Interactive case studies

Swisstransfusion, 6 September 2013

Haemovigilance

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Case 1

A 42-year-old patient with AML developed generalised urticaria, angio-oedema of the lips, difficulties swallowing, and abdominal pains 5 minutes after the beginning of a platelet transfusion. This was accompanied by tachycardia (133/min) and hypotension (85/50 mmHg). No bronchospasm observed.

What are your thoughts?

1. Hypotensive TR
2. Allergic TR
3. Not transfusion related
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- The blood pressured normalised within 15 minutes of administration of antihistamines, corticosteroids and infusion of 500 ml of saline. No need for adrenaline.
- No other concomitant medication that could have caused an allergic reaction.
- Tryptase elevated to 39.3 ng/ml
- IgA-level normal (determined before transfusion)
- Previous platelet transfusions uneventful
- Known allergy to Imipenem
Case 1

How would you classify this reaction?

1. Hypotensive TR
2. Allergic TR
3. Not transfusion related
Case 1

How would you classify this reaction?

1. Hypotensive TR
2. Allergic TR, anaphylactic
3. Not transfusion related

Severity: grade 3

Imputability: probable

Preventive measures for the future:
• premedication with antihistamines and steroids
• closer observation of the patient during transfusion
Case 2

An 86-year-old patient with anaemia following diverticular haemorrhage (Hb 66 g/L) receives a RBC-transfusion. Of note in her medical history is an endocarditis with staphylococcus aureus, valvular and hypertensive heart disease with moderate aortic stenosis and light-grade aortic insufficiency, stage 3 renal failure.

After transfusion of approx. 240 ml over 1 hour she presents rigors, hypertension and tachycardia (BP rises from 110/64 to 200/100 mmHg, P from 105 to 130/min). Temperature: 36.5 ▶ 37.3° C
Case 2

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After transfusion of approx. 240 ml over 1 hour: rigors, hypertension and tachycardia (BP rises from 110/64 to 200/100 mmHg, P from 105 to 130/min). Temperature: 36.5 ▶ 37.3°C

What would you do / investigate?

• check immune-haematology, check for haemolysis
• chest X-ray
• bacterial cultures
• stop transfusion
• anything else?
Case 2

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What would you do / investigate?

• check immune-haematology, check for haemolysis
• chest X-ray
• bacterial cultures
• stop transfusion
• administer diuretics?
Case 2

Results:

• immune-haematology: nothing particular
• check for haemolysis: Bili tot. 3.9 µmol, LDH 252 IE/l, Haptoglobin 2.57 g/l
• chest X-ray: not done
• bacterial cultures: product cultures negative
• stop transfusion: doesn’t say, but hope so (TR is classed as life-threatening !)
• anything else ? Pro-BNP (1 hr after TR): 8753 ng/l
Case 2

Classification: TACO

Severity: life-threatening
   (according to local HV team)

Imputability: probable
Case 2

And what if the patient needs further transfusions?

Patient at risk for circulatory overload
- limit transfusion rate to 1 ml/kg BW/h
- consider premedication with diuretics
- but first: check Hb ➤ 85 g/l after transfusion, stable conditions, so perhaps no immediate need for further transfusion
Case 3

A regional blood transfusion service is notified of a grade 3 transfusion reaction in a 58-year old patient following transfusion of 2 RBC, classified as TRALI, imputability probable

- symptoms: dyspnea with hypoxia 1 hour after transfusion of 2 RBC (over 2 hours) in a patient with thoraco-abdominal aneurysm of the aorta.
- temp. 36.7 / 36.8° C, BP 120/55 ▶ 135/80 mmHg, P 76/72
- Hb before transfusion 97 g/l, after 139 g/l
- severity: life-threatening
- no further information
Case 3

A regional blood transfusion service is notified of a grade 3 transfusion reaction in a 58-year old patient following transfusion of 2 RBC, classified as TRALI, imputability probable. Symptoms: dyspnea with hypoxia 1 hour after transfusion of 2 RBC (over 2 hours) in a patient with thoraco-abdominal aneurysm of the aorta. Temp. 36.7 /36.8° C , BP 120/55 ▶ 135/80 mmHg, P 76/72, Hb 97 g/l ▶ 139 g/l. Severity life-threatening

Do you agree with the initial suspicion (probable TRALI) ?

