

Deep Vein Thrombosis in Bilateral Legs Associated with Acute Brucellosis: Review of the Literature.**Manju¹, Nikhil Kumar², Akshit Gupta³, Gopal Singh⁴**¹Assistant Professor Department of Medicine Dr. RPGMC, Kangra at Tanda, H.P.²Junior Resident, Department of Medicine, Dr. RPGMC, Kangra at Tanda, H.P.³Junior Resident, Department of Medicine, Dr. RPGMC, Kangra at Tanda, H.P.⁴Senior Resident Department of Anesthesia, Dr. RPGMC Kangra at Tanda H.P.

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Abstract

Brucellosis caused by species of *Brucella*, is among the most prevalent zoonotic disease that can involve any organ. Here we present a case of deep vein thrombosis as a complication of brucellosis. We reported a 44 years old male patient diagnosed with brucellosis with deep vein thrombosis on his bilateral legs with features of polyarthrititis. The patient was treated with anticoagulants. The patient was discharged with warfarin therapy and antibrucellosis treatment. Although rare, some infectious agents may cause vascular pathologies. Patients presenting with symptoms of DVT or similar vascular pathologies should be assessed for infectious agents, particularly in those coming from *Brucella*-endemic areas.

Keywords: Deep vein thrombosis, brucellosis, polyarthrititis and zoonosis.

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Introduction

Brucellosis is a cosmopolitan zoonotic disease that mainly affects people in close contact with domestic animals and their products. It is endemic in Mediterranean countries and caused by bacteria of the *Brucella* genus.[1] Brucellosis is a systemic infection and the clinical presentation varies widely from asymptomatic to severe disease. Human brucellosis is a multisystem disease that may present with a broad spectrum of clinical manifestations and its complications can affect almost all organs and systems, with varying incidence. Careful attention must be paid to any sign or symptom of thrombosis in patients affected by brucellosis, regardless of the presence of endocarditis and cardiovascular risk factors. Vascular complications of *Brucella* infection have rarely been reported in the medical literature.

Case Report:

A 44-years old male was hospitalized complaining of pain in his back and multiple small & large joints of both upper and lower limbs. Pain preceded by fever. Fever was documented as 100 to 102 degrees F. The fever lasted for three days, which subsided after taking medicine from his native primary health center. But there was no relief for joint pain which was further exacerbated when walking. It was associated with swelling in both calves. For these complaints, the patient took admission to a rural

tertiary care hospital Kangra at Tanda. Pain was sudden in onset, starting with low back followed by the left and right elbow joints, eventually spreading to joints of both legs. History of painful swelling of both lower calves developed four days later of onset of pain in joints. Left calf swelling settled itself but swelling of the right calf persisted. No history suggesting urinary tract involvement and congestion of the conjunctiva. The patient and his family owned goats and cows. The patient also reported that he had ingested unpasteurized cow milk, as well as he used to help in cattle rearing. On clinical examination upon admission, general physical examination was within normal limits. Right-sided sacroiliac joint was painful on palpation. The circumference of right calf was 1.5 cm more than the left leg with tenderness on palpation. Other system on examination was unremarkable. Baseline laboratory analysis showed the following results: erythrocyte sedimentation rate 32 mm in first hr., red blood cells 3.8×10^6 /micro Liter, hemoglobin 11.9 g/dl, white blood cells 11.2×10^9 /L (81% neutrophils), C reactive protein 3.5 mg/L, platelets 243×10^3 /micro L, hematocrit 35.5%, aspartate aminotransferase 47 U/L, alanine aminotransferase 45 U/L. Anticardiolipin and lupus anticoagulant antibodies were negative and protein C, protein S, and antithrombin III activities were within the normal ranges. Rose Bengal tested positive, eventually

