CORRESPONDENCE

Venous Thrombosis in Hematopoietic Stem Cell Transplantation

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To The Editor,

There is paucity of data on thrombotic events in patients undergoing hematopoietic stem cell transplant (HSCT). There is a new interest in venous thrombosis events in HSCT setting. A recent meta analysis has found an incidence of 5 % venous thromboembolism (4 % each in autologous and allogeneic HSCTs) amongst all HSCT patients [1]. There is no such information available from India. We share our data of venous thrombotic events in HSCT setting.

Over last 4 years 120 patients underwent bone marrow transplantation at our center. Five patients developed venous thrombotic events (Table 1). None of the patients developed arterial thrombosis. Patient with aplastic anemia developed ethmoid and sphenoid sinusitis. He developed dipopia. There was a debate whether he should be anticoagulated or not in view of inflammation related thrombus and thrombocytopenia. His platelet counts were 42,000 received one dose of low molecular weight heparin and platelet count dropped to 32,000 next day and was not anticoagulated any further. He gradually recovered over a period of 4 months. Catheters were removed in all patients when a catheter related venous thrombosis was diagnosed. Hypercoagulable work-up was not performed on any of these patients. All patients recovered well. Since precipitating factor was present in most patients, duration of anticoagulation was much shorter (Table 1). There was no pulmonary embolism. There was no bleeding episode

secondary to anticoagulation. Venous thrombosis in patient 1 recurred after 2.5 years in same site in setting of dehydration. He was on thalidomide maintenance. His hypercoagulable work-up was negative at this time. Follow-up of our patients is from 4 months to 2.5 years.

The incidence of venous thrombosis has been reported at 47 % in acute graft versus host disease (GVHD) and 35 % in chronic GVHD [1]. Labrador et al. [2] described clotting events in HSCT patients unrelated to catheter. Another review identified prior venous thrombosis, GVHD, infections and indwelling venous catheters are risk factors for thrombosis [3].

There are certain unique findings in this small data. All patients are young, had one or another precipitating factor for thrombosis and were high risk for thrombosis. Three patients had multiple myeloma which in itself is considered a hypercoagulable state in view of thalidomide or lenalidomide along with other medicines used in these patients. One patient had paroxysmal nocturnal hemoglobinuria with a 100 % CD 55 and CD 59 deficient clone and presented as transfusion dependent aplastic anemia. Patients with high clone size are at high risk of thrombosis [4]. There is a strong correlation between inflammation and thrombosis [5]. Patient with aplastic anemia developed thrombosis in setting of sinusitis.

The challenges posed are great once someone develops thrombosis as many times patients are thrombocytopenic due to conditioning regimen or immunosuppressive agents like mycophenolate mofetil. It is difficult to anticoagulate these patients as was the case with our fifth patient. Thrombosis was probably unrelated to any of the transplantation variable as it developed in both autologous and allogeneic setting. All patients received peripheral blood hematopoietic stem cell transplantation. Since both allogeneic patients got thrombosis early in the course it is

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Table 1 Thrombosis in bone marrow transplant unit

	Age/gender	Diagnosis	Transplant	Infection	Site	Risk factor	Comment
1	47/M	Myeloma	Autologous	<i>Acinetobacter baumannii</i> in blood, <i>E. coli</i> UTI	Femoral vein	Primary disease Femoral catheter Prolonged immobilization	DVT 6 days after catheter removal Warfarin × 12 weeks Recurrence after 2.5 years
2	40/F	Myeloma	Autologous	<i>Staph epidermidis</i> blood	Femoral vein	Primary disease Femoral catheter Prolonged immobilization	Day 18 of BMT Warfarin × 12 weeks
3	53/M	Myeloma	Autologous	<i>E. coli</i> , VRE UTI	Left external iliac vein	Primary disease Femoral catheter Prolonged immobilization	Warfarin × 12 weeks
4	22/M	Aplastic anemia	Allogeneic	Blood—CRE; sinusitis	Cavernous sinus Right IJ thrombosis	Sphenoid and ethmoid sinusitis	Could not anticoagulate due to thrombocytopenia
5	28/F	PNH	Allogeneic	None proven	@ RIJV and subclavian vein	Primary disease Hickman catheter	Warfarin × 6 weeks

CRE carbapenem resistant enterobacteriaceae, VRE vancomycin resistant enterococci, UTI urinary tract infection, PNH paroxysmal nocturnal hemoglobinuria, DVT deep venous thrombosis, IJV internal jugular vein

difficult to comment on role of graft versus host disease (GVHD) (incidentally none developed during follow-up), or stem cell dose or conditioning regime (all autologous patients received myeloablative conditioning and allogeneic patients received reduced intensity conditioning).

Patient 1 was on thalidomide maintenance. Thalidomide is known to be a risk factor for thrombotic events even though risk is low in certain Asian populations [6].

In early phase of our program we were inserting femoral catheters for peripheral blood stem cell harvest for multiple myeloma and in some patients used the same catheter during transplant in patients with difficult venous access. A major pitfall of this approach was that some patients were not keen to mobilize out of bed and that added an extra risk factor for thrombosis. We have revised our policy since then. Now all our patients get a permacath inserted in internal jugular vein which is used both for stem cell harvest and as a venous access for transplant for 3 weeks. This has taken away the immobilization factor and we have not noticed any venous thrombosis since then.

Conclusions

Venous thrombosis in our patients was largely interplay of hypercoagulable state due to primary disease, a central venous catheter and prolonged immobilization.

Compliance with Ethical Standards

Conflict of interest Author Manoj Singh that he has no conflict of interest. Author Rahul Naithani declares that he has no conflict of interest.

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