Sarcoid Myopathy Mimicking Polymyositis: A Case Report and Pool Analysis of the Literature Reviews

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Abstract- A 59-year-old man presented with proximal myopathy, myalgia, and weight loss, with the initial markedly elevated serum creatine kinase at 11,000 U/L. Due to his refusal for muscle biopsy, he was initially treated as inflammatory myositis and responded well with the corticosteroids. However, he subsequently had a relapse of the symptoms with more extensive systemic involvement, i.e., hypercalcemia, lymphadenopathy and subcutaneous nodules. Finally, a biopsy of the thigh and subcutaneous nodule revealed non-caseating granulomatous inflammation, consistent with sarcoidosis. He responded well to the corticosteroids, and finally, azathioprine was added as a steroid-sparing agent. Including our series, there are 103 cases of symptomatic muscle involvement in sarcoidosis patients published in the English literature to date. Further pool analysis of the cases will be reported in this review.

Keywords: Granuloma; Myopathy; Sarcoidosis; Subcutaneous nodules

Introduction

Sarcoidosis is a granulomatous inflammatory disease involving multiple organ systems. Beside organ-specific symptoms, non-specific constitutional complaints such as fatigue and general weakness are frequent (1). The granuloma formation in sarcoidosis is driven by an array of cytokines such as tumor necrosis factor (TNF)-α, interleukin (IL)-6, interferon (INF)-γ and others (2-4). The exact etiology and mechanism that leads to either progression or spontaneous resolution of the disease are not known.

Musculoskeletal involvement of sarcoidosis is usually asymptomatic and resolves spontaneously, although granulomas are commonly demonstrated by biopsy in 50-80% of sarcoid cases (5). On the other hand, symptomatic involvement of musculoskeletal system in sarcoidosis is rare, with the reported cases of around 0.5-2.3% (7-9). Acute inflammatory myopathy is resembling polymyositis, as well as palpable myopathic nodules and a chronic progressive myopathy, have been described in sarcoidosis (6-8). The extremities muscle are commonly involved in sarcoidosis. However, there are few reported cases of respiratory muscle involvement (9,10) and is one reported case of abdominal muscle involvement (11).

We described a case of sarcoïd myopathy with the initial presentation resembling polymyositis. The diagnosis of sarcoïd myopathy was finally revealed by the muscle and subcutaneous nodule biopsy. We also reviewed the English language literature using PubMed database with keywords of “sarcoid myopathy” “musculoskeletal sarcoidosis,” “muscular sarcoidosis” and “sarcoïd myositis.” We also included pertinent articles obtained from searching references in the articles found in the primary search.

Case Report

A 59-year-old gentleman first presented to another hospital in October 2010 with proximal myopathy, myalgia and photosensitive rashes over the face and anterior chest. He was treated as inflammatory myositis based on clinical presentation and elevated serum creatine kinase of 11,000 U/L. He refused muscle biopsy but subsequently improved with prednisolone 60
mg daily.

Approximately one year later, after the prednisolone was tapered to 5 mg daily, he started to have recurrent muscle weakness and myalgia. It was associated with prolonged fever of more than three months, which did not resolve despite multiple courses of antibiotics, together with weight loss. Subsequently, his left thigh muscle became swollen and tender. At that time, he also developed left knee swelling but the knee aspiration yield no growth. His septic workup including sputum, urine and blood cultures were all negative. Subsequently, he was referred to Rheumatology after he had consulted several physicians for the past 8 months due to his worsening symptoms.

On physical examination, he was afebrile with normal vital signs. His muscle power was 4/5 at the upper limbs and 3/5 over the proximal lower limbs. Another neurological examination was normal. Multiple non-erythematous subcutaneous nodules were noted over the upper limbs and lower limbs. The sizes of the nodules range from 1-3 cm in diameters. An erythematous rash was also noted covering the anterior chest. Multiple inguinal lymph nodes were also palpable but no hepatosplenomegaly. Cardiovascular and respiratory examinations were normal. Further blood investigations revealed that he had anemia of chronic disease, hypercalcemia (serum Calcium 2.81 mmol/L), and elevated erythrocyte sedimentation rate (ESR) of 97 mm/hour. His serum creatine kinase and chest radiograph were normal (CK 154 U/L). On serological analysis, rheumatoid factor (RF) and anti-nuclear antibody (ANA) were negative and complemented (C3 and C4) were within the normal ranges. A repeat TB work-up including Mantoux test and sputum TB cultures/polymerase chain reaction (PCR) were all negative.

