A Case Series of Sarcoidosis with Pulmonary Involvement: Various Clinical and Radiographic Manifestations

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Background: *Sarcoidosis is a multisystem granulomatous disease of unknown etiology. The disease is rare in East Asian populations. Patients have many clinical presentations and 90% of patients have pulmonary involvement. There are few reports in Thailand that collected the data about chest imaging and pathological findings of sarcoidosis.*
Material and Method: *The data of patient with sarcoidosis with pulmonary involvement, who followed-up between September 2008 and December 2011, were retrospectively reviewed.*
Results: *Ten patients with sarcoidosis and pulmonary involvement were reviewed. Three patients presented with abnormal chest x-ray without respiratory symptom or other organ involvement. One patient was suspected to be sarcoidosis secondary to etanercept therapy. The majority of patients had cutaneous involvement. The most common finding on chest x-ray is bilateral hilar lymphadenopathy (90%). Seven patients had stage 2 disease and three patients had stage 1 disease. The diagnoses of all patients were confirmed by histopathology and exclusion of tuberculosis and fungal infection. Spirometry showed normal in seven patients, irreversible obstruction in one patient, and impaired diffusing capacity in six patients. There was no indication of systemic corticosteroids or immunosuppressive drug in most patients.*
Conclusion: *Sarcoidosis has various clinical manifestations. The pulmonary and cutaneous involvement is common and the diagnosis is made by a combination of clinical, radiological, and histopathologic findings. The treatment of systemic corticosteroids is not required in most patients. The patients should be regularly followed-up in order to follow the course of disease.*

Keywords: *Sarcoidosis, Pulmonary involvement, Granulomatous disease, Non-necrotizing granuloma, Etanercept*

J Med Assoc Thai 2013; 96 (8): 888-97
Full text. e-Journal: *http://jmat.mat.or.th*

Sarcoidosis is a multisystem granulomatous disease of unknown etiology. The incidence of the disease in United States among whites ranges from 10 to 14 cases per 100,000 persons that is less than American Africans (64 cases per 100,000 persons)[1-3]. The disease is rare in East Asian populations. Patients have many clinical presentations and 90% of patients have pulmonary involvement that may be no symptom[4,5]. The diagnosis of sarcoidosis requires combination of clinical, radiological and histopathologic findings. In Thailand, the diagnosis of pulmonary sarcoidosis needs to be differentiated from pulmonary tuberculosis because there is high incidence of tuberculosis and these diseases have many similar clinical presentations, radiographic, and histopathologic findings. There were few reports in Thailand that collected the data about chest imaging[6] and pathological findings[7] in patients with sarcoidosis. This study was conducted to retrospectively review the data of patients with sarcoidosis who have pulmonary involvement included clinical presentations, staging of pulmonary involvement, spirometry, treatment, and progression of disease.

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Material and Method

The data of patient with sarcoidosis with pulmonary involvement, who were followed-up at the Division of Respiratory Disease and Tuberculosis, Department of Medicine, Faculty of Medicine Siriraj Hospital, were retrospectively reviewed.

Statistical analysis

This study was approved by the ethics committee of our institution. The continuous variables

were presented as the mean ± SD. The categorical data were presented as proportions. All statistical analyses were performed using statistical software (SPSS for windows, version 13.0; SPSS; Chicago, IL).

Results

Ten patients of sarcoidosis with pulmonary involvement, who follow-up at Division of Respiratory Disease and Tuberculosis, Department of Medicine, Faculty of Medicine Siriraj Hospital between September 2008 and December 2011, were reviewed. There were seven females (70%) and three males (30%) as shown in Table 1. Mean age was 46.6 (range 26-75).

Clinical manifestations

Three patients presented with respiratory symptoms. One patient (case 1) had chest tightness with constitutional symptoms and the others (case 4 and 8) had chronic non-productive cough. All patients had no desaturation.

Three patients (case 2, 7, and 10) had abnormal chest x-ray at presentation but no abnormal symptoms either from pulmonary or other organs involvement. During follow-up, one patient (case 7) developed subungual hyperkeratosis and periungual swelling (Fig. 1A). One patient (case 2) developed fatigue, small cervical lymphadenopathy and skin nodules on her shins and blood chemistry showed acute rising of creatinine (serum creatinine 3.6 mg/dL) and hypercalcemia (serum total calcium 15.6 mg/dL, phosphate 3.5 mg/dL and parathyroid hormone level 7.6 pg/mL (normal range 15-65 pg/mL)).

