SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2016; 33; 297-301

Subacute sarcoid myositis with ocular muscle involvement. A case report and review of the literature

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Abstract. Sarcoidosis is a chronic granulomatous disease that can affect multiple organs. The lungs, eyes, and skin are known to be highly affected organs in sarcoidosis. There have been reports based on random muscle biopsy that 32-80% of systemic sarcoidosis comprises noncaseating granulomas; however, muscle involvement in sarcoidosis is generally asymptomatic and has an unknown frequency. We describe a case of acute to subacute sarcoid myositis of the skeletal and extraocular muscles. Typical ophthalmic involvement (manifested by infiltration of the ocular adnexa, intraocular inflammation, or infiltration of the retrobulbar visual pathways) and extraocular sarcoid myositis (as with the present case) is infrequently reported. It is important to keep in mind the rare yet perhaps underestimated entity of sarcoid myositis, and to utilize muscle biopsy and imaging tests for appropriate diagnosis and management of patients with sarcoidosis. *(Sarcoidosis Vasc Diffuse Lung Dis 2016; 33: 297-301)*

Key words: sarcoidois, myositis, extraocular muscle

Introduction

Sarcoidosis is a chronic multisystem disease of undetermined etiology that is pathologically characterized by noncaseating granulomatous inflammation. Asymptomatic sarcoid myopathy is seen in 32-80% (1-3) of systemic sarcoidosis by random muscle biopsy, whereas symptomatic sarcoid myopathy is relatively rare. Symptomatic sarcoid myopathy is classified into three categories (3): palpable muscle nodules, acute myositis, and chronic myopathy. Palpable muscle nodules are the most common form of sarcoid myopathy. The latter two are so rare that their clinical features remain unclear.

About a third of patients with sarcoidosis have ophthalmic involvement that manifests either by infiltration of the ocular adnexa, intraocular inflammation, or infiltration of the retrobulbar visual pathways (4). As far as we know, extraocular myositis due to sarcoidosis is very rarely reported. Presented is a rare case of subacute sarcoid myositis with external ocular muscle involvement.

Case Report

A 70-year-old Japanese woman was admitted to our hospital in June 2011 with a one-year history of prolonged worsening myalgia of the bilateral lower limbs and with fluctuating and acute onset diplopia. Two years before the admission, clinical diagnosis of systemic sarcoidosis was substantiated by dem-

Received: 28 October 2014
Accepted after revision: 17 February 2016
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onstration of uveitis, bilateral lymphadenopathy on chest x-ray, and elevated serum angiotensin-converting enzyme and calcium levels.

Physical examination revealed no remarkable findings except for grasping pain in both the proximal and distal skeletal muscles of the bilateral lower limbs. Her muscles showed neither atrophy nor hypertrophy, and no palpable muscle nodules were identified. On neurological examination, she had a slight limitation of abduction of both eyes. She had no other cranial nerve disorders, no other muscle weaknesses, and deep tendon reflexes were normal.

Laboratory findings on admission revealed marked elevation in creatine phosphokinase at 6,653 U/L with a myoglobin level of 1,691 ng/mL. The lactate dehydrogenase level was also elevated at 968 U/L, and aspartate aminotransferase was elevated at 316 U/L. Serum angiotensin-converting enzyme was elevated at 41.0 U/L and soluble interleukin-2 receptor was also elevated at 4,425 U/mL. The erythrocyte sedimentation rate was slightly elevated at 16 mm/h and C-reactive protein was normal. Anti-acetylcholine receptor antibody was within the normal limit. Antinuclear antibody was ×160 (speckled pattern). Other antibodies related to autoimmune diseases including anti-Jo-1 antibody were all negative.

Magnetic resonance imaging (MRI) showed diffuse streaky high intensity areas in skeletal muscles of her hip, thighs, and lower thighs (Fig. 1A). Additionally, head MRI showed esophoria, mild swelling of external ocular muscles and small high intensity nodules in her left lateral rectus muscle (Fig. 1B). An electromyogram of the deltoid and biceps revealed a myopathic pattern with fibrillations and positive sharp waves with spontaneous activity and short-duration, low-amplitude and poly-phasic motor unit action potentials with volitional activity. Biopsy of the left vastus muscle showed marked infiltration of macrophages and lymphocytes, and non-caseating granulomas were found in the muscle fibers and stroma (Fig. 2). The resulting diagnosis was subacute sarcoid myositis of skeletal muscles with orbital sarcoid myopathy.