CT scan of lower abdomen and pelvis did show thickening of the right erector spinae muscles, left iliopsoas muscle and left thigh muscles, as well as multiple left inguinal lymph nodes (Figure 1). Finally, biopsy of the left quadriceps muscle and subcutaneous nodules were performed, and they revealed non-necrotizing granulomatous inflammation (Figure 3). Tuberculosis (TB) smear, cultures and polymerase chain reaction (PCR) from the lesions were negative. Fungal staining and cultures were also negative. Therefore, the diagnosis of sarcoidosis was made, and the prednisolone was increased to 15 mg daily and later added on azathioprine 50 mg daily. Serum Angiotensin Converting Enzyme (ACE) level was normal 29 U/L (10-70 U/L). Clinically he responded to the treatment with improving muscle power and regression of the subcutaneous nodules. His serum calcium and ESR normalized to 2.31 mmol/L and 33 mm/hr respectively. His post-treatment CT scan also revealed resolved inflammatory changes in all previous soft tissues and muscles (Figure 2).

![Figure 1. Computed tomography abdomen in axial view shows isodense thickening (white arrows) of the right erector spinae muscles (a), left iliopsoas muscle (b) and left thigh muscles (c,d) as well as multiple left inguinal lymph nodes (black arrow).](image-url)
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We found 103 well-described reported cases (1,5,7,12-62) in the English language literature of sarcoidosis involving the muscles and we are describing another one case in this review. The largest case series was reported by Otake et al., (46) in a single cohort of 28 Japanese patients with muscular sarcoidosis, amongst their 457 sarcoidosis patients. The cohort consisted of 27 women and one man, aged 30 to 80 years (mean 56 years). A total of 20 patients had nodular type, and eight had the myopathic type.

Due to the unavailability of the specific demographics details of each patients in Otake et al., case series, analysis of the other 76 individual cases of sarcoid myopathy including ours revealed that majority of the patients were female (n=50, 66.7%) with the mean age of presentation of 43.7±15.3 years (range 16 to 80 years). The commonest type of muscular sarcoidosis published in the literature was the nodular type (n=49, 65.3%) followed by chronic myopathy and myositic type (n=13, 17.3% respectively). Large proportion of the patients presented with muscle weakness (n=49, 64.5%) followed by muscle swelling, mass or nodules (n=34, 44.7%). Two cases reported respiratory muscles involvement while one dysphagia. Only 7 (9.2%) cases presented as isolated sarcoid myopathy while 21 (27.6%) had sarcoid myopathy as the onset of disease.

Only 45 cases reported the race/ethnicity of the patients. 15 of them (33.3%) were Caucasians and Asians, while 12 (26.7%) were African-American or blacks. The rest were Spanish (n=2, 4.4%) and West

Figure 2. CT abdomen post treatment shows complete resolution of the muscle thickenings and left inguinal lymphadenopathy (arrows)

Figure 3. Subcutaneous nodule biopsy showed non-caseating granulomatous lesion
Indies (n=1, 2.2%). Serum creatine kinase (CK) was available in 35 cases. Only seven (20%) reported an increase in the CK level and the majority of them were in patients with acute myositis (5/9 patient). Serum Angiotensin Converting Enzyme (ACE) was only available from 24 cases, and 14 (58.3%) of them had documented an increase in the enzyme level.