Four patients (case 1, 4, 5, and 9) received antituberculous treatment before the diagnosis of sarcoidosis was made. In these four patients, three patients were found to derive no improvement of bilateral hilar lymphadenopathy from chest x-ray after a complete course of treatment. Another patient (case 1) developed uveitis and skin lesion after 3-month of TB treatment and her constitutional symptoms were not improved.

Seven patients had skin involvement that was found at multiple parts of body and had various physical findings (Table 1, Fig. 1).

No neurologic and cardiac involvement was found in this review. Electrocardiogram was done in all patients and found no abnormalities.

One patient was suspected to be sarcoidosis secondary to etanercept therapy for his spondylo-arthropathy. He developed erythematous indurated nodules at scrotum (Fig. 1C) and skin biopsy showed non-necrotizing granulomatous inflammation. AFB staining and culture were negative for *Mycobacterium tuberculosis*. He had reticular infiltrates at right upper and middle lobes and bilateral hilar lymphadenopathy on chest x-ray (Fig. 2A) and HRCT showed multiple mediastinal lymphadenopathy and diffuse centrilobular nodules (Fig. 2B, 2C). Transbronchial lung biopsy (TBLB) showed non-necrotizing granuloma and bronchoalveolar lavage (BAL) fluid staining and culture were negative for mycobacteria and fungus.

Chest imaging

Most common finding on chest x-ray was bilateral hilar lymphadenopathy (90%) (Table 2). One patients (case 6) had normal chest x-ray but found multiple mediastinal lymphadenopathy from HRCT chest. According to staging by radiographic findings, seven patients (70%) had stage 2 disease (presence of

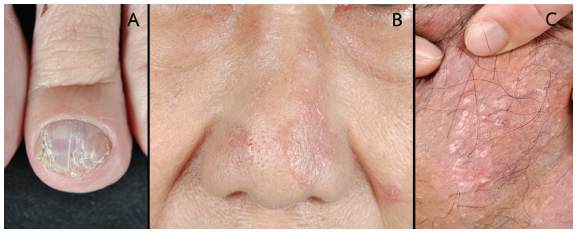

Fig. 1 Skin manifestation of sarcoidosis: A) subungual keratosis with periungual swelling (case 7); B) scaly erythematous plaque at nose and face (case 6); C) erythematous indurated nodules at scrotum (case 10).

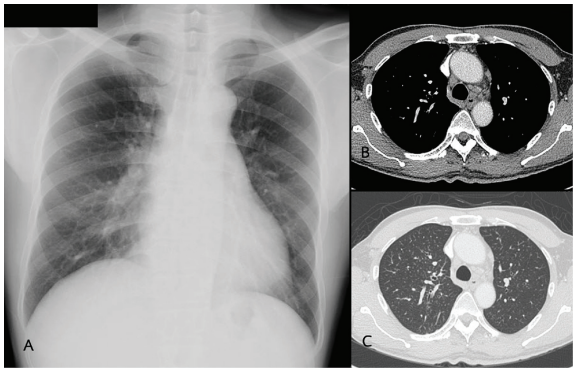

Fig. 2 Chest x-ray and HRCT chest of patient with sarcoidosis associated with etanercept therapy (case 10): A) chest x-ray showed bilateral hilar lymphadenopathy and reticular infiltrates at right upper and middle lobes; B) HRCT chest with contrast showed multiple mediastinal lymphadenopathy; C) HRCT chest showed diffuse centrilobular nodules at both upper lobes.

Table 1. Clinical data of 10 patients

Case	Sex	Age (years)	Presenting symptom	Stage of pulmonary involvement	Skin manifestation	Other organs involvement	Immunosuppressive drugs (indication)	Course of pulmonary involvement	Follow-up
1	F	45	Chest discomfort and fatigue with weight loss 16 kgs for 5 months	2	Discrete ill-defined scaly erythematous patch on both legs	Uveitis	Yes (eye)	Improved	3 years
2	F	60	Abnormal chest x-ray	2	Discrete well-defined erythematous translucent nodule on both shins	- Superficial lymphadenopathy - Hypercalcemia (symptomatic)	Yes (hypercalcemia)	Improved	3 years
3	M	26	Rash at abdominal wall and extremities	2	Non-tender skin-colored subcutaneous nodules on abdomen, back, arm and thigh	No	No	Stable	2 years
4	F	46	Non-productive cough for 2 months	2	Multiple discrete with confluent non-tender erythematous papule at nose	No	No	Stable	3 years
5	F	41	Uveitis	1	No	Uveitis	Yes (eye)	Stable	2 years
6	F	69	Rash at face	1	Scaly erythematous plaque at nose and face (Fig. 1B)	No	No	Stable	1 years
7	F	31	Abnormal chest X-ray	2	Subungual hyperkeratosis with periungual swelling (Fig. 1A)	No	No	Worsen	7 years
8	M	24	Uveitis and non-productive cough	2	No	Uveitis	No	Stable	10 months
9	F	75	Abnormal chest X-ray	1	No	No	No	Stable	6 months
10	M	49	Spondyloarthropathy and treatment with etanercept for 7 months then he had skin lesion at scrotum	2	Non-tender erythematous indurated nodules at scrotum	No	No (off etanercept)	Stable	6 months

