

Deep Vein Thrombosis Complicating Recurrent Erythema Nodosum Leprosum

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Recurrent erythema nodosum leprosum (ENL) is a type 2 leprosy reaction, which often poses a challenge for the treating physician. Patient may be non-ambulatory due to systemic symptoms like fever, body aches, joint pains, and painful skin lesions. Moreover, drugs like corticosteroids and thalidomide in refractory cases pose an increased risk of deep vein thrombosis (DVT). We have described a case who developed DVT in due course of the treatment.

Keywords : Leprosy, Thalidomide, Erythema Nodosum Leprosum (ENL), Deep Vein Thrombosis (DVT)

Introduction

Recurrent erythema nodosum leprosum (ENL) is a type 2 leprosy reaction, which often requires the addition of some medication other than the usual oral corticosteroids. Thalidomide is a useful drug in recurrent ENL. Deep vein thrombosis (DVT) is one of the life-threatening serious adverse events encountered in our difficult to treat a case of refractory ENL.

Case Report

A 66-year-old male, a diagnosed case of lepromatous leprosy 6 months back, had a history of hypoaesthesia of hands and feet for 2 years. The patient was on multidrug therapy (MDT) for 6 months and had a bacteriological index (B.I) of

2+ on slit skin smear at 6 months of MDT, when he presented with the sudden appearance of tender red raised lesions over the trunk, upper and lower limbs along with fever and joint pains. Patient was diagnosed clinically and confirmed histopathologically with the findings of polymorphonuclear infiltration on the background of macrophage granuloma as erythema nodosum leprosum (ENL). Patient was started on oral prednisolone at a dose of 60mg (1mg/kg/day) along with multidrug therapy. The reaction was controlled in a week but recurred on tapering prednisolone to 40mg/day. Increment in the dosage to 60mg led to control of ENL. There were multiple episodes of ENL in the past 4 months. Thalidomide was added at a dose of 400mg/day

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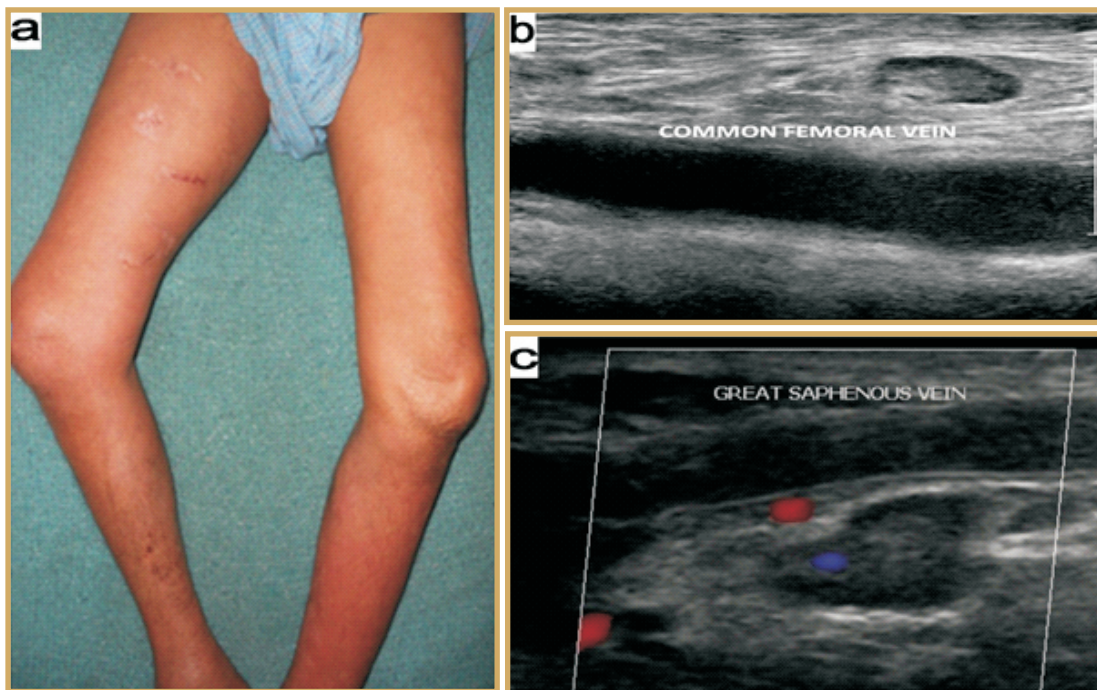


Fig. 1 (a-b) : Mild erythema, swelling over right lower limb. Acute thrombosis seen in (a) common femoral vein on doppler study extending into sapheno-femoral junction and proximal great saphenous vein (b, c).

