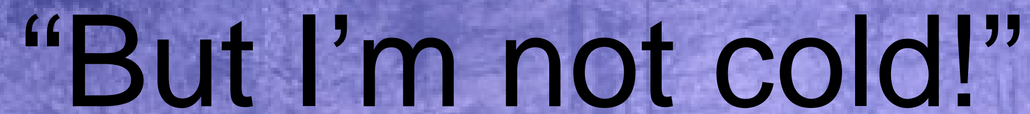


ESIM 2009

Dr Simon Dalton,

Christchurch, New Zealand

Hiroki_Suzuki

Mrs V – 40 years old

- GP referral with "Anaemia and SOB"
- (Hb=57g/L, normal WCC/platelets)

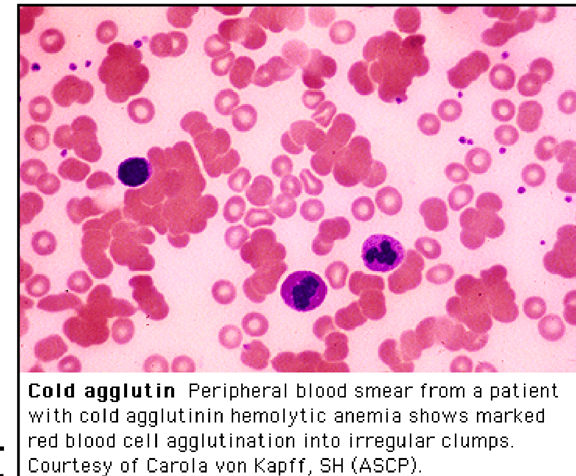
- Well until 2 weeks ago, now increasing SOB at rest, difficult to walk around
- No bleeding, bruising, malaena
- Donated blood 1/12 prior with Red Cross
  - "Rejected in a letter as I was DAT (I think…) positive"

Mrs V

- No PHx/Meds/FHx. Smoker 5/day.
- Examination
  - Pale. Scleral icterus.
  - No lymphadenopathy, no bruising.
  - P=124/min regular, BP 120/80
  - RR=24/min, on O_2 via mask.
  - HS S1+S2+?added sound, JVP +1cm.
  - Chest NAD.
  - Abdomen - large, soft, non-tender ?spleen
    - PR – no blood, malaena. Normal findings.
  - No oedema

Blood film

- WBC corrected for the presence of erythroblasts.
- Atypical and reactive lymphocytes +
- Granulocytes show toxic granulation and vacuolation +
- Polychromasia ++
- Red cell agglutination +++
- Unable to perform reticulocyte count agglutinins. Morphology and results are consistent with Cold Haemagglutinin Disease



Cold agglutin Peripheral blood smear from a patient with cold agglutinin hemolytic anemia shows marked red blood cell agglutination into irregular clumps. Courtesy of Carola von Kapff, SH (ASCP).

- CBC - Hb = 50g/L, WCC = 11.7, Platelets = 403, Nucleated RBCs = 1.6, Myelocytes = 0.7

Other Investigations

- Biochem
  - LFT's: Bilirubin 76, otherwise normal
  - U&E's: normal, LD: 1200
  - SPE: Inflammatory response with low haptoglobin
- Coagulation normal
- Haematinics – low folate , low/normal B12, high iron, low transferrin, saturation 100%.
- Direct AHG Test: Strongly Positive (IgG: +, C3d: +++)
- Cold Agglutinin Screen: Positive, Anti-I, titre: 1:256
- Thermal Amplitude: Reacting up to 37°C

Other Investigations

- Bone Marrow: Erythroid hyperplasia secondary to cold haemagglutinin disease.
- CT Chest/Abdo/Pelvis:
  - Splenomegaly with splenic infarct.
  - No lymphadenopathy. Otherwise normal.
- Mycoplasma serology - negative
- EBV serology – evidence of past contact

Treatment

- 4 units PRC's via blood warmer
- Keep patient warm!!
- After 4 units, Hb only increased by 9g! (59)
- Still SOB, pale and very icteric.
- After a further 4 units, Hb now 72g/L
- Further blood whilst investigations in progress. 4 units results in gain of 6-10g/L

Progress

- Refusing to keep warm. Finds it difficult. Nurses not helping. Next to window, nightie only. Given ice to suck!!
- 20 units in total of blood. Hb has a net increase of 14g/L.
- In room with heater – set to 32. Nurses turn down to 19° as “patient hot”.

- Medical Registrar understandably frustrated.
- Patient understandably depressed.

- Further discussions with Haematologist
  - Initiate therapy – not optimistic of response
    - Prednisone 100mg/day
    - Cyclophosphamide

Cardiac Arrest

- Nurse in room. Not had medication yet.
- Last bag blood 3-4 hours prior.
- Suddenly very SOB. Unresponsive.
- PEA – bradycardic ~25 min on monitor.
- CPR incl external pacing, K+ normal
- Rhythm degenerated (never an output) and became asystolic.
- After 17 minutes CPR, declared dead.
- ?PE ??infected bag blood ??MI

- Coroners Post Mortem

Cold Agglutinin Disease

- A type of autoimmune haemolytic anaemia
- IgM antibodies against polysaccharides on the red cell surface

- "Cold" as the antibody-antigen reaction occurs more readily or more strongly as temperature is reduced

- Each antibody has a "thermal amplitude"
  - This is the highest temperature at which antibody reacts with antigen (ie the Red Cell).
    - Mrs V's antibody has a thermal amplitude of 37°c

Arise in two clinical settings…

- Associated with malignancy (monoclonal antibodies)
- In response to infection (polyclonal antibodies)
  - Commonly seen in two infections:
    - Mycoplasma pneumonia
    - Infectious mononucleosis
  - Other viral infections and Listeria
- Symptoms are related to:
  - Agglutination, anaemia, any underlying disease

Treatment

- Cold avoidance – including emigration to warm country!!
- Treat the underlying disease
- Cytotoxic agents (cyclophosphamide or chlorambucil, with prednisone) or Rituximab (anti-CD20 Antibody)
- Plasmapharesis

- What not to use:
  - Prednisone alone does not diminish antibody
  - Splenectomy
  - Exceptions to the above:
    - Low titre high thermal amplitude patients
    - Rare patient with IgG anitbodies: prednisone and splenectomy may be useful.

Prognosis

- Usually unremitting
- Overall prognosis dominated by underlying lymphoma or other disease process. Even in those without, malignant lymphoma may develop after several years.

- Would we have changed any of our management? Anticoagulation?
  - After discussion with Haematologist – no change.
  - Very difficult disease to treat.
  - This patient had a particularly severe case.
- Very difficult to get other staff to understand and appreciate significance of the cold.