Acute haemolysis, DIC and renal failure after transfusion of uncross-matched blood during trauma resuscitation: illustrative case and literature review

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SUMMARY

Aims/Objectives: The aims of this study were to report a patient with acute haemolytic transfusion reaction (HTR) after transfusing uncross-matched red blood cell (RBC) units and to identify the frequency of this complication.

Background: Uncross-matched RBC units are commonly transfused in emergencies, but the frequency of acute HTR is unknown.

Methods: We describe a male stabbing victim who received three units of uncross-matched RBC units complicated by acute intravascular HTR, disseminated intravascular coagulation (DIC) and renal failure. We identified 14 studies evaluating the frequency of acute HTR post-emergency transfusion of uncross-matched RBC units.

Results: Acute HTR was shown by haemoglobinuria, free-plasma haemoglobin and methemalbumin, with anti-K and anti-Fya eluted from recipient red cells; acute DIC featured severe hypofibrinogenemia, thrombocytopenia, elevated fibrin D-dimer and multiple bilateral renal infarcts. Two of the three transfused units reacted with pre-existing RBC alloantibodies [anti-K (titre, 128), anti-Fya (titre, 512)], explained by transfusion 25 years earlier. Our literature review found the frequency of acute HTR following emergency transfusion of uncross-matched RBC units to be 2/3998 [0.06% (95% CI, 0.01–0.21%)].

Conclusions: Although emergency transfusion of uncross-matched blood is commonly practiced at trauma centres worldwide, with low risk of acute HTR (<1/1000), our well-documented patient case demonstrates the potential for acute HTR with severe complications.

Key words: alloimmune haemolytic transfusion reaction, disseminated intravascular coagulation, emergency transfusion, renal failure, uncross-matched blood.

In this report, we estimate the frequency of acute haemolytic transfusion reaction (HTR) after receipt of emergency uncross-matched red blood cell (RBC) units. Our study was prompted by observing a male patient develop severe acute HTR with disseminated intravascular coagulation (DIC) and acute renal failure after the standard practice of transfusing uncross-matched RBC units in an emergency setting.

The emergency provision of uncross-matched group O RBC units is a common practice at trauma centres as the perceived risk of a clinically significant adverse reaction is relatively low and outweighed by the potential benefits of immediate RBC transfusion to a patient at high risk of fatal haemorrhage (Murthi et al., 2008; Boisen et al., 2015). This is particularly the case given that young males are most often trauma victims (Norton & Kobusingye, 2013) and less likely than females to harbour RBC-reactive alloantibodies (Barnes, 1973) that could be harmful when an incompatible RBC unit is given before completing serological testing. Although clinicians are cognizant of the potential for life-threatening acute HTR if a recipient with pre-existing alloantibodies is transfused with one or more incompatible units, well-documented examples of this complication are difficult to find in the literature.

We present a male stabbing victim who developed acute alloimmune HTR, DIC and acute renal failure after receiving three units of uncross-matched blood, two of which were incompatible with the recipient's pre-existing RBC-reactive alloantibodies. This unusual event prompted us to perform a systematic review of HTR following emergency transfusion with uncross-matched blood.
METHODS

Patient information

This study satisfies the ethical requirements of the Hamilton Integrated Research Ethics Board (HiREB).

Laboratory investigations

Serological testing by routine blood bank methods included: blood grouping by tube method (Immucor, Norcross, GA, USA). Antibody detection/identification was performed using solid-phase (Immucor) methodologies per manufacturer's specifications. The polyspecific and monospecific direct antiglobulin tests (DATs) (Immucor) and eluates (Gamma Elu-kit II; Immucor) were performed using commercially available reagents and kits. Antibody titration of the patient's anti-Fy^a^ and anti-K were performed using a tube anti-human globulin method. Testing for haemolysis was performed using a semi-quantitative gel electrophoretic method; evidence for haemolysis using this method includes detection of free-plasma haemoglobin and methaemalbumin, as well as showing reduced haptoglobin (<0·3 g L\(^{-1}\); reference range, 0·3–2·0 g L\(^{-1}\)) (Dacie & Lewis, 1995).

