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Case Report

Deep vein thrombosis as a rare complication of scrub typhus

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ABSTRACT

Scrub typhus is a common re-emerging, acute febrile infectious disease, caused by orientia tsutsugamushi, transmitted by bite of chiggers of trombiculid mite. The clinical presentation of infection can vary from mild symptoms to severe multi organ failure, shock, encephalopathy, meningoencephalitis, DIC and various thromboembolic complications. We describe a rare hematological complication of deep vein thrombosis (DVT) caused by scrub typhus in a 61-year-old female. Vasculitis and perivasculitis with endothelial dysfunction could be considered as the main pathologic mechanism causing this complication.

Keywords: Scrub typhus, Endothelial injury, DVT

INTRODUCTION

Rickettsiae are a heterogenous group of obligate intracellular, gram-negative coccobacilli, which are transmitted by a tick, mite, flea or louse vector. Among rickettsiae, *Coxiella burnetii*, *Rickettsia prowazekii* and *Rickettsia typhi* will survive for prolonged period outside the reservoir or vector and are extremely infectious. Scrub typhus, murine flea-borne typhus, Indian tick typhus and Q fever are common in India.[1] Scrub typhus is caused by the rickettsia, Orientia tsutsugamushi, and is transmitted to humans by the bite of larval stage of trombiculid mites. Systemic dissemination occurs by lymphatic and hematogenous spread. Scrub typhus has a latent period of 5-20 days, whose symptoms vary from mild to severe and include general malaise, fever, headache, rash and lymphadenopathy.[2] Severe scrub typhus manifestation includes pulmonary edema, interstitial pneumonia, meningoencephalitis, glomerulonephritis, acute renal failure, hypotensive shock and coagulopathy. The most characteristic skin rash is eschar caused by the bite of the larval mite. Eschar is seen in about 04-46% of patients with scrub typhus.[3]

The proliferation of Orientia tsusugamushi in endothelial cells of the microvascular system is the main pathologic mechanism causing vasculitis and perivasculitis in scrub typhus infection.[4] This Rickettsial vasculitis affects the microvascular system of skin, lungs, liver, kidneys, central nervous system, skeletal and cardiac muscles.[5] Endothelium has potent anticoagulant properties and any injury to endothelium alters the efficiency of anticoagulation property. Injury to endothelium, by apoptosis exposes membrane phosphatidylserine which leads to activation of factor X by factor IX. Apoptosis of endothelial cells leads to exposure of procoagulant subendothelial matrix, with or without cell detachment, and through cell retraction, apoptotic leukocytes and endothelial cells circulate as procoagulant bodies. Changes in endothelium following infection are associated with activation of the coagulation system.[6]

We report a case of a 61-year-old female diagnosed to have right lower limb DVT developed secondary to scrub typhus infection. Prompt and timely management with antipyretics, antibiotics and anticoagulants encouraged successful treatment.

CASE REPORT

A 61-year-old female presented with complaints of fever, breathlessness and bilateral leg swelling associated with pain on right leg for past three days. She reported symptoms of fatigue, myalgia and headache. She has a medical history of ventricular septal defect and systemic hypertension. On examination, patient was conscious, oriented and tachypnoeic with the GCS of 15/15. Her pulse rate was 108 beats per minute, blood pressure was 110/70 mmHg, respiratory rate - 32 cycles per minute, SpO_2-71% in room air. General examination revealed an eschar over the medial aspect of right thigh region and bilateral pitting pedal odema (right more than left) (Figure 1). On systemic examination, auscultation of the chest revealed pan systolic murmur in pulmonary area and basal crepitations over bilateral infrascapular area.