• Yes
• No
• Yes, but…
Case 3

A regional blood transfusion service is notified of a grade 3 transfusion reaction that had occurred the day before in a 58-year old patient following transfusion of 2 RBC, that was classified as probable TRALI.
Symptoms: dyspnea with hypoxia 1 hour after transfusion of 2 RBC (over 2 hours) in a patient with thoraco-abdominal aneurysm of the aorta. Temp. 36.7 /36.8° C , BP 120/55 ► 135/80 mmHg, P 76/72, Hb 97 g/l ► 139 g/l. severity life-threatening

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Other possibilities ?

1) Allergic TR
2) TACO
3) TAD
4) Respiratory distress non transfusion-related

More information needed
Case 3

Further information:
• intubation necessary due to worsening dyspnoea
• Echocardiography shows pulmonary hypertension, normal LVEF
• Pro-BNP > 4000 ng/l (post-transfusion and following day, no previous count)
• Chest X-ray: repeatedly no bilateral infiltrates, but signs of increasing pulmonary hypertension
• pre-existing mild hypoxia (PaO$_2$ 9.7, reference 10-12.9 kPa)
Case 3

TRALI ↔ TACO ?
## Case 3

<table>
<thead>
<tr>
<th>TRALI</th>
<th>TACO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute dyspnoea, hypoxia and</td>
<td>Acute dyspnoea</td>
</tr>
<tr>
<td>Bilateral infiltrates in chest X-ray and</td>
<td>Hypertension / Tachycardia, -arrhythmia</td>
</tr>
<tr>
<td>Begin during or within 6 hours of transfusion and</td>
<td>Begin during or within 6 hours of transfusion</td>
</tr>
<tr>
<td>No signs of cardiac insufficiency and</td>
<td>Chest X-ray / echo: Signs of acute or worsening pulmonary oedema / pulmonary hypertension</td>
</tr>
<tr>
<td>No pre-existing ALI and no risk factors for ALI (acute lung injury)</td>
<td>Positive fluid balance</td>
</tr>
<tr>
<td></td>
<td>additional: chest pains, cough, headache, cyanosis, BNP ↑↑</td>
</tr>
</tbody>
</table>
Case 4

A 70-year old patient with pancytopenia of unknown origin is transfused with 1 PC and 2 RBCs. After these transfusions the patient presented fever (temperature 37.9° → 39.6°C), a rise in BP (108/62 → 129/75 mmHg) and heart rate (82 → 118)

In which direction would you investigate ?

1) Bacterial infection
2) Haemolytic TR
3) TACO
4) FNHTR
5) Other cause for fever
Case 4

A 70-year old patient with pancytopenia of unknown origin is transfused with 1 platelet concentrate and 2 RBCs. After these transfusions the patient presented fever (temp. from 37.9 to 39.6°C), a rise in BP from 108/62 to 129/75 mmHg, P 82 to 118

In which direction would you investigate?

1) Bacterial infection
2) Haemolytic TR
3) TACO
4) FNHTR
5) Other cause for fever
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A 70-year old patient with pancytopenia of unknown origin is transfused with 1 platelet concentrate and 2 RBCs. After these transfusions the patient presented fever (temp. from 37.9 to 39.6° C), a rise in BP from 108/62 to 129/75 mmHg, P 82 to 118

Which of the following investigations would you do?

1) Check documentation ✔
2) Repeat T&S pre- and post ✔
3) Check for haemolysis ✔
4) Bacterial cultures ✔
5) Chest X-ray
6) Echocardiography
7) Check fluid balance ?
Case 4

Results:

• Documentation: no discrepancies
• Haemolysis: bilirubine tot 43 µmol/l, LDH 150 IE/l, haptoglobin < 0.058 g/l
• Immune-haematology:
  – DAT pre-transfusion, monospec.: IgG 1+, ab-screen neg.
  – DAT post-transfusion, monospec.: IgG 1+, antibody screen positive ▶ Anti-C (only enzyme-enhanced)
• Bacterial cultures: negative for patient‘s blood and blood components

• One of the transfused RBCs was positive for C antigen !
Case 4

How come a C-positive product was issued?