Search strategy, study selection and data extraction

Using the key words 'uncross-matched' 'emergency release' and 'transfusion reactions', as well as a review of reference lists within relevant papers, we identified 12 studies (Blumberg & Bove, 1978; Gervin & Fischer, 1984; Schwab et al., 1986a,b; Lefebre et al., 1987; Unkle et al., 1991; Dutton et al., 2005; Goodell et al., 2010; Ball et al., 2011; Miraflor et al., 2012; Radkay et al., 2012; Mulay et al., 2013) that evaluated the frequency of acute HTR following emergency receipt of uncross-matched RBC units; a 13th study (Meyer & Uhl, 2015) evaluated the frequency of significant alloantibodies being present at transfusion. A 14th study (Schmidt et al., 1988) was brought to our attention during peer review of our manuscript. We were particularly interested in estimating: (i) the frequency of clinically significant RBC-reactive alloantibodies being detected in the pre-transfusion specimen, (ii) the frequency of patients receiving incompatible RBCs and (iii) the frequency of acute HTR and associated clinical consequences among patients receiving one or more incompatible RBC units. Clinically 'significant' RBC-reactive alloantibodies were defined as per Mulay et al. (2013), namely, those known to be associated with HTR, decreased RBC survival and/or haemolytic disease of the newborn, i.e., Rh, Kell, Duffy, Kidd, Ss, certain low-incidence antigens (e.g., Wr\(^e\)), MN and A1 (if reactive at 37°C).

RESULTS

Clinical case

A 47-year-old male was brought to a regional trauma centre (Hamilton General Hospital) for management of a deep, 2 cm-wide stab wound to the right side of the neck caused by an 18-cm hunting knife. On arrival, the patient was hypotensive and overtly bleeding. He immediately received two units of uncross-matched group O RhD-negative RBC units and (after determining the patient's blood type as group A RhD-negative) received a third uncross-matched but group-specific (group A RhD-negative) RBC unit.

He was taken urgently to the operating room, where a lacerated right anterior jugular vein was repaired. Upon arrival to the intensive care unit, the patient was observed to have dark red urine [urinalysis: 3+ blood (reference range, negative), with no significant increase in red cells], elevated blood lactate (10·3 mmol L\(^{-1}\)) and a haemoglobin of 77 g L\(^{-1}\). The transfusion medicine (TM) laboratory determined that the patient had high-titre anti-Fy\(^a\) and anti-K alloantibodies and that two of the RBC units had been incompatible for one or both antigens. Thus, haemolysis investigations were performed, which showed strong evidence of intravascular haemolysis on two different blood samples obtained 65 h apart: free-plasma haemoglobin [detected by gel electrophoresis as well as by visual inspection of the centrifuged whole blood specimen, the latter classified as 'gross haemolysis' (the greatest of three classifications, 'gross', 'moderate' or 'slight', in relation to the normal value of 'absent'), methaemalbumin, reduced plasma haptoglobin of <0·3 g L\(^{-1}\) (reference range, 0·3–2·0 g L\(^{-1}\)), elevated lactate dehydrogenase (LDH) of 1422 U L\(^{-1}\) (reference range, 100–220; peak LDH, 3275 U L\(^{-1}\) measured 65 h later) and peak total bilirubin of 412 μmol L\(^{-1}\) (reference range, <21 μmol L\(^{-1}\)), with elevated indirect bilirubin of 133 μmol L\(^{-1}\) (reference range, <12·4 μmol L\(^{-1}\)). Figure 1a summarises the patient's clinical course over the first 10 h post-admission.

Laboratory testing also showed evidence of acute DIC: fibrinogen nadir, 0·5 g L\(^{-1}\) (reference range, 1·5–4·0); peak international normalized ratio (INR) of 2·4 (reference range, 0·8–1·2) and fibrin D-dimer >4000 μg L\(^{-1}\) fibrinogen-equivalent units (reference range, <500); the platelet count fell precipitously within 8 h of admission to 13 × 10\(^{10}\) L\(^{-1}\) (nadir; reference range, 150–400) (Fig. 1a). The patient was actively resuscitated with 10 units of cross-match-compatible Fy\(^a\)–K–RBCs. 11 units frozen plasma, 10 units cryoprecipitate and four adult doses of (group O) buffy-coat platelets. Consulted for anuria and azotemia [with serum urea and creatinine abruptly rising from admission values of 7·8 mmol L\(^{-1}\) (reference range, 3·2–7·4) and 90 μmol L\(^{-1}\) (reference range, 64–111), respectively, to 20·2 mmol L\(^{-1}\) and 408 μmol L\(^{-1}\) by 30 h post-admission], the nephrologist opined that the patient likely suffered 'pigment nephropathy secondary to acute HTR'; after the serum urea and creatinine levels rose further to 22·8 mmol L\(^{-1}\) and 557 μmol L\(^{-1}\), respectively, over the next 17 h, haemodialysis was started. A CT scan showed that the kidneys had a cortical rim of hypoattenuation with multiple tiny wedge-shaped hypoattenuating foci (Fig. 1b), consistent with numerous DIC-associated micro-infarcts. The patient was discharged on day 53 but required further intermittent haemodialysis for 4 months, at which point sufficient renal recovery rendered him haemodialysis-independent.
Acute haemolysis after uncross-matched blood

Hours after admission

Platelet count (x10^9 L^-1)

0 100 200 300

0 50 100 150

1.1 4.7 n.d. 1.6

1.3  n.d.

