COLD ANTIBODIES: AN UNCOMMON FACTOR IN TRANSFUSION SAFETY IN THE TROPICS-A REPORT OF TWO CASES

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Introduction

• Cold antibodies or Cold agglutinins are either Immunoglobulin G or Immunoglobulin M antibodies with a thermal optimum 0°C that bind to erythrocytes with consequent haemolysis.
• At 20-25°C complement is fixed – Donath-Landsteiner antibody
Physico-chemical Characteristics

- Cold antibodies are usually harmless
- In cold haemagglutinin disease (CHAD), they induce red cell agglutination, and haemolysis.
- Infections-related agglutinins (e.g. Mycoplasma) are transient and polyclonal
- Monoclonal agglutinins are associated with autoimmune haemolytic anaemia (AIHA) of the cold antibody type, or the lymphoid malignancies.
- These auto-antibodies are against I, i and H antigens, precursors of the ABH and Lewis blood group substances, on erythrocytes.
Pathophysiology

• Haemolysis due to cold antibodies is complement mediated, and enhanced by acidification;
• Erythrocytes from individuals with CHAD acquire resistance to complement mediated lysis which is manifested in a biphasic pattern,
• Initial rapid phase through a later slow phase and final nil haemolysis.
• The diminished haemolysis may be due to erythrocyte coating with C3dg which confers resistance on them.
Pathophysiology

• Intravascular haemolysis with consequent haemoglobin anaemia results in endothelial damage and reduced production nitric oxide synthase.

• The depletion of nitric oxide (a natural vasodilator), coupled with the cooling of the extremities in cold weather causes a narrowing (vasoconstriction) of the peripheral blood vessels with resultant cyanosis termed acrocyanosis or Raynaud’s phenomenon.

• Recurrent episodes of Raynaud’s phenomenon cause digital deformity, and ulceration.
Clinical Features and Epidemiology

- Haemoglobinemia due to intravascular haemolysis is a cause of haemoglobinuria and renal failure with fatal outcomes and this adversely affects the outcome of transfusion.
- Therefore, transfusion management of individuals with cold agglutinins involves the storage of the blood unit at temperatures above the thermal threshold for agglutination.
- Nursing the patient in a surrounding of forced air surface warming prevents agglutination and vasoconstriction in such patients.
- Concurrent conditions like respiratory infection or malignancy should be appropriately treated.
- CHAD accounts 15-20% of AIHA
CN a 30-year-old health worker with Sickle Cell Anaemia presented in her third pregnancy with vaso-occlusive crisis of two weeks duration due to urinary tract infection in the 31st week.

Management included analgesics, antibiotics, antimalarials and exchange blood transfusion of two units to reduce the concentration of circulating haemoglobin S-containing erythrocytes.

Agglutination was observed in only the tube that contained the patient’s serum crossmatched with a 2% suspension of group compatible donor red cells that was kept at room temperature of 25°C.

The units of blood used for transfusion were stored in a warm place with a temperature of 38°C to raise the temperature for 45 mins prior to transfusion; thereafter the transfusion took place uneventfully.

Nine years later, she presented to the haematology department on a cold harmattan morning (T=16°C) with extensive maroon-coloured, pruritic macular lesions over the dorsa of both feet and the extensor surface of both forearms and hands.

At the time of second presentation, the environmental temperature was 16°C and intense itch coupled with the background sickle cell anaemia resulted in ulcers. Anti-fungal and anti-scabietic agents provided no relief. LE cells and antinuclear antibodies were absent.

Management consisted of warm dressings and anti-histamines while the routine health maintenance therapy for sickle cell anaemia continued. She was lost to follow-up.
• AA was 76 year old community leader with suspected colonic carcinoma with cachexia and haematochezia
• Red cell transfusions to correct severe anaemia for laparotomy
• Haemolysis in the tube kept at room temperature.
• Blood removed from the blood bank refrigerator and immersed in warm water to raise the temperature and subsequently transfused.
• This method of warming blood for all red cell transfusions till a histological diagnosis was made and definitive chemotherapy commenced.
• On achieving clinical remission, the haemolysis in the cold abated.
Discussion

- Rare occurrence (2 patients in a decade)
- Patients
- Acrocyanosis limited to just the digits
- Ulceration and sickle cell anaemia present confounding diagnosis
- Although lymphomas are more common co-morbidity states with cold agglutinins carcinomas may also be found
- Patients with carcinomas who have cold agglutinins should be screened for the acquired B antigen
- None of our patients had immunosuppressive chemotherapy
- The sickle cell patient is still being followed up for cold related exacerbations in the harmattan season
Limitations

- Confirmatory tests are absent
- Serum Ig assay takes a minimum of 6 weeks
- Sudden unexpected haemolysis with ominous outcomes
- Forced air warming facilities absent – Room heaters
- Blood warming
Conclusion

• Cold agglutinins may be uncommon but can constitute a delay which interferes with transfusion safety.

• The intense pruritus that accompanies the Raynaud’s phenomenon may simulate endemic conditions like scabies, and fungal infections.
References

• Special thanks to Dr B Augustine
• Luzzatto L., Haemoglobinopathies and Thalassaemias in Clinics in Haematology by Luzzatto L (ed) 1981 Vol.10(3) 757-784.
• Thank you