CASE REPORT

HISTOPLASMOSIS MYOSITIS: A CASE REPORT AND LITERATURE REVIEW

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Abstract. Disseminated histoplasmosis is an AIDS-defining illness that can affect multiple organ systems. Myositis due to histoplasmosis is rare in HIV infected patients. We report here an HIV-infected patient who presented with myositis caused by *Histoplasma capsulatum*. Her HIV was under poor control and her CD4 cell count was only 11 cells/mm^3. She responded well to treatment but later succumbed to another opportunistic infection. The literature on disseminated histoplasmosis is reviewed.

Keywords: *Histoplasma capsulatum*, AIDS, myositis

INTRODUCTION

Histoplasmosis is an opportunistic infection caused by *Histoplasma capsutalum*, a dimorphic fungus (De Monbreun, 1934). The disease is usually asymptomatic but disseminated histoplasmosis may occur among immunocompromised individuals including those with AIDS, hematologic malignancies and post-transplantation (Kauffman *et al,* 1978; Wheat *et al,* 1983; Wheat *et al*, 1990). Patients with histoplasmosis commonly presented with fever, cough, dyspnea, hepatosplenomegaly and lymphadenopathy (Kauffman, 2007). There are only a few reports of Histoplasma myositis in the literature (Voloshin *et al*, 1995; Wagner *et al*, 1996; Goel *et al*, 2007; Bourre'-Tessier *et al*, 2009). Of these, only one case occurred in an HIV-infected person (Goel *et al*, 2007). We describe here a case of myositis caused by *H.capsulatum* in an AIDS patient.

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CASE REPORT

The patient is a 33-year-old Thai female who had a history of HIV infection for 18 years. She was started on treatment with GPO-VIR-S (stavudine, lamivudine and nevirapine) in December 2005 at which time she had a CD4 T-lymphocyte count of 106 cells/mm^3 (15%). One year later, her antiretroviral therapy (ART) was changed to GPO-VIR-Z (zidovudine, lamivudine and nevirapine) due to lipodystrophy. She apparently did well on this new regimen and her CD4 T-lymphocyte count increased to 321 cells/mm^3 by April 2008. However, her CD4 T-lymphocyte count decreased to 103 cells/mm^3 in October of 2008 and 85 cells/mm^3 in January 2009. Despite an

undetectable viral load, the physician was concerned about immunological failure, and her regimen was changed to tenofovir, lamivudine and ritonavir-boosted indinavir in January 2009. Unfortunately, she discontinued the ART and was lost to follow-up because of economic problems.

The patient presented to our hospital in May 2012 with a 3 month history of low-grade fever, headache, and diffuse myalgia. The rest of her history was unremarkable. On examination, her temperature was 38ºC, heart rate was 80/min, blood pressure was 110/80 mmHg and respiratory rate was 20/min. No abnormalities were found in the oral cavity except for oral candidiasis. The cardiovascular and respiratory examinations revealed no apparent abnormalities. There was no hepatosplenomegaly or lymphadenopathy. She was conscious with no sign of meningeal irritation. Her strength was 5/5 for all extremities. Her deep tendon reflexes and sensory examination were normal and the Babinski's sign was negative.

Her complete blood count (CBC) revealed a hemoglobin (Hb) level of 11.3 g/dl, a platelet count of 221,000 cells/mm^3, and a white blood cell count (WBC) of 5,420 cells/mm^3 (88% neutrophils, 9% lymphocytes, 2% eosinophils and 1% monocytes). Her liver function tests were: albumin of 4 g/dl, globulin of 4 g/dl, alkaline phosphatase of 130 U/l, aspatate aminotransferase (AST) of 85 U/l and alanine aminotransferase (ALT) of 96 U/l. Her CD4 T-lymphocyte count was 11 cells/mm^3. Her chest X-ray was normal. A computed tomography scan of her brain demonstrated mild dilatation of the third ventricle and a lacunar infarction in the left pons. A lumbar puncture was done and the opening pressure was 12 cmH_20. The cerebrospinal fluid (CSF) showed no white blood cells, the protein was 43 mg/dl, the glucose was 56 mg/dl (the serum glucose was 87 mg/dl). The CSF PCR for *Mycobacterium tuberculosis* (TB) and cryptococcal antigen were negative.

While awaiting the CSF culture results, the patient was diagnosed with TB meningitis and anti-TB drugs (isoniazid, rifampicin, pyrazinamide and ethambutol) were prescribed. Her headache then improved but her fever and muscle pain grew worse. Her muscle strength deteriorated to 4/5 in the upper extremities and 3/5 in the lower extremities. A repeat CBC revealed a Hb level of 7.4 g/dl, a platelet count of 195,000 cells/mm^3, and a wbc count of 2,880 cells/mm^3 (85% neutrophils, 8% lymphocytes, 5% monocytes and 2% eosiophils). A bone marrow study demonstrated normocellularity. There were no granulomas or organisms seen.

A muscle biopsy was performed, which revealed foamy histiocytes packed with multiple intracellular, oval shaped, yeast-like organisms compatible with *H.capsulatum* (Fig 1a,b,c). The patient was then diagnosed with histoplasma myositis. The patient was treated with amphotericin B 0.7 mg/kg/day for 2 weeks. The patient responded well to therapy, her muscle pain subsided by 1 week. She was discharged home on itraconazole oral solution (400 mg daily). She was given combination ART (tenofovir, lamivudine, ritonavir-boosted lopinavir) and itraconazole for 4 weeks. Four weeks later her CD4 T-lymphocyte count had increased to 15 cells/mm^3. Unfortunately, she developed community acquired pneumonia and sepsis and died 3 months after being diagnosed with histoplasma myositis.

DISCUSSION

Determining the etiology of myopathy among HIV-infected patients is cru-

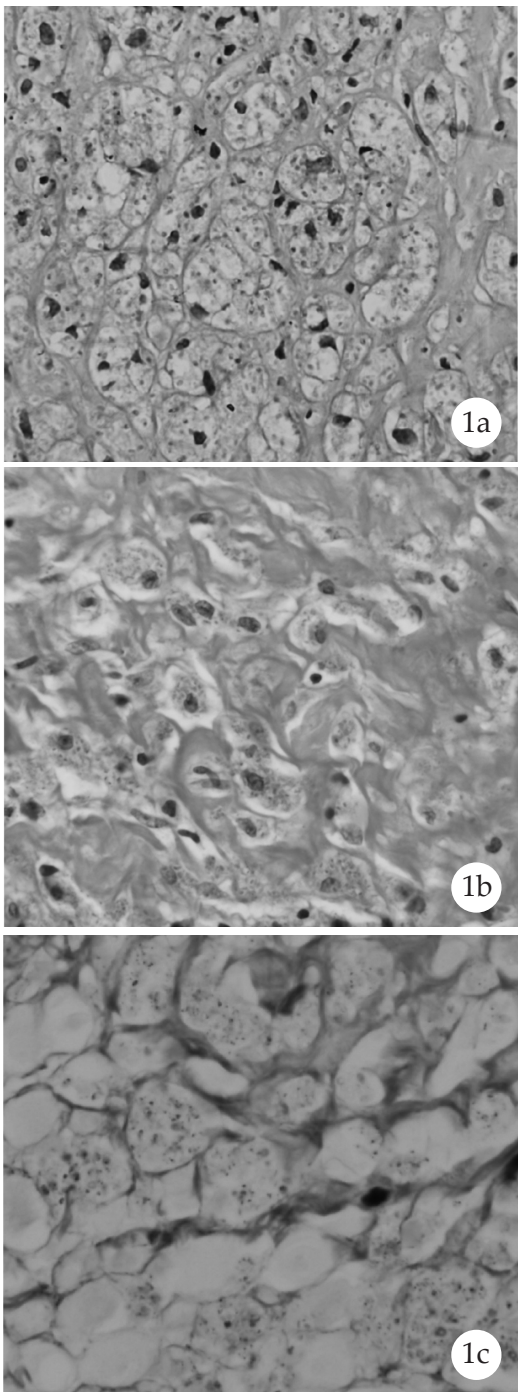

Fig 1–Multiple intracellular, oval shaped, yeast liked organisms within histiocytes. (1a) Hematoxylin and eosin staining. (1b) Periodic acid-Schiff staining. (1c) Gomori methenamine silver staining.

cial, since there are a variety of etiologies. These included disorders unrelated to HIV infection, such as endocrine disorders (thyroid, parathyroid, adrenal and pituitary diseases), inflammatory myopathies, electrolyte abnormalities (hypokalemia) and drug-induced myopathies (such as, due to corticosteroids, statins, colchicine and chloroquine); disorders related to HIV infection include those directly associated with HIV infection (HIV-associated polymyositis), adverse effects of ART (zidovudine) and opportunistic infections (Colmegna *et al*, 2006; Chawla, 2011; Louthrenoo *et al*, 2008). Many infectious agents can cause myositis, such as bacteria, parasites and viruses. Although fungal myositis is uncommon, there have been reports of fungal myositis caused by *Cryptococcus neoformans, Histoplasma capsulatum*, *Aspergillus* spp and *Pneumocystic jiroveci* (Crum-Cianflone *et al*, 2010).

Histoplasmosis is a granulomatous disease caused by *H.capsulatum*. Infection is usually contracted through inhalation of the spores from soil contaminated with organisms (Goodwin *et al*, 1981). Clinical presentations varies from asymptomatic to progressive severe disease and commonly affects immunosuppressed individuals, including those infected with HIV, transplant recipients, those with hematologic malignancies and those on immunosuppressive agents (Kauffman *et al*, 1978; Wheat *et al*, 1983; 1990). Virtually any organ system may be involved; common symptoms include fever, diarrhea, cough, hepatosplenomegaly, lymphadenopathy, mucous membrane ulcerations, skin lesions (ulcers, nodules and molluscum-like papules) and pancytopenia (Mootsikapun and Srikulbutr, 2006; Kauffman, 2007; Rangwala *et al*, 2012).

Myositis is a rare manifestation of disseminated histoplasmosis, only 4 cases

Table 1
Reported cases of histoplasma myositis.

Author, Year	Age (y), sex	Underlying disease/ risk factor	Prominent clinical features	Duration of illness	Diagnosis	Antifungal therapy	Outcome
Voloshin *et al*, 1995	54, M	Dermatomyositis, corticosteroids	Fever, myalgia, weakness, necrotizing fasciitis of gluteus muscle	ND	Muscle biopsy, culture	Antifungal therapy	ND
Wagner *et al*, 1996	ND	Renal transplant recipient	Necrotizing fasciitis of upper limb	ND	ND	Surgical debridement, Amphotericin B	Death
Goel *et al*, 2007	42, M	HIV infection, CD4 66 cells/mm^3	Fever, myalgia, lower limb weakness, multiple painful nodules	ND	FNA	Fluconazole	Improved
Bourré-Tessier *et al*, 2009	67, M	RA, TNFα inhibitor	Panniculitis, focal myositis of left arm and leg, no fever	1 month	Muscle biopsy, culture	Itraconazole	Improved
This study	33, F	HIV infection, CD4 11 cells/mm^3	Fever, myalgia, generalized weakness	3 month	Muscle biopsy	Amphotericin B and itraconazole	Death

M, male; F, female; ND, no data available; RA, rheumatoid arthritis; FNA, fine needle aspiration.

have been reported in the English literature (Table 1). The first case was reported in 1995. Only 1 of the 4 reported cases had HIV infection. The most common symptoms include fever (80%), myalgia (60%) and weakness (60%) (Voloshin *et al*, 1995; Wagner *et al*, 1996; Goel *et al*, 2007; Bourré-Tessier *et al*, 2009). Other manifestations included necrotizing fasciitis (40%), multiple painful nodules (20%), panniculitis and focal myositis (20%) (Voloshin *et al*, 1995; Wagner *et al*, 1996; Goel *et al*, 2007; Bourré-Tessier *et al*, 2009). Diagnosis is made by obtaining tissue samples for morphological examination and fungal culture (Voloshin *et al*, 1995; Wagner *et al*, 1996; Goel *et al*, 2007; Bourré-Tessier *et al*, 2009). Unfortunately, not all the reported cases provided information about demographics, duration of infection or outcomes. Of the patients for whom the clinical outcome was available, 2 (of 3) died (Wagner *et al*, 1996; Goel *et al*, 2007; Bourre'-Tessier *et al*, 2009).

In conclusion, we describe severely immunosuppressed HIV-infected patient presented with myositis due to *H.capsulatum*. Prompt and accurate diagnosis is crucial. A high index of suspicion for this infection is needed; diagnosis is typically confirmed by histopathology and fungal culture.

REFERENCES

Bourré-Tessier J, Fortin C, Belisle A, Desmarais E, Choquette D, Senecal JL. Disseminated *Histoplasma capsulatum* infection presenting with panniculitis and focal myositis in rheumatoid arthritis treated with etanercept. *Scand J Rheumatol* 2009; 38: 311-6.

Chawla J. Stepwise approach to myopathy

in systemic disease. *Front Neurol* 2011; 2: 49.

Colmegna I, Koehler JW, Garry RF, Espinoza LR. Musculoskeletal and autoimmune manifestations of HIV, syphilis and tuberculosis. *Curr Opin Rheumatol* 2006; 18: 88-95.

Crum-Cianflone NF. Nonbacterial myositis. *Curr Infect Dis Rep* 2010; 12: 374-82.

De Monbreun WA. Cultivation and cultural characteristics of Darling's *Histoplasma capsulatum. Am J Trop Med Hyg* 1934; S1-14: 93-125.

Goel D, Prayaga AK, Rao N, Danodaram P. Histoplasmosis as a cause of nodular myositis in an AIDS patient diagnosed on fine needle aspiration cytology. A case report. *Acta Cytol* 2007; 51: 89-91.

Goodwin FA, Loyd JE, Des Prez RM. Histoplasmosis in normal hosts. *Medicine* (Baltimore) 1981; 60: 231-66.

Kauffman CA. Histoplasmosis: a clinical and laboratory update. *Clin Microbiol Rev* 2007; 20: 115-32.

Kauffman CA, Israel KS, Smith JW, White AC, Schwarz J, Brooks GF. Histoplasmosis in immunosuppressed patients. *Am J Med* 1978; 64: 923-32.

Louthrenoo W. Rheumatic manifestations of human immunodeficiency virus infection. *Curr Opin Rheumatol* 2008; 20: 92-9.

Mootsikapun P, Srikulbutr S. Histoplasmosis and penicilliosis: comparison of clinical features, laboratory findings and outcome. *Int J Infect Dis* 2006; 10: 66-71.

Rangwala F, Putcharoen O, Bowonwatanuwong C, *et al*. Histoplasmosis and penicilliosis among HIV-infected Thai patients: a retrospective review. *Southeast Asian J Trop Med Public Health* 2012; 43: 436-41.

Voloshin DK, Lacomis D, McMahon D. Disseminated histoplasmosis presenting as myositis and fasciitis in a patient with dermatomyositis. *Muscle Nerve* 1995; 18: 531-5.

Wagner JD, Prevel CD, Elluru R. *Histoplasma capsulatum* necrotizing myofasciitis of the upper extremity. *Ann Plast Surg* 1996; 36: 330-3.

Wheat LJ, Smith EJ, Sathapatayavongs B, *et al*. Histoplasmosis in renal allograft recipients. Two large urban outbreaks. *Arch Intern Med* 1983; 143: 703-7.

Wheat LJ, Connolly-Stringfield PA, Baker RL, *et al*. Disseminated histoplasmosis in the acquired immune deficiency syndrome; clinical findings, diagnosis and treatment, and review of the literature. *Medicine* (Baltimore) 1990; 69: 361-74.