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Another case of acute cardiopulmonary toxicity with cord blood infusion: *Is dextran the culprit?*

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Infusion-related adverse reactions associated with cord blood (CB) transplants are considered to be less frequent and less severe when compared to cryopreserved bone marrow or peripheral blood stem cells.[1] The true incidence of these reactions is unknown, although it is reported that 30-60% of CB recipients are affected by infusion reactions.[1,2] Recently, there have been six published reports of severe, life-threatening cardiopulmonary reactions associated with CB infusions (Table 1).[3,4] A review by the National Marrow Donor Program (NMDP) and the Food and Drug Administration (FDA) of 13 serious CB-associated infusion reactions events showed that the majority of cases (92%; 12/13) involved infusion of at least one RBC-replete CB unit.[3] As a consequence, the NMDP and FDA provided recommendations for thawing and washing RBC-replete CB units.[3] We report a case of a seventh, cardiopulmonary reaction associated with the infusion of a RBC-depleted, CB unit diluted with human serum albumin (HSA)-Dextran 40.[2]

The patient was a 16-year old, 46 kg, group O Caucasian female with acute biphenotypic leukemia. As part of a clinical trial, the patient was randomized to receive a 5/6 HLA-matched, double CB transplant (Table 1). Both CB units were RBC-depleted and cryopreserved in a solution containing 10% DMSO and 10% Dextran-40. After thawing, both CB units were diluted 1:3 with 5% HSA-8% Dextran 40 solution, for a combined final infusion volume of 411 ml and less than 3% DMSO per unit. The total transplant dose was 2.6×10^5 CD34 per kg and 5.7×10^7 TNC per kg of recipient weight.

The patient was pre-medicated with acetaminophen, diphenhydramine, hydrocortisone, and mannitol per institutional clinical practice guidelines. Less than five minutes after starting the first CB unit, the patient experienced a severe anaphylactic reaction characterized by nausea, vomiting, dyspnea, wheezing, chest tightness, tachycardia, and tachypnea. The infusion was immediately stopped and the patient was treated with hydrocortisone, diphenhydramine, ativan, atrovent, and albuterol, and placed on 4 liters of oxygen by nasal cannula. After 10 minutes, the patient's symptoms improved and the infusion of CB unit #1 was slowly restarted and subsequently completed within 60 minutes. After additional premedication, the patient received the second CB unit over 60 minutes. The second infusion was uneventful except for hypertension and a few hives two hours post-infusion. Both were successfully treated with additional antihistamine and anti-hypertensive medications.

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Diagnostic studies at the time of the infusion reaction showed a prolonged QTc (baseline 0.416 to 0.514 sec), elevated troponin (baseline <0.01 to 1.7 ng/mL) and B-type natriuretic peptide (baseline 110 to 592 pg/mL). An echocardiogram revealed regional hypokinesis of the basal half of the posterior two-thirds of the septum, with overall mildly depressed left ventricular systolic function. The patient had no evidence of electrolyte abnormalities, renal insufficiency, intravascular hemolysis or acute pulmonary changes. Pertinent EKG and laboratory studies returned to baseline within 48 hours and were attributed to transient myocardial ischemia.

Our patient's symptoms were consistent with a severe, anaphylactic reaction. We believe the reaction was precipitated by Dextran 40. Acute, severe reactions to Dextran 40 have a reported incidence of 1/2000 and can be associated with cardiac ischemia, pulmonary and renal injury.[4,5] It is noteworthy that the majority (6/7) of cardiopulmonary infusion reactions reported to date were associated with CB units frozen and/or diluted in HSA-Dextran. As observed by Ma et al,[4] reports of severe CB infusion reactions "coincide with the introduction of dextran in cryopreservation", and include more recent protocols for dilution or washing CB products in HSA-Dextran.[2] Ongoing investigations into severe CB reactions should include the potential role of Dextran in such reactions, as well as possible prophylaxis with Dextran-1, a hapten known to significantly decrease the risk of Dextran reactions.[4,5]