1.6

INR

Fibrinogen (g L^-1)

0 1 2 3 4 5 6 7 8 9 10

11 FP units

10 Cryo units

Platelets

26 14 13 20

2.4 (peak)

0.5 (nadir)

0.13

1.6

Fig. 1. Clinical course of patient who developed acute HTR and DIC following receipt of three units of uncross-matched RBCs. (a) Summary of clinical course. A 47-year-old stabbing victim received three units of uncross-matched RBCs, the first two O RhD-negative and the third A RhD-negative (after patient’s group A RhD-negative blood group ascertained). Two of the three units were incompatible with the patient’s anti-Fy^a and anti-K alloantibodies, resulting in an acute HTR (including: haemoglobinuria/acute renal failure, free-plasma haemoglobin, reduced haptoglobin, anti-Fy^a and anti-K eluted from the patient’s RBCs) and acute DIC (platelet fall to 13 × 10^9 L^-1 (nadir), INR rise to 2.4, fibrinogen fall to 0.5 g L^-1 (nadir) and fibrin D-dimer >4000 𝜇g L^-1 fibrinogen equivalent units) (D-dimer values are not shown in the figure). (b) Computed tomography (CT) scan showing bilateral renal cortical necrosis (white arrows) and bilateral renal infarcts (black arrows). The radiologist and nephrologist opined that these abnormalities were consistent with the clinical and laboratory picture of haemolysis-associated pigment nephropathy and acute DIC.

Subsequent patient history included an admission 25 years earlier for 45 days to a hospital elsewhere in Canada when he was a pedestrian struck by a motor vehicle. That hospital’s TM laboratory confirmed patient receipt of nine units of RBC units during that admission, presumably triggering alloimmunisation.

Laboratory investigations confirming alloimmune haemolysis

The patient’s pre-transfusion blood sample showed blood group A RhD-negative, with a positive alloantibody screen and negative direct antiglobulin test (DAT). The patient’s plasma contained anti-Fy^a (titre 512) and anti-K alloantibodies (titre, 128). Phenotyping and serological cross-match of the three uncross-matched RBC units (two group O, one group A) showed that two units (typed as Fy^a+/K+ and Fy^a+/K−) were incompatible (Fig. 1a). Three days post-uncross-matched RBC transfusion, the DAT was positive [Immunoglobulin G (IgG), complement]. Elution studies revealed anti-Fy^a 3 days post-trauma, both anti-Fy^a and anti-K 6 days post-trauma and anti-Fy^a at 3 months post-trauma. Three months post-trauma,
the patient’s anti-Fya and anti-K titres rose to 8192 and 2048, respectively.

Literature review

Table 1 summarises our literature review. The pooled data (see last line of Table 1), show that 3-7% of evaluable recipients had detectable RBC-reactive alloantibodies in their pre-transfusion specimen. However, only 0-6% (16/2643) of patients received one or more incompatible RBC units as a consequence of transfusion with uncross-matched units. Of these 16 patients who received incompatible RBC units, however, only 2 developed acute HTR, the consequences of which ranged from trivial (laboratory evidence for haemolysis only) (Goodell et al., 2010) to consequential (overt HTR, renal failure and death) (Radkay et al., 2012). Thus, the overall probability of a patient developing an acute HTR, with or without consequence, was only 2/3398 (0·06%; 95% CI, 0·01–0·21%) or less than one in 1000 patients receiving one or more uncross-matched RBC units in an emergency setting.

