Netherlands Journal of Critical Care
Submitted July 2021; Accepted January 2022

CASE REPORT

Rescue plasmapheresis for massive shear stress-induced haemolysis following paravalvular leak closure

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Keywords - **Haemolysis, plasmapheresis, valvular interventions, mechanical circulatory support**

Abstract

Given the increasing use of transcatheter (para)valvular interventions and mechanical circulatory support, haemolysis is becoming a more frequently encountered complication. In this setting, patients should be actively monitored for signs of haemolysis, given the potential major adverse consequences. Although not commonly used, plasmapheresis is a very effective rescue method to remove plasma free haemoglobin from the circulation and preserve renal function while the underlying cause is being addressed, as illustrated in this case report.

Introduction

Intravascular mechanical haemolysis or the destruction of red blood cells by mechanical (non-physiological) shear stress, despite their flexibility and deformation, is becoming a clinical challenge in the new era of transcatheter valvular interventions and mechanical circulatory support (MCS). In this case report on massive haemolysis after closure of a paravalvular leak (PVL), we provide an illustration of the potential benefit of plasmapheresis in reversing the renal dysfunction while the underlying cause of haemolysis is being addressed, and also emphasise the importance of proactive surveillance in this setting for signs of haemolysis.

Case

An 82-year-old female patient was admitted to our hospital for closure of a large paravalvular mitral leak. Four months earlier, the patient underwent mitral valve replacement with a bioprosthesis (Abbott Epic Mitral, 31 mm) due to symptomatic, severe degenerative mitral regurgitation. Three months after the procedure, she was readmitted with decompensated heart failure, and echocardiography revealed a severe prosthetic PVL, measuring 14x8 mm in diameter, with a regurgitant orifice area of 0.75 cm^2 and regurgitant volume of 97 ml. This large lateral PVL was thought to originate in suture dehiscence in a zone of severe mitral annular calcification. There were no signs of infective endocarditis. Transapical closure of the PVL was performed via a small thoracotomy with a closure device normally used for ventricular septal defects (Occlutech 71 muscular VSD occluder, 14 mm) *(figure 1A)*, with mild residual regurgitation between the device and the prosthesis and mainly through the device itself *(figure 1B)*. Approximately 12 hours after the procedure, the patient's urine appeared dark-red and she developed oliguric renal failure with a serum creatinine of up to 1.4 mg/dl (123.8 µmol/l) (reference 0.51-0.95 mg/dl or 45.1-84.0 µmol/l; baseline value 0.8 mg/dl or 70.7 µmol/l). Massive haemolysis was diagnosed, reflected by the strong elevation of plasma free haemoglobin (pfHb) (up to 190 mg/dl (29.5 µmol/l); reference <5 mg/dl or 0.775 µmol/l) and other haemolysis parameters (including lactate dehydrogenase and bilirubin), and fully suppressed haptoglobin. An initial attempt with hydration, forced diuresis and intravenous nitroprusside for left ventricular afterload reduction was unsuccessful. Approximately 24 hours after the procedure, membrane plasmapheresis was initiated. The plasma volume was calculated based on height (165 cm) and weight (58 kg) to be 2.94 litres. Plasma was substituted with 1500 ml of fresh frozen plasma and 1500 ml of albumin. Fresh frozen plasma was chosen in order to promote clotting of the paravalvular leakage. In the following hours, there was a rapid recovery of the diuresis with the urine colour returning to normal *(figure 2A)*. Normalisation of pfHb levels was obtained about nine hours after the institution of plasmapheresis, and restauration of serum creatinine to baseline values 48 hours later. The effluent was notable for a 'cola' coloured liquid, indicating efficient removal of pfHb from the patient's circulation *(figure 2B)*. One two-hour session of plasmapheresis proved to be sufficient, given spontaneous clotting and obliteration of the remaining PVL after withholding anticoagulation. Transfusion of packed cells was not required.

