Thalassaemia Case Scenarios

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With transfusion and chelation therapy, thalassemia patients can be expected to have a normal life, shifting the focus to managing the disease complications.
Resources for the patient and the clinician

http://www.ukts.org/

http://thalassaemia.org.cy/
Case 1

- 25 year old lady with TDT beta-thalassaemia major comes to clinic with her new husband
- They want to start a family
- How would you approach this?
Case 1: Pre-conception counselling

- Risk of having an affected child (20-30/year thalassaemia in UK)
- Risk to mother
  - Previous history/severity
- Thalassaemia
  - Transfusion history – antibodies
  - Cardiac iron overload
  - Chelation
Case 1: Risks to women with thalassaemia

- Cardiac problems (cardiomyopathy and arrhythmias), given the 40% increase in cardiac workload during pregnancy
- Worsening osteoporosis
- Iron overload
- Small stature – difficult labours
- Infertility
- Thrombosis – especially post splenectomy in intermedia patients
Case 1: Risks to the fetus

- The possibility of having a major haemoglobin disorder, depending on the globin genotype of the other parent.
- If the mother has diabetes, there is a four-old increased risk of fetal anomaly and three-fold increase in perinatal mortality (NICE 2008).
- If ovulation induction results in a multiple pregnancy, there is increased risk of premature delivery, growth restriction, and disability in the infants.
What do we do? PREPARATION!

- Iron – and chelation thereof
  - T2* >20ms and a liver iron as measured by Ferriscan of <5mg/g/dw and a serum ferritin close to 1000μg/L
  - Stop chelation – desferral when preg test positive
- Hormones – insulin (OGTT) and thyroid function
- Vitamins
  - Vit D
  - Folic Acid
- Spleen
  - Vaccines
- Other medications
What do we do?  PREGNANCY

- Refer to specialist for ovulation induction
  - Clomifine
  - Gonadotrophins (if hypogonadal)
  - U/S and then HCG to trigger ovulation

- Reassess iron load at 28/40 and cardiology review - LVEF

- Consider restarting desferral in 2nd or 3rd trimester
  - T2* of <10ms should start on low dose subcutaneous desferrioxamine (20mg/kg/day) on a minimum of 4 to 5 days
  - T2*> 10ms but < 20ms should be assessed for risks T2*>20ms no chelation unless there is a high risk of cardiac complications.
What do we do?  PREGNANCY and DELIVERY

• Joint specialist clinic – high risk pregnancy
• Anticoagulation
  – Aspirin +/- LMWH
• Keep Hb >100g/L trough
• Monthly fructosamines
• Remember allo antibodies!!!
• Normal vaginal delivery is possible
• Commence desferral when labour commences
Case 2:

• Male patient 23 years old presents to A&E with back pain
• Found to have splenomegally and anaemia
  – Hb 70g/L
  – Spleen 3 finger breadths below diaphragm
• Slightly thalassaemic features
• Hb electophoresis shows HbF and HbA and raised HbA2
Case 2:

- Thalassaemia intermedia or poorly transfused thalassaemia major?
- Or TDT or NTDT?
Case 2: NTDT

• Treatment options in NTDT
  – Hydroxyurea
  – New agents – luspatercept, suspatercept
• When to transfuse?
• Role of chelation
• Splenectomy?
• What can modulate severity of NTDT?
• Why might this chap have back pain?
Case 3:

- 40 year old female TDT beta thalassaemia
- Presents with puffy face and increasing SOB
- Poorly tolerant to s/c desferral

PMH: splenectomy aged 5 years old, previous iron overload (now resolved)

What could be cause of symptoms?
Case 3:

- Port-a-cath in situ for 7 years (4 previous ports)
- Stopped warfarin 7 months ago
- Significant thrombosis: Superior vena cava obstruction seen on venogram
Case 3: Hypercoagulable state

1. Red blood cells
   Hemichrome causes oxidative stress to RBC membrane, resulting in exposed phosphatidylserine (PS)

2. Platelets
   Increased platelet activation and aggregation

3. Endothelium
   Increased endothelial activation and endothelial microparticles; resulting in increased tissue factor

4. Nitric oxide (NO)
   Hemolysis decreases arginine leading to decreased NO; decreased NO causes vasoconstriction

5. Splenectomy
   Increased abnormal RBCs in circulation; high platelet counts

6. Organ function
   Cardiomyopathy and cardiac arrhythmia increased risk of thrombosis

7. Thrombophilia
   Genetic of thrombophilia such as factor V Leiden, prothrombin A20210G, decreased protein C and S; high incidence of antiphospholipid antibody

Case 3: What do we do?

- Avoid central lines if possible
- Anticoagulate all patients with indwelling lines
- Ask radiologist to make sure the tip of line is NOT in the right atrium
- Low threshold for imaging of patient presents with symptoms
- Avoid splenectomy
Case 4:

• 57 year old TM
  – Presents with weight loss and diarrhoea
  – Investigate for diabetes (negative, look for cancer-negative, endoscopy and colonoscopy negative,)

• What to do now??
  – Is this endocrine, thyroid normal, IGF1B reduced but normal response on stimulation
  – Iron (ferritin <500 ug/l now but not in the past!)
Case 4:

• Side effects of drugs- deferiprone, deferasirox
  – Nausea vomiting diarrhea, stomach ulcers

• Pancreatic exocrine insufficiency
  – Presents with weight loss
  – Diarrhoea
  – Common in diabetes, cystic fibrosis, post operative, chronic pancreatitis settings, ETOH
Case 4:

Fecal elastase used to confirm diagnosis (200-99999 ug/g)
- 100-200 is moderate insufficiency
- Severe <100

- Treated with pancreatic enzyme replacement using Creon if symptomatic from moderate range downward
  - Dose often needs titrating upwards! And don’t forget snacks....
Any Questions?