CASE REPORT

Muscular sarcocystosis: an index case in a native Malaysian

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SUMMARY

A previously healthy 20-year-old man presented with prolonged intermittent low grade fever and cough for 6 months. He had bilateral calf pain and lower limb weakness 2 days prior to admission. Physical examination revealed multiple enlarged lymph nodes with hepatomegaly. There was bilateral calf tenderness with evidence of proximal myopathy. Full blood picture showed lymphocytosis with reactive lymphocytes and eosinophilia. Creatine kinase and lactate dehydrogenase were markedly elevated. Over 2 weeks of admission, patient was treated symptomatically until the muscle biopsy of right calf revealed eosinophilic myositis with muscular sarcocystosis. He was treated with albendazole and high-dose corticosteroids. Symptoms subsided on reviewed at 2 weeks and the dose of corticosteroid was tapered down slowly over a month. Due to poor compliance, he was readmitted 1 month later because of relapsed. High-dose corticosteroid was restarted and duration for albendazole was prolonged for 1 month. His symptom finally resolved over 2 weeks.

BACKGROUND

Human muscular sarcocystosis is a rare infection caused by coccidian parasites in the family of Sarcocystidae. *Sarcocystis* species are an intracellular protozoan, classically have a life cycle based on a prey–predator relationship. Humans may be involved either as definitive or intermediate hosts. Humans succour as definite hosts for *Sarcocystis hominis* and *S. suihominis* acquired after eating indecorously cooked sarcocyst-infected beef or pork. Likewise, humans may also aid as accidental intermediate hosts for other *Sarcocystis* species by consuming food or drinks contaminated by sporozoites, leading to muscular sarcocystosis.¹

As a disease, sarcocystosis is notable in diversity of animals² but symptomatic human disease seems to be less common, with lesser than 150 cases described in the literature. The typical biphasic pattern of muscular sarcocystosis are the initial flu-like symptoms and second, the chronic phase of eosinophilic myositis.³ Corresponding to this biphasic clinical aspect is the biphasic cytokine response.⁴ This serves as important highlight for potential treatment. The initial phase may to some extent be curable with antiparasitic medicine, whereas in chronic myositis phase the symptoms seems to arise from overacting of human immune system. The cornerstone of treatment is corticosteroids.

It is also difficult to establish the prevalence of incidental sarcocystosis in humans. This case highlights necrotising eosinophilic myositis in a previously healthy man, suggesting that sarcocystis infection may result in a remarkable prolonged clinical illness in humans. This case also reflects that it may occur in isolation without being caused by a postexposure outbreak, making the diagnosis difficult due to lack of suspicion.

CASE PRESENTATION

A previously healthy 20-year-old male Malay presented to our hospital in July 2015 with a main complain of intermittent fever which was relieved only temporarily with antipyretic. The fever was primarily during mid-day which lasted for 2 to 3 days and associated with non-productive cough for total of 6 months duration. He had no significant weight lost, night sweats, recent travelling to neighbouring areas and tuberculosis contact. The patient also had bilateral lower limb weakness, malaise and lethargy for the past 2 months prior to admission, which restricted him from sport events and normal activities of daily living. He had received multiple antibiotic cycles, since the onset of fever, although it never subsided. He denied high-risk behaviour, smoking and alcohol intake. He comes from East Coast of Peninsular Malaysia and he is a student. His late mother died due to parotid carcinoma. On further questioning, he recently went camping at a waterfall with his friends and had barbecues at the camping site. However, none of his companions were sick.

On physical examination, he had low-grade temperature with multiple enlarged lymph nodes in the cervical and inguinal regions with hepatomegaly. There was also bilateral calf tenderness with symmetrical weakness of both proximal upper and lower limbs. Other physical examinations were unremarkable.

