2021 Annual SHOT Report – Supplementary information

Chapter 17b: Pulmonary Complications of Transfusion: (Non-TACO)

Additional case studies not included in the main 2021 Annual SHOT Report.

Deaths related to transfusion n=7

Case 17b.1: TACO/TRALI cannot be distinguished, antibody-negative: Death probably due to transfusion in a patient with a history of heart failure.

A female in her 40s with a history of systemic lupus attended for an outpatient transfusion for autoimmune haemolysis, with diuretic cover. She was 150kg and had a diagnosis of normal systolic function cardiac failure for which she was on 200mg frusemide daily. At the start of the third unit of red cells, she became hypotensive, borderline fever, tachypnoea with hypoxia (80% saturations on air. Chest X-ray was a white out. There was no clinical improvement despite 2.5L diuresis, and despite non-invasive ventilation she died 2 days after transfusion.

All donors were negative for red cell antibodies. There were no troponin or ECG changes but there was a rise in BNP 483 to 2692pg/mL.

The reporters commented 'we recognise that she was at risk of cardiac failure, however, the lack of any response to diuresis, even temporary, along with unchanged chest X-ray appearances and normal troponin made us suspicious of TRALI. The acute medical HDU team also felt that TRALI more in keeping with clinical picture.'

In the RC schema it could arguably be classified as 'TRALI type 1' depending on the subjective judgement of whether 'left atrial hypertension was not judged to be the major contributor.' It would not meet SHOT TRALI criteria because of the absence of antibodies and presence of an alternative explanation. The RC classification of 'TACO and TRALI cannot be distinguished' is a reasonable description. There does seem to be a relationship to the transfusion but whether it is due to fluid overload is unclear.

Case 17b.2: TRALI type 2: antibody-positive. Death probably related to transfusion in a patient with HLA class 1 antibodies, sepsis and large volume transfusion.

A female patient in her 50s with myelodysplasia being treated for sepsis became acutely hypoxic during transfusion. Two units of red cells, four units of FFP and one pooled platelet had been given in the preceding 3 hours. Chest X-ray showed bilateral infiltrates. There was no improvement in respiratory state to diuretics and the patient died within 48 hours of transfusion. One female donor contributing to the platelet pool had multiple HLA antibodies with HLA A24, B52 cognate. The cause of death was recorded as 'sepsis' but the respiratory deterioration was considered to have contributed.

This case has the 'full house' of potential explanations for bilateral lung infiltrates with a large volume of transfusion over a short period of time, sepsis and cognate antibodies. In addition, the

large number of donors investigated increases the chance of an incidental finding of a cognate antibody. The case would be classified as ‘equivocal TRALI’ in the SHOT schema or ‘TRALI type 2’ in the IRC nomenclature.

Case 17b.3: TRALI type 2: antibody-negative. Death possibly related to transfusion in patient with end stage liver disease.

A female patient in her 60s, known to have alcohol related cirrhosis and recurrent anaemia was admitted with a Hb of 47g/L. She had worsening respiratory status with increasing oxygen requirement within 2 hours of starting one unit of red cell transfusion. She had no pre-existing lung disease and there was no clinical evidence of fluid overload. CXR post event showed bilateral pulmonary opacifications, small pleural effusions, appearances suggestive of pulmonary oedema. Echocardiogram showed left ventricular ejection fraction >55%, no suggestion of valvular disease or ventricular compromise. The patient was managed with high flow oxygen, diuretics and no information was available about the response to diuretic. The patient was not considered suitable for ITU/HDU because of the underlying cirrhosis, and died with worsening clinical status. The female donor was negative for leukocyte antibodies.

The case meets criteria for TRALI type 2 in the RC schema but would not be considered TRALI in the SHOT schema due to the absence of antibodies and the presence of an alternative explanation. Decompensation of liver disease due to a GI bleed would be a valid reason to develop ARDS irrespective of transfusion.

Case 17b.4: TAD-IC: Death possibly related to transfusion in patient with lung consolidation, cardiac failure and liver disease.

A male patient in his late 50s with a history of alcoholic liver disease, portal hypertension, previous varices and multiple co-morbidities including COPD, colostomy due to diverticular perforation, myocardial infarction with a percutaneous coronary intervention in 2007, AF, heart failure, large parastomal hernia with stomal bleeding. The patient developed fever, rigors, dyspnoea, wheeze, cough approximately 25 minutes into a transfusion of red cells. The transfusion was stopped appropriately, and the patient treated for suspect sepsis. CXR showed perihilar consolidation. The patient deteriorated despite treatment (received IV antibiotics, diuretics, high flow oxygen), care was not escalated to ITU due to multiple comorbidities and the patient died.

Case 17b.5: TAD-IC: Death possibly related to transfusion in patient with deteriorating COVID-19 infection.