M = male (30%); F = female (70%)

Table 2. Pulmonary manifestations

Pulmonary manifestations	n (%)
Total number of patients	10 (100)
Respiratory symptom	
No respiratory symptom	7 (70)
Non-productive cough	2 (20)
Chest discomfort	1 (10)
Dyspnea on exertion	1 (10)
Constitutional symptom	1 (10)
Chest radiograph	
Normal	1 (10)
Bilateral hilar adenopathy	9 (90)
Reticular or reticulonodular infiltrates	1 (10)
Alveolar or patchy infiltrates	1 (10)
HRCT chest	
Perilymphatic distribution of centrilobular nodules	6 (60)
Upper lung field	2 (20)
Middle lung field	4 (40)
Lower lung field	5 (50)
Mediastinal lymphadenopathy	
Right paratracheal lymph node	9 (90)
Subcarina lymph node	8 (80)
Aortopulmonary window	7 (70)
Hilar lymph node	8 (80)
Pulmonary function tests	
Normal	7 (70)
Obstruction	1 (10)
Restriction	2 (20)
Decreased TLC	3 (30)
Impaired diffusion capacity	6 (60)

HRCT = high-resolution computed tomography; TLC = total lung capacity

both mediastinal lymphadenopathy and parenchymal involvement) and three patients (30%) had stage 1 disease (presence only of mediastinal lymphadenopathy). Most common mediastinal lymph node stations that were found on HRCT chest were right paratracheal, hilar, and subcarina lymph nodes. Four of six patients that had no infiltration on chest x-ray showed parenchymal involvement from HRCT chest. Most of those with parenchymal involvement were reticulonodular or reticular infiltrates on chest x-ray and centrilobular nodules on HRCT. However, one patient (case 8) had diffuse patchy infiltrates. Furthermore, HRCT showed diffuse flame-shaped consolidation and centrilobular nodules at both lungs with multiple lymphadenopathy (Fig. 3). The lower and middle lobe distribution of centrilobular nodules were the most common location of parenchymal involvement.

Pulmonary function tests (Table 3)

Spirometry showed normal in seven patients (70%), restriction in two patients (20%), and irreversible airflow obstruction in one patient (10%). Patients with normal spirometry had decreased TLC and/or DLCO in four cases (57%). In patients with stage I disease, two patients had normal spirometry, but mildly decreased TLC and/or DLCO and one patient had mild irreversible airflow obstruction. In patients with stage 2 disease, three patients had normal spirometry, TLC and DLCO. Pulmonary function tests in one patient who had clinical of dyspnea (case 1) showed normal spirometry, mildly decreased TLC (73% predicted), and moderately decreased DLCO (53% predicted).

Bronchoalveolar lavage (BAL) fluid

Bronchoalveolar lavage was performed in seven patients (70%). Mean cell count was 241 cell/mm^3 (range 60-635) and BAL lymphocytosis was found in six patients (range 11-82%). The CD4/CD8 ratio was evaluated in six patients and none of these patients had a ratio of more than 3.5 times (range 1.49-2.57). All cultures were negative for mycobacteria and fungus.

Histopathology

Pathologic examination was performed in all cases. Tissue biopsy for the pathologic study was obtained from various sites including lung, lymph node, skin, and nail bed. Histologic evaluation from more than one site was accomplished in nine cases. All cases revealed similar histologic features of granuloma.