Discussion

Intravascular mechanical haemolysis is becoming a clinical challenge in the new era of transcatheter valvular interventions and mechanical circulatory support (MCS). Subclinical haemolysis

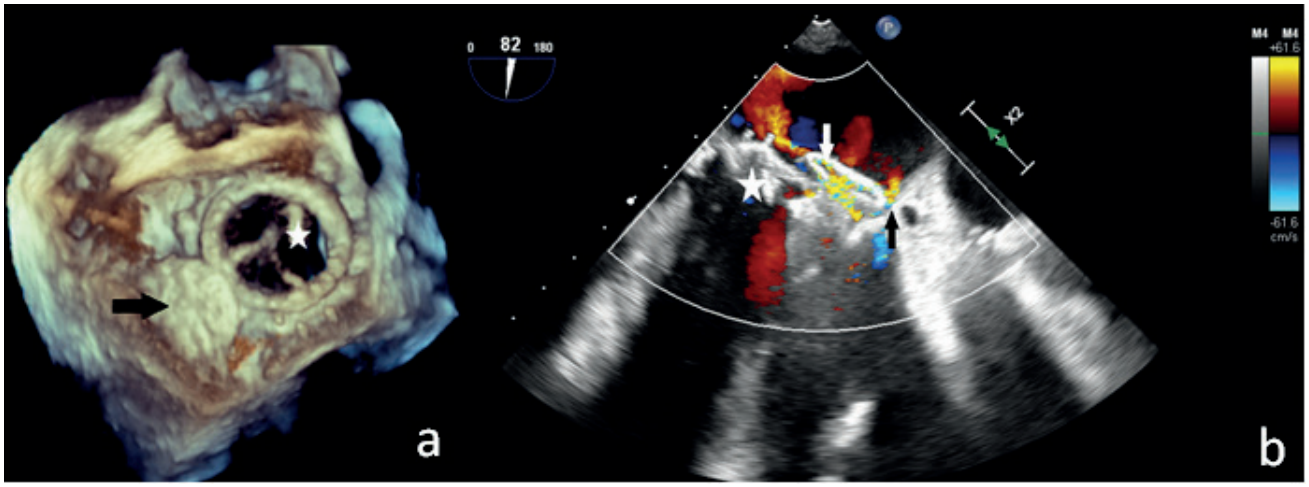

Figure 1. A) 3D transoesophageal echocardiography image of the closure device in situ (black arrow) next to the mitral bioprosthesis (asterisk). B) Residual regurgitation between the mitral bioprosthesis (asterisk) and the closure device, with one large jet (white arrow) through the device and one small jet (black arrow) to the lateral side of the device

was present in 15% of 122 patients after balloon-expandable transcatheter aortic valve replacement.[1] In registries of HeartMate® II, haemolysis was noted in 13-18% of cases, while in HeartMate® III less than 1% of the cases were complicated with haemolysis.[2,3] Haemolysis is reported at meaningful frequencies of 8 to 63% in patients who receive short-term percutaneous MCS with the Impella® device.[4] Haemolysis is associated with increased mortality, along with an increased incidence of haemolytic anaemia (and increased blood product transfusions), acute kidney injury and, in cases of MCS, oxygenator failure and pump thrombosis.[5]

Elevation of pfHb (>40-50 mg/dl or >6.2-7.8 µmol/l) and haemoglobinuria are both tell-tale signs of haemolysis and therefore should be frequently and proactively monitored in those patients. Circulating free haemoglobin is very prothrombotic and can cause acute kidney injury through pleiotropic mechanisms.[5] First, it exerts a direct toxic effect on proximal tubular cells by the deposition of haemosiderin, with resultant oxidative stress (formation of reactive oxygen species) and release of pro-inflammatory markers, cast formation and tubular obstruction. Furthermore, pfHb causes vasoconstriction of the renal microcirculation through quick and irreversible nitric oxide (NO) scavenging and impaired NO synthesis.[5] Last but not least, it also has prothrombotic properties through binding of von Willebrand factor (vWF) and blockage of the cleavage of vWF by ADAMTS-13 protease, resulting in augmented platelet adhesion, activation and formation of microthrombi.[5]

