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Case Report

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Myositis and rhabdomyolysis in scrub typhus infection: A case report

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ABSTRACT

Rationale: Fever with myositis and rhabdomyolysis is a medical emergency requiring prompt diagnosis and management. Scrub typhus associated myositis with rhabdomyolysis is rare.

Patient concerns: A 36-year-old female presented with intermittent fever up to 38.6 °C, jaundice and progressive weakness of all four limbs.

Diagnosis: Scrub typhus associated myositis and rhabdomyolysis.

Intervention: Doxycycline 100 mg twice daily and injection of ceftriaxone 1 gm twice daily along with continuous intravenous fluids.

Outcome: Fever resolved with normalization of liver function and recovery of muscle power.

Lessons: Presence of myositis and rhabdomyolysis is uncommon in scrub typhus; high clinical suspicion should be kept in patients with atypical manifestations of scrub typhus.

KEYWORDS: Scrub typhus; Myositis; Rhabdomyolysis; Doxycycline; Transaminitis; Vasculitis

1. Introduction

Scrub typhus infection has re-emerged as an important cause of acute febrile illness in South East Asia. It is caused by *Orientia tsutsugamushi* and spread by the bite of the larval form of the *Leptotrombidium* mite, called 'chigger'. Scrub typhus is prevalent in distinct geographical region, termed 'tsutsugamushi triangle', which includes Pakistan and Afghanistan in the West, Japan and Russia in the North, and Australia in the South[1]. Organism primarily infects the endothelial cells. It leads to activation of endothelial cells causing adhesion of leucocytes, transmigration, platelet aggregation and cytokine release resulting in various complications. Scrub typhus is usually categorized by the acute febrile illness with chills, rash and eschar. Myositis or rhabdomyolysis associated with renal involvement in scrub typhus has been sporadically reported in literature[2–6]. Here, we report a case of scrub typhus infection in a female in her mid-30s presenting with myositis and rhabdomyolysis.

2. Case presentation

A 36-year-old female with a history of hypothyroidism and bicuspid aortic valve with severe aortic stenosis, and moderate aortic regurgitation was admitted with an intermittent fever up to 38.6 °C, jaundice associated with insidious onset, gradually progressive weakness of all 4 limbs. On examination, she was hemodynamically stable, had icterus with tenderness, and decreased power all over the muscle groups (proximal>distal). Motor power at bilateral shoulders was 4/5, bilateral hip flexors were 2/5, and bilateral knees were 3/5. The sensory system, cranial nerve examination, and cerebellar system were normal. Laboratory investigations showed hemoglobin of 9.4 gm/dL (normal range: 12-16 g/dL), total leucocyte count of $12.5 \times 10^9/L$ (normal range: $4.0-11.0 \times 10^9/L$), platelet count of $272 \times 10^9/L$ (normal range: $150-450 \times 10^9/L$), elevated C-reactive protein: 28.96 mg/L (normal range: 0-5 mg/L), serum creatinine: 1.5 mg/dL (normal range: 0.5-1.2 mg/dL), total bilirubin: 13.2 mg/dL (normal range: 0.2-1.2 mg/dL) conjugated bilirubin: 8.9 mg/dL (normal range: 0-0.3 mg/dL), aspartate aminotransferase: 1411 U/L (normal range: 2-40 U/L), alanine aminotransferase: 571 U/L (normal range: 2-41 U/L), alkaline phosphatase: 785 U/L (normal range: 42-128 U/L), elevated creatinine kinase enzyme: 34341 U/L (normal range: 26-308 U/L), serum myoglobin: 37462 ng/mL (normal range: 25-58 ng/mL) and urine myoglobin: 1046 ng/mL (normal range: none) all of which are indicative of rhabdomyolysis.