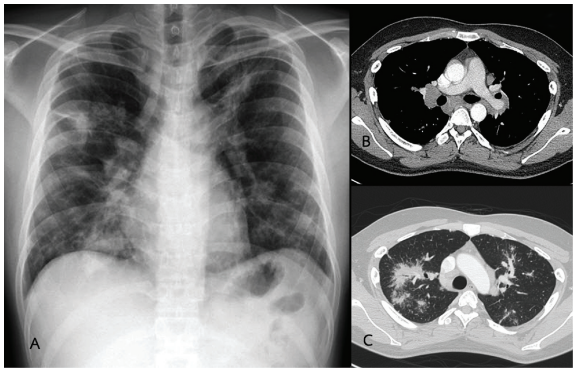

Fig. 3 Chest x-ray and HRCT chest of case 8: A) chest x-ray showed diffuse patchy infiltrates at both lungs and bilateral hilar lymphadenopathy; B) HRCT chest with contrast showed multiple mediastinal lymphadenopathy; C) HRCT chest showed flame-shaped consolidation and diffuse centrilobular nodules at both lungs.

Table 3. Pulmonary function tests of 10 patients

Case	Stage	Corticosteroids or immunosuppressive drugs	Follow-up time*	FEV_1/FVC (%)**	FEV_1 (L)***, % of predicted	FVC (L)[#], % of predicted	TLC (%)[##]	DLCO (%)[###]
1	2	Yes	Diagnosis	92	2.77 (115.7)	3.02 (107.2)	73	53
			10 months	87	2.52 (107.3)	2.88 (104.2)	81	76
2	2	Yes	Diagnosis	77	1.92 (92.9)	2.48 (99.2)	62	67
			6 months	81	2.11 (103.3)	2.59 (104.7)	71	79
			12 months	79	1.98 (99.1)	2.52 (104.1)	74	85
			22 months	80	1.91 (96.9)	2.39 (99.8)	77	76
3	2	No	Diagnosis	70	3.21 (85.0)	4.58 (102.4)	83	95
				NA	NA	NA	NA	NA
4	2	No	Diagnosis	78	1.85 (82.5)	2.36 (90.5)	85	85
				NA	NA	NA	NA	NA
5	1	Yes	Diagnosis	80	1.98 (82.4)	2.41 (87.9)	67	73
			8 months	78	1.96 (81.6)	2.50 (89.3)	68	68
6	1	No	Diagnosis	66	1.33 (81.7)	2.00 (100.6)	87	86
			6 months	66	1.22 (74.3)	1.84 (92.1)	94	88
7	2	No	Diagnosis	95	2.69 (95.2)	2.84 (87.4)	92	89
			13 months	NA	NA	NA	NA	65
			7 years	87.5	2.24 (83.0)	2.56 (81.1)	64	56
8	2	No	Diagnosis	83	2.30 (64.9)	2.77 (66.6)	55	63
			NA	NA	NA	NA	NA	NA
9	1	No	Diagnosis	74	1.47 (103.1)	1.98 (113.7)	82	75
			NA	NA	NA	NA	NA	NA
10	2	No	Diagnosis	79	2.12 (77.2)	2.70 (79.9)	65	75
			6 months	83	2.09 (76.1)	2.53 (74.9)	64	NA

* Median follow-up time was 9 months (range 6-84 months; mode 6 months), ** Mean FEV_1/FVC was 79.4 (range 66-95), *** Mean FEV_1 was 2.16 L (range 1.33-3.21; median 2.05 L), [#] Mean FVC was 2.71 L (range 1.98-4.58; median 2.59 L), [##] Mean TLC was 75.1% (range 55-92; median 77.5%), [###] Mean DLCO was 76.1% (range 53-95; median 75%)
FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity; L = litre; TLC = total lung capacity; DLCO = carbon monoxide diffusing capacity; NA = not available

Fite acid fast and Gomori methenamine silver stains were performed in all cases to demonstrate acid fast bacilli and fungi, respectively. No microorganisms were identified. Cultures were negative in all cases.

Transbronchial lung biopsy

Seven cases had TBLB performed and all histologic findings were non-necrotizing granulomas. The biopsy site was determined by the location of centrilobular nodules in HRCT. In three patients with stage I disease, random TBLB and bronchial biopsy were performed in case 6 and 9, respectively. The result of bronchial biopsy was negative for granuloma.

Microscopic findings of the lung lesion displayed non-necrotizing granulomas comprising compact nodular aggregates of epithelioid histiocytes variably rimmed by sparse lymphocytes or hyaline fibrosis (Fig. 4A). Multinucleated giant cells of both Langhan's type, peripherally arranged nuclei in the cell, and foreign-body type, haphazardly arranged nuclei in the cell, were present in the granulomas. The granulomatous nodules were repetitively similar in the same stage. No necrosis was identified. The nodules were confluent and coursed along interlobular septa in proximity with the pulmonary vein (Fig. 4B), and submucosa of the bronchial wall. Vascular involvement by the granulomas was not present.

