Case report

Managing a patient with thrombotic thrombocytopenic purpura requiring large amounts of blood in Oman

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Introduction

Providing adequate amounts of safe blood is the prime objective of any blood transfusion service. Over the last two decades, efforts have been directed at decreasing the risk of transmission of diseases through transfusion. Reducing viral risks through expansion of donor history screening, improvements in testing for infectious disease markers and virus inactivation of blood products have met with much success [*1,2*]. However, transfusion of blood components still bears a certain element of risk. None of the current practices of donor selection or testing guarantee zero risk. There are several reports of transfusion-transmitted diseases, with varying incidence, contracted even after the transfusion of properly tested blood [*2,3*]. There are no such reports from the population in Oman.

Shortage of blood is a global problem. It is more common in developing countries, as a result of rapid industrialization and advances in technology leading to the establishment of more modern medical facilities. As a consequence, transfusion services frequently experience pressure to mobilize blood and blood products at short notice.

We report our experience from Oman in the management of a case of thrombotic thrombocytopenic purpura (TTP) that highlights the importance and the problems in organizing and supplying enough safe blood and blood components. For this patient, large amount of blood components had to be mobilized at short notice. Although the patient received blood components and products originated from several hundred donors, she did not contract any transfusion-transmitted disease.

Management of the case

A 23-year-old female patient of Omani nationality was referred to the Royal Hospital, Muscat, from a regional hospital, suffering from anaemia and thrombocytopenia with episodes of generalized convulsions and loss of consciousness. TTP was considered likely.

She was initially given supportive treatment with platelet and packed-cell transfusions, antibiotics and prednisolone. On the 3rd day, fresh-frozen plasma (FFP) infusion was started at a dose of 15 mL/kg body weight, followed by intravenous immunoglobulin 0.4 g/kg body weight. Subsequently, haematological and biochemical parameters, peripheral blood film and a bone marrow aspirate examination helped

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confirm the diagnosis of TTP. Hence it was decided to start aggressive plasma exchange therapy immediately.

FFP was used as replacement solution for the first 6 sessions of plasma exchange and cryoprecipitate-poor plasma (CPP) for subsequent sessions. After 6 days of plasma exchange the patient started showing improvement. A total of 11 plasma exchange sessions were carried out over a period of 13 days. After discontinuation of plasma exchange, CPP infusion at 15 mL/kg body weight was given for a week. The amount of blood components and blood products given are shown in Table 1. She was discharged with advice to take 10 mg prednisolone daily and to check her blood count periodically.

Eight months later she relapsed. Plasma exchange was started on the first day with FFP as replacement solution for the first 3 sessions and CPP subsequently. From the 9th day onwards she improved. She received 8 units of packed red cells, but she developed severe febrile non-haemolytic transfusion reaction. Hence the next 4 transfusions given were washed red cell preparations. There were no reactions to these.

Thirty months after the 1st episode, she again came to the hospital as her platelet count had dropped. As the plasma exchange facility was temporarily unavailable, daily infusion of CPP was immediately started at a dose of 15 mL/kg body weight. After 3 days she started showing improvements and was discharged on 10 mg prednisolone daily, with advice to get her blood counts tested at regular intervals.

Fifty months after the first episode she came back with multiple bruises and a very low platelet count. CPP infusion was given at 15 mL/kg body weight for 2 days and plasma exchange was started from the 3rd day onwards, with CPP as replacement solution. Oral prednisolone, methyl prednisolone infusion, intravenous immunoglobulin and vincristine were given as adjuvant therapy. Phenytoin and intravenous diazepam was used to control the convulsions she developed. Her illness had a much more protracted course during this episode. Splenectomy was planned, but consent denied.

