

## James Price

Factor X deficiency.

## Case 1 - IM

- HPC
  - Marked periumbilical bleeding noted Day 3 of life
  - Ongoing bleeding from heel pricks and venepuncture sites
  - Bruising noted left side of back
  - Transferred by NETS to RNSH for further investigation and management

## Perinatal history

- Pregnancy
  - Mother on lamotrigine for epilepsy; dose increased early in pregnancy due to two episodes of seizures
  - Otherwise uncomplicated
- IOL at 37<sup>+5</sup> for IUGR
  - Mona Vale Hospital
- SVD
  - no instrumentation required
  - Birthweight 2.49kg, Apgars 9<sub>1</sub>9<sub>5</sub>
  - IM Vitamin K and HBV uncomplicated

## Family history

- First child of nonconsanguineous Caucasian parents
  - No bleeding history in extended family
- Mother
  - No history of abnormal bruising or menorrhagia
  - Uncomplicated scoliosis surgery as teenager
- Father
  - Splenectomy at 14 years post trauma
  - Laparoscopic cholecystectomy complicated by haematoma requiring evacuation
  