- Routine pre-transfusional antibody screen performed with 4 Coombs cells was negative (no enzyme enhanced cells)

- Positive antibody screen only became evident on examining the transfusion reaction screen with 6 cells of which 2 are enzyme enhanced
Classification local HV:
‟Although antibodies only detectable in the enzyme phase are not usually associated with acute haemolysis, the clinical presentation and laboratory findings strongly suggest the occurrence of an acute haemolytic transfusion reaction‟.

Imputability „possible‟
Case 5

A 77-year old patient in haemorrhagic shock due to lower GI-bleeding required massive transfusion, in the course if which he also received an FFP. After transfusion of approx. 30 ml, the patient presented generalised urticaria, swelling of the chin and lips, no dyspnoea. BP rose from 130/60 to 150/80 mmHg, P from 60 to 65/min. Patient has a history of allergy to penicillin (rash) and had gastroenteritis 4 days previously.

What actions do you propose?

- Stop the transfusion
- Apply antihistamines / steroids, Adrenaline
- Give diuretics
- Bacterial cultures
Case 5

A 77-year old patient was admitted in haemorrhagic shock due to lower GI-bleeding and was transfused with FFP. After transfusion of approx. 30 ml, the patient presented generalised urticaria, swelling of the chin and lips, no dyspnoea. BP rose from 130/60 to 150/80 mmHg, P from 60 to 65/min. 4 days previously the patient had gastroenteritis. Patient has a history of allergy to penicillin (rash).

What actions do you propose?

• Stop the transfusion
• Apply antihistamines / steroids (Adrenaline)
• Give diuretics
• Bacterial cultures
Case 5

The transfusion was stopped immediately and Tavegyl, Solumedrol and Zantic were administered, with favourable effect.

The immune-haematological investigations showed no incompatibility, the bacterial cultures of the product remained sterile.

The TR was classified as:

Allergic TR, anaphylactoid, grade 1 (or mild allergic?)
Case 5

3 days later, the same patient received a RBC. This time, towards the end of the transfusion he develops dyspnoea, swelling enoral, of the face and eyelids. No haemodynamic problems. Hb count 101 ▶ 122 g/l

Suggested investigations:
• chest X-ray
• IgA, anti-IgA and tryptase
• Bacterial cultures
• Immune-haematology
3 days later, the same patient received a **RBC**. This time, towards the end of the transfusion he develops **dyspnoea, swelling enoral**, of the face and eyelids. No haemodynamic problems. Hb count 101 ➤ 122 g/l

**Suggested investigations:**
- chest X-ray
- IgA, anti-IgA and tryptase
- Bacterial cultures
- Immune-haematology
Case 5

3 days later, the same patient received a RBC. This time, towards the end of the transfusion, he develops dyspnoea, swelling enoral, of the face and eyelids. No haemodynamic problems. Hb count 101 \( \rightarrow \) 122 g/l

Results:

- chest X-ray
- IgA, anti-IgA and tryptase: within the normal range
- Bacterial cultures (product) negative
- Immune-haematology no particular findings
Case 5

Diagnosis / future management:

Classification: anaphylactoid TR
Severity: grade 1
Imputability: probable

- Consider premedication with antihistamines.
- In case of re-occurrence of allergic TRs, discuss administration of washed cellular blood components with blood transfusion service.
Case 6

Blood products are ordered daily from a haematology ward using a form that lists all the patients currently on the ward with their respective blood counts. The number of required RBCs or PCs is marked in the corresponding column. This particular day, the blood bank staff member responsible for preparing the blood products missed a line and issued a PC for patient AB instead of patient ZZ, although no blood products were ordered for AB that day. The delivery arrived on the ward round about lunch time; several components were sent together and the number of staff was reduced.
Case 6

The nurse responsible would like to get the platelet transfusion done before lunch. It is her first day back at work after a period of absence and she omits to check the prescription and also doesn‘t look at patient AB‘s blood count. The PC is administered to the patient AB without any problems.

After a while, the ward notices that the PC ordered for the patient ZZ has not yet been delivered. On checking with the lab, the error comes to light.