standard tube agglutination testing of initial samples resulted positive for antibodies to Brucella with titer 1:320. Rheumatoid factors, Anti CCP, and ANA profile were found negative. Chest X-ray, ECG, ECHO and abdominal ultrasound were normal; pelvis X-ray showed sacroiliitis of the right sacroiliac joint. The computed tomography scan of the lumbar/sacral part of the vertebral column showed a slight medial disc L4/L5 protrusion and outpatient treatment with analgesics and anti-inflammatory non-steroids did not result in substantial improvement of his condition. On color Doppler USG of lower limbs suggestive of DVT of the right leg. Based on the patient's history of ingesting unpasteurized cow milk and rearing cattle, together with the exhibited symptoms and clinical

signs, the presence of sacroiliitis, positive Rose bengal plate test (RBPT) and positive serum agglutination test (SAT), a diagnosis of brucellosis with right calf deep vein thrombosis was made. The patient was initially treated with low molecular weight heparin (LMWH) for 5 days followed by warfarin for DVT and simultaneously treated with Rifampicin and doxycycline, Patient was discharged on treatment with Doxycycline, Rifampicin, and Warfarin for next three months. On the 5th day of discharge, the patient developed pain, edema and redness in his left leg accompanied by a fever of up to 38.5°C. Doppler USG of lower limbs veins resulted in acute thrombosis of CFV and the popliteal vein showed echogenic contents and is not compressible on transducer pressure bilaterally.

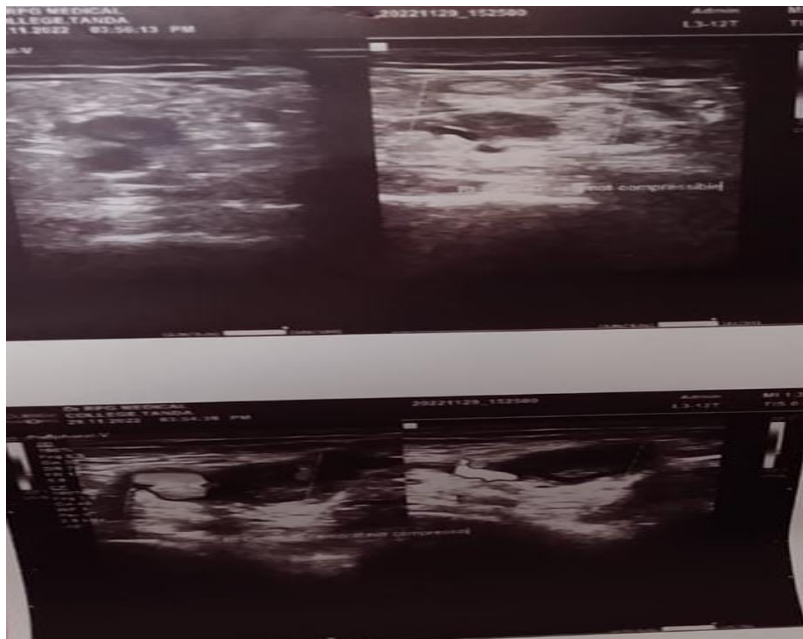


Figure 1: B/L CFV, SFV, and popliteal veins show echogenic contents and are not compressible to gentle transducer pressure.

The treatment durations for both anticoagulant and brucellosis were extended to 3 months. On follow-up in OPD after one month, repeat color Doppler of legs was normal and the patient was free from joint pain. Vascular complications of brucellosis are rare; the arteries are more affected than veins. Arterial complications of brucellosis include aneurysm formation in the aorta, and cerebral arteries, brachial, and tibioperoneal, with or without underlying endocarditis.

Review of Literature and Discussion

Brucellosis is among the most prevalent zoonotic diseases all around the world. India is an endemic region for disease, and the annual incidence rate of human and animal infection is still considerable. [2] Deep vein thrombosis is a rare complication of brucellosis and its pathogenesis has not been described well. [3] The mechanisms of thrombosis