Treatment modalities were documented in 52 cases. The majority were treated with oral corticosteroids (n=44, 84.6%). Methotrexate (12-14,17,54) and azathioprine (13,14,59) were used in combination with corticosteroids in 6 cases. Two patients received hydroxychloroquine in combination with steroid treatment (7). Three patients were treated conservatively as they improved without any specific treatment (32,37,56). Four cases of nodular sarcoid myositis were treated with surgical debridement or excision (7,31,53,62). One of them also received radiotherapy (62). The majority had a very good response to corticosteroid, and only 2 cases reported partial response with the treatment (33,62). One patient responded to intra-lesional corticosteroid (48). Infliximab was used successfully in a case of sarcoïd myositis who had relapsed with methotrexate and steroid (55).

Discussion

The first published case of sarcoidosis of the skeletal muscles was reported as early as 1908 by Licharew who presented a girl with many palpable nodules in the muscle (63). Asymptomatic muscular involvement is the most common type as granulomas can be found in the skeletal muscles up to 80% of patients with sarcoidosis (64). In patients with symptomatic muscle involvement of sarcoidosis, the most common type of presentation is chronic myopathy, and the less common types are the myositic type (16) and the nodular type (54,62).

Chronic myopathic type occurs mainly in women aged between 50 and 60 years and is characterized by a slow progressive symmetrical weakness and atrophy of the proximal muscle groups (14,65). Similarly, in our case, it may mimic polymyositis or muscular dystrophy (13). The diagnosis of inflammatory myositis was first considered in this patient as there was no other organ especially pulmonary involvement, which is the commonest system involvement in sarcoidosis (13,66). Furthermore, symptomatic muscle involvement in sarcoidosis occurs in the chronic multi-systemic form of the disease and is rarely at its initial or as isolated presentation (67,68). In the prospective ACCESS study, only one of 215 patients had initial muscle involvement (69). Therefore, muscle biopsy is crucial in clinching the diagnosis.

Not all patients with muscular sarcoidosis experienced elevated muscle enzymes. High serum creatine kinase (CK) typically occurs in the acute myositis of sarcoidosis (19). This is consistent with our analysis of the literature in which majority of the patients with acute myositis (55.5%) reported an increase in CK level. Therefore, not surprisingly, our patient only developed high CK level at the initial acute presentation of sarcoid myositis, but later the level normalized despite persistent symptoms of muscle weakness. Due to poor sensitivity of muscle enzymes in chronic sarcoid myopathy, magnetic resonance imaging and gallium scintigraphy are the useful tools that can demonstrate muscle involvement in chronic myopathy (70,71).

Sarcoidosis is a diagnostic challenge in countries where tuberculosis is endemic. However, physicians still need to keep sarcoidosis in the differential diagnosis due to clinical, histological and radiological similarities between the two conditions. As in our South East Asia setting, tuberculosis still has to be considered, but as Ziehl Neelson staining was negative, Sarcoidosis is more likely the diagnosis for our patient. There was no immunohistological staining done for our patient. But there are few immunohistochemical studies of the muscle biopsies from sarcoidosis patients, though Takanashi et al., (10) and Tews and Pongratz (11) did study the subset of lymphocytes immunohistochemically in biopsied muscles using the monoclonal antibody for the antigen on the lymphocytes' surface markers. showed that the majority of infiltrating cells were macrophages and CD4-positive cells. They studied the distribution of these cells and found that CD4-positive cells accumulated in the center of granulomas, while CD8-positive cells accumulated at the periphery of granulomas. These findings are similar to the reported findings on granulomas within the lymph nodes or bronchoalveolar lavage fluid of sarcoidosis patients (12).

For symptomatic muscle involvement of sarcoidosis, systemic corticosteroids are the treatment of choice, but relapses are commonly reported when the dose is tapered down (7,72).

The evidence for other immunosuppressive agents, i.e. methotrexate, azathioprine and hydroxychloroquine are limited to few case series and some case reports (73). Experimental biological approaches with anti-tumor necrosis factors (infliximab and adalimumab) have been successfully used in refractory cases of sarcoidosis (55,74).
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In conclusion, the clinical picture of sarcoidosis is variable as it is a complex multi-organ disease. Physicians should be aware of this diagnosis as it has a good response to corticosteroid treatment and delay in diagnosis may lead to chronic muscle atrophy and permanent sequelae of muscle weakness.

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