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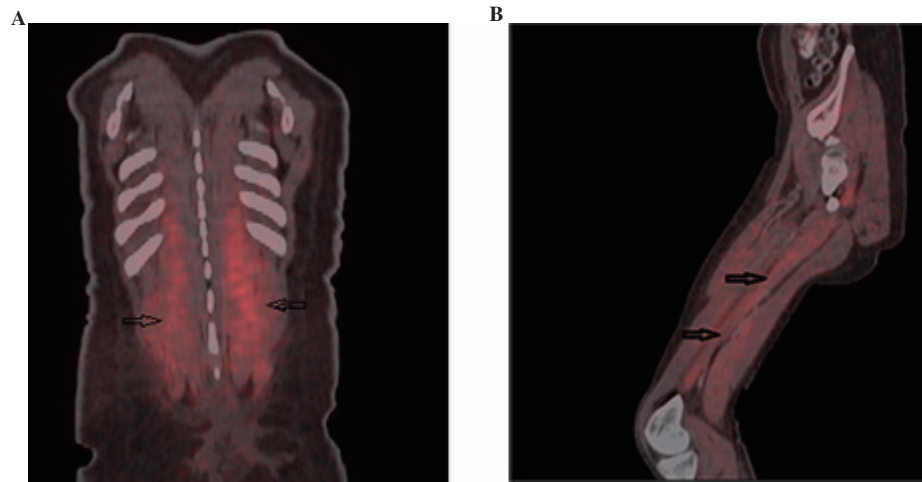


Figure 1. Whole body positron emission tomography scan of a 36-year-old female with scrub typhus and myositis. A) Increased fluorodeoxyglucose uptake noted in latissimus dorsi, quadratus lumborum, and erector spinae muscles (black arrows). B): Increased fluorodeoxyglucose uptake noted in gluteal and thigh muscles (black arrows).

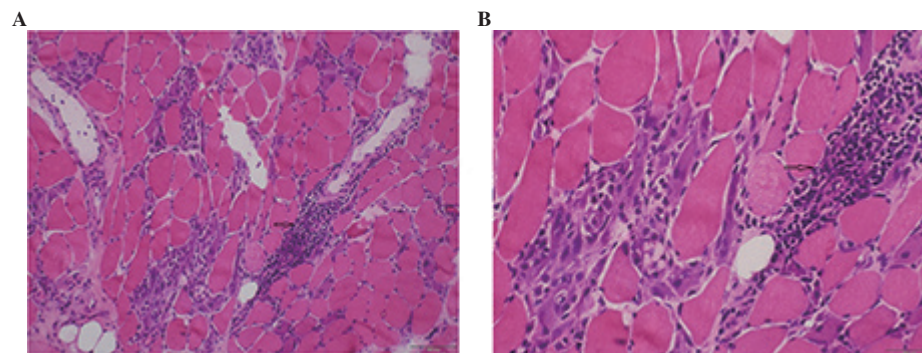


Figure 2. Snap frozen muscle biopsy of a 36-year-old female with scrub typhus and myositis. A) Transversely and obliquely oriented myofibers; moderate increase in endomysial connective tissue and fat infiltration; modest endomysial inflammation composed of histiocytes and lymphocytes along with myophagocytosis (H&E×40). B): Inflammation is seen in endomysium and perivascular locations and is composed of predominant lymphocytes. Many degenerating and regenerating fibres are also seen (H&E×200).

On further investigations scrub IgM turned out to be positive; a diagnosis of a probable case of scrub typhus infection with myositis and rhabdomyolysis was considered and she was started on doxycycline 100 mg twice daily and injection of ceftriaxone 1 gm twice daily along with continuous intravenous fluids and supportive care. Workup for other causes of hepatitis like hepatitis A, B, C, E, and autoimmune hepatitis was negative. Investigations for dengue, malaria, enteric, and leptospirosis were also negative. Further, the positron emission technology scan showed increased fludeoxyglucose uptake of multiple muscle groups (Figures 1A and 1B). Electromyogram displayed a myogenic pattern, and muscle biopsy showed modest endomysial, and perimysial inflammation with overall features suggestive of inflammatory myositis (Figures 2A and 2B). Her myalgia and motor power started to improve in 3-4 days of initiation of doxycycline along with the improvement in the renal and liver functions, reduction of creatinine kinase (960 U/L), serum myoglobin, and urine myoglobin. In the next 12-14 days, she was able to walk without any support and was discharged.