for a week, which led to control of ENL. It was tapered to 300mg/day for 1 month and 100mg/month dose reduction thereafter, along with 60 mg of prednisolone. Prednisolone was then successfully tapered to 40 mg after 2 weeks. Patient developed excruciating pain in right lower limb after 1.5 months. Examination revealed mild erythema, warm, tender, and swollen right lower limb (Fig. 1a). Colour doppler revealed acute thrombosis of deep veins of the right lower limb (Figs. 1b, 1c, 2a). Blood investigations including protein C and S activity, and antiphospholipid antibody were within normal limits. With these findings, the diagnosis of deep vein thrombosis (DVT) induced by thalidomide in recurrent ENL was established. Thalidomide was stopped

immediately while oral prednisolone continued at the dose of 40 mg/day. Patient was administered an injection of enoxaparin 60 mg/0.6 mL subcutaneously twice a day for 5 days along with warfarin (5 mg), which was continued. Compression hosiery were provided. Combined enoxaparin and warfarin therapy were continued for 5 days after which enoxaparin was stopped. The International normalized ratio was maintained between 2.5 to 3.5. After about two weeks of therapy, the patient improved symptomatically with subsidence of swelling and pain. Repeat color doppler after a month showed recanalization (Fig. 2b). The patient developed 2 episodes of ENL during the DVT which were controlled with increased prednisolone doses.

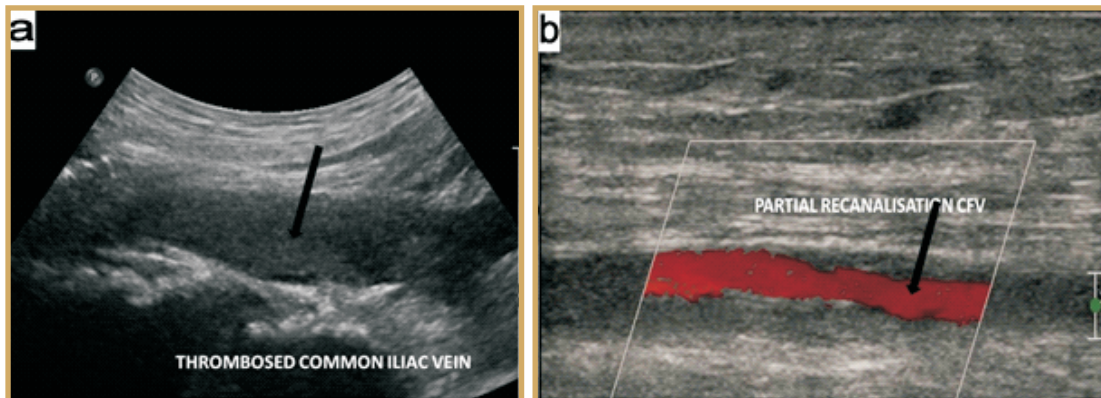


Fig. 2 (a-b) : Thrombosed common iliac vein on doppler study. Partial recanalization seen in (a) common femoral vein and (b) superficial femoral vein after treatment on doppler study.

He was discharged on multidrug therapy, prednisolone 40 mg/day and warfarin 5 mg/day with advice to regular follow up.

Discussion

Thalidomide was licensed by US FDA for the management of ENL in 1998. The reported side effects of thalidomide other than teratogenicity are DVT, constipation, sedation, skin rash, peripheral neuropathy and fatigue (Franks et al 2004). DVT is seen after the use of thalidomide, especially in cases of malignancies, but it is rare in other non-malignant conditions. The risk of DVT has been considered around 1% when used alone and around 20-30% when used in combination with dexamethasone or chemotherapy (Weber et al 2003). Sharma et al (2004) reported a case of resistant ENL with DVT who was being treated with thalidomide and dexamethasone, cyclophosphamide pulse therapy. In a cross-sectional study of 110 patients of ENL on thalidomide, 10 patients developed DVT and 9/10 patients were on prednisolone concomitantly and only 1 patient developed ENL with thalidomide alone (Drummond et al 2019). Glucocorticoids in high

doses are also considered as an independent risk factor for thromboembolism (Johannesdottir et al 2013).

Thalidomide worked as a precipitating factor in the development of DVT in the index case. In such a scenario, patient should be carefully observed for the risk of development of DVT. Ambulation and mechanical methods of DVT prophylaxis may prove very useful. Prophylactic anticoagulation is not recommended in patients of Hansen's disease with ENL receiving glucocorticoids and thalidomide. Therefore, pharmacovigilance is crucial in preventing severe adverse events.

Conclusion

There should be careful monitoring of the recurrent ENL patients on drug therapy for redness, swelling and tenderness over lower limbs. High dose corticosteroids and thalidomide are the risk factors for DVT. Compression ultrasonography and doppler study assist in the diagnosis of DVT. Prophylactic anticoagulation is not recommended in ENL patients. Compression stockings and ambulation of ENL patients on thalidomide may decrease the risk of DVT.

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