Respiratory Failure due to Diaphragm Sarcoidosis Diagnosed by a Computed Tomography-guided Needle Biopsy

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Abstract:
Sarcoidosis is a multisystem noncaseating granulomatous disorder of unknown etiology that can be found in almost any organ, but symptomatic respiratory muscle involvement is rare. We herein report the case of a 77-year-old woman with diaphragm sarcoidosis diagnosed by a computed tomography (CT)-guided needle biopsy that was successfully treated with a corticosteroid. The patient presented with dyspnea that lasted for two weeks and respiratory failure. CT revealed diffuse diaphragm thickening with contrast enhancement, which might be a characteristic imaging finding for diaphragm myopathy/myositis, including sarcoidosis. A CT-guided needle biopsy proved useful for the diagnosis of diaphragm sarcoidosis.

Key words: sarcoidosis, diaphragm, muscle, CT-guided needle biopsy, corticosteroid

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Introduction
Sarcoidosis is a multisystem noncaseating granulomatous disorder of unknown etiology and can manifest in almost any organ, including the lungs, lymph node, eyes, and skin (1). It has been estimated that skeletal muscle is involved in 50-80% of sarcoidosis cases but is symptomatic in only 0.5-2.5% of cases (2-4). We herein report a case of respiratory failure caused by diaphragm sarcoidosis, which was diagnosed by a computed tomography (CT)-guided needle biopsy.

Case Report
A 77-year-old woman visited our emergency room because of dyspnea that had lasted for two weeks. Three years previously, she had been clinically diagnosed with pulmonary sarcoidosis at our hospital based on bilateral hilar mediastinal lymphadenopathy with an increased uptake on gallium scintigraphy; elevated levels of serum soluble interleukin-2 receptor (sIL-2R) (1,150 U/mL), angiotensin-converting enzyme (ACE) (29.7 IU/L), and lysozyme (14.6 μg/mL); lymphocytosis; and a high CD4/CD8 ratio in her bronchoalveolar lavage fluid. Serum levels of aspartic aminotransferase (AST), lactate dehydrogenase (LDH), creatine phosphokinase (CPK), and C-reactive protein (CRP) were not elevated. At that time, she was also diagnosed with cardiac sarcoidosis, and a pacemaker was placed for complete atrioventricular block. She was not treated with corticosteroid or immunosuppressive agents.

At her recent visit to the emergency room with dyspnea, a physical examination revealed her to be overweight (body mass index, 26.6 kg/m²), with hypertension and fine crackles at the bilateral inferior lung fields but without a fever, muscle pain, or muscle weakness in her limbs. Her oxygen saturation measured by pulse oximetry on room air was 93% while sitting and 88% in the supine position, and her respiratory rate was 24 breaths per minute. After inhalation of oxygen at 3 L/min in the supine position, an arterial blood gas analysis revealed a pH of 7.422, carbon dioxide partial pressure (pCO₂) of 35.3 mmHg, partial pressure oxygen (pO₂) of 66.1 mmHg, HCO₃⁻ of 22.6 mmol/L, and base excess of −1.2 mmol/L. Laboratory test results revealed that
blood cell counts were within normal ranges, with elevated serum levels of AST (70 IU/L), LDH (405 IU/L), CPK (1,412 U/L), CRP (5.23 mg/mL), sIL-2R (1,360 U/mL), ACE (28 IU/L), and lysozyme (17.1 μg/mL). The serum level of CPK-MB isozyme (63 U/L) and plasma level of brain natriuretic peptide (31 pg/mL) were not significantly elevated. The patient’s serum was negative for antinuclear and anti-aminocarboxy tRNA synthetase antibodies. A lung function test revealed a restrictive disorder, and her vital capacity (%VC) were 1.27 L and 62.0%, respectively. An electrocardiogram showed atrial sense ventricular pace without ST-segment elevation. Echocardiography showed an ejection fraction of 58.6% without either ventricular septum thinning or inferior vena cava dilation. Chest X-ray showed dull bilateral costophrenic angles, and CT revealed atelectasis at the bilateral lower lobes and diffuse diaphragm thickening with contrast enhancement (Fig. 1). Mediastinal and retrocrural lymphadenopathy was observed without lung parenchyma involvement of sarcoidosis.