Transbronchial needle aspiration (TBNA)

Specimens for cytology were obtained by conventional transbronchial needle aspiration (TBNA) in two cases and endobronchial ultrasound (EBUS)-guided TBNA in two cases. The microscopic findings showed granuloma in two cases (50%) (one by conventional TBNA and one by EBUS-TBNA). Cytologic examination revealed aggregates of

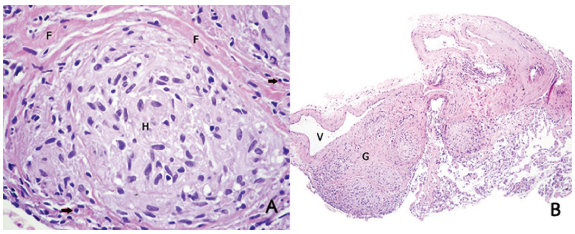

Fig. 4 Transbronchial lung biopsy in case 2: A) nodular aggregate of tightly packed epithelioid histiocytes (H) without necrosis. Hyaline fibrosis (F) and sparse lymphocytes (arrow) are noted at periphery of the nodule; B) non-necrotizing granulomas (G) coalescing to form mass along an interlobular septum where pulmonary vein (V) runs along beside.

epithelioid histiocytes (Fig. 5) scattered in a background of many small lymphocytes and stromal connective tissue fragments. Granular appearance of necrotic debris was not apparent. Neither malignant cells nor microorganisms were found. These findings indicated non-necrotizing granulomatous inflammation.

In two cases for which negative results of TBNA, the diagnosis of sarcoidosis was done by obtaining the specimens from mediastinoscopy, skin biopsy, or TBLB.

Skin and nail bed biopsy

Microscopic findings of the skin displayed confluent non-necrotizing granulomas along dermo-epidermal junction (Fig. 6) and variable extension into deep dermis and subcutaneous tissue. Islands of the granulomas were well-demarcated. A moderate number of giant cells were detected, some contained calcium oxalate crystals (Fig. 7).

Treatment

Seven patients (70%) were only treated with topical treatment of uveitis or skin lesions. In case 10, which was sarcoidosis associated with etanercept therapy, etanercept was discontinued. Three patients required systemic corticosteroids. Two of these patients (case 1 and 5) were treated due to panuveitis that did not response to topical treatment and all of them received immunosuppressive drugs (one received methotrexate and another received azathioprine) due to incomplete response after prednisolone monotherapy. Another patient (case 2) received prednisolone due to severe hypercalcemia. There was no treatment of corticosteroids or immunosuppressive drugs due to indication of pulmonary involvement.

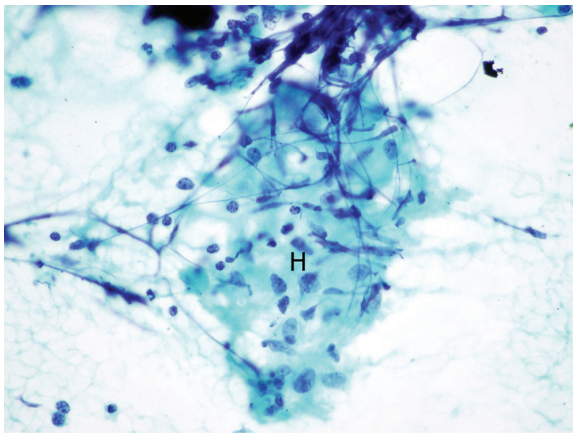

Fig. 5 Fine needle aspiration of the lymph node revealing aggregate of epithelioid histiocytes (H) associated with sparse inflammatory cells and connective tissue fragments. Note clean background.

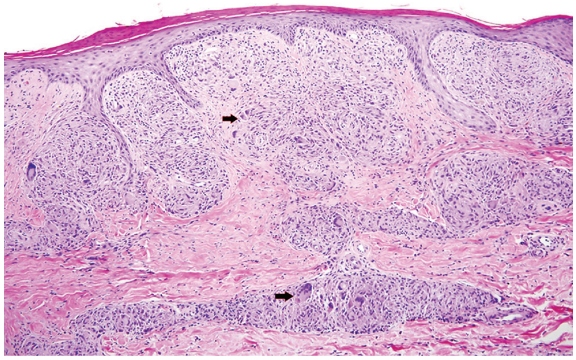

Fig. 6 Islands of confluent non-necrotizing granulomas infiltrating upper and deep dermis. Giant cells (black arrow) are readily detected at scanning magnification.

