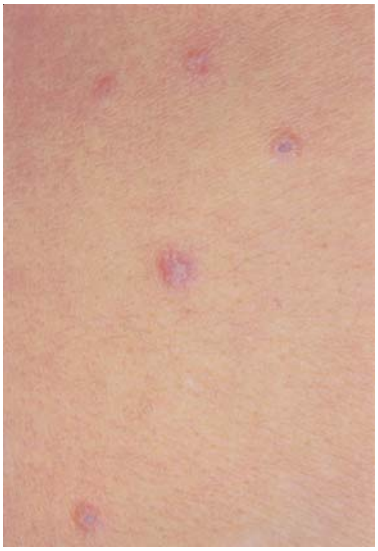

Fig. 2 Some papules had central necrosis

unremarkable. Histopathology of skin lesions at the back revealed multiple naked granulomas composed of epithelioid histiocytes and multinucleated giant cells (Fig. 3). Complete blood count (CBC) revealed mild anemia, leukopenia, neutropenia and lymphopenia. ESR was 62 mm/hr. Chest radiograph showed diffuse bilateral reticulonodular opacities in both lungs with bilateral hilar lymph node enlargement (Fig. 4). High resolution computed tomography (HRCT) of the lungs was performed and showed diffuse irregular, nodular peribronchovascular interstitial thickening with multiple enlarged lymph nodes in paratracheal, paraaortic, subcarinal and hilar regions(Fig. 5). Sputum for acid fast bacilli (AFB) were negative. Serum calcium level was 12 mg/dl (normal 8.5-10.5 mg/dl) and anti HIV was negative. Monotest (PPD) was negative. Bronchoscopy showed no endobronchial lesion and bronchoalveolar lavage was performed with 150 ml of normal saline, of which 50 ml were removed. Bronchoalveolar lavage fluid analysis revealed increased numbers of lymphocytes and macrophages (95% and 5% respectively). Lymphocyte count was 1,513 cells/mm^3, predominately with CD_4 T lymphocytes (CD_4 T cells and CD_8,72% and 26% respectively). Bronchoalveolar lavage cultures for bacteria, mycobacteria, and fungus were all negative.

She was treated with isoniazid, 300 mg/day, rifampicin, 600 mg/day, ethambutol, 800 mg/day and pyrazinamide, 1000 mg/day for 2 months. Her signs

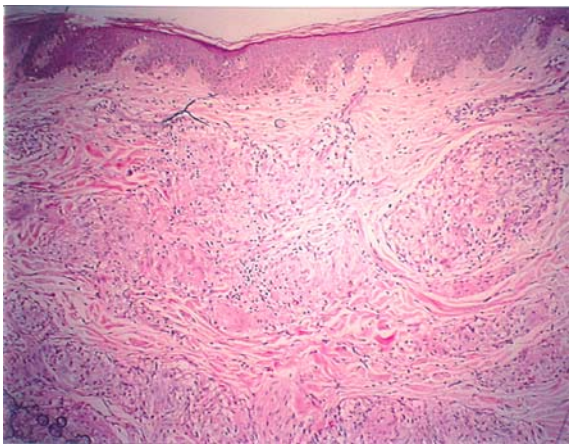

Fig. 3 Histopathology of skin lesion at the back showed multiple naked granulomas with multinucleated giant cells (Hematoxyline and eosin stain)

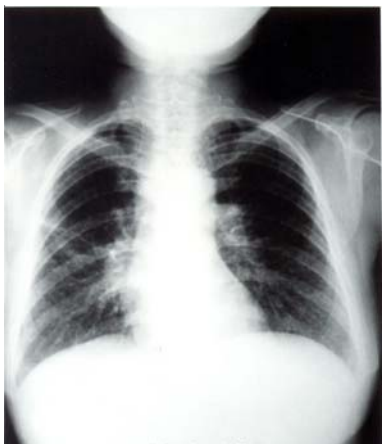

Fig. 4 The chest radiograph showed diffuse bilateral reticulonodular opacities in both lungs with bilateral hilar lymph node enlargement

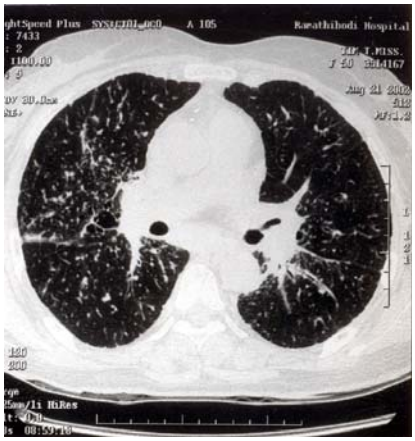

Fig. 5 HRCT of lungs showed diffuse, nodular peribronchovascular interstitial thickening with multiple lymph nodes enlargement

and symptoms including chest radiographic findings did not improve. Prednisolone 45 mg/day (1mg/kg/day) was then administered while she still took isoniazid, 300mg/day and rifampicin, 600 mg/day. Two weeks after starting the prednisolone, the signs and symptoms including chest radiographic findings improved. The papules became flatter and later healed. No new lesions developed. The CBC and serum calcium level returned to normal. After 6 months of corticosteroid treatment, her constitutional symptoms markedly improved; the papules healed with scar formation in some lesions (Fig. 6). Chest radiograph and HRCT showed remarkable decrease in pulmonary lesions and decrease in the size of lymph nodes at mediastinal and hilar regions (Fig.7,8).