Her diplopia disappeared gradually and spontaneously a few days after admission. Prednisolone therapy, 40 mg daily, was initiated, resulting in a gradual improvement of muscle tenderness. The elevated serum creatine phosphokinase level also gradually decreased, and the dose of prednisolone was slowly tapered. Two months after the start of treatment, her serum creatine phosphokinase level finally decreased to normal levels. She had no recurrence of diplopia.

Discussion

Muscular involvement in sarcoidosis has been divided into two general classifications: asymptomatic and symptomatic. While sarcoid granulomas are frequently observed histologically in skeletal muscles, they are not often associated with muscle symptoms such as tenderness, weakness, or wasting. Asymptomatic sarcoid muscle involvement is reported to be seen in 32-80% of patients with systemic sarcoidosis by random muscle biopsy (1-3). Today, 'blind' muscle biopsy of asymptomatic patients with sarcoidosis is not recommended, and muscle involvement is found incidentally by ^{67}Ga-scintigraphy or fluorodeoxyglucose-positron emission tomography. On the other hand, symptomatic sarcoid muscle involvement is reported in only 1.4-2.3% of patients with systemic sarcoidosis, and has been divided into three clinical entities: palpable muscle nodules, acute myositis, and chronic myopathy (4, 5). The most common type is palpable muscle nodule and the latter two are so rare that their clinical features are not clear. Making a diagnosis of palpable muscle nodules is not too difficult because the nodules can be identified from the surface of the body and are used to identify an exact biopsy location. Moreover, enhancement of skeletal muscle MRI is a specific finding, and palpable muscle nodules appear as intensely bright nodules on T2-weighted images. Meanwhile, acute to subacute myositis and chronic myopathy has no specific findings on MRI or electromyography. It is sometimes difficult to distinguish palpable muscle nodules from other types of inflammatory myositis, such as that seen with autoimmune diseases.

There is an increasing number of case reports of sarcoidosis complicated by various autoimmune diseases, such as Sjögren syndrome (6, 7) and mixed connective tissue disease (8). There are a few reports of dermatomyositis complicated with sarcoidosis (9, 10), a case of cardiac sarcoidosis in a patient with progressive systemic sclerosis, Sjögren syndrome, and polymyositis (11), and a case of pulmonary sarcoidosis in a patient with dermatomyositis under