There are a limited number of management approaches to address intravascular shear stress-induced haemolysis.[2] In the setting of MCS, optimisation of device position, flow, volume status and anticoagulation are paramount.[4] In valvular heart disease, appropriate afterload reduction, e.g. with nitroprusside or beta blockers, is indicated.[2,6] Of course, intervention to correct the underlying cause should always be considered, such as the closure of a PVL or pump exchange in case of thrombosis in MCS. Alkalinisation of urine or forced diuresis can be used to prevent cast formation. Pentoxifylline is sometimes described to improve the blood viscosity and red blood cell deformability.[2]

Only a few case reports mention therapeutic plasma exchange or plasmapheresis as a possible treatment approach in the setting of massive haemolysis, especially in MCS.[7-9] Plasmapheresis can accomplish three goals: direct removal of circulating pfHb, repletion of haptoglobin stores and regeneration of NO with improved vasodilation and microvascular blood flow. It consists of the withdrawal of venous blood, followed by the separation of plasma from blood cells (by membrane filtration or centrifugation), and the reinfusion of cells plus a replacement fluid.[10] This replacement fluid can be either human albumin 5% or other plasma derivatives, crystalloid solutions or, as in this case and preferentially, fresh frozen plasma. Anticoagulation with unfractionated or low-molecular-weight heparin is used to prevent the circuit from clotting, but should be used at a minimal dose in this setting to promote clot formation of the residual PVL.

Conclusion

Haemolysis is becoming a more commonly encountered complication in the era of transcatheter (para)valvular interventions and MCS. Signs of haemolysis should be actively monitored, given the potential major adverse consequences. This case report describes, for the first time, the successful use of plasmapheresis as rescue treatment for massive shear stress-

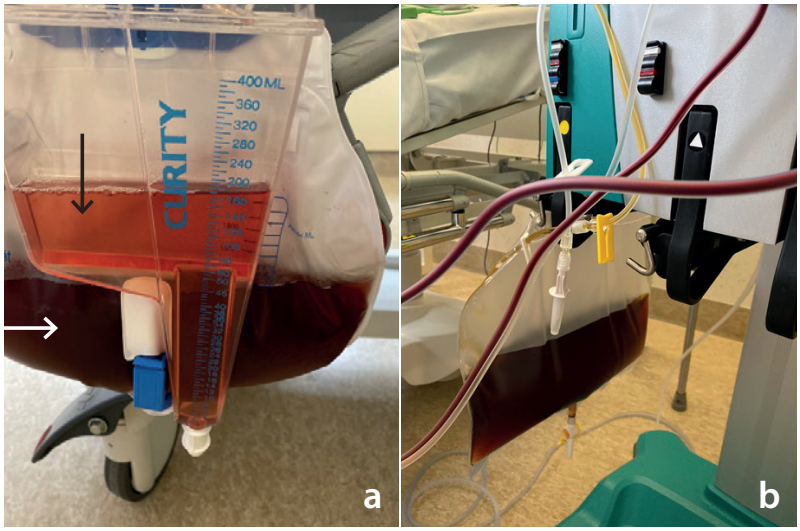

Figure 2. A) Dark urine before (white arrow) and after (black arrow) the initiation of plasmapheresis; colour attenuation was in parallel with a decrease in plasma free haemoglobin levels. B) Plasmapheresis effluent collector

induced haemolysis in the setting of percutaneous PVL closure, confirming it is a very effective method to remove the pfHb from the circulation and restore the renal function, while the underlying cause is being addressed.

Disclosures

W. Budts reports being proctor for Abbott and Occlutech. On behalf of the other authors, the corresponding author states that there are no conflicts of interest. No funding or financial support was received.

The institutional ethical committee waived the need for informed consent; thus, according to local ethical guidelines for this case report, no written informed consent was obtained.

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Video 1. Colour flow transoesophageal echocardiography before closure of PVL

https://njcc.nl/sites/nvic.nl/files/21-35%20Couck%209953182C-79DD-46D1-AD25-03796059B21E.mov

Video 2. Colour flow transoesophageal echocardiography after closure of PVL

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