Based on these findings, we suspected a diaphragm lesion as the cause of respiratory failure and performed a CT-guided needle biopsy of the diaphragm. We approached the right crus of the diaphragm at the Th12/L1 level with an 18-gauge needle (Fig. 2). The pathological findings revealed infiltration of lymphocytes and histiocytes, as well as epithelioid granulomas with multinucleated giant cells (Fig. 3). Acid-fast staining, culture, and tuberculosis polymerase chain reaction of the needle washing solution were negative. Therefore, the patient was diagnosed with diaphragm sarcoidosis and treated with 125 mg of methylprednisolone for 8 days and 60 mg for 7 days. Her respiratory status rapidly improved, accompanied by normalization of the serum CPK levels. The corticosteroid dose was then reduced to 40 mg of prednisolone. At 17 days after commencing corticosteroid administration, CT revealed that the atelectasis of the bilateral lower lobes and diaphragm thickening had improved (Fig. 4); at 26 days, her VC and %VC had improved to 1.86 L and 90.3%, respectively. Thereafter, the disease was well controlled with a low dose of oral corticosteroid.

Discussion

In a survey of 1,027 patients with pathologically proven sarcoidosis in Japan, the most commonly involved organs were the lungs (86.1%), followed by the eyes (54.8%) and skin (35.4%); muscle involvement was observed in 4.2% of cases (5). Similarly, in a study of a large cohort of patients with sarcoidosis in the United States, muscle involvement was observed in only 0.4% of cases (6). Conversely, other studies have reported muscle involvement in 50-80% of patients with sarcoidosis (2-4). Because muscle involvement is typically asymptomatic, it can be underestimated. Muscle involvement in patients with sarcoidosis is generally classified into three types: chronic myopathy, acute myositis, and palpable nodules (7). The most common of these is chronic myopathy, which presents as indolent proximal muscle weakness and wasting. Acute myositis, observed most com-
monly in women, is associated with muscle weakness and elevated muscle enzymes. The least common type is palpable nodules, which can present as single or multiple painful nodules. Respiratory muscle involvement in sarcoidosis that includes the intercostal muscle and diaphragm can cause respiratory symptoms or respiratory failure even without lung parenchyma involvement. Previous reports of respiratory muscle involvement of sarcoidosis have described both respiratory symptoms and muscle weakness in the limbs; the myopathy findings were confirmed by a limb muscle biopsy, and respiratory muscle involvement was determined using electromyography (8-10). Although the absence of muscle weakness of the limbs in our patient was atypical compared with the previous reports, the patient was believed to have acute myositis because of the rapid appearance of respiratory symptoms, elevated levels of serum CPK, and diaphragm biopsy findings. Lymphadenopathy spread from mediastinum to retrocrural space, suggesting that it might be involved in the development of diaphragm sarcoidosis. Respiratory muscle involvement in sarcoidosis generally responds well to corticosteroid treatment, as demonstrated in the present case and previous reports (9, 10). Pathologically confirmed diaphragm involvement in sarcoidosis has rarely been reported, with only two reported cases of diaphragm sarcoidosis diagnosed by an autopsy (11, 12). To our knowledge, the present case is the first report of diaphragm sarcoidosis diagnosed by a CT-guided needle biopsy while the patient was alive.

Imaging studies are useful for detecting muscle involvement in sarcoidosis. Magnetic resonance imaging (MRI) can detect inflammatory lesions in muscle (13). On MRI, palpable nodules present a characteristic finding: a star-shaped area of low signal intensity centered within the nodule surrounded by areas of high intensity (14). Positron emission tomography can be useful for detecting asymptomatic muscle involvement in sarcoidosis (15). Although the CT findings of diaphragm sarcoidosis have not been described, diffuse thickening of the diaphragm with contrast enhancement is considered a characteristic finding of diaphragm myopathy and myositis, including sarcoidosis, polymyositis or der-
matomyositis, immune-mediated necrotizing myopathy, and sporadic inclusion body myositis. A biopsy of the diaphragm is required to perform a differential diagnosis. The diaphragm moves dynamically with respiration, but the crura of the diaphragm are fixed and can be safely approached, as in the present case.

We herein described for the first time a case of diaphragm sarcoidosis diagnosed by a CT-guided needle biopsy. If respiratory symptoms or respiratory failure appear during the course of known sarcoidosis, both lung involvement and respiratory muscle involvement should be suspected. Diffuse diaphragm thickening with contrast enhancement on CT might be a characteristic imaging finding of diaphragm myopathy and myositis, and a CT-guided needle biopsy is useful for the diagnosis of diaphragm sarcoidosis.

The authors state that they have no Conflict of Interest (COI).

References


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