Patient AB had a platelet count of > 200 and did not need the transfusion.
Case 6

2 deviations:
1) PC issued for the wrong patient
2) Administration of the PC without checking the prescription and also without noticing that transfusing a patient who had a normal platelet count was not feasible.

Any suggestions for corrective measures?
• Remodelling of the order form, so that it is not so easy to miss a line
• No transfusion without prescription / checking the prescription
## Case 6

<table>
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<th>Patient</th>
<th>Geschlecht</th>
<th>Eingangsdatum</th>
<th>Auftragser</th>
<th>Leukozyten</th>
<th>Hämoglobin</th>
<th>Thrombozyten</th>
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**Old list**
## Case 6

### New list

<table>
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</table>

Columns for number of requested BP is closer to name of patient.
Case 7

Male donor, born in 1984, about to undertake his first platelet apheresis donation. He had donated whole blood on several occasions, the last time a few years ago. On the donor questionnaire he noted chronic sinusitis, no signs at the moment. No other problem comes up during the pre-donation check and he is considered fit to donate.

During the first re-infusion (flow rate 150 ml/min), his lips start tingling, shortly after he has a sensation of trembling on his chest.
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Male donor, born in 1984, about to undertake his first platelet apheresis donation. He had donated whole blood on several occasions, the last time a few years ago. On the donor questionnaire he noted having chronic sinusitis, no signs of exacerbation at the moment. He is considered fit to donate.

During the first re-infusion, flow rate 150 ml/min, his lips start tingling, shortly after he has a sensation of trembling on his chest.

What do you think could be wrong and what would you do?

• first, mild signs of citrate toxicity ► the flow rate is reduced to 100 ml/min, which helps straight away. The donor is given 2 soft tablets of calcium (Calcimagon)
Case 7

During the second re-infusion, the sensations of tingling and trembling appear again, a bit milder, this time combined with slight dyspnoea, followed by a dry cough and red eyes (red conjunctiva).

Would you continue or stop the apheresis?

The flow rate is reduced further to 70 ml/min and the donor feels a bit better.

The third re-infusion caused recurrence of all symptoms plus oedema of both eyelids. The apheresis is stopped after a total duration of 24 minutes.
Case 7

The symptoms persisted for over an hour after breaking off the apheresis. The donor also had to vomit once. He was treated with 500 mg of Solumedrol and Tavegyl iv and inhalations with Dospir for persistent bronchospasm. The donor had gone back to work, but had to leave and go home about 2 hours later.

By late evening the symptoms had receded completely and the donor was able to go to work the next day free of complaints.

How would you classify the reaction?
Case 7

- Generalised allergic (anaphylactoid) reaction
- Severity: grade 2

- Caused by citrate? An other solution? Plasticisers?

- It turned out the donor had an atopic disposition with a history of various allergic manifestations, including asthma. However, he had neither mentioned this on the questionnaire nor during the pre-donation check. He had also taken 2 soft tablets of calcium 2 hours before the donation.
Case 7

What can we learn from this case?

- Question every first-time apheresis donor directly on a possible history of allergies.

Assessment of the deputy chief medical officer at the transfusion service:

- Blood products containing plasma that were donated by donors with atopic disposition can possibly cause allergic reactions in recipients. Donors whose blood products cause allergic reactions in patients may need to be deferred from donation or at least barred for the specific patient.
Case 8

Due to previous clopidogrel-medication, a 47-year old patient receives one pooled PC post-operatively after successful and uneventful mitral valve reconstruction.

5 minutes after the beginning of the transfusion he presents:
- shock, MAP drops from >60 to <40 mmHg
- hypoxia

The patient has to be re-intubated.

Which is your first assessment?

1) hemorrhagic shock  4) TAD
2) anaphylactic shock  5) TRALI
3) septic shock  6) don’t know
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6) don’t know
Case 8

Effusion of copious/massive amount of fluid from tubus indicating pulmonary oedema

Chest X-ray shows bilateral infiltrates.

Worsening of the respiratory situation necessitates re-installment of ECMO (extracorporeal membrane oxygenation).

The patient requires high dosed catecholamine treatment over the next 2 days.
Case 8

Effusion of copious/massive amount of fluid from tubus indicating pulmonary oedema. Chest X-ray shows bilateral infiltrates. Worsening of the respiratory situation necessitates re-installment of ECMO (extracorporeal membrane oxygenation). The patient requires high dosed catecholamine treatment over the next 2 days.

