Multiple Organ Failure Associated with Dimethylsulfoxide and Hydroxyethyl Starch in Autologous Blood Stem Cell Transplantation

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Dear Sir,

Autologous blood stem cell transplantation (ABSCT) is reported to have less contamination by tumor cells [1] and more rapid recovery of marrow function than autologous bone marrow transplantation [2]. Life-threatening complication associated with the infusion of bone marrow grafts or peripheral blood stem cells (PBSC) preserved with a mixture of dimethylsulfoxide (DMSO) and hydroxyethyl starch (HES) has not yet been documented. We describe the case of multiple organ failure (MOF) after the infusion of PBSC preserved with a mixture of DMSO and HES.

A 22-year-old male was admitted, complaining of pain in the lower right quadrant of the abdomen, where a tender tumor was palpable. He was diagnosed as having malignant lymphoma Burkitt type originating in the terminal ileum. High-dose ablative chemotherapy consisting of pirarubicin, rani-mustine, carboplatin and etoposide was performed. On day 9 of the chemotherapy, PBSC, which had been harvested via peripheral blood by means of apheresis and stored at -80°C with 5% DMSO and 6% HES (Kyokuto Pharma. Indust. Co., Tokyo, Japan), were rapidly thawed in a 37°C water-bath and infused through a central venous catheter for 60 min. The infused volume was 759 ml containing 38.0 g of DMSO (0.70 g/kg) and 45.5 g of HES (0.84 g/kg).

An hour and a half after completion of the infusion the patient developed pulmonary edema and was in respiratory failure with arterial blood gas showing pH 6.86, PO2 48 mm Hg, PC02 99 mm Hg, HC03 16.6 mmol/l and with blood pressure 120/70 mm Hg, pulse rate 170/min. He was shocked with marked hypotension and required mechanical ventilation. Three days later he became independent of both mechanical ventilation and inotropic support. However, the investigations showed anemia, nonoliguric renal deterioration and liver dysfunction: hemoglobin 7.7 g/dl, hematocrit 21.7%, white cell count 100/µl, platelets 1.2 × 104/ µl, blood urea nitrogen 77.9 mg/dl, creati-nine 6.3 mg/dl, serum bilirubin 3.9 mg/dl, asparate aminotransferase 3,573 IU/l, alanine aminotransferase 2,219 IU/l, lactic de-hydrogenase 20,340 IU/l and prolonged pro-
thrombin time (PT) and partial thromboplastin time (APTT). Urinalysis was positive for protein and blood. Plasma exchange for the same volume of fresh frozen plasma for 2 successive days (the first day 4.2 l, the next day 3.6 l) and hemodialysis were performed. Over subsequent days liver enzymes, PT, APTT all returned to near normal values and after 10 days the patient became independent of dialysis (fig. 1).

It seemed likely that the pulmonary edema and subsequent MOF were attributable to the infused cryoprotectants. Minor to moderate toxicities of DMSO infusion in human such as intravascular hemodialysis, hyperosmolality and mild increase of serum transaminase have been reported [3, 4]. However, the dose of DMSO in our case was not beyond the range of these reported cases. It is reported that grafts infusion with DMSO decreases forced vital capacity [3], and that DMSO causes characteristic breath odor soon after being administered [5]. These findings may suggest that DMSO rapidly distributes and accumulates in pulmonary interstitial spaces and alveoli, which causes an influx of fluid from plasma to these spaces by means of osmotic force of DMSO. In addition to pulmonary damage by DMSO, acute ventricular failure induced by HES, which is an artificial colloid and a plasma expander, appeared to have caused clinically manifested pulmonary edema, acute respiratory failure and respiratory acidosis.

Nephrotoxicity attributable to hemolysis caused by DMSO has been reported [4]. The patient showed hemoglobinuria with decrease of hemoglobin level from 10.0 g/dl on the day of transplant to 7.7 g/dl on the 4th day posttransplant, when plasma exchange and hemodialysis were initiated. It is likely that hemolysis with hemoglobinuria and hypotension were responsible for the acute renal failure. The patient probably had ischemic liver damage secondary to severe pulmonary edema and shock. We performed plasma exchange followed by hemodialysis because DMSO is strongly bound to plasma proteins and its clearance by hemodialysis or peritoneal dialysis is poor [6].

This is, to our knowledge, the first published case of MOF about infusion-related toxicity in ABSCT. Our experience may suggest that development of processing and technique for reducing the volume of cryoprotectant and enriching PBSC in ABSCT is required to decrease the risk of infusion-related toxicity, as the use of ABSCT is expanding.

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ABSCT
4,000 3,000 2,000 1,000
0
8,000
- 6,000 [a]
$4,000 [b]
0 [c] 4,000 $5,000
2,000 0

Fig. 1. Changes in creatinine (Cr), asparate aminotransferase (AST), hemoglobin (Hb), white blood cell count (WBC) and urine output at the time of plasma exchange (PE) and hemodialysis (HD) after autologous blood stem cell transplantation (ABSCT). CRC means concentrated red cell transfusion.
References

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