Investigation and management of acute transfusion reactions

BCSH guidelines
What this talk will cover

- Definition
- Flow chart
- Key clinical features
- Four cases, hopefully indicating key features
Acute transfusion reactions are defined as those occurring at any time up to 24 hours following a transfusion of blood or components excluding cases of acute reactions due to incorrect component being transfused, haemolytic reactions, transfusion related acute lung injury (TRALI), TACO, TAD or those due to bacterial contamination of the component.
Patient exhibiting possible features of an acute transfusion reaction, which may include: Fever, chills, rigors, tachycardia, hyper- or hypotension, collapse, flushing, urticaria, pain (bone, muscle, chest, abdominal), respiratory distress, nausea, general malaise

STOP THE TRANSFUSION: Undertake rapid clinical assessment, check patient ID/blood compatibility label, visually assess unit

Evidence of:
Life-threatening Airway and/or Breathing and/or Circulatory problems and/or wrong blood given and/or evidence of contaminated unit

Yes

Inform medical staff

SEVERE/LIFE-THREATENING
- Call for urgent medical help
- Initiate resuscitation-ABC
- Is haemorrhage likely to be causing hypotension? If not, discontinue transfusion (do not discard implicated units)
- Maintain venous access
- Monitor patient e.g. TPR, BP, urinary output, oxygen saturations

If likely anaphylaxis/severe allergy-follow anaphylaxis pathway
If bacterial contamination likely start antibiotic treatment
Use BP, pulse, urine output (catheterise if necessary) to guide intravenous physiological saline administration
Inform hospital transfusion department
Return unit with administration set to transfusion laboratory
If bacterial contamination suspected contact blood service to discuss recall of associated components
Perform appropriate investigations (see Table 1)

MODERATE
- Temperature ≥39°C or rise of ≥2°C and/or
- Other symptoms/signs apart from pruritus/rash only

Consider bacterial contamination if the temperature rises as above and review patient’s underlying condition and transfusion history
Monitor patient more frequently e.g. TPR, BP, oxygen saturations, urinary output

MILD
- Isolated temperature ≥39°C and rise of 1-2°C and/or
- Pruritus/rash only

Continue transfusion
Consider symptomatic treatment (see text)
Monitor patient more frequently as for moderate reactions
If symptoms/signs worsen, manage as moderate/severe reaction (see left)

Not consistent with condition or history
Discontinue (do not discard implicated units)
Perform appropriate investigations (see Table 1)

If consistent with underlying condition or history, transfusion can be continued at same or slower rate with appropriate symptomatic treatment

Continue Transfusion

Review at HTC
Report to SHOT/MHRA as appropriate

Transfusion-related event

Transfusion unrelated

Document in notes that no HTA/TTC review SHOT report necessary
Breathlessness

• Related to transfusion or to underlying illness?
• TACO?
• TRALI?
• Anxiety?
• Initial Investigations
  – CXR, ECG, oxygen sats
Fever

- Feeling of heat
- Mild rigors
- **Severe, uncontrollable rigors**
- Shock

**Investigate:**
- As for suspected bacterial contamination
- Possible haemolytic reaction
Pain

• Pain associated with transfusion often noted
  – Around IV site
  – Back, loin, abdomen, chest

• Treat as serious, esp if shock
  – Bacterial TTI
  – Acute haemolytic reaction

• Feeling of “impending doom”
Case 1
Case 1, initial information

- Female, aged 75
- Treated for CLL
- Hb 89 g.L, wbc 25, plts 17 x 10⁹/L
- She is group B neg with known anti E and an unspecified auto antibody
- B neg irradiated CMV negative platelet requested
- A neg irradiated CMV negative platelet issued
- Pre-transfusion, temp 37.5C, BP 138/85
- Three minutes into the transfusion, she complained of tingling around the mouth, then became dyspnoeic and collapsed
- Crash team called
- Whilst the team are awaited, she begins to recover
- Temp 37.2C, BP 90/45, oxygen sats 88%
Case 1

- What are the possible diagnoses?
- How would you manage the immediate reaction?
- What further management would you give?
- What investigations would you perform?
Dramatic collapse

- Possible causes include
  - Anaphylaxis
  - Transfusion transmitted bacterial infection
  - Acute haemolytic reaction
  - TACO (unlikely with 1 platelet unit)
  - TRALI
  - Cause unrelated to transfusion
Dramatic collapse

- Possible causes include
  - Anaphylaxis
  - Transfusion transmitted bacterial infection
  - Acute haemolytic reaction
  - TACO (unlikely with 1 platelet unit)
  - TRALI
  - Cause unrelated to transfusion
Case 1 continued

