Indwelling catheter-related central venous thrombosis during bone marrow transplantation

Venous thrombosis is uncommon in Chinese. Two patients with thrombocytopenia developed catheter-related thrombosis during bone marrow transplantation, which resolved after catheter removal and anticoagulation. There was no change in protein C, protein S and antithrombin levels. Endothelial trauma plays an important role in causing catheter-related thrombosis in our patients.

Indwelling central venous catheters (CVC) are associated with thrombosis with an incidence as high as 21%.[1,2] During bone marrow transplantation (BMT), CVC is required for delivery of chemotherapy, stem cells and parenteral nutrition. Venous thrombosis is uncommon in Chinese patients[3] and during thrombocytopenia, most patients are at risk of bleeding complications. We report two thrombocytopenic patients who developed thrombosis at the site of CVC (Hickman® Dual Lumen CV Catheter, Bard Access Systems, Utah, USA) during BMT. Both had no antecedent history of thrombosis with no anticoagulant prophylaxis during BMT.

Patient #1 was a 41-year old woman with acute myeloid leukemia M2 in second remission who received an allogeneic BMT from a matched unrelated donor. Two months before transplantation a CVC was inserted into the superior vena cava (SVC). Because of partial blockage, the catheter was replaced a week prior to BMT with another one through the right cephalic vein. On day 13 post-BMT (platelet count 34x10^9/L), she developed sudden right arm swelling with progressive involvement of the other arm, the face and the neck. A venogram confirmed deep vein thrombosis (DVT) of the distal right subclavian vein around the CVC, right brachiocephalic vein and SVC (Figure 1a). The catheter was removed and she received intravenous heparin. Two weeks later a spontaneous subdural hemorrhage developed requiring surgical drainage and cessation of anticoagulation. A venogram on day 51 revealed significant resolution of the thrombus (Figure 1b).

Patient #2 was a 28-year-old man who received BMT from an HLA-identical sibling for chronic myeloid leukemia in accelerated phase. Two months before BMT, a CVC was inserted into the SVC through the right external jugular vein. On day 15 post-BMT (platelet count 20x10^9/L), he developed DVT of the proximal right subclavian vein extending into the proximal right internal jugular vein. The CVC was removed and he was given intravenous heparin followed by oral warfarin. Ultrasonongraphy on day 41 revealed significant improvement of thrombosis and he remained asymptomatic thereafter.

To assess the role of natural anticoagulants in thrombosis, antithrombin III (ATIII), protein C (PC) and protein S (PS) levels were measured. (ATIII and PC by chromogenic assays Stachrom ATIII and Stachrom Protein C; total and free PS by Asserchrom Total Protein S and Asserchrom Free Protein S; Diagnostica Stago, France). Figure 2 shows the average levels of ATIII, PC and PS and serum albumin in patient #1 together with four other control patients undergoing BMT. There was no significant change in their levels from day 0 to day 35.

Thrombosis complicating BMT is uncommon in Chinese patients. It appears paradoxical for thrombosis to occur during thrombocytopenia. However, hypercoagulability has been shown in BMT recipients related to the decrease in PC, PS and AT.[4-8] These factors reached a nadir at the end of the second week