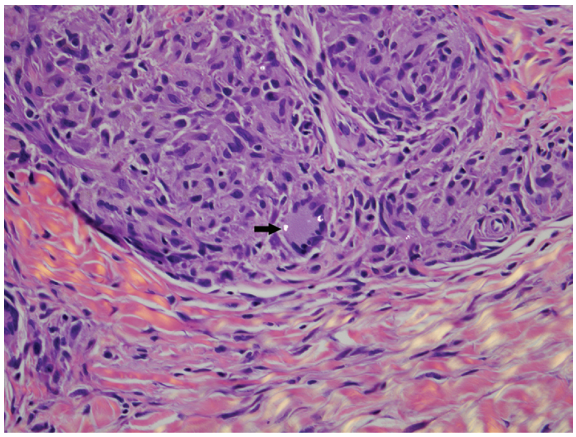

Fig. 7 Crystalline particle (black arrow) in a giant cell seen under polarized light.

Median follow-up time was nine months (range 6-84 months). Findings from chest imaging (both chest x-ray and HRCT) were stable in seven patients (70%), worsening in one patient (10%) and improved in two patients (20%). All patients that had chest x-ray improvement received treatment with corticosteroids and/or immunosuppressive drugs. Pulmonary function tests were followed-up in seven patients (Table 3). FVC, TLC, and DLCO were no significant change in four patients. One patient (case 7), who had worsening chest x-ray that was progression of reticulonodular infiltrates at both upper lobes, had progressively decreased TLC and DLCO, but no respiratory symptoms and no decline in functional class. TLC and DLCO of case 1 and 2, who received systemic treatment, were improved from baseline more than 10% and 15%, respectively.

Discussion

Sarcoidosis is a multisystem disease of unknown etiology. Patients have various clinical presentations and 90% of the patients have pulmonary involvement that may be asymptomatic[4,5]. The present study showed that 70% of the patients had no respiratory symptom. All patients with radiographic stage I were asymptomatic and 57% of the patients with radiographic stage II had respiratory symptoms. These findings were similar to a previous study[8]. The most common findings on chest x-ray is hilar or paratracheal lymphadenopathy and reticular or reticulonodular infiltrates. HRCT of chest has more sensitivity than chest x-ray. The findings from HRCT are multiple mediastinal lymphadenopathy and perilymphatic distribution of centrilobular nodules. Other HRCT findings are variable and include solitary or multiple nodules, bronchiectasis and air-space consolidation[9]. The present study reported one patient with diffuse alveolar and patchy infiltrates on chest x-ray and HRCT chest showed multiple flame-shaped consolidation at both lungs with multiple mediastinal lymphadenopathy.

The cutaneous involvement is a common manifestation that reported in 25 to 35% of patients with sarcoidosis[10]. There is variability of the lesions and maculopapules are the most common type of skin lesions[11,12]. The lesions may arise as single isolated lesions or in groups and commonly involve the nape of the neck and upper back, extremities, and trunk, and may appear in scars or tattoos[11-13]. Lupus pernio and erythema nodosum were not found in this study. The present study reported one patient with nail involvement that is a rare manifestation[14]. Nail changes are variable and include nail thickening, longitudinal ridging, discoloration, splinter hemorrhages, onycholysis, subungual hyperkeratosis, onychodystrophy, nail pitting, and brittleness of the nails[12]. Genital sarcoidosis is an unusual manifestation that can be hypopigmented plaques, enlargement of the scrotum and penis, and genital ulcerated lesion[13]. The present study reported one patient who had indurated papule at the scrotum but no abnormalities at the penis.

The characteristic histologic finding of sarcoidosis is a discrete, compact, non-caseating epithelioid cell granuloma. The tissue for histologic diagnosis of pulmonary sarcoidosis can be obtained by bronchoscopic procedure including bronchial biopsy, TBLB, TBNA (with or without EBUS-guided) and bronchoalveolar lavage (BAL). Bronchial biopsy has positive for non-caseating granuloma in 41 to 57% of patients[5,15].The diagnostic yield depends on stage of disease (higher in stage II disease) and number of specimens[16]. TBLB is the recommended procedure that has diagnostic yield about 46 to 90%[17]. The diagnostic yields for sarcoidosis by conventional TBNA have ranged from 42 to 76% with a higher yield in the stage I disease[16,18]. In present study, all TBLB showed granulomas and the majority of these patients were stage II disease. Cytologic examination of mediastinal lymph nodes that obtained by conventional and EBUS-TBNA show granulomas in 50% of cases. The combination of diagnostic procedures, such as TBLB with TBNA, can increase the diagnostic yield[16].