formation include the occurrence of inflammation and injury of perivascular tissue, a transient hypercoagulable state, granulomatous end phlebitis, or the immune reaction in the vessel wall to the Brucella antigen. In a recent review of the literature, Koubaa et al. [4] described 9 reported cases of vein thrombosis associated with brucellosis, from 1973 to 2014. Ratio male female was 4/3 (in 2 cases this information was lacking), age ranged from 18 to 52 years (median 41 years). Deep vein thrombosis involved legs in 5 cases, brain in 2 cases, lower limb in 1 case and portal vein in one case. Deep vein thrombosis of one leg is the main represented feature in the literature, but our case, that developed this complication on both lower limbs. Cem Gul et al. [5] reported a similar case of a male patient of 21 years of age, who developed a deep vein thrombosis on the left leg, in which the *B. melitensis* was isolated from the blood culture thus ruling out other possible

causes of vein thrombosis. Ertek et al. reported that out of 216 adults with brucellosis treated in their clinic, seven of them had cardiovascular system complications, while deep vein thrombosis developed in only two of the cases. [6] Further cases pertaining to deep vein thrombosis were reported by Odeh et al. (right leg, related to acute brucellosis). [7] Memish et al. has also reported a case of 41 years old male patient with the venogram resulted in deep vein thrombosis of left calf. Although the blood

culture was negative, the patient developed high Brucella antibody titres. [8] In 1973, Romem et al. [9] reported the first case of brucellosis complicated with central vein thrombosis. Since this publication, nine further cases of vein thrombosis due to brucellosis have been reported. Table 1 shows demographic data and clinical and laboratory findings of the nine case reports of brucellosis complicated with vein thrombosis. The tenth one is the case reported by us.

Table 1:

Author	Years	Country	Gender	Age	DVT	Serology	Antibiotic Therapy (in wk)
Romem et al. [1]	1973	Israel	NM	NM	Central retinal vein	NM	Not mention (NM)
Gregori et al. [2]	1990	Spain	NM	NM	Portal vein	NM	NM
Zaidan et al. [3]	1999	Saudi Arabia	F	23	Cerebral vein (sagittal sinus)	1:320	R + D + TS (NM)
Sen et al. [4]	2011	Turkey	F	43	Left leg	1:320	Doxy+Rifampicin
Marfil Rivera et al. [5]	1986	Mexico	F	18	Lower limb	1:160	NM T (NM)
Odeh et al. [6]	2000	Israel	M	52	Right leg	1:160	R + D
Memish et al. [7]	2001	Saudi Arabia	M	21	Right leg	1:1280	Doxy +Rifampicin
Gul et al. [8]	2008	Turkey	M	21	Right leg	1:400	Doxy+Rifampicin
LlirTolaj.et.al.[9]	2014	Prishtina, Kosovo	M	37	Left	1:640	Doxy+Rifampicin

F, female; M, male; R, rifampicin; D, doxycycline; T, tetracycline; TS, trimethoprim-sulfamethoxazole; NM, not mentioned;

Thrombosis involved the portal vein, the central retinal vein, the cerebral vein and the lower limb veins, in one case each. Acute brucellosis was associated with DVT in the legs in four patients (three men and one woman). The diagnosis of DVT in the leg was made before the onset of other clinical features of brucellosis in one case and concomitant with the diagnosis of brucellosis in two. [10] The duration between DVT diagnosis and the occurrence of brucellosis clinical features was about 4 weeks. Infectious processes in adjacent tissues, direct endothelial damage, granulomatous endophlebitis, compression from a local soft tissue mass or abscess, induction of a transient hypercoagulable state, and an immune reaction in the vessel wall to a Brucella antigen. In the present case protein C, protein S, and antithrombin III levels, were normal, and no antiphospholipid and anti-lupus antibodies were detected. In his illness, no local infection was observed adjacent to his both calves' deep veins. [11] Thus, it is possible that granulomatous Endophlebitis or a possible immune reaction in the vessel wall to a Brucella antigen was responsible for the patient's DVT.

Conclusion

DVT is a rare complication of brucellosis. We report a new case of bilateral leg deep vein thrombophlebitis with acute brucellosis. The present

case and the previously reported other cases suggest that there must be high suspicion of brucellosis in patients suffering from DVT, particularly in patients from Brucella-endemic areas like India.

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