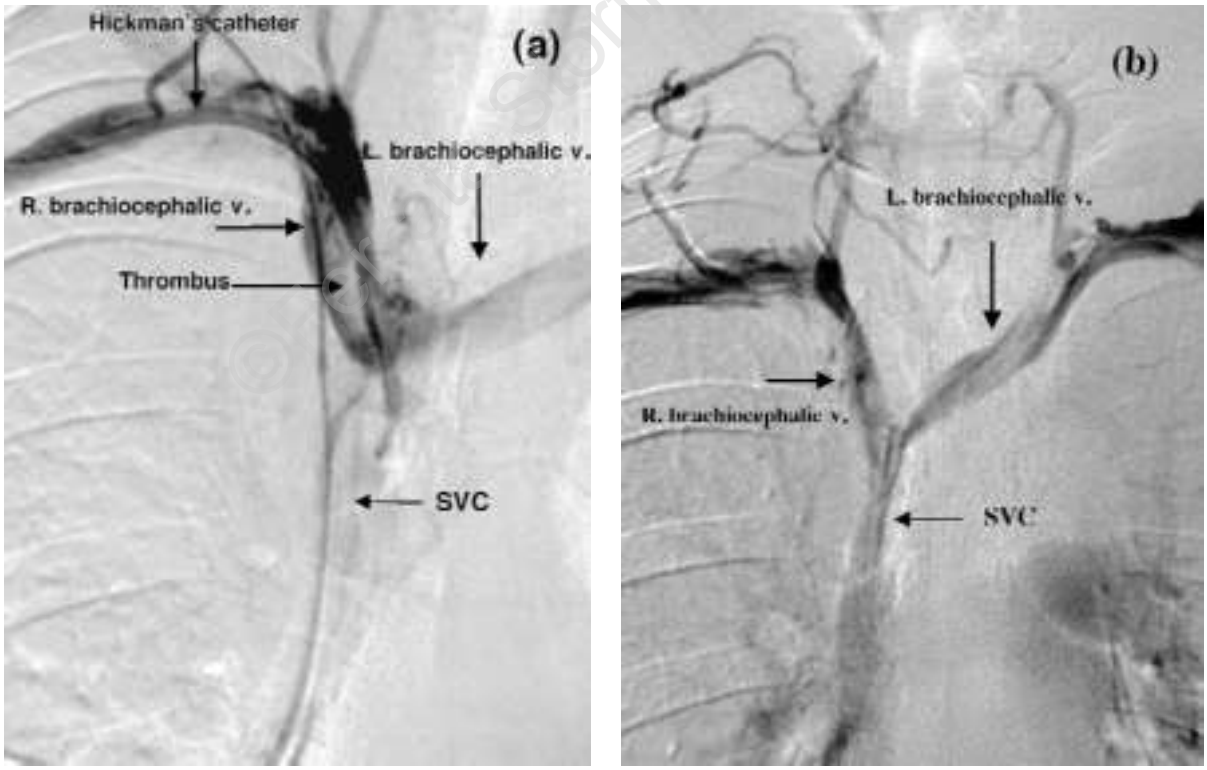

Figure 1. (a) Central vein venogram showing a thrombus in the right (R) brachiocephalic vein (V) that blocked the passage of contrast to the superior vena cava (SVC). Intravenous contrast was injected into the vein of the ipsilateral upper limb. As a result, the SVC was not opacified; (b) central vein venogram showing resolution of thrombosis 38 days after removal of the Hickman's catheter with free passage of contrast into the SVC.

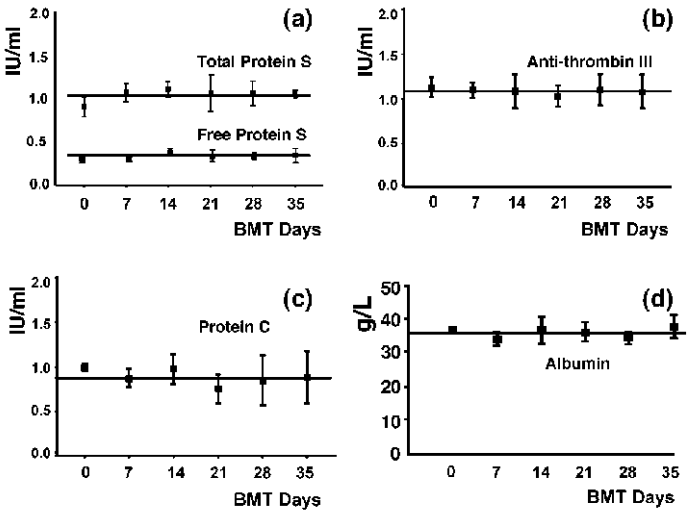

Figure 2a-d. Protein C (a), antithrombin III (b), total and free protein C (c) and albumin (d) levels during the course of BMT. The result represented the average value of the five patients in Table 1. There was no significant change in these parameters from day 0 to day 35. Each error bar represents one S.E.M.

post-BMT and remained low until one month post-BMT. In our series, however, there was no change in natural anticoagulants during BMT. Therefore, hypercoagulability did not appear to be an important mechanism. In fact, venous thrombosis in general is uncommon in Chinese as compared within Caucasians.[3] The ethnic difference is genetically related, as the prevalences of PC, PS and AT deficiencies are lower than those in Caucasians, and factor V Leiden mutation is absent in Chinese people.[9]

A risk factor in our patients may be related to local injury to the endothelial wall. DVT was limited to the site of CVC insertion and none of the patients developed systemic thromboembolism, suggesting that endothelial trauma may have played a pivotal role in the formation of thrombus. In patient #2, repeated catheter insertions might have increased the severity and extent of the thrombosis. Another risk factor may be related to the advanced disease status in these patients at the time of BMT.

Whether thrombosis is related to systemic hypercoagulability or vascular trauma might be relevant in treatment. Although we could not distinguish the therapeutic effects of catheter removal from anticoagulation, in our patient who developed subdural hemorrhage requiring cessation of anticoagulation, removal of the CVC was apparently adequate to stop the thrombotic process. As we could not demonstrate a hypercoagulable state, it might be argued that in Chinese BMT patients with catheter-related thrombosis, prompt removal of the catheter without immediate anticoagulation might be a reasonable strategy, in order to avoid bleeding complications in these thrombocytopenic patients. Close monitoring after catheter removal is warranted as pulmonary embolism has been reported after CVC removal.[10] This proposal will have to be tested with further studies of DVT in Chinese BMT patients.

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