- Of these, anaphylaxis is most likely
- Call for urgent help
- Intramuscular adrenaline is the first line drug
- Appropriate investigations for breathlessness include oxygen sats, CXR and ECG if prolonged
Further information

• She was investigated per local protocol, including
  – u&e/LFTs/fbc
  – Repeat group and screen:
    – Blood cultures
    – Unit cultures performed locally
    – Immunoglobulin A level
    – Haptoglobin
    – Mast cell tryptase
Further information

- She was investigated per local protocol, including
  - u&e/LFTs/fbc (no change)
  - Repeat group and screen: no new antibodies found
  - Blood cultures: negative
  - Unit cultures performed locally Staph epidermidis and staph aureus
  - Immunoglobulin A level 0.5 g/L (normal 2-4 g/L), IgG 2.8 g/L (normal 6-12 g/L), IgM 0.5 g/L (normal 0.6-1.5 g/L)
  - Mast cell tryptase 13 µmol/L (normal 6-13 µmol/L)
Case 1 Comments on results

- Micro results suggest faulty sampling
- If you do suspect bacterial TTI you must contact blood service re possible recall
- IgA low but all lgs low as can occur in CLL so no diagnostic help here
- Single MCT no help
- Probable anaphylaxis
- Was transfusion appropriate?
- Did she need CMV negative platelets?
Review of actions

• This was likely to be anaphylaxis
• Testing protocol needs to be revised
• If you suspect bacterial contamination, first step is to contact the blood service
• Was the platelet indicated?
• Was the group suitable? (A neg to B neg patient)
• Why was it CMV negative?
Number of bacterial TTI incidents, by year of report and type of unit transfused (Scotland included from 10/1998)
Review of tests

• Red cell serology or unit culture needed only where symptoms and signs suggest possible haemolytic reaction or bacterial contamination
  – Shock
  – Rigors
  – Pain
Clinical features of bacterial transfusion transmitted infection

- Temperature rise >2°C and/or severe shivering, rigors
- Back or abdominal pain
- Severe hypotension, shock
- Tachycardia
- Occasionally symptoms are milder
  - Pathogenicity, number of bacteria, underlying clinical state
Case 2

- 36 year old woman had emergency LSCS at 37 weeks for PET
- She had intraoperative cell salvage set up
- Experienced heavy interoperative blood loss
Transfusion history

- Given: 2L crystalloid, 2 flying squad O neg units, 500 mls salvaged blood, 10 units group specific (A pos) red cells
- 2 units of group A plasma
- 1 A pos platelet, ordered from blood centre 50 miles away, was given after 3 hours
- By then, haemorrhage was controlled.
Subsequent transfusion

• In recovery, 45 minutes after platelet transfusion, she was receiving the first of 2 further units of group specific red cells
• She became very short of breath
  – Oxygen sats (on 24% oxygen) dropped from 95% to 84%
  – BP rose from 110/68 to 185/105
Case 2

• What are the likely causes of her dyspnoea?
• How will you investigate the reaction?
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  – Unrelated to transfusion (Amniotic fluid embolism)
  – TRALI
  – TACO

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Case 2

• What are the likely causes of her dyspnoea?
  – Unrelated to transfusion (? Amniotic fluid embolism)
  – TRALI
  – TACO

• How will you investigate the reaction?
  – CXR
  – Fbc
  – A: HLA test the patient, identify donors of all blood components, and test for HLA antibodies or:
  – B: Just HLA screen the platelet donor
  – C: No HLA testing
Case 2

- What are the likely causes of her dyspnoea?
  - Unrelated to transfusion (Amniotic fluid embolism)
  - TRALI
  - TACO

- How will you investigate the reaction?
  - CXR: bilateral pulmonary infiltrates
  - Fbc: Hb 7.2 g/L, wbc 21, plts 56
  - ?? HLA test the patient, identify donors of all blood components, and test for HLA antibodies
  - ?? Just HLA screen the platelet donor

- How will you treat her?
Management

- The team decided this was TACO and gave her diuretics
- She required 3 days on HDU but made a good recovery and went home with baby 10 days later
Case 2 Commentary

- SHOT is increasingly seeing TACO associated with major haemorrhage
- Raised fluid volume in pregnancy (esp PET) a likely risk factor
- Note large volumes of colloid and crystalloid used prior to blood components
- Do you think ICS helped here?
- The transfusion team should ensure there is a workable major obstetric haemorrhage protocol
Unexpected dyspnoea

- Teenage boy with history of liver disease transfused with female apheresis platelets for an elective surgical procedure
- Developed hypoxia, hypotension and pyrexia within 30 minutes of transfusion. Hb increased from 8g/dl before procedure to 18 after
- Required cardio-respiratory support on ITU
- When ET tube inserted, developed fountain like pulmonary oedema
30 mins post transfusion
What is the most likely diagnosis?