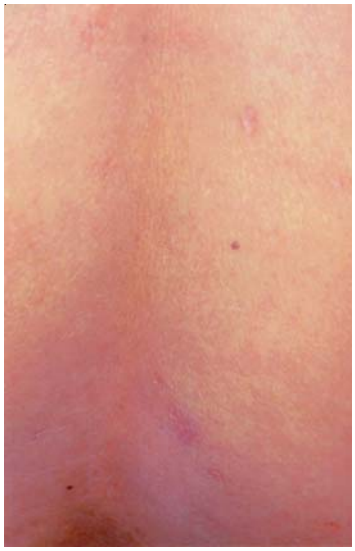

Fig. 6 The papules healed with scar after treatment with corticosteroid for 6 months

Discussion

Sarcoidosis is characterized by the formation of small noncaseating epithelioid granulomas that involve many organs. The etiology of this disease is unknown. There are many factors that may be involved in the pathogenesis of this disease such as genetic predispositition, immunological alteration, infectious agents and environmental factors[2]. The clinical manifestations are usually asymptomatic. Many cases of sarcoidosis are discovered during routine chest radiography.

The epidemiology of sarcoidosis may be underestimated because many cases are asymp-

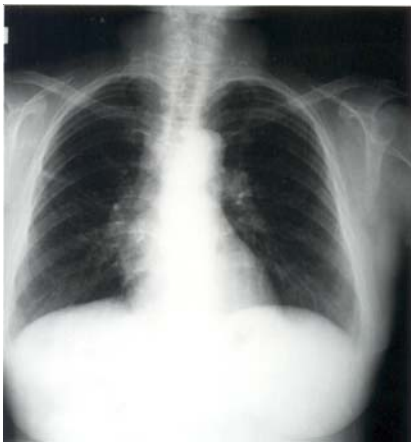

Fig. 7 The chest radiograph showed remarkable decrease in pulmonary infiltrations

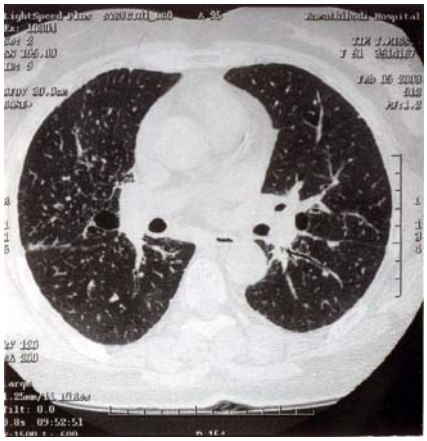

Fig. 8 The HRCT showed remarkable decrease in pulmonary infiltrations and decrease in the size of mediastinal and hilar lymph nodes

tomatic and are never reported. The incidence rate of sarcoidosis is reported as follows: Sweden 64/100,000; United Kingdom 20/100,000; Israel 0.8/100,000; United States 10/to 14/100,000 for white persons and 35.5/ to 64/100,000 for African Americans[4-7]. There is a higher incidence of sarcoidosis in Chinese, Russian and Indian people but sarcoidosis is rarely reported in the Middle East, Korea, Taiwan and Southeast Asia[8-17]. In Thailand, the incidence of sarcoidosis is unknown. The first case of sarcoidosis in Thailand was reported in 1959[18], since then there has been scattered case reports. Most of the cases reported in Thailand had pulmonary, lymph nodes or internal organs involvement, only one case had cutaneous lesions[14, 19-23].

Pulmonary involvement and hilar lymphadenopathy occurs in about 90% of patients with saroidosis[24]. Pulmonary infiltration can lead to lung fibrosis. The most common symptoms are shortness of breath and persistent dry cough. Other organs involvement includes eyes, nasal mucosa, skin, liver, spleen, peripheral lymph nodes, bone marrow and parotid glands. Less frequent manifestations occur in the central nervous system, heart, kidney, musculoskeletal, gastrointestinal tract, endocrine and reproductive systems. There are racial differences in the severity of sarcoidosis. The studies from two London clinics showed that sarcoidosis was more frequent, severe and extensive in black West Indian, African, Indian and Pakistan patients than in Caucasians[25,26]. In the United States, blacks are affected more often than whites[24].

