

Deep vein thrombosis - a rare post transplant complication

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Abstract

Deep vein thrombosis (DVT) is a rare post transplant multifactorial disease and often results from a combination of risk factors causing venous stasis. Venography and doppler ultrasound are reliable and accurate procedures for detecting venous thrombosis. Once DVT has been established, these patients should be treated with anticoagulants atleast for a limited duration particularly in high risk post transplant patients with previous episodes of thrombotic events.

We report here a case of a 7 years old boy with B-thalassaemia major, who developed deep vein thrombosis at 04 month post SCT. He was treated with low molecular weight heparin and oral warfarin sodium and INR was stabilized between 2.5 - 3.0. Two months later, he presented with bleeding diathesis and died of intracranial haemorrhage. Excessive unchecked anticoagulation was the cause of death. It is recommended that patients on anticoagulation therapy require strict monitoring with PT/INR to avoid bleeding complications related to unchecked over anticoagulation.

Introduction

Deep vein thrombosis (DVT) is a rare post transplant complication. It is a multifactorial disease and often results from a combination of risk factors like venous stasis due to prolonged immobilization, vascular endothelial damage by preparative regimens/use of indwelling catheters, prolonged glucocorticoids therapy for GVHD and hypercoagulability states including factor V Leiden, deficiency of natural anticoagulant proteins (C and S) and anti thrombin III deficiency.^{1,2}

DVT either involves one or both legs and it is characterised by painful swelling with normal or raised local temperature and dilation of superficial veins.³ Because clinical diagnosis is unreliable, accurate diagnostic tests are required when DVT is suspected. Venography is the most accurate and reliable technique for assessing the presence of venous occlusion. Doppler ultrasound is also a reliable, non-invasive procedure for detecting venous thrombosis.⁴ If the patient has a proven venous thrombosis, it is necessary to exclude thrombophilic conditions. Once DVT has been established, these patients should be treated with anticoagulants atleast for a limited duration (3 months), particularly in high risk patients with previous episodes of thrombotic events.^{5,6}

Case Report

A 7 years old boy with B-thalassaemia major, had received multiple irregular transfusions along with chelation therapy was eventually subjected to splenectomy for massive splenomegaly. Liver biopsy showed bridging fibrosis. On the basis of pre-transplant Pesaro risk group classification criteria, he was placed in Pesaro risk class III. He was conditioned with Hydroxy urea, 30 mg/kg daily (day - 45 till day -11), Azathioprine, 3 mg/kg daily (day - 45 till day -11), Fludarabine, 20 mg/m² daily (day - 17 till day - 13) followed by Busulphan, 4 mg/kg daily for 4 days and Cyclophosphamide 40mg/kg daily for next 4 days. He received allogeneic stem cell transplant (allo-SCT) from his HLA matched sibling brother in March 2004. After successful early engraftment, he was discharged from the hospital on day + 20 post - SCT. There after patient was on regular follow up in out patient department. His post transplant period remained uneventful for four months post-SCT, when he developed painful swelling of right calf and popliteal region. Ultra sound

guided doppler studies and venography confirmed the diagnosis of deep vein thrombosis. His thrombophilia screening was negative. Hypercoagulability states and infective causes were ruled out. Patient was treated with low molecular weight heparin (Clexan), 1.5 mg/kg subcutaneous dose daily and was switched over to oral warfarin sodium over next week. His INR was stabilized between 2.5 - 3.0 and was discharged after 15 days with an advice to regularly monitor his INR. He however, did not report for follow up and was brought to emergency room two months later in a state of shock with fresh bleeding per rectum, epistaxis, haemoptysis and marked pallor. Detailed clinical history was suggestive of warfarin over dosage. His haemoglobin at the time of admission was 3.1 g% with normal platelet and white blood cell counts. His coagulation profile showed INR of > 6.0 and grossly deranged PTTK. He was given red cell concentrates, vitamin K and fresh frozen plasma (FFP). His condition worsened over the next few hours. He suddenly had generalized seizure with cessation of breathing. Resuscitation was unsuccessful and patient expired within an hour. CT scan brain could not be carried out due to critical state of the patient. Most probable cause of death was intra cranial bleeding due to excessive anticoagulation with unchecked warfarin over dosage.

Discussion

Thrombotic events have been reported at various time intervals after haematopoietic stem cell transplantation (HSCT).⁷ Venous thromboembolism results from a combination of risk factors which include hyperglycaemia and hyperlipidaemia associated with post- HSCT glucocorticoid treatment for GVHD as well as prolonged inactivity due to fatigue in these patients.⁸

Once DVT is diagnosed, the goals of treatment are relief of symptoms, prevention of embolisation and recurrence. The corner stone of initial therapy is either unfractionated or low molecular weight heparin, followed by oral anticoagulant therapy. Thrombolytic therapy should be considered for patients who have limb threatening circulatory compromise. Inferior vena caval filters should be inserted in patients with contraindications to anticoagulations and in those who require urgent surgery that precludes anticoagulation.⁹

Initial management of DVT include complete bed rest with elevation of affected leg. Unfractionated heparin is usually given intra venously by continuous infusion after a loading dose has been administered. Heparin, is initially given in loading dose of 5000-10000 units (100 units/kg) I/V over 5 minutes, followed by heparin I/V infusion 100 units/hour for 06 hours and then dose of heparin is regulated according to PTTK. On third day of heparin therapy,

warfarin sodium is added at an initial dose of 9 mg daily for 03 days and then readjusted according to PT/INR. When patient achieves therapeutic levels of PT/INR with warfarin, heparin therapy is stopped and patient is monitored with warfarin therapy.¹⁰

Low molecular weight heparin (LMWH) is usually used for initial management of patients with DVT. Fixed dose, subcutaneous LMWH is an effective and safe treatment regardless of whether the patient has pulmonary embolism or a history of venous thromboembolism.⁵

In summary DVT is a rare delayed post transplant complication and the risk factors for DVT associated with allo-SCT are transient. We used low molecular weight heparin (LMWH) in our patient which is safe and equally effective as that of unfractionated heparin. More over the administration of LMWH in a single daily dose is quite easy. Our patient was successfully treated with LMWH and was switched over to warfarin sodium. Oral anticoagulant therapy requires strict anti coagulation control with regular PT/INR monitoring. Unfortunately this patient did not follow the doctor's advice for oral anticoagulation therapy. We, therefore recommend that before subjecting these patients on oral anticoagulants in our patient department, it should be ensured that patients and their relatives clearly understand the complications related to under and over dosage of oral anticoagulant therapy. Strict PT/INR control is recommended in all patients who are on oral anticoagulants.

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