Which investigations would you propose ?

1) Check T&S, check for haemolysis
2) Echocardiography, post-operative bleeding ?
3) Bacterial cultures (patient and product)
4) IgA
5) HLA- /HNA-antibodies
6) Donor histories
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Which investigations would you propose?

1) Check T&S, check for haemolysis
2) Echocardiography, post-operative bleeding?
3) Bacterial cultures (patient and product)
4) IgA
5) HLA-/HNA-antibodies
6) Donor histories
Case 8

Results:

- **IH:** pre- and post transfusion: BG A pos, T&S negative, DAT negative, crosscheck +
- **Echo:** “good”. Post-op ejection fraction was 60%. The mitral valve is functioning fine, cardiologists exclude cardiac origin of the pulmonary oedema
- **HLA-ab:** HLA-ab class I and II negativ (Luminex)
- **HNA-ab:** HNA-ab negative (Flow-GIFT/SASGA) for all 5 donors and patient
- **Donors:** 4 female, one male (number of donations 10-62, no known complications)

- Bacteriology and IgA not done
Case 8

What is your assessment now?

1) haemorrhagic shock
2) anaphylactic shock
3) septic shock
4) TAD
5) TRALI
6) still don’t know
Case 8

What is your assessment now?

1) haemorrhagic shock
2) **anaphylactic shock** ??
3) septic shock
4) TAD
5) TRALI
6) still don’t know
Case 8

Further course:

• the patient was on ECMO for 10 days, off respiratory support after 12 days

• further FFP-transfusions were uneventful ▶ allergic reaction due to IgA-deficiency unlikely

• he suffered renal failure requiring haemodialysis, 3 weeks after event renal function is recovering

• restitutio ad integrum expected
Assessment Swissmedic:

Classification: TRALI, non immune

Severity: grade 3

Imputability: probable

BUT: possibly also an allergic component?
Case 9

A 56-year old patient suffering from leucemia received a RBC transfusion after which a rise in temperature from 38.3 to 39.6 °C was observed.

Which possible TR would you want to prove / exclude ?

1) FNHTR
2) HTR
3) Bacterial infection
4) TRALI
5) other ?
Case 9

A 56-year old patient suffering from leucemia received a RBC transfusion after which a rise in temperature from 38.3 to 39.6 °C was observed.

Which possible TR would you want to prove / exclude ?

1) FNHTR
2) HTR
3) Bacterial infection
4) TRALI
Case 9

A 56-year old patient suffering from leucemia received a RBC transfusion after which a rise in temperature from 38.3 to 39.6 °C was observed.

What would you check?

1) Paperwork
2) Immune-haematology
3) Haemolysis
4) Bacteriology
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What would you check?

1) Paperwork
2) Immune-haematology
3) Haemolysis
4) Bacteriology
Case 9

Results:

Paperwork: No discrepancies

IH pre:
• DAT poly (+)
• T&S pos: known Anti-c and Anti-E detected, Anti-Jka and Anti-Kpa not ruled out
• Crossmatch with 2 chosen RBC (c-,E-,Jka-) was negative

IH post:
• DAT mono pos (C3d), titre neg
• Antibody testing same as before transfusion
• Crossmatch with transfused RBC negative

Bacteriology: Patient blood cultures and cultures of products negative
Case 9

Classification: FNHTR

Imputability: Possible

Severity: Non-severe
Case 9

BUT:

Haemolysis: The day before this transfusion the blood service was notified that the patient showed signs of haemolysis:
- Bilirubin 93 µmol/l
- LDH 312 IE/l
- Haptoglobin 0.98 g/l

2 days earlier she had already received 2 RBC T&S for these transfusions was checked
Case 9

Results:
• DAT: IgG negative
• positiv findings for anti-c and anti-E
• anti-Lua and anti-Kpa could not be excluded and were taken into account

• both transfused RBC had been Jka positive with neg crossmatch before transfusion
Case 9

Probable delayed haemolytic transfusion reaction due to boostering of an undetectable Anti-Jka prior to the first transfusions.

Anti-Jka is still detectable several months later