After 18 sessions of plasma exchange over a period of 20 days without improvement, we felt that she has developed resistance to plasma exchange and she was

Table 1 **Number of blood components and products given to a patient with thrombotic thrombocytopenic purpura during each episode of illness in hospital**

Blood component/product	No. of products given			
	1st episode	2nd episode	3rd episode	4th episode
Packed or washed red cells	16	12	0	13
Platelet concentrates	77	0	0	6
Fresh-frozen plasma	102	54	0	0
Cryoprecipitate-poor plasma	59	157	54	308
Intravenous immunoglobulin	Yes	Yes	No	Yes

started on cyclosporin A at 5 mg/kg body weight by intravenous infusion. She responded readily to cyclosporin A and marked improvement was noticed from the 3rd day onwards. Plasma exchange sessions were tapered and later discontinued. She was discharged on the 40th day but is regularly followed up in the clinic. She was negative for serological markers of hepatitis B, hepatitis C and human immunodeficiency virus 1, 2 and 0 and remains so. Screening for red cell antibodies was negative. The liver function tests done at regular intervals were normal. She is currently taking 200 mg cyclosporin A, 300 mg aspirin and 10 mg prednisolone daily.

Procedures

Plasma exchange procedures were done by removing 1–1.5 plasma volume and infusing FFP or CPP as the replacement fluid in a 1:1 ratio. It was performed with a discontinuous-flow cell separator machine (V50 Plus, Haemonetics Corp, Braintree, Massachusetts, USA) using a low-volume component collection set. A double-lumen catheter (Quinton) was placed in the femoral vein for access. CPP, also known as cryosupernatent plasma, was obtained after centrifugation and removal of cryoprecipitate from FFP. Washed red cells were prepared by a cell washing protocol using low-volume component collection set (Haemonetics V50 Plus). During the course of her hospital stay, the patient received blood components derived from 858 donors (Table 1).

Blood collected by the blood transfusion service in Oman is regularly tested by microparticle enzyme immunoassay for human immunodeficiency virus (HIV) 1, 2 and 0 (AxSYM HIV 1/2 gO, Abbott Diagnostics, Illinois, USA), hepatitis B (AxSYM HBsAg version 2, Abbott Diagnostics), hepatitis C (AxSYM HCV version 3.0, Abbott Diagnostics) and the *Treponema pallidum* haemagglutination assay (Immutrep-TPHA, Omega Diagnostics, Alva, Scotland). Screening of the patient's serum for red cell antibodies was by the gel method (ID Micro Typing System, DiaMed, Switzerland) and was done at each admission and at 3-monthly intervals.

Discussion

The introduction of plasma infusion and exchange to the management of TTP has boosted survival rates to more than 90% [*4*]. Plasma exchange continues to be the mainstay of treatment although several adjuvant treatment modalities are in practice [*5*]. Plasma exchange-resistant TTP has been reported recently [*6*]. Our patient responded well in the first 3 episodes but showed resistance to plasma exchange in the 4th episode. Cyclosporin A, splenectomy and stem cell transplantation have been tried successfully in patients resistant to plasma exchange [*7–9*].

Large volume, frequent plasma exchanges put tremendous pressure on the blood transfusion services for resources and manpower. The CPP is prepared by overnight thawing of FFP, centrifuging and separating it into another bag, which is time-consuming. Such cases can easily deplete our blood reserves very quickly. In Oman, stocks of blood are low during the summer and long holidays when schools and colleges are closed. Finding enough blood components at short notice is a problem, so too is the availability of well-trained staff out of normal working hours. The staff of the haemapheresis section have to devote several hours per day to a single patient. This means that only 1 machine will

be available for other patients or donors. A sudden rise in the consumption of disposable sets can also cause procurement problems. We have to consider the cost for a department with a predetermined fixed budget. Cost constraints are a major concern in developing countries.

