Myositis and immune reconstitution inflammatory syndrome in an immuno compromised patient: A therapeutic conundrum

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ABSTRACT

Microsporidia are ubiquitous fungi that may infect animals, fish, insects as well as humans. Human infection is uncommon and only seen in the immunocompromised individual. Here, we report the case of a 40-year-old known AIDS patient presented with severe myalgia and inability to walk. Investigations revealed microsporidial myositis. Her treatment was further complicated by the development of acute inflammatory demyelinating polyneuropathy (AIDP) 2 weeks later. However, treating human immunodeficiency virus, microsporidiosis, and AIDP as a consequence of immune reconstitution inflammatory syndrome concomitantly led to clinical improvement.

Key words: *Fungus, Microsporidiosis, Myositis*

Microsporidia are the fungi which have 1200 species and 400 genera. They are ubiquitous and may infect animals, fish, insects as well as humans [1]. Human infection is uncommon and only seen in the immunocompromised individual. The most commonly involved systems in human are the gastrointestinal, urinary, and respiratory systems.

We present this case as the involvement of skeletal muscle by microsporidia is very rare and documented only in isolated case reports since 1985 [2]. Furthermore, we want to highlight certain specific hurdles such as the development of immune reconstitution inflammatory syndrome (IRIS) during therapy.

CASE REPORT

A 40-year-old female presented with the complaint of pain in both the legs for the past 1 month, especially in both calf muscles. The pain was of a continuous, aching character aggravated with movement and not relieved completely even by analgesics. The patient was unable to walk for the same duration. On further inquiry, it was found that she was also unable to stand from squatting for the past 1½ months. She also complained of tingling sensations in her feet. She had been admitted to a local hospital 6 months back with severe shortness of breath for 7 days along with a history of intermittent low-grade evening rise of temperature and cough for 15 days. On subsequent investigations, she was diagnosed to be immunocompromised with *Pneumocystis jiroveci* pneumonia. At that time, her CD4 count was only 7/µl. She was non-diabetic, non-hypertensive, and euthyroid. There was no history of imbalance, vertigo, headache, vomiting, convulsion, back pain, diurnal variation of weakness, or history suggestive of cranial nerve disorders. Bladder and bowel habits were normal.

On general examination, the patient was alert, conscious, and well oriented. She had poor nutrition (body mass index or BMI 15.3 kg/m^2) and pallor. The pulse was 96/min, regular, normal volume, and BP was 100/60 mmHg in the right arm in the supine posture. Respiratory rate was 16/min, which was of thoracoabdominal. Tenderness was present over both calf muscle regions. Examination of the nervous system revealed decreased tone in all four limbs; power was 4/5 in distal muscles and (4-)/5 in proximal muscles in all the four limbs. All jerks were preserved except both the ankle jerks. There was some distal sensory loss bilaterally in the lower limbs.

On investigations, hemoglobin was 6.3 g/dl, packed cell volume 22.8%, mean corpuscular volume 108.1 fl, mean corpuscular hemoglobin 29.9 pg/dl, and mean cell hemoglobin concentration 27.6 g/dl. Peripheral blood smear showed macrocytic normochromic anemia with anisopoikilocytosis. Complete blood count was otherwise non-contributory. Electrolytes level, liver function test, renal function test, and lipid profile tests were found normal. Serum phosphate was 4.0 mg/dl, calcium was 7.8 mg/dl, and Vitamin D3 was 43.53 ng/ml. Free T4 was 1.02 ng/dl, and thyroid-stimulating hormone was 13.2 µIU/ml. The serum creatine phosphokinase was 498 U/L (normal level up to 167), and C-reactive protein 6.58 mg/dl (<0.3 mg/dl). Antinuclear antibodies was negative, p-ANCA- 4+, but the levels of myeloperoxidase and PR3 were negative. Serum folate level was 1.73 ng/ml (2–20 ng/ml), and serum Vitamin B12 was >200 ng/ml (200–900 ng/ml). Latest CD4 cell count was found to be 50 cells/µl. Ultrasonogram (USG) of both the legs

revealed heterogeneous hypoechoic lesions noted in between calf muscle region without any obvious collection. Magnetic resonance imaging (MRI) of both the lower limbs showed extensive muscle edema with shaggy intermuscular planes in calf muscles and thigh as well. No marrow edema was found. Normal cortices of bones were reported (Figs. 1 and 2).

Electromyogram (EMG) was suggestive of the myopathic pattern. Antibody for myositis, i.e., anti-Jo 1 and overlap of systemic sclerosis and myositis, i.e., anti PM/Scl were sent but came to be non-contributory. Muscle biopsy was done and histopathology report of formalin-fixed skeletal muscle showed

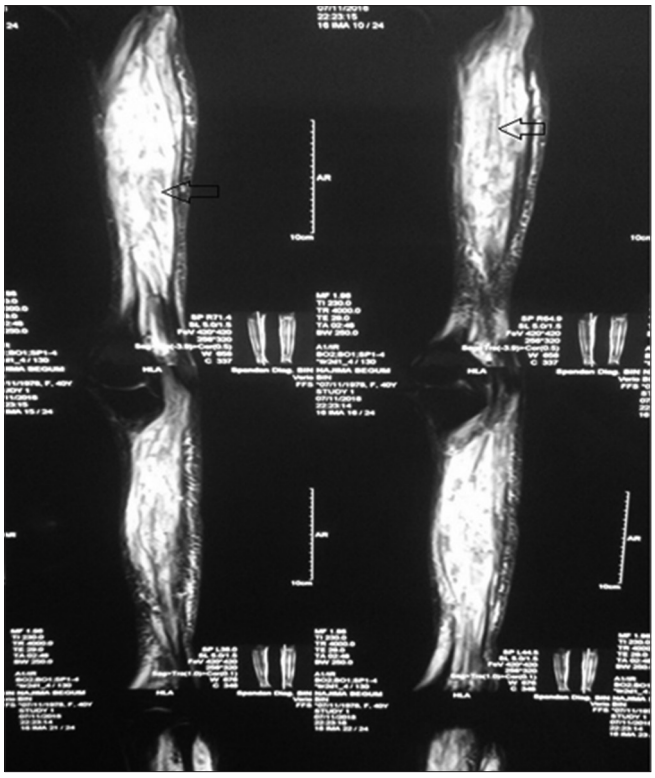

Figure 1: Magnetic resonance imaging of calf muscles' longitudinal cut showing extensive muscle edema with shaggy intermuscular planes

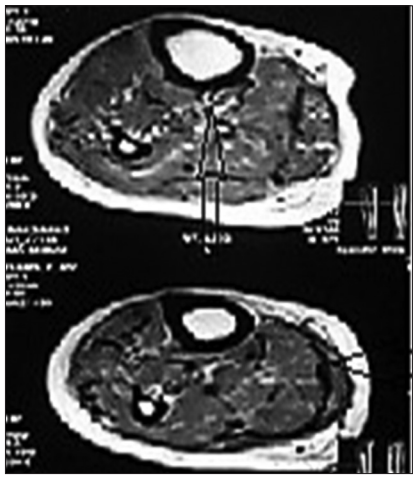

Figure 2: Magnetic resonance imaging of thigh muscles' transverse cut showing patchy areas of muscle edema and no marrow edema with normal cortices

longitudinally, obliquely, and transversely cut fibers. Myofibers were polygonal with internalized nuclei. The fascicular architecture was partly effaced by fat infiltration. There was marked edema separating the muscle fibers. Polyfocal necrosis and myophagocytosis were present. Scattered atrophic fibers were present. Several of the myofibers were bloated and showed clusters of pale oval bodies (spores) 2–3 μ wide and 3–5 um in length in the sarcoplasm. These microsporidial spores were highlighted on special stains and were of red color (weak acid fast), black color (Grocott-Gomori's methenamine silver stain [GMS]), and magenta color (Periodic Acid Schiff). The spores showed dark staining at the narrow end or waistband area close to the tip. There was no evidence of budding in these spores. Mild interstitial and perivascular lymphoplasmacytic and histiocytic inflammatory infiltrate was seen. There were no eosinophils, giant cells, or neutrophils. The inflammatory response to the pathogen was minimal considering the immunocompromised status of the patient. Masson's trichrome stain highlighted the microspoidial spores as red color. There were mild endomysial creeping fibrosis and focal fat infiltration.

Based on the above-mentioned clinical, radiological, and histological investigations, a diagnosis of myositis and IRIS was made and the patient was put on oral albendazole therapy along with the antiretroviral therapy (ART) and sulfadiazine pyrimethamine. Unfortunately, the patient suddenly developed acute onset, progressive weakness of all four limbs after 7 days. Deep tendon reflexes were absent in all four limbs. No sensory involvement or bladder and bowel involvement was found. Examination of the patient showed acute onset areflexic quadriparesis without any sensory and bladder and bowel involvement. Nerve conduction study documented acute motor axonal polyradiculoneuropathy.

The sequence of events led to the marked clinical deterioration of the patient. She was put on intravenous immunoglobulin G (IVIG) after consulting neurologist. The improvement was suboptimal even though the patient was on albendazole, sulfadiazine pyrimethamine IVIG, and ART. The possibility of IRIS was considered, and a cautious dose of steroids was added. Thereafter, the patient started to improve significantly. The patient was found asymptomatic on further follow-up at 3 months.

DISCUSSION

The rapid decrease in viral load after starting ART leads to the phenomenon of IRIS comprising clinical deterioration, opportunistic infections, and autoimmune phenomena. The CD4 count of our patient had improved from 7 to 50 in 6 months, but she deteriorated due to the acute inflammatory demyelinating polyneuropathy (AIDP) and microsporidial infection. Microsporidia are obligate intracellular parasites now classified as fungi. The sources of fungal spores are water, undercooked food, and pets [3]. The majority of microsporidial infections involve the small gut gallbladder, sinuses, cornea, urinary, and respiratory tracts [4]. Involvement of muscles by this organism is extremely rare.

The first case was reported in an AIDS patient in 1985 [2]. Since then, isolated anecdotal reports have been published regarding microsporidial myopathy. The incriminated species are Trichopleistophora hominis, Pleistophora ronneafiei, Brachiola vesicularum, and Tubulinesema acridophagus [5-9]. No specific culture or serological test is available, and species are the only electron microscopically identified.

On presentation, our initial impression of the patient was that her muscle involvement was a part of the human immunodeficiency virus spectrum. However, the new onset of severe myalgia and weakness in 2 months led us to look for other causes. Marked pain and tenderness of calves may be due to pyomyositis, inflammatory muscle disease, deep venous thrombosis, and painful neuropathy [10-12]. USG Doppler study of the legs gave us the first clue to look for myositis which was later confirmed by MRI, EMG, and biopsy.

CONCLUSION

Treatment of the immunocompromised patients even after diagnosis poses many challenges to the clinician. The development of AIDP after starting therapy for microsporidiosis as a result of IRIS demonstrates the immense complexity in the treatment strategy of AIDS patients where a fine balance is to be struck to get optimum results.

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