DISCUSSION

Our patient’s clinical course suggested acute intravascular haemolysis and DIC beginning soon after the administration of three uncross-matched units of blood, two of which were incompatible with pre-existing RBC alloantibodies [anti-K (titre, 128), anti-Fya (titre, 512)] explained by transfusion 25 years earlier. Although it is difficult to distinguish adverse consequences of acute intravascular haemolysis secondary to incompatible transfusions from similar events that could be attributable to DIC secondary to trauma-related tissue injury and/or hypotension per se, the striking clinical and laboratory features we observed, which included multiple bilateral renal infarcts, precipitous platelet count fall, severely reduced plasma fibrinogen, marked elevation in LDH and detection of free-plasma haemoglobin and methemalbumin, are consistent with clinically significant intravascular haemolysis with associated DIC. We cannot exclude the possibility that this dramatic clinical picture represented the interaction of acute intravascular haemolysis (secondary to receipt of incompatible blood) and trauma-related tissue injury and hypotension. Although the laboratory picture of haemolysis is not entirely specific in the setting of trauma, our patient’s clinical profile of dramatically rising LDH and reduced haemoglobin far exceeded that usually seen in male trauma patients who receive incompatible RBC transfusions (Seheult et al., 2017).

A noteworthy laboratory feature was the particular temporal pattern of alloantibody elution we observed: whereas anti-Fya alloantibodies could be eluted on three different blood samples (obtained 3 days, 6 days and 3 months post-trauma), anti-K alloantibodies could only be eluted on the single sample obtained 6 days post-trauma. This picture implies that the anti-K alloantibodies, rather than the anti-Fya alloantibodies, were primarily responsible for causing the intravascular haemolysis.

Also consistent with this view is the mechanism of haemolytic anaemia associated with anti-K (intravascular and extravascular) versus anti-Fya (predominantly extravascular) (Regan, 2017). Finally, as our patient’s DAT was positive both for IgG and complement, it indicates that either (or both) of our patient’s anti-K and anti-Fya alloantibodies were complement-fixing (Mollison et al., 1987), potentially also contributing to the severe clinical course.

When patients require blood on a non-urgent basis, pre-transfusion testing includes investigation for unexpected RBC-reactive alloantibodies. However, certain emergency situations may require urgent transfusion of RBC units prior to the opportunity to perform this testing. ABO group-specific units (based on previous results and/or rapid testing for ABO grouping) or group O (‘universal donor’) RBC units, either RhD-positive or RhD-negative, depending on institutional policy, can be used for emergency release. However, patients who receive uncross-matched group-specific or group O RBC units are still at risk of atypical (i.e., non-ABO) alloantibody-mediated HTRs (Boisen et al., 2015). Despite this risk, standard policy is to provide emergency release blood in urgent situations, and indeed, this practice is relatively common in trauma centres.

The relative safety of using group O uncross-matched blood in emergency situations was initially established largely from military studies (Crosby & Akeroyd, 1954; Barnes & Allen, 1968). However, the population prevalent in these studies was mostly young healthy males, which differs significantly from the civilian population encountered in hospitals. Indeed, pre-existing RBC-reactive alloantibodies are infrequent in young males, compared with older men, multiparous women or previously transfused patients, as shown by Saverimuttu et al. (2003). These investigators studied the prevalence of non-ABO alloantibodies in 15 966 patients in the trauma suite, emergency department (ED), haematology–oncology and antenatal settings. They found the overall prevalence of alloantibodies to be 1·9%, with an even lower frequency (0·6% overall) of certain alloantibodies (e.g., Kell, Kidd, Rhesus, Duffy, MNS) being present, which could cause an immediate or delayed HTR (Saverimuttu et al., 2003). However, the frequency ranged from as low as 0·5% (for patients <30 years of age presenting to the ED) to as high as 5% for previously transfused haematology–oncology patients >30 years of age.

Table 1 summarises our review of 14 studies evaluating uncross-matched blood transfusion from the perspectives of identifying the (i) frequency of clinically significant RBC-reactive alloantibodies being detected in the pre-transfusion specimen (column 4), (ii) the frequency of patients receiving incompatible RBCs (column 5) and (iii) the frequency of acute HTR (column 6) and associated clinical consequences (‘Comment’, column 7). Remarkably, the overall frequency of an emergency blood recipient having clinically significant RBC-reactive alloantibodies and receiving one or more incompatible alloantibodies is relatively low, at 0·6% (16/2643), i.e., less than 1 in 100 RBC recipients. Moreover, only 2 of the 16 patients (described subsequently) developed acute HTR, which
### Table 1. Literature summary