The bronchoalveolar lavage fluid lymphocyte marker specifically the CD4/CD8 ratio has been used as an adjunct to support the diagnosis of sarcoidosis. All the patients in this study had a BAL CD4/CD8 ratio lower than 3.5. A previous study[19] reported that the BAL CD4/CD8 ratio greater than 3.5 has a sensitivity 53% and a specificity of 94% for diagnosis of sarcoidosis. However, 29% of the TB patients also had values greater than 3.5[20].

The chest imaging study, BAL fluid analysis, histopathology or blood tests are not useful investigations for making definite diagnosis of sarcoidosis because many diseases exhibit similar clinicoradiological presentations and histopathologic findings. Other granulomatous conditions, such as mycobacterial or fungal infection, should be excluded before making a final diagnosis of sarcoidosis. Special stains and cultures for mycobacterium and fungi are necessary. In this study, four patients (40%) received antituberculous treatment before the time of diagnosis

of sarcoidosis. In three of these patients, chest x-ray were not improved after completing treatment of TB and one patient had worsening symptoms of fatigue and weight loss and developed panuveitis during 3-month of TB treatment.

Pulmonary function tests are an important physiologic measurement of lung impairment and help physicians to assess an improvement or deterioration of the pulmonary involvement because the radiographic findings have no correlation with pulmonary function tests[21]. So sequential studies are important to follow the course of disease and assess response to therapy[22,23]. Abnormalities in pulmonary function tests are found in 20% of stage I disease and 40-70% of patients with stage II, III, and IV disease[5]. Both restrictive and obstructive pulmonary function abnormalities can be found. The most common parameters indicating functional impairment are the diffusion capacity and the vital capacity. This study found abnormal pulmonary function tests in all patients with stage I disease and in 57% of patients with stage II disease, respectively. All patients had no desaturation or dyspnea on exertion.

Patients with mild disease, such as skin lesions or anterior uveitis, may be treated with topical corticosteroids alone. Systemic therapy with corticosteroids and/or immunosuppressive drugs is indicated for hypercalcemia, cardiac and neurologic involvement or eye involvement that are not responding to topical treatment. According to pulmonary involvement, patients who have significant respiratory symptom, persistent pulmonary infiltrates, or progressive loss of lung functions may require systemic treatment[24]. In present study, the majority of patients did not require systemic treatment and indications for systemic treatment were panuveitis that did not responded to topical therapy (2 cases) and hypercalcemia (1 case).

Etanercept is a soluble tumor necrotic factor alpha (TNF-α) receptor antagonists that increasingly used in the treatment of inflammatory rheumatologic diseases. There were several studies that reported the development of sarcoidosis associated with TNF-α inhibitors therapy[25-27]. Members of a French rheumatologic association estimated an incidence of sarcoid-like granulomatous reactions following TNF-α inhibitors at 1 in 2,800 persons[25]. Discontinuation leads to granulomatosis resolution in most cases. Corticosteroids can be required in cases of severe symptoms[25]. The present study reported one patient with etanercept-induced sarcoidosis that presented with indurated nodules at scrotum and bilateral hilar lymphadenopathy on chest x-ray without respiratory symptom. The diagnosis was confirmed by histopathology of cutaneous nodule and TBLB. All cultures for mycobacteria and fungus were negative. Etanercept was discontinued and the treatment was topical steroid for cutaneous nodules. During 6-month follow-up, the cutaneous nodule was resolved and no change in chest x-ray findings and pulmonary function tests. Other two available TNF-α inhibitors (adalimumab and infliximab) are anti-TNF monoclonal antibodies. All these three TNF-α inhibitors have been reported to cause sarcoid-like granulomatous reactions. The review of literature by Tong[28] found that the implicated agents were etanercept in 22 cases (59.5%), infliximab in 10 cases (27.0%) and adalimumab in five cases (13.5%). This suggested that a soluble TNF-α receptor antagonist had a higher risk of inducing new granulomatosis compared with anti-TNF monoclonal antibodies.

Spontaneous remissions occur in nearly two-thirds of patients, but the course is chronic or progressive in 10 to 30%[5]. In several studies, one-third to one-half of patients with sarcoidosis were treated with systemic corticosteroids and most patients stabilized or improved with treatment, but relapse occurred in 16 to 74% of patients when the drug was tapered off or discontinued[5]. Criteria for assessing response or improvement have not been validated. Most investigators define improvement of FVC or TLC ≥10% or DLCO ≥15% as significant[29]. The present study, TLC and DLCO of case 1 and 2, who that were treated with prednisolone and/or immunosuppressive drugs, were significantly improved from baseline.