Cutaneous involvement occurs in 10-100% of patients with sarcoidosis depending upon whether an internist or dermatologist is the observer[24] and may occur without systemic involvement[27]. The lesions may be specific or nonspecific. Specific lesions include maculopapules, nodules, plaques, subcutaneous nodules, infiltrative scars and lupus pernio. Other uncommon manifestations includes acquired ichthyosis, ulceration, hypopigmentation, psoriasiform, folliculitis, erythroderma, lichenoid, verrucous, erythematous plaques of palms and soles, lupus erythematosus- like lesion, granulomatous cheilitis[2], sarcoidosis of the scalp[28], genital sarcoidosis[29], scarring alopecia[30], cutaneous manifestation with severe osseous destruction of the midface[31], and granulomatous tattoo reaction[32]. Non specific lesions include erythema nodosum (which is a hallmark of acute and benign sarcoidosis), calcification, prurigo and erythema multiforme.

Papulonecrotic tuberculid is a skin manifestation that appears as a reaction to tuberculous infection in other organs. The skin lesions of papulonecrotic tuberculid are asymptomatic crops of hard, dusky-red papules with central necrosis and usually appear symmetrically on elbows and knees. These lesions heal leaving pigmented, and sometimes atrophic scars. Stain for acid fast bacilli and culture for mycobacteria from the papulonecrotic tuberculid lesions are negative; delayed hypersensitivity skin tests for tuberculosis are positive. Recently, using the PCR technique, mycobacterium DNA has been identified in some lesions[33]. Histopathology of a papulonecrotic tuberculid lesion reveals vascular involvement. Subsequently, a wedge-shaped area of necrosis forms its broad base toward the epithelium. As the wedge is cast off, epithelioid and giant cells gather around its periphery. Ziehl-Neelsen stain is negative[34].

The presented patient had skin manifestations that looked like papulonecrotic tuberculid but the distribution of skin lesions was unusual for papulonecrotic tuberculid. She had skin lesions on the trunk instead of extensor surface of the extremities and the histopathology of skin lesions showed multiple naked granuloma. The sputum examination and bronchoalveolar lavage fluid did not show acid fast bacilli; Monotest was negative. She did not respond to antituberculous therapy, instead, she responded well to corticosteroid with improvement of skin and lung lesions. The authors, therefore, concluded that she had systemic sarcoidosis with skin involvement that looked like papulonecrotic tuberculid by evidence of cutaneous histopathology, pulmonary involvement, chest radiograph, HRCT of the lungs compatible with sarcoidosis, bronchoalveolar larvage fluid analysis that showed increase CD_4 T lymphocytes and the good response to corticosteroid therapy. This case is a rare cutaneous manifestation of sarcoidosis which presented like papulonecrotic tuberculid.

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รายงานผู้ป่วย 1 รายที่เป็น systemic sarcoidosis ซึ่งมีรอยโรคที่ผิวหนังลักษณะคล้าย papulonecrotic tuberculid

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รายงานผู้ป่วย 1 ราย เป็นหญิงไทยคู่อายุ 50 ปี อาชีพแม่บ้าน เข้ามาพบแพทย์เนื่องจากมีรอยโรคที่ผิวหนังลักษณะคล้ายแพบพูโลเน็คโครติคทูเบอร์คูลิดบริเวณหลังและใต้ราวนม ร่วมกับมีไข้ ไอ น้ำหนักลด การถ่ายภาพรังสีทรวงอกพบเงาต่อมน้ำเหลืองบริเวณขั้วปอดโตขึ้นและมีเงาทึบแบบเรติคูล่าร์กระจายทั่วไปที่ปอดทั้งสองข้าง ตรวจเสมหะไม่พบเชื้อแบคทีเรียที่ย้อมติดสีแอซิดฟาสท์ การทดสอบผิวหนังด้วยวิธีโมโนเทสต์ให้ผลลบ ผู้ป่วยได้รับการรักษาด้วยไอโซไนอาซิด ไรแฟมปิซิน อีแทมบูทอลและไพราซินามายด์นาน 2 เดือนแต่รอยโรคที่ผิวหนัง ไข้ ไอ น้ำหนักลดรวมทั้งภาพถ่ายรังสีทรวงอกไม่มีการเปลี่ยนแปลง จึงได้เพิ่มเพรดนิโซโลนร่วมกับไอโซไนอาซิด ไรแฟมปิซิน หลังจากได้รับเพรดนิโซโลนเพียง 2 สัปดาห์ รอยโรคที่ผิวหนังและในปอดดีขึ้นอย่างชัดเจน ผู้ป่วยสามารถหยุดยาเพรดนิโซโลนได้ภายใน 6 เดือน อาการทั่วไปดีขึ้น ตุ่มที่ผิวหนังยุบลงหมด รวมทั้งภาพถ่ายทางรังสีปอดดีขึ้นอย่างชัดเจน