<table>
<thead>
<tr>
<th>Study</th>
<th>No. pts. given uncross-matched RBCs</th>
<th>Total no. uncross-matched RBCs given</th>
<th>Frequency of significant alloantibodies (pre-transfusion)</th>
<th>No. of pts. receiving ≥1 incompatible RBCs</th>
<th>Frequency of acute HTR (per patient transfused)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blumberg &amp; Bove, 1978</td>
<td>49</td>
<td>221</td>
<td>Not reported</td>
<td>Not reported</td>
<td>0/49</td>
<td>Group-specific (ABO/Rh) blood only was transfused</td>
</tr>
<tr>
<td>Gervin &amp; Fischer, 1984</td>
<td>160</td>
<td>875</td>
<td>Not reported</td>
<td>0/160 (0%)</td>
<td>0/160</td>
<td>Group-specific (ABO/Rh) blood only was transfused</td>
</tr>
<tr>
<td>Schwab et al., 1986a,b</td>
<td>99</td>
<td>410</td>
<td>0/99</td>
<td>0/99 (0%)</td>
<td>0/99</td>
<td>Two papers with overlapping study periods, with data from later, larger study presented</td>
</tr>
<tr>
<td>Lefebre et al., 1987</td>
<td>133</td>
<td>537</td>
<td>0/122 (0%)</td>
<td>0/122 (0%)</td>
<td>0/133</td>
<td>Group O blood only was transfused; 11 recipients had no blood available for antibody testing; in seven patients who received eight or more group O units, transient positive DATs were observed (presumably due to anti-A and/or anti-B) but without apparent overt haemolysis</td>
</tr>
<tr>
<td>Schmidt et al., 1988</td>
<td>449</td>
<td>1717</td>
<td>6/418</td>
<td>2/418 (0.5%)</td>
<td>0/449</td>
<td>Group O RhD-positive blood only was transfused. Neither patient with clinically significant alloantibodies (anti-c; anti-E\textsuperscript{a}) who received incompatible blood developed evidence of haemolysis</td>
</tr>
<tr>
<td>Unkle et al., 1991</td>
<td>135</td>
<td>Not reported (at least 135)</td>
<td>0/135</td>
<td>0/135 (0%)</td>
<td>0/135</td>
<td>Although three patients had detectable alloantibodies on the pre-transfusion specimen, these were anti-Le\textsuperscript{a} (n = 2) and anti-Sd\textsuperscript{a} (n = 1), which were regarded as being clinically insignificant</td>
</tr>
<tr>
<td>Dutton et al., 2005</td>
<td>161</td>
<td>581</td>
<td>Not reported</td>
<td>Not reported</td>
<td>0/161</td>
<td>Group O blood only was transfused</td>
</tr>
<tr>
<td>Ball et al., 2011</td>
<td>153</td>
<td>511</td>
<td>Not reported</td>
<td>Not reported</td>
<td>0/153</td>
<td>Fifteen incompatible RBCs given to seven patients with one or more clinically significant alloantibodies (anti-D, n = 6; anti-E, n = 4; anti-c, n = 1; anti-K, n = 4; anti-I\textsuperscript{k}, n = 4, anti-Jk\textsuperscript{a}, n = 1; anti-Fy\textsuperscript{a}, n = 1); only one patient (with anti-c and anti-Jk\textsuperscript{a}) had laboratory evidence of haemolysis (although clinical relevance was not clear)</td>
</tr>
<tr>
<td>Goodell et al., 2010</td>
<td>265</td>
<td>1002</td>
<td>17/265 (6.4%)</td>
<td>7/265 (2.6%)</td>
<td>1/265</td>
<td>Fifteen incompatible RBCs given to seven patients with one or more clinically significant alloantibodies (anti-D, n = 6; anti-E, n = 4; anti-c, n = 1; anti-K, n = 4; anti-I\textsuperscript{k}, n = 4, anti-Jk\textsuperscript{a}, n = 1; anti-Fy\textsuperscript{a}, n = 1); only one patient (with anti-c and anti-Jk\textsuperscript{a}) had laboratory evidence of haemolysis (although clinical relevance was not clear)</td>
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<tr>
<td>Miraflor et al., 2012</td>
<td>132</td>
<td>Not reported (at least 132)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>0/132 (0.8%)</td>
<td>Although one patient developed delayed HTR secondary to anamnestic anti-Jk\textsuperscript{a} alloantibodies, these were not detectable in the pre-transfusion work-up; thus, HTR occurrence cannot be attributable to emergency release</td>
</tr>
<tr>
<td>Mulay et al., 2013</td>
<td>1444</td>
<td>4144</td>
<td>73/1444 (5.1%)</td>
<td>7/1444 (0.5%)</td>
<td>0/1444 (0%)</td>
<td>Ten incompatible RBCs given to seven patients with one or more clinically significant alloantibodies (most often, anti-K and anti-E; further details not given); however, no acute HTR episodes were observed; although one patient developed delayed HTR secondary to anti-c and anti-E alloantibodies, these were not detectable in the pre-transfusion work-up; thus, HTR occurrence cannot be attributable to emergency release</td>
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is an overall frequency of only 2/3398 (0.06%), or less than 1 in 1000 RBC recipients, receiving uncross-matched blood.

