Sarcoidosis Acutely Involving the Musculoskeletal System

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Abstract

A 69-year-old man complained of knee pain, subsequent polyarthralgia, and pains of the muscles of the pelvic girdle and thighs. At the same time, erythema of the face and hands appeared. Biopsy of the skin and muscle revealed non-caseating granuloma of epithelioid cells. The level of serum angiotensin-converting enzyme was normal, but that of lysozyme was elevated. Chest X-ray and CT did not show bilateral hilar lymphadenopathy (BHL) but revealed infiltrative ground glass appearance-like shadows of both lungs, and a Ga scintigram disclosed accumulation in the right hilar region, but not in the muscles. These complaints were quickly ameliorated by the administration of prednisolone. The present patient represented a rare case of acute musculoskeletal system involvement in sarcoidosis not typical of Löfgren's syndrome.

Key words: erythema, arthralgia, myalgia, sarcoidosis

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Introduction

Sarcoidosis is a systematic, granulomatous disease of unknown etiology (1). In sarcoidosis, the prevalence of symptomatic musculoskeletal involvement of muscle, bone, and joints is infrequent and is less than 0.5% (2-10). Patterns of musculoskeletal involvement include: asymptomatic with microscopic granuloma, acute polymyositis-like syndrome, chronic progressive myopathy, and nodular or tumorous sarcoidosis (2-10). Chronic progressive myopathy has been a frequently reported type of sarcoid myopathy; however, acute myopathy is rare. Acute onset sarcoidosis with typical manifestations of bilateral hilar lymphadenopathy (BHL), arthritis, and erythema nodosum, were described as Löfgren's syndrome (11, 12). We report a case of sarcoidosis with acute manifestations involving the musculoskeletal system and skin erythema, without the typical enlargement of BHL and erythema nodosum as in Löfgren's syndrome, whose symptoms were quickly ameliorated with the administration of prednisolone. We think that cases such as in the present patient might be more frequent than reported and underestimated.

Case Report

A 69-year-old man complained of arthralgia of both knees, subsequent polyarthralgia, and muscle pains of the pelvic girdle and thighs, and could not stand up, squat, or walk one month previously, and visited the Department of Orthopedics. Edema of the knees and legs was observed. At the same time, erythema with induration appeared on the face, hands (Fig. 1), and around the knee joints. Heliotrope rashes and Gottron's papules were not observed. Cranial, central, or peripheral nerve palsies were not observed. The pain was refractory to the administration of non-steroidal anti-inflammatory agents (NSAIDs), and the patient was referred to our department and subsequently hospitalized. Laboratory data on admission is shown in Table 1. CBC was normal. Blood chemistry revealed normal creatinine phosphokinase (CK) and aldolase activities and a normal Ca concentration. The level of serum angiotensin-converting enzyme (ACE) was normal. The concentration of serum lysozyme was elevated. The values of CRP and the erythrocyte sedimentation rate (ESR) were elevated. The tuberculin skin test was negative. Serological studies for collagen disease were negative. The electromyogram (EMG) was normal. Magnetic resonance imaging (MRI) did not reveal any changes in muscles of the thigh. Biopsy of the skin of the

Table 1. Laboratory Data on Admission

CBC		Serology	
RBC($\times 10^4/\mu\text{l}$)	475	ANF	—
Hb(g/dl)	11.8	Sm	—
Ht(%)	38.5	SCL 70	—
Plt($\times 10^4/\mu\text{l}$)	26.8	Jo-1	—
WBC($/\mu\text{l}$)	7800	PR3-ANCA	—
Chemistry		MPO-ANCA	—
		SS-DNA IgG	—
		SS-DNA IgM	—
		DS-DNA IgG	—
		DS-DNA IgM	—
		RNP	—
		ACE($\mu\text{g/dl}$)	12.8
		Lysozyme($\mu\text{g/dl}$)	26.3
		CRP(mg/dl)	11.8
		ESR 1h(mm)	64
TP(g/dl)	6.8	2h(mm)	94
Alb(g/dl)	2.5		
Glb(g/dl)	4.3		
AST(IU/l)	34		
ALT(IU/l)	22		
LDH(IU/l)	218		
ALP(IU/l)	460		
γ -GTP(IU/l)	90		
UA(mg/dl)	5.8		
CK(IU/l)	58		
Aldolase(IU/l)	3.8		
BUN(mg/dl)	10.2		
Cre(mg/dl)	0.62		
Na(mmol/l)	139		
K(mmol/l)	3.4		
Ca(mg/dl)	8.8

Figure 1. Indurative erythema of the hand.

hand and thigh muscle revealed a non-caseating granuloma of epithelioid cells (Fig. 2). Transbronchial lung biopsy (TBLB) was not performed.

Chest X-ray and CT did not reveal enlargement of bilateral hilar lymphadenopathy (BHL), but showed infiltrative ground glass appearance-like shadows of both lungs (Fig. 3), and a Ga scintigram disclosed accumulation in the right hilar region (Fig. 4), suggesting stage II of pulmonary change in sarcoidosis (13), but accumulation was not observed in the quadriceps muscles. These results supported the diagnosis of definite acute type of sarcoid myopathy (10). Serologically-determined HLA antigens were: A2 (A*02), B39 (B*39), B60 (B*40), DR4(DRB1*04), and DR8 (DRB1*08).

The administration of prednisolone, 30 mg/day, was started, and the pains were resolved; the level of CRP became negative and the levels of lysozyme and ESR were

Figure 2. The pathology of the biopsied skin showing non-caseating granuloma of epithelioid cells.

normalized within two weeks. Then, the dose of prednisolone was decreased, and the patient was discharged. The patient is being followed-up at the out-patient clinic and is currently well without any recurrence of symptoms of the musculoskeletal system for 6 months.

Discussion

Although the asymptomatic involvement of muscles has been reported in 25 to 75% of patients, symptomatic involvement is rare (2-10). In four large series of sarcoid patients, symptomatic myopathy was reported in only three of 800 (4), two of >500 (5), two of 807 (6), and three of 143 patients (7). There are two main types of sarcoid myopathy based on the clinical course: 1] the rarest form is acute onset of inflammatory myositis with myalgia, muscle tenderness, and polyarthralgia, with a benign clinical course, 2] and the commonest case is chronic myopathy with slowly progressive weakness and disability over months or even years (4, 8-10).

The true incidence of muscle involvement in sarcoidosis is not clear since muscle biopsies such as that of the gastrocnemius have not been performed routinely, and the lesion has not been pathologically confirmed (8). The histological picture of sarcoid myopathy is non-caseous granuloma (NCG) located in the perimysial connective tissue, often near a blood vessel or beneath the sheath of muscles (2-5, 8, 10). Large granulomas compress and destroy adjacent muscle fibers, resulting in degeneration and focal lymphocyte infiltration, and foci of necrosis or fibrosis may also be observed (2-5, 8, 10). The main features distinguishing sarcoid myositis from polymyositis or dermatomyositis are the presence of sarcoid granulomas in skeletal muscle or at other sites (8). In the present patient, granuloma was observed in the connective tissue around muscles. Serial sections of biopsy specimens may be necessary to observe the location of granuloma in the muscles or degenerative changes of the muscle (3). Skin manifestations in sarcoidosis patients are observed in 25% of patients, ranging from

Figure 3. Chest X-ray (left) and CT (left) of the chest did not reveal enlargement of bilateral hilar lymph (BHL) nodes but showed infiltrative ground glass appearance-like shadows of both lungs.

Figure 4. Ga scintigram revealed accumulation in the right hilar region.

typical erythema nodosum, plaques, subcutaneous nodules, macules, and papules (1). Thus, it is evident that the present patient showed acute involvement of the musculoskeletal system in sarcoidosis, although MRI and Ga scintigram did not reveal any significant changes in the muscles, and neurological manifestations were not observed.

The present patient does not represent a typical case of Löfgren's syndrome. Typical Löfgren's syndrome is rare in Japanese, since only 6 cases have been reported (14-20), and it is more common in young Caucasian women from the Nordic countries, Ireland, and Spain (11, 12, 20). Among Japanese patients with sarcoidosis, arthralgia is infrequent (1.6%), and typical erythema nodosum is rare (2.2%), although other skin lesions are observed occasionally (13.8%) (19). Japanese tend to present with asymptomatic and

chronic disease, so Löfgren's syndrome may be underdiagnosed (20). The rate of an exact diagnosis of Löfgren's syndrome might be different between dermatologists, orthopedists, rheumatologists, or pulmonologists (20). Thus, diseases similar to but not typical of Löfgren's syndrome, as in the present patient, may be more frequent than reported (19, 20).

In Japanese patients with sarcoidosis, a strong association with the serologically determined HLA antigens: DR52, DR 52-associated antigens (DR3, DR5, DR6), and DR8, has been reported (21). Löfgren's syndrome is associated with special HLA antigens: B8 and DR3 in Caucasians, correlating the acute onset of the disease with arthritis (22). The frequency of these HLAs is very low in the Japanese population, which may reflect the low incidence of this syndrome in Japan (19). In the present patient, the significance of HLA is unknown.

The prognosis in patients with acute manifestations of sarcoidosis is favorable, and it is usually a self-limiting disease becoming inactive within the first year, with a mean duration ranging from 3 weeks to 3.7 months, (9, 12). However, 8% of patients continued to have active disease (12). These patients require NSAIDs, but steroids rarely need to be administered (9, 12, 19). In the present patient, acute manifestations of the musculoskeletal symptoms were refractory to NSAIDs initially but responded quickly to the later administration of prednisolone, the values of CRP became negative, and lysozyme and ESR were normalized, showing a favorable therapeutic effect for the acute manifestation of sarcoidosis, as in typical cases of Löfgren's syndrome.

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