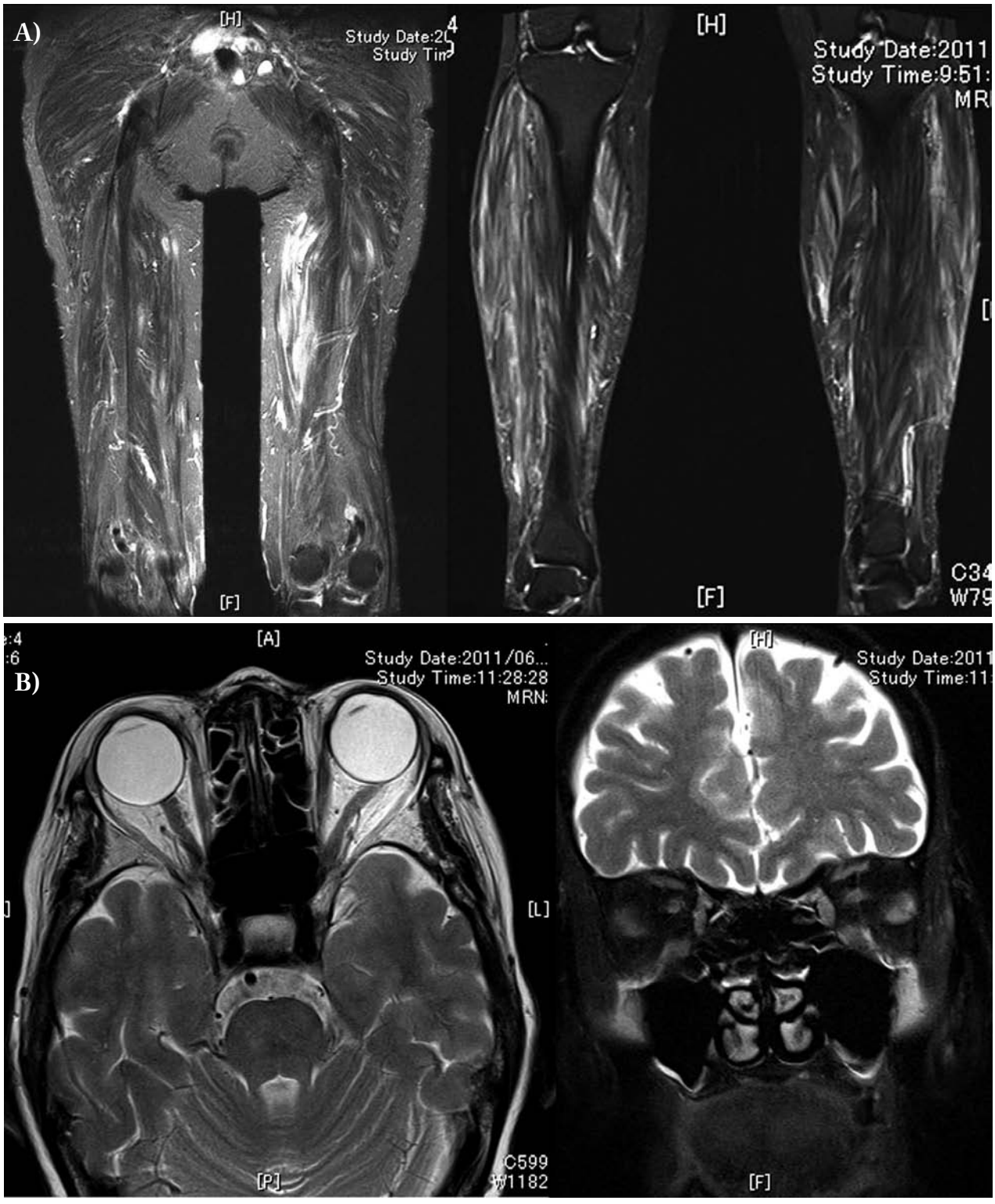

Fig. 1. (A) MRI reveals diffuse streaky high intensity areas in the skeletal muscles of the hips, thighs, and lower thighs. (B) Head MRI shows esophoria, mild swelling of the external ocular muscles, and small high intensity nodules in the left lateral rectus muscle.
*MRI; magnetic resonance imaging

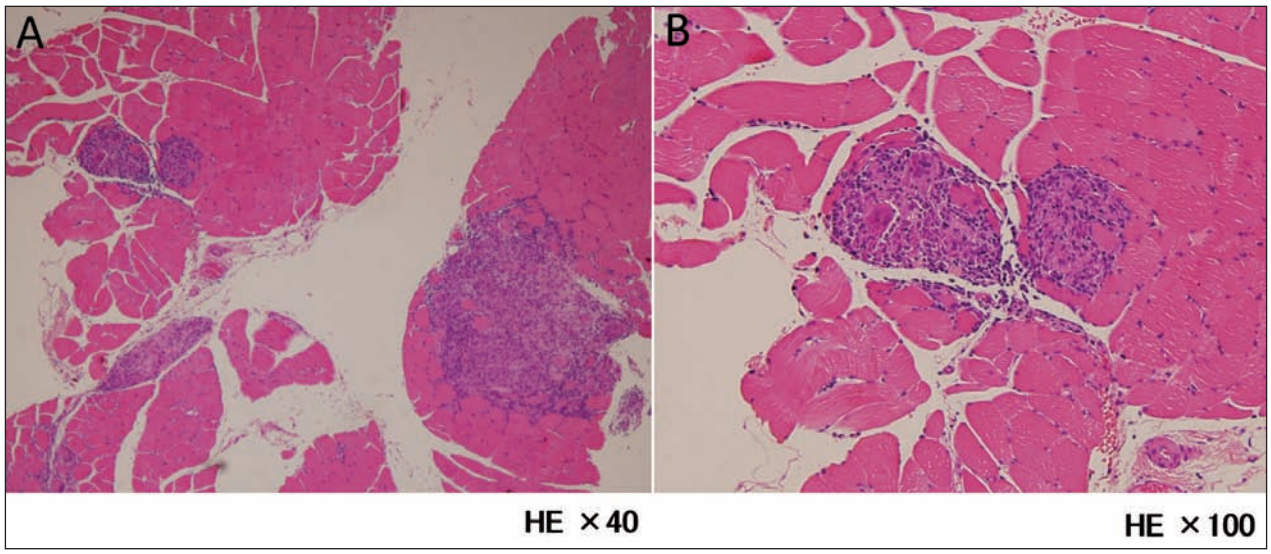

Fig. 2. Specimen obtained from the left vastus muscle shows marked infiltration of macrophages and lymphocytes, and non-caseating granulomas were found in the muscle fibers and stroma (hematoxylin and eosin stain, A; 40, B; ×100)

long-term steroid therapy (12). In the case of acute sarcoid myositis, it is important to distinguish this disease process from polymyositis/dermatomyositis because therapeutic strategies, complications, and disease prognoses are different between the two diseases. In order to make a definite diagnosis, clinicians should not hesitate to perform a muscle biopsy.