Goodell et al. (2010) reported one transfusion episode that appeared to have been complicated by clinically overt haemolysis, as suggested by positive testing for haemolysis parameters (e.g., LDH level of 1057 U L\(^{-1}\), total bilirubin level of 38 \(\mu\)mol L\(^{-1}\) and haptoglobin concentration of less than 23-5 \(\mu\)mol L\(^{-1}\), up from a baseline LDH level of 110 U L\(^{-1}\) and total bilirubin level of 10 \(\mu\)mol L\(^{-1}\) a week before the transfusion). However, this 68-year-old patient had anti-c, anti-E and anti-Jk\(^a\) alloantibodies eluted from his pre-transfusion RBC specimen, and he had also received multiple recent RBC transfusions. Thus, he may already have had a delayed HTR occurring at the time of emergency transfusion of uncross-matched blood, and so, no clear adverse consequence from the uncross-matched RBC unit was apparent. However, we classified this patient as having had an acute HTR.

Only one additional study, performed by Radkay et al. (2012), identified a patient who appeared to have developed a clinically significant acute HTR as a result of receiving uncross-matched RBC units. The patient was a 72-year-old man who received three uncross-matched RBC units because of gastrointestinal bleeding. The pre-transfusion sample contained anti-K, anti-Fy\(^a\), anti-E and anti-C\(^w\), all of which had been detected previously. The patient’s haemoglobin rose post-transfusion from 72 to 108 g L\(^{-1}\) but then decreased to 82 g L\(^{-1}\), without further evidence of bleeding, during the 2 days post-transfusion. Whereas the pre-transfusion eluate was negative, a post-transfusion eluate (performed because of clinical suspicion of haemolysis) demonstrated both anti-E and anti-Fy\(^a\). The patient’s serum creatinine increased from 168 to 212 \(\mu\)mol L\(^{-1}\) on the day after transfusion, at which time haemodialysis was initiated. The patient died within 1 week of the transfusions, with the authors concluding that the ‘decline in hemoglobin after uncross-matched RBC transfusion, the increased bilirubin, and the worsening renal function [were] highly suggestive of immune-mediated hemolysis’.

Thus, this patient case represents a rare example of a patient whose adverse clinical course can be causally attributed to the consequences of acute HTR related to receipt of uncross-matched blood.

Indeed, in our review of 3398 patients who received almost 12 000 units of uncross-matched blood (Table 1), this was the only patient recognised as having a clinically relevant HTR (frequency, 0.03%). Overall, these studies suggest that uncross-matched, ABO-compatible blood transfusions are extremely safe. A caveat is that many patients who receive uncross-matched blood die due to their admitting emergency illness or post-trauma state, and it remains possible that the extreme clinical circumstances make the recognition of acute HTR challenging.

Despite the apparent safety profile of uncross-matched blood, the patient case we present here is a rare example that illustrates the risk of a severe acute HTR related to the common clinical practice of using emergency-release uncross-matched blood. Our patient developed renal failure, with strong evidence of alloimmune-mediated HTR, including biochemical markers of confirmed intravascular haemolysis and DIC. In addition, the radiological imaging of multiple renal infarcts indicates a microvascular renal injury consistent with acute haemolysis and DIC. Although our experience should not argue against the use of emergency-release uncross-matched blood.
of such transfusions in an emergency-release fashion (given the strong likelihood that many lives are saved by this practice), clinicians should be attuned to the small but potentially serious risk of an alloantibody-mediated acute HTR, with the potential for associated morbidity and mortality.

ACKNOWLEDGMENTS

J. F. and T. E. W. summarised the clinical, and A. L. E. the laboratory (transfusion medicine), aspects of the original patient case reported. J. F. and A. L. E. performed the literature review, and all three authors reviewed the papers identified and interpreted the data. All three authors critically revised the manuscript and approved the final version. We thank Jo-Ann I. Sheppard for preparing the figure. We thank Prof. Nancy M. Heddle for her helpful comments.

CONFLICT OF INTEREST

The authors have no competing interests.

REFERENCES