Since 1991 the importation of blood and blood products to Oman has been prohibited by law, except coagulation factor concentrates, immunoglobulins and vaccines. Oman became self-sufficient in red cells, platelets and plasma preparations such as CPP. WHO guidelines for donor recruitment and selection (non-remunerative) are followed. Special attention is given to public relations and the local media is used efficiently and quickly when a large amount of blood products are needed at short notice. The availability of the haemapheresis service also helps in making certain quality products available for selected patients.

The risk of transmitting hepatitis B virus in blood screened by modern methods is relatively low (1:63 000 units donated in a low prevalence population such as the USA for such infections) [*2*]. An incidence of hepatitis B infections of 0.06% has been reported in patients receiving FFP [*10*]. Raphael et al. observed a higher incidence of complications when FFP was used as a replacement solution in plasma exchange; 5 of the 52 patients receiving FFP developed anicteric hepatitis [*11*].

There are no reports on the incidence of transfusion-transmitted disease in the Omani population. In a study published in 1997 in Oman, it was found that voluntary donors represent 86.5% while 13.5% were replacement donors. The combined incidence of hepatitis B surface antigen (HBsAg) and anti-heptitis C virus (HCV) antibody positive donations were reported as 5.9% among replacement donors and 4.3% among voluntary donors [*12*]. The study did not distinguish between the 2 infections. More recently, the number of donations and donors deferred because of positive infection markers was published in the 2002 annual report of the Ministry of Health in Oman [*13*]. A total of 81.6% of the donors were Omani nationals, the rest were expatriates. Out of a total 32 944 donations, 3647 were not used. The HBsAg-positive donations were 1269 representing 3.9%, HCV-positive donations were 229 representing 0.79%, and HIV-positive donations were 13 representing 0.04% of the total donations. These figures came from people willing to donate who usually are well-informed and motivated. The prevalence of HBsAg as an example is better reflected by a sero-surveillence study carried out in pregnant women in Oman that showed 8.9% of them to be positive for HBsAg [*14*]. As a result we would expect that the chances of acquiring transfusion-transmitted disease after exposure to 858 donors in our patient to be significant. However, this theoretical chance never materialized during her prolonged course of treatment and 2 years of follow-up after her last plasma exchange session. Her liver enzymes remained normal and no irregular red cell antibodies were detected.

The white cell associated reactions are responsible for febrile non-haemolytic transfusion reactions. The reported incidence is from 0.025 to 1 per 100 units of blood transfused [*15*]. In the 2nd episode since the patient developed severe febrile non-haemolytic transfusion reactions, we transfused washed red cells only. In the treatment of TTP, washed red cells have been used by others also to remove white cells and plasma [*16*]. White cell filtration at source using blood collection sets with built-in filters or filtration at the blood bank during component preparation has not yet been introduced in Oman. Bedside filtration

of white cells is widely available. It is usually used for all neonates and children, and to multiply transfused and immunocompromised patients.

Successful management of TTP is a challenge not only to clinicians but also to the blood transfusion and haemapheresis services in developing countries. Our experience in Oman highlights the importance of having a properly organized blood transfusion service. Such a service must have adequate stocks and trained staff to prepare and supply the necessary components at short notice without compromising the product safety. The successful outcome of this patient's management is a testimony to the competence and quality of the blood transfusion service in Oman.

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World Blood Donor Day

The 14 June 2004 has been designated as the first World Blood Donor Day. It is being held as a worldwide celebration to honour and thank those people who donate their blood on a voluntary, unpaid basis. The aim of World Blood Donor Day is to give particular thanks to these individuals, particularly those who give blood regularly. The objective is not to attract a big influx of new blood donors on 14 June, but to create wider awareness of the importance of voluntary unpaid blood donation and encourage more people to become regular donors. World Blood Donor Day is supported by the collaborative efforts of four international organizations working for the provision of safe blood globally: the World Health Organization, the International Federation of Red Cross and Red Crescent Societies, the International Federation of Blood Donor Organizations (FIODS) and the International Society of Blood. Information about World Blood Donor Day can be obtained at: http://www.wbdd.org/index.html