Her blood reports revealed hemoglobin-15.3 gm/dl, total leukocyte count-8410 cells/microlitre, platelet-1.50 lakh cells/microliter, urea-125 mg/dl, creatinine-1.9 mg/dl, total bilirubin-3.76 mg/dl, direct bilirubin-3.10 mg/dl, SGOT-71 U/L, SGPT-34 U/L, ALP-239 IU/L, total protein-6 gm/dl, albumin-2.5 gm/dl, ESR-12 mm/hr, CRP- 82 mg/L, D-dimer->4200 ng/ml, PT-13.6 seconds, APTT-33.6 seconds, INR-1.18, HbA1c-5.6%, serum procalcitonin-0.2 (<0.5 ng/ml), troponin I-0.032 (<0.94 ng/ml), CKMB-0.38 (2-10 U/L). Electrolytes and urine routine were within normal limits. Her HIV I, II, HBsAg/anti HCV antibody were negative. Scrub typhus IgM antibodies were positive. Dengue profile (NS1, IgM, IgG) and Leptospira IgM antibodies were negative. Serum homocysteine, protein C and protein S levels were found to be in normal limits. Her blood and urine culture revealed no growth. ECG revealed premature ventricular complexes. Chest X-ray revealed increased cardiothoracic ratio. CT Chest revealed subpleural fibroatelectactic changes in left lower lobe. Echocardiography revealed perimembranous VSD with bidirectional shunt, concentric left ventricular hypertrophy, normal LV systolic function with EF-60%, dilated right atrium and right ventricle, moderate PAH (pulmonary artery hypertension)-50 mmHg. Right lower limb venous doppler revealed an echogenic thrombus noted in both right distal superficial femoral vein and great saphenous vein in mid-thigh for a length of 10 cm. As the patient is having acute kidney injury, CT pulmonary angiography was not done.

She was started on supplemental oxygen at rate of 12 L/min, back rest, IV furosemide 40 mg OD, IV doxycycline 100 mg BD, IV cefoperazone sulbactam 3 gm BD, IV unfractionated heparin 5000 U BD, antiplatelets, antiemetics and other supportive measures. During stay in hospital she improved symptomatically with her renal and liver parameters in decreasing trend. IV doxycycline 100 mg BD and IV cefoperazone sulbactam 3 gm BD were given over a period of 10 days. IV unfractionated heparin 5000 U BD were given over a period of 12 days along with overlap therapy of oral warfarin 2 mg per day. On day 8 of stay in hospital, her urea-36 mg/dl, creatinine-0.6 mg/dl, total bilirubin-1.45 mg/dl, direct bilirubin-0.58 mg/dl, SGOT-39 U/L, SGPT-39 U/L, total protein-7.1 gm/dl and albumin-2.9 mg/dl. On day 13, repeat right lower limb venous doppler revealed no evidence of DVT. On day 14, patient was symptom free and was discharged. She was advised to continue oral warfarin for a period of 3 months with serial INR monitoring. After one month, she was doing significantly better on proper evaluation and her blood parameters were found to be within normal limits with repeat right lower limb venous doppler revealing no evidence of DVT. She was followed up at the outpatient department once a month with INR report.

Figure 1: Eschar seen over the medial aspect of right thigh.

DISCUSSION

Antithrombotic property of endothelium is altered with introduction of inflammatory mediators, vascular injury, infection and endotoxins. The main pathologic findings in scrub typhus are systemic vasculitis and perivasculitis, which are caused by proliferation of O. tsutsugamushi in endothelial cells of the microvascular system.[7]

Honnutagi and his colleagues published a similar case report where left lower limb DVT occurred secondary to scrub typhus infection in a 24-year-old male patient, where he was successfully treated with oral doxycycline and IV unfractionated heparin.[8]

Chowdhury published a case report where a 52-year-old male developed acute ischemic stroke and right lower limb DVT simultaneously as a complication of scrub typhus infection, where he was successfully treated with low molecular weight heparin injection and IV doxycycline.[9]

Mounika and her colleagues published a case report where a 17-year-old female developed pulmonary thromboembolism as a complication of scrub typhus infection and was treated with low molecular weight heparin injection (enoxaparin).[10]

Biswas et al published a case report where a 21-year-old female developed cerebral venous sinus thrombosis as a complication of scrub typhus infection and was successfully treated with injection low molecular weight heparin (enoxaparin) and overlap therapy with oral warfarin.[11]

Das published a case report where a 32-year-old female developed cerebral venous sinus thrombosis as a complication of scrub typhus infection and was successfully treated with injection clexane and warfarin.[12]

In most of the cases published, the cause of this venous thrombosis is likely to be vasculopathy, resulting from endothelial injury caused by cytokine release due to rickettsia infection. There is localised platelet aggregation, polymorph and monocyte proliferation, leading to focal occlusive and angiitis causing microinfarcts in various tissues.

CONCLUSION

Scrub typhus are emerging infection in India, with wide range of clinical presentation varying from non specific presentation to severe life threatening conditions like shock, pulmonary embolism, meningoencephalitis, DIC, ARDS and DVT. This case reminds the importance of suspecting scrub typhus as one of the causes for thromboembolic disease and to recognize scrub typhus early and initiate the treatment early to prevent the severe disease.

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