INVESTIGATIONS

Initial blood investigations showed leucocytosis with predominant lymphocyte. Full blood film revealed eosinophilia with no obvious dysplastic features. Erythrocyte sedimentation rate was elevated (150 mm/hour), C reactive protein was high (100 mg/L). Sputum for acid-fast bacilli and Mantoux test for tuberculosis screening were negative. Antinuclear antibody and extractable nuclear antigen were also negative. Serology tests including

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Table 1 Laboratory results

	24/3	20/7	28/7	3/8	6/8	7/8	8/8	9/8	10/8
Total protein (60 to 83 g/L)	78	69	68	76	67	74	75	64	60
Albumin (35 to 55 g/L)	44	38	44	41	37	41	42	36	34
Aspartate aminotransferase (10 to 40 IU/L)	251	68	48	68	959	1865	2946	2670	989
Alkaline phosphate (44 to 147 IU/L)	159	127	105	100	83	93	104	81	76
Alanine aminotransferase (7 to 56 IU/L)	318	52	39	27	170	415	787	846	751
Total bilirubin (0.3 to 1.9 mg/dL)	9	5	5	8	13	10	8	5	4
Creatine kinase (38 to 174 U/L)		2669			42 670	>42 670		>42 670	
Lactate dehydrogenase (140 to 280 U/L)		789	747		3704			10 354	

hepatitis C and B, HIV and syphilis were all unremarkable. No pathogens were isolated from blood and urine cultures.

Table 1 showed abnormal liver function, markedly raised creatine kinase (CK) and lactate dehydrogenase (LDH) levels.

Ultrasound of neck revealed multiple shotty cervical lymph nodes with the largest measuring (5 mm x 2.7 mm x 7.8 mm). Ultrasound of abdomen has shown hepatomegaly. MRI of bilateral thigh muscles demonstrated symmetrical heterogeneous increase in signal intensity of bilateral thigh muscles with subcutaneous fluid on lateral and posterior aspects of both thighs consistent with polymyositis (figure 1). Ultimately, histopathology examination of right thigh biopsy confirmed diagnosis with sarcocyst seen within a muscle fibre. (figure 2)

DIFFERENTIAL DIAGNOSIS

- ▶ Autoimmune myositis;
- ▶ Infective myositis such as toxocariasis, trichinellosis, leptospirosis, rickettsial disease and toxoplasmosis;
- ▶ Drugs such as alcohol, cocaine, antimalaria, penicillamine, statin may induced myositis;
- ▶ Toxin-induced myositis for example in Haff disease; Haff disease is an unexplained acute rhabdomyolysis following ingestion of shellfish or fresh water fish. This is unlikely in our patient as he has no history of fish ingestion or rapid deterioration of rhabdomyolysis symptoms and signs.

Other differentials such as dengue and chikungunya were unlikely in this case because of duration of fever. These two viral infections, though common in this region, are very unlikely

to be more than 7 days duration even though in chikungunya arthralgia may persist up to 6 weeks despite resolution of fever.

TREATMENT

Patient was given bolus intravenous hydrocortisone 100 mg thrice daily for 5 days followed by oral prednisolone 60 mg daily. Oral albendazole 400 mg twice daily for 1 month was commenced.

OUTCOME AND FOLLOW-UP

During admission, the patient's initial symptoms resolved with liver enzymes normalisation. He remained afebrile after commencement of treatment throughout his hospital stay. He was followed up in our clinic 2 weeks later and his oral prednisolone was reduced 10 mg every fortnightly. However, he was readmitted again 1 month later for symptom relapsed likely because he missed the medications. CK was again elevated. Inevitably he was given intravenous hydrocortisone for 5 days followed by high-dose oral prednisolone and albendazole similar to previous regime.

He was seen in outpatient clinic and was started on oral azathioprine 50 mg daily then increased to 100 mg daily. He was no longer on albendazole. Azathioprine was started as a steroid sparing agent. Prednisolone was gradually tapered to 5 mg daily. We planned to repeat his muscle biopsy to see evidence of histological improvement in a few months time.

DISCUSSION

South-East Asia has a highest prevalent of human muscle sarcocystosis. The spectrum of acute muscular sarcocystosis in humans may range from asymptomatic, which may characterise most infected patients⁵⁻⁷ to debilitating and relapsing illness lasting for years.⁸ The amplified prevalence of muscle infection in Malaysia propose that muscular sarcocystosis is a common aetiology;

Figure 1 MRI bilateral thigh (axial T2 turbo spine view). Symmetrical heterogeneous increase in signal intensity of bilateral thigh muscles with subcutaneous fluid on lateral and posterior aspects of both thighs consistent with polymyositis (arrow).

Figure 2 A single sarcocyst (arrow) within a muscle fibre. There is a mild myositis near the sarcocyst. H&E stains: x40 objective lens.

however, rarely recognised and reported especially in native Malaysians.