- TACO (Transfusion Associated Circulatory Overload)
- Chest infection
- Acute myocardial infarction
- TRALI (Transfusion-Related Acute Lung Injury)
TRALI

- Serious complication of transfusion, almost always with plasma rich components
- Donor has antibody to recipient leucocytes
  - HLA or HNA
- Reduced
  - Universal leucodepletion
  - Male donors
- Dyspnoea, hypoxia (pyrexia) usually within 6 hours
- Commoner in certain groups of patients-”two-hit” hypothesis
Figure 15.1
Number of suspected TRALI cases and deaths at least possibly related to TRALI by year of report.
# Features of TACO and TRALI

<table>
<thead>
<tr>
<th></th>
<th>TRALI</th>
<th>TACO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of component</td>
<td>Usually plasma or platelets</td>
<td>Any</td>
</tr>
<tr>
<td>BP</td>
<td>Often reduced</td>
<td>Often raised</td>
</tr>
<tr>
<td>Temperature</td>
<td>Often raised</td>
<td>Normal</td>
</tr>
<tr>
<td>Echo</td>
<td>Normal</td>
<td>Abnormal</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Worsen</td>
<td>Improve</td>
</tr>
<tr>
<td>Fluid loading</td>
<td>Improves</td>
<td>Worsens</td>
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</tbody>
</table>
Case 3
Case 3

- A 55 year old man with MDS (Group A Rh neg) is receiving weekly platelet transfusions as his count usually runs 5-10, he is bruising badly and getting occasional nose bleeds.
- On the last 2 occasions, he had an itchy rash which appeared during transfusion and lasted several hours, despite being given “hydrocortisone and piriton” cover.
- This week, no A neg platelets are available and the decision is made to transfuse him with a unit of A pos platelets.
- He rapidly develops the rash again, with swelling of the eyelids and lips.
Case 3

- What would you call this reaction?
- What is the likely cause?
- What investigations could you perform?
- How best to manage future platelet transfusions?
Case 3

• This is suggestive of angioedema, and would fit into the category of moderate allergic transfusion reaction.
• Often difficult to determine cause
• Investigations:
  – Immunoglobulin A normal
  – Post-transfusion platelet count pre Tx $9 \times 10^9$/L, at 1 hour post $35 \times 10^9$/L
  – HLA studies of the patient show he had Class 1 HLA antibodies to HLA-B44
Case 3: stop this happening!

- This is likely to be angioedema

Advice:
- Firstly, are transfusions appropriate as BCSH guidelines suggest stable thrombocytopenia not an indication: depends how severe the nosebleeds are
- Satisfactory platelet increment, so not refractory
- HLA antibody studies on the patient are therefore not indicated.
Case 3 continued

- HLA matched platelets not indicated
- If platelets are clinically indicated, try PAS platelets
- The team may wish to continue prophylaxis against reactions (no evidence to support it) but Piriton alone may be just as beneficial
- Tranexamic acid may help reduce epistaxis
Case 4
Severe reaction

- A male patient is receiving a top up red cell transfusion
  - Myelodysplasia
  - Known anti-c
  - Given blood negative for c
- 30 minutes in, complains of feeling unwell
- Pain in abdomen, shaking
- BP dropped from 125/82 to 95/??
- What is going on?
- How will you investigate?
What causes should you consider?

- Haemolytic transfusion reaction to new antibody other than c
- Bacterial infection
- Unrelated to transfusion
- Massive haemolytic reaction because of ABO incompatibility
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- Haemolytic transfusion reaction to new antibody other than c
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First steps

- Stop the transfusion
- Check patient ID
- Check compatibility label on unit
Severe reaction

- Initial observations: Unit is group B, patient is group O
- Patient advises he has not had a recent blood test
- Transfusion sample was a WBIT, labelled with his details but from another patient
In conclusion

- If a patient has an adverse reaction to a transfusion, you initially do not know the cause.
- Stop and check!
- Manage the symptoms and signs.
- Most important action is to recognise and treat anaphylaxis
  - I.M. adrenaline
- If you suspect there is something wrong with the unit, contact the blood service to consider a recall.
Most important not to miss

- Wrong blood
- Anaphylaxis
- TACO
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