3. Discussion

Scrub typhus infection usually presents with an acute febrile illness with thrombocytopenia, bleeding diathesis and may have complications in the form of interstitial pneumonia, acute kidney injury, deranged liver functions, myocardial damage, and meningoencephalitis[7]. *Orientia tsutsugamushi*, the causative pathogen is primarily located in the endothelial cells of the lung, kidney, heart, brain, and skin[8]. There are only few case series or reports about involvement of muscles in patients of scrub typhus infections; with uncommon occurrence of rhabdomyolysis[2-6]. In a study from South Korea in 208 patients with scrub typhus; myalgia was present in 77% and 26.4% had elevated serum creatinine kinase levels[2]. In a case series by Kalita *et al*[3], muscle involvement was seen in 39% of patients with various degrees of myalgia or muscle weakness including quadriparesis along with elevations in creatinine kinase (CK) levels. Factors associated with significant muscle involvement in scrub typhus infection were lower platelet counts, significantly lower glasgow coma scale scores, and greater disability at the time of discharge as compared to those without muscle involvement.

They also found a correlation between muscle power with serum CK levels[2]. Electromyography revealed fibrillations and short duration, polyphasic multiple unit pellet systems with early interference pattern, suggestive of myopathy/myogenic pattern. The precise mechanism of muscle dysfunction in scrub typhus is not fully understood, but the histopathology findings are suggestive of vasculitis. Like other bacterial or viral infections causing myositis, possible mechanisms for muscle dysfunction can be due to the release of proinflammatory cytokines (like IL-1, TNF- α), myotoxins, hypotension, autoimmunity, molecular mimicry, impaired metabolism, and hyperosmolar state[3,10]. Bacterial infections have been described to cause rhabdomyolysis occasionally but its association with scrub typhus infection is uncommon[4,6]. Myositis and myonecrosis leading to rhabdomyolysis results in complications like hyperkalaemia, hypocalcaemia, hyperphosphatemia, and hyperuricemia. IgM by ELISA is the more common test used in clinical practice for the diagnosis of scrub typhus with comparable specificity and sensitivity of indirect immunofluorescence. Polymerase chain reaction from serum or eschar targeting specific antigen genes of *Orientia tsutsugamushi* is used for diagnostic confirmation of the disease during the first week of illness[9]. The patient having rhabdomyolysis presents with generalized weakness, myalgia, dark-coloured urine, raised CK and myoglobin levels, and acute renal failure as was seen in the index patient. The mechanism of rhabdomyolysis remains the same as for other vasculitic complications. Adequate hydration and avoidance of potentially nephrotoxic agents are vital in patients with rhabdomyolysis. Although there was documentation of vasculitis on muscle biopsy in the study by Kalita *et al.*, there was no need for steroids or other immunomodulation[3]. Although our patients did not fit in to the typical presentation of muscle involvement in scrub typhus infection as described in literature[2,3]; our patient belonged to endemic area, presented in post monsoon season and had supporting clinical, laboratory features with response to doxycycline therapy. Oral or intravenous doxycycline 100 mg twice daily is the drug of choice; Azithromycin is used as an alternative agent in children and pregnancy. With the timely and early treatment with doxycycline and comprehensive supportive care, the prognosis of these patients is fairly good.

4. Conclusions

Clinicians should be aware of the other uncommon and unusual manifestations of scrub typhus like myositis and rhabdomyolysis. Awareness of unusual presentation helps in early diagnosis and treatment. Despite the demonstration of inflammation and vasculitis on muscle biopsy; steroids may not be required as the majority of the patients have a response to doxycycline.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Ethics approval and consent to participate

Informed consent was obtained from the patient for the publication of this case report and any accompanying images.

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Authors' contributions

TRB: Data collection, formal analysis and original draft of manuscript; SB: Data collection, formal analysis; HS: Data analysis, review of manuscript and supervision; VS: Supervision and review of manuscript; AB: Supervision and review of manuscript; DC: Data collection and analysis.

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