Clinicopathological Case Conference of Haematological Medicine

Case 4:

Transfusion challenge in a solid organ transplant recipient

Date 14th August 2020

Dr Amin Islam MBBS, MRCP UK, FRCP London, FRCPath UK

Senior Consultant Haematologist and BMT

Hon Clinical Senior Lecturer

Queen Mary University, London, UK

Case presentation

- A 66 year-old male with primary sclerosing cholangitis received an orthotopic liver transplant (donor blood type O+, recipient blood type A+)
- 12 days post transplant
- Presented to Emergency with fatigue and dizziness

Clinical evaluations

- Patient denied symptoms of infection or bleeding.
- Vitals :Normal
- Physical exam was normal except for mild jaundice.
- Concern of graft rejections

further investigation

- Hb 5.3 g/dL (it was 11.3 g/dL 4 days prior),platelets 359,
- WCC : Normal
- INR 1.2, Fibrinogen : Normal
- Cr 0.75 mg/dL, total bilirubin 6.6 mg/dL: Increased
- Direct bilirubin 3.3 mg/dL: Increased
- AST 96 IU/L, ALT 128 IU/L, alkaline phosphatase 90 IU/L,
- LDH 785 IU/L: Increased
- Reticulocytes : Increased

Pre transplant

- Blood transfusion laboratory findings
- Received 2 unit RBC, compatible pre transplant

Recipient :Blood group A RhD positive
Donor : O RhD positive
Antibody screen: Negative

Haemolytic causes considered

- Acute or delayed haemolytic transfusion reactions
- Autoimmune haemolysis
- MAHA
- Drug induced haemolysis
- Steroid started

Progress under renal team

- Despite multiple transfusions, haemoglobin continued to trend down over the next couple of days
- Repeat HB 4.4 g/dL

Haematology opinion sought

- Haematology was consulted
- Direct antiglobulin test: Positive
  For IgG and anti-C3 with
- Elution study revealing :Anti-A antibodies
- Blood film: Evidence of haemolysis: NO MAHA

Diagnosis

Passenger Lymphocytes Syndrome

- Given the severity and timing of the HA in the setting of a minor ABO-incompatible liver transplantation (O into A),
- PLS was most likely the cause.
- After a week of supportive care and transfusions the patient's haemoglobin stabilized at 9.8 g/dL and he was discharged home with plan for close follow up
- Given O RhD positive bloods (donor type)

Suggested treatment approach

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Treatment:

- Conservative if haemoglobin stable

Transfusion support with **DONOR** blood group if required (e.g Hb< 8 and/ or symptomatic anaemia)

- Increase steroids – prednisolone 1mg/ kg

If not resolving

- Stop CNI
- Plasmapharesis / Rituximab

Discussions

- PLS is part of the differential diagnosis of HA after solid organ transplant, especially in the early setting (within 1-3 weeks),
- With biochemical evidence (low haptoglobin, high transaminases, and unconjugated bilirubin) seen in 30-40% of these patients.

Discussions

- Donor B-lymphocytes within the liver produce antibodies against the patient's red blood cells.

- While only a small subset of patients presents with severe anaemia, those who do, will require early diagnosis and transfusion for a favourable outcome

Discussions

- PLS is a cause of HA in recipients of minor ABO-incompatible solid organs.
- The diagnosis can be easily missed and only few patients require transfusion.
- However, clinicians should have a high index of suspicion for PLS in any recipient of an ABO organ mismatch presenting with haemolysis in the first 3 weeks following organ transplant

Passenger Lymphocyte Syndrome (PLS)

Definition

The PLS refers to the clinical phenomenon of alloimmune haemolysis resulting from the antibodies produced by viable donor B lymphocytes “passenger lymphocytes” in a primary or secondary immune response against the recipient’s red blood cell antigens

History

- The appearance of unexpected antibodies of A and B specificity in recipients of kidney allografts from ABO minor mismatched donors was first reported in the early 1980s.
- Then, more than 100 cases involving liver, kidney, pancreas, spleen, heart, lung, and heart-lung were published in 1991.

PLS can occur after

- Solid organ transplant
- Stem cell transplant
- Administration of B cell rich cellular therapeutic infusions
- PLS most often seen in solid organ transplantation with minor ABO mismatch
- Donor Group O / Recipient Group A,
- Also reported with other blood group systems like Rh, K, Fy, Kidd
- Donor lacks recipient's antigens
- Donor can form antibodies against recipient's red blood cell antigens

Pathophysiology

- PLS is heterogeneous
- Donor B-lymphocytes are detected in recipients but antibody production is either delayed or is never detectable
- Both donor B-lymphocytes and antibody are detected but haemolysis may not occur
- The triggers for antibody production and haemolysis is still incompletely understood

PLS – risk factors

Table 2: Risk factors for PLS

Risk factors
• Blood group O to A transfer • Possible sensitizing events: Pregnancy, blood transfusions • Cyclosporin use • Infection in the immediate posttransplantation period

Nadarajah et al. American Journal of Transplantation 2013; 13: 1594–1600

PLS - Solid organ transplantation

- PLS following solid organ transplantation has been reported to be;
- 09% for kidney transplants
- 29% for liver transplants
- 70% for heart-lung transplants

Nadarajah et al. American Journal of Transplantation 2013; 13: 1594–1600

- These differences are likely to reflect the amount of lymphoid tissue implanted with the corresponding organ transplant

PLS – Worth anticipating

- Be vigilant about ABO and minor blood group incompatibilities
- Identify the risk factors
- Daily DAT starting 3 – 4 days post op aids early detection
- Use of donor-compatible RBCs prophylactically in the perioperative and immediate postoperative setting might reduce the development of graft associated immune haemolysis, but remains an untested hypothesis.

Fung et al. Transfusion 2004;44:1635-1639

References and good read

- *Nadarajah et al. American Journal of Transplantation 2013; 13: 1594–1600*
- *Maxime Audet et al. Clinical & Developmental Immunology 2008; ID 715769*
- *Fung et al. Transfusion 2004;44:1635-1639*
- *Gniadek et al. Transfusion 2017;57;1262–1266*