Conclusion

Sarcoidosis is a multisystemic granulomatous disease for which the clinical manifestations were widely variable. The diagnosis of sarcoidosis was made by combination between clinicoradiographic and histopathologic findings. The diagnosis of other granulomatous diseases such as mycobacterial or fungal infection should be excluded. The pulmonary and cutaneous involvement of sarcoidosis is common and the treatment of systemic corticosteroids is not required in most cases. The patients should be regularly followed-up and sequential studies of chest x-ray and pulmonary function tests are important to follow the course of disease and assess response to therapy.

Potential conflicts of interest

None.

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กรณีผู้ป่วยโรค sarcoidosis ที่มีความผิดปกติของระบบการหายใจ

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ภูมิหลัง: โรค sarcoidosis เป็นโรค granulomatous disease ชนิดหนึ่งซึ่งทำให้มีความผิดปกติกับอวัยวะต่าง ๆ หลายระบบในร่างกายโดยยังไม่ทราบสาเหตุ การเกิดโรคชัดเจนและมีอุบัติการณ์ของโรคต่ำในประเทศไทย โรคนี้มีลักษณะทางคลินิกได้หลากหลายและมีความผิดปกติทางระบบการหายใจได้มากกว่า 90% ของผู้ป่วยทั้งหมด

วัสดุและวิธีการ: *เก็บรวบรวมและวิเคราะห์ข้อมูลผู้ป่วยโรค sarcoidosis ที่มีความผิดปกติของระบบการหายใจที่มาติดตามการรักษาที่สาขาวิชาโรคระบบการหายใจและวัณโรค ภาควิชาอายุรศาสตร์ โรงพยาบาลศิริราช ตั้งแต่ เดือนกันยายน พ.ศ. 2551 ถึง ธันวาคม พ.ศ. 2554*

ผลการศึกษา: *การศึกษานี้รวบรวมผู้ป่วยจำนวน 10 ราย พบผู้ป่วยที่มีความผิดปกติของภาพรังสีทรวงอก โดยไม่มีอาการทางระบบการหายใจและระบบอื่น ๆ ทั้งหมด 3 ราย (30%) มีผู้ป่วย sarcoidosis ที่สัมพันธ์กับการรักษาด้วยยา etanercept จำนวน 1 ราย โดยผู้ป่วยส่วนใหญ่ (70%) มีรอยโรคทางผิวหนังหรือเล็บร่วมด้วย ลักษณะที่พบบ่อยที่สุดจากภาพรังสีทรวงอกคือ ต่อมน้ำเหลืองบริเวณขั้วปอดโต โดยมีระยะของโรคที่แบ่งตามความผิดปกติของภาพรังสีทรวงอกคือ ระยะที่ 2 พบ 7 ราย (70%) และระยะที่ 1 พบ 3 ราย (30%) การยืนยันการวินิจฉัยโรคโดยใช้ลักษณะทางพยาธิวิทยาร่วมกับลักษณะทางคลินิกอื่น ๆ และผู้ป่วยทุกรายไม่พบหลักฐานการติดเชื้อวัณโรคหรือเชื้อรา การตรวจสมรรถภาพปอด (spirometry) ผลปกติจำนวน 7 ราย และมีการอุดกั้นแบบ irreversible จำนวน 1 ราย มี total lung capacity ลดลงจำนวน 3 ราย และ diffusion capacity ลดลงจำนวน 6 ราย ผู้ป่วยส่วนใหญ่ได้รับการรักษาเฉพาะที่มีเพียง 3 ราย ที่ต้องใช้ systemic corticosteroids และ/หรือ ยากดภูมิคุ้มกันชนิดอื่นโดยมีข้อบ่งชี้ทางตาซึ่งไม่ดีขึ้นโดยการรักษาเฉพาะที่และภาวะแคลเซียมในเลือดสูง*

สรุป: *การวินิจฉัย sarcoidosis จำเป็นต้องใช้ข้อมูลร่วมกันระหว่างลักษณะทางคลินิคภาพรังสีทรวงอกและลักษณะทางพยาธิวิทยาโดยความผิดปกติของอวัยวะต่าง ๆ ที่พบได้บ่อยคือ ระบบการหายใจและผิวหนัง และควรมีการติดตามการดำเนินโรคและผลการรักษาอย่างใกล้ชิด*