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Biography

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References

1. Chrysler, GR.; McKenna, DH.; Scheierman, T.; Kadidlo, D.; Askari, S.; Miller, J.; Clay, ME.; McCullough, J. Umbilical cord blood banking. In: Broxmeyer, HE., editor. Cord Blood: Biology, Immunology, Banking and Clinical Transplantation. AABB Press; Bethesda MD: 2004. p. 219-257.
2. Barker JN, Abboud M, Rice RD, Hawke R, Schaible A, Heller G, La Russa V, Scaradavou A. A "no-wash" albumin-dextran dilution strategy for cord blood unit thaw: high rate of engraftment and a low incidence of serious infusion reactions. Biol Blood Marrow Transplant. 2009; 15:1596–602. [PubMed: 19896084]
3. Miller, JP. National Marrow Donor Program. Minneapolis, MN: Jul. 2009 A centralized cord blood registry to facilitate allogenic, unrelated cord blood transplantation, BB-IND #7555 Safety Report.
4. Ma RW, Kwan JM, Ma DD, Fay KC. Acute life-threatening cardiovascular toxicity with umbilical cord blood infusion: the role of dextran. Am J Hematol. 2010; 85:722–4. [PubMed: 20661918]
5. Zinderman CE, Landow L, Wise RP. Anaphylactoid reactions to Dextran 40 and 70: Reports to the United States Food and Drug Administration, 1969 to 2004. J Vasc Surg. 2006; 43:1004–1009. [PubMed: 16678697]

Table 1

Summary of Cord Blood Infusion Reactions with Cardiopulmonary Symptoms*

Patient			Cord Blood Characteristics					Infusion Reaction		
Case	Age	Sex	CB Unit	ABO Compatible	RBC Depleted	CB Processing	Final Volume	Onset	Symptoms	Ref
1	16	F	1	N	Y	Both diluted 1:3 HSA-Dextran 40	169 mL	< 5 min	Nausea, vomiting, hypertension, chest pressure, tachycardia, ↑QTc, ↑troponin, septal hypokinesis, ↓ left ventricular function.	This Report
			2	Y	Y		201mL	2 hours	Hives.	
2	55	M	1+2	Y	Y	None	209 mL	10 min	Chest pain, hypertension, nausea, hypoxia, pulmonary edema, ↑troponin, ARI.	3
3	44	F	1	Y	N	Both diluted HSA-Dextran 40	251 mL 52 mL	50 min	Chest pain, ↑troponin, hypoxia, ↓EF (69→15%), pulmonary infiltrates, ARI.	4
			2	Y	NA					
4	65	M	1	Y	NA	Both diluted HSA-Dextran 40	200 mL	First unit	Chest pain, ↑troponin, ↓EF (25%), ST changes, hypoxia, pulmonary edema, ARI.	4
			2	Y	NA		50 mL			
5	34	F	1	N	N	Both diluted 1:4 HSA-Dextran 40	Total 500 mL	50 mL	Chest pain, ↓EF (66→50%).	4
			2	Y	N			During infusion	Hypoxia, nausea, vomiting, chest pain, ↑troponin, ↓EF (50→40%), pulmonary infiltrates, global myocardial hypokinesis.	
6	20	F	1	NA	N	None	50 mL	During infusion	Chest pain, hypertension, hypoxia, nausea, vomiting, hemoglobinuria.	4
			2	NA	Y	Diluted HSA-Dextran 40	NA			
			3	NA	N	Diluted HSA-Dextran 40	114 mL			
7	60	NA	1	NA	N	Centrifuged, resuspended HSA	175 mL	15 min	Nausea, vomiting, abdominal pain, hypertension, hypoxia, ST depression, ↑troponin, mild atrial hypokinesia.	3

*Abbreviations: CB, cord blood; EF, cardiac ejection fraction; HSA, human serum albumin; NA, not available; ARI, acute renal injury.