A woman in her mid-40s with alcoholic liver disease was admitted with upper GI bleeding and COVID-19 infection. She received three units of FFP and deteriorated around 24 hours following transfusion. Her respiratory status was worsening prior to transfusion and the patient continued to deteriorate and died within 48 hours despite supportive measures.

Death was most likely related to COVID-19 infection but due to the temporal nature of the transfusions and difficulty in assessing the imputability, this has been recorded as possible and with paucity of details available regarding investigations, has been included as TAD-IC.

Case 17b.6: TAD-IC: Death possibly related to transfusion in patient with decompensated heart failure and COVID-19.

A woman in her 90s was admitted with COVID-19 pneumonitis and a Hb of 79g/L. The patient was also known to have decompensated heart failure and developed worsening respiratory status approximately 2 hours after red cell transfusion. There was a paucity of information provided with no CXR, no fluid balance and no change in status following diuretic, antihistamine and bronchodilator.

It is difficult to assess the relationship of the transfusion to respiratory and cardiovascular symptoms in this patient with COVID-19 pneumonitis who was not expected to survive. This case was submitted to SHOT under TACO but did not meet sufficient criteria for TACO and has been included as TAD-IC.

Case 17b.7: TAD-IC: Death possibly related to transfusion in patient with GI bleed, cardiac and renal impairment and positive fluid balance.

A female patient in her 50s had an episode of GI bleeding and was being transferred to another hospital for an upper GI endoscopy. A unit of red cells was given prior to transfer over 3 hours, the patient departed for transfer on room air and stable. En route in the ambulance shortly following the transfusion the patient desaturated to 76% on air. The patient had a number of risk factors for developing TACO, renal impairment, cardiac impairment, low albumin and a positive fluid balance. No post-transfusion CXR was available but there was suspicion of pre-transfusion pulmonary oedema. Limited information was available and the response to the diuretic was unknown.

This case was submitted to SHOT under TACO but did not meet sufficient criteria for TACO and has been included as TAD-IC.

Other cases - deaths unrelated to transfusion n=2

Case 17b.8: TAD IC: Death not related to transfusion in patient with lung consolidation, sepsis and cardiac disease.

A man in his 70s known to have hypertension, AF, CCF, COPD, eczema, bronchiectasis, adrenal insufficiency was admitted with shortness of breath and a productive cough. Following a single unit red cell transfusion for stable anaemia (Hb 80g/L), a worsening in respiratory status was noted. CXR showed right upper lobe consolidation and presumptive Staph aureus was reported in the blood culture consolidation. No cardiovascular changes were noted, and no details had been provided about fluid balance. The patient improved clinically after diuresis but deteriorated later with acute kidney injury and died. Death was not related to the transfusion.

Case 17b.9: Death not related to transfusion - ATRA differentiation syndrome

A woman in her 60s was diagnosed with acute promyelocytic anaemia with a high WCC (30) and received multiple blood components (FFP, cryoprecipitate, platelets) for severe coagulopathy and thrombocytopenia. The patient developed respiratory distress less than 2 hours after the last transfusion. The patient had been on ATRA and had evidence of fluid overload prior to transfusion. The worsening respiratory status was also associated with significant drop in BP by >30. CXR showed bilateral consolidation which was extensive in all lobes on the right and suggested aspiration. Unilateral pulmonary oedema seemed less likely. Differentiation syndrome was highly likely as the cause of the patient's deterioration and death.

Differentiation syndrome (DS), formerly known as retinoic acid syndrome, is a relatively common and potentially severe complication seen in patients with acute promyelocytic leukaemia treated with all-trans retinoic acid and/or arsenic trioxide. The full-blown syndrome consists of unexplained fever, weight gain, dyspnoea with pulmonary infiltrates, pleuropericardial effusion, hypotension, and renal failure. A preventive strategy with corticosteroids, especially for patients with leukocyte levels higher than from 5 to $10x10^9$/L is recommended. DS diagnosis should be suspected in the presence of any of the above-mentioned signs and symptoms, and pre-emptive treatment with dexamethasone should be started immediately (Sanz and Montesinos 2014).

Transfused ARDS (n=1)

Case 17b.10: Transfused ARDS with worsening status in the 12 hours prior to transfusion as per redefinition consensus criteria

A known patient with atrial fibrillation and cardiac disease presented to the emergency department acutely unwell with a Hb of 50g/L, raised lactate, and was being investigated for a GI bleed. The patient was noted to have a deteriorating respiratory status in the 12 hours prior to transfusion. Two hours into the second unit of red cells, the patient became dyspnoeic, and wheezy with increasing oxygen requirements. CXR showed evidence of ARDS. A diuretic was given and the patient improved.

Imputability in this case was possibly related to the transfusion.

References

Sanz MA, and Montesinos P. How we prevent and treat differentiation syndrome in patients with acute promyelocytic leukemia. *Blood* 2014;123(**18**):2777–2782. https://doi.org/10.1182/blood-2013-10-512640 [accessed 04 July 2022].