In the present case of a patient with a diagnosis of sarcoidosis, sarcoid myositis was suspected at the beginning. However, it is difficult to distinguish sarcoid myositis from polymyositis only by symptoms, laboratory data, MRI findings, and electromyography. Therefore, muscle biopsy was performed and a definite diagnosis of sarcoid myositis was made. Her muscle tenderness had been sustained for about a year, and was acute-on-chronic at the time of diagnosis. Despite her chronic clinical course, she showed no muscle atrophy or weakness. Her muscle samples revealed dominant cellular inflammation without a particular distinction of myolysis. Considering her clinical and pathological findings, a diagnosis of subacute sarcoid myopathy was made.

Sarcoidosis often involves ocular tissues, but most of them are due to uveitis and iritis, and ophthalmoplegia is rare. In the case of ophthalmoplegia externa in patients with sarcoidosis, two situations should be considered: the possibility of sarcoid neuropathy of the oculomotor nerve, trochlear nerve, or abducens nerve, and that of sarcoid myopathy in the extraocular muscles. In the latter case, according to the head MRI findings, the diagnosis of sarcoid myopathy of the extraocular muscles was made. Viral or bacterial infections, drugs, IgG4-related disease, and other systemic inflammatory diseases such as Crohn's disease may also cause extraocular myositis. These possibilities were ruled out based on the clinical course and laboratory data.

Extraocular sarcoid myositis is rare, and as far as we know only eight cases have been reported (13-19) (Table 1). There are no specificities in the age or sex of the patients. All of the cases presented symptoms such as blepharedema, external ophthalmoplegia, blepharoptosis and diplopia. Some cases were diagnosed by ocular muscle biopsy, whereas with some cases in recent years the diagnoses were made by clinical symptoms and findings from MRI or scintigraphy. All the cases showed not only ocular defects but also involvement of other organs. Ocular sarcoid myopathy complicated with skeletal muscle sarcoid myositis is rare, and the present case is only the second report worldwide.

Patients with asymptomatic sarcoid myopathy of the 'palpable nodular type' usually receive follow-up with no medication under the expectation of natural improvement. On the other hand, for patients with symptomatic sarcoid myositis, systemic steroid therapy, such as a moderate to high dose of oral prednisolone, is adapted. Some cases respond well to ster-

Table 1. Case reports of ocular sarcoid myositis

Author (year)	Age/Sex	Ocular manifestations	Diagnosis	Another involvement	Response to steroid
Stannard K, et al (1985) (13)	39/M	blepharedema	ocular muscle biopsy	lung	Good
Cornblath WT, et al (1993) (14)	15/M	external ophthalmoplegia	ocular muscle biopsy	lacrimal gland, lung	Good
Patel SA, et al (1994) (15)	43/F	diplopia	ocular muscle biopsy	-	Good
Takahashi T, et al (1999) (16)	62/F	diplopia, blepharedema	^{99m}Tc pyrophosphate scintigraphy, MRI	skeletal muscle	Good
Hayashi E, et al (2001) (17)	63/F	blepharoptosis	MRI	skin, brain stem, cervical cord	Good
Tamura A, et al (2009) (18)	59/M	diplopia	MRI	Lung, skeletal muscle	Good
So WL, et al (2012) (19)	36/F	vague lump below left eye	ocular muscle biopsy	-	Good
Present case	*70/F*	*diplopia*	MRI	*uveitis, skeletal muscle, lung*	Good

oid therapy, whereas others exhibit a poor response to steroid therapy alone and are treated successfully with combination therapy of steroids and methotrexate (20, 21).

Conclusions

Reported is a rare case of subacute sarcoid myositis of the skeletal muscles with ocular involvement. Acute or subacute sarcoid myositis is relatively rare, and muscle biopsy is useful to distinguish it from other systemic inflammatory diseases that can cause myositis, such as polymyositis/dermatomyositis. With ocular involvement of sarcoidosis, extraocular myositis is extremely rare. It is important to consider this possibility, and to make a diagnosis using MRI or muscle biopsy.

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