A large clustered outbreak of acute muscular sarcocystosis was reported by Mark K Arness *et al* in 1999 involving six American military servicemen involved in a Malaysian jungle mission.⁹ Clinically most of them had prolonged fever, muscle aches and bronchospasm while the laboratory markers showed elevated eosinophil counts and abnormal liver enzymes. Sarcocysts of an undetermined *Sarcocystis* species were demonstrated in skeletal muscle biopsies of the index case.

The largest recent outbreaks was from Tioman Island, Malaysia which reported more than 100 foreign persons with an acute muscular Sarcocystis-like illness after returning from Tioman Island between 2011 and 2012. This report suggested either possible re-emergence of infection or increase recognition of endemic disease; whereby infection in this outbreak was likely due to consumption of water contaminated by snake faeces or consumption of raw food.

Another major outbreak of sarcocystosis in human ever described was possibly due to the infection caused by *Sarcocystis nesbitti* as the aetiological pathogen. This outbreak involved 89 patients including college students and teachers after retreat in Pangkor Island, Malaysia in January 2012.¹⁰

As clinical and laboratory investigations may be non-specific, isolated cases of muscular sarcocystosis could be easily missed, hence the condition can easily be under diagnosed. Our patient presented with non-specific symptoms, fever of unknown origin together with myalgia, making initial diagnosis difficult. Further evidence of myositis supported with elevated liver function test, creatine kinase, eosinophilia and lymphocytosis were then suggestive of diagnosis. The risk of exposure in our patient was probably the ingested contaminated food during his camping event. He might also exposed to drinking contaminated water at the waterfall during the event. Subsequent MRI demonstrating myositis correlates with our diagnosis. Histopathology examination of muscle biopsy demonstrated pericyclic inflammation suggestive of sarcocystocytes within a muscle fibre. PCR was negative. We are unable to proceed with species differentiation on the muscle biopsy. However, the pathological findings in this patient were morphologically similar to the previously reported human cases from Malaysia with myositis and eosinophilia, having the same characteristic disseminated foci of sarcocystis, cyst morphology and pericyclic inflammation.^{9–11}

We concluded that muscular sarcocystis was the aetiological agent of the eosinophilic myositis syndrome of this patient, based on simultaneous onset of symptoms and/or laboratory abnormalities and identical clinical features. This is yet another case of muscular sarcocystosis in Malaysia. Although few outbreaks were reported in this country, the rarity of this case is our utmost interest. Moreover, there have been no conclusive recommendations for the treatment of sarcocystosis. Although previous reports highlights the possibility of clinical improvement with steroids and albendazole but recovery was not rapid.

Recognising the biphasic nature of cytokine responses in muscular sarcocystosis, there may be only a short window of opportunity for curative treatment during the acute/intermediate phase with antiparasitic treatment. And, it seems that the only immunomodulatory treatment of choice in the chronic phase is the immunosuppression (corticosteroids). Therefore, a prolonged antiparasitic cycle are unlikely to confer benefits due to the dormant stage of the parasites within the sarcocystocytes without relevant metabolism. Nevertheless, we elected to use short-term albendazole in

combination with corticosteroids and using azathioprine thereafter as steroid sparing agent in our patient. It is uncertain whether this treatment will cure systemic infection with *Sarcocystis*, but it did appeared to have clinical benefit evidenced by laboratory and symptomatic improvement in our patient.

It is also noted that most reported symptomatic cases previously have been showing predilection towards travellers and expatriates, signifying that there may be a role of host immunity in disease manifestations in high prevalence countries like Malaysia. However, this would need further studies to prove. We also plan to repeat the muscle biopsy after maintenance phase to see whether sarcocyst remains despite improvement of clinical symptoms.

Learning points

- Muscular sarcocystis is a rare parasitic disease in Malaysia caused by sarcocystis species in humans as an accidental intermediate host.
- Although typically reported as incidental findings, this case reflects it may also cause a remarkable prolonged clinical illness in humans.
- Increased awareness is important in muscular sarcocystosis infection especially in patients who have recently lived in or travelled to Southeast Asia.
- Typical clinical symptoms and laboratory findings are myositic complaints with eosinophilia and elevated muscle enzymes.
- Muscle biopsy remains as a gold standard for confirmation of diagnosis.
- *Sarcocystis* eosinophilic myositis is a potential threat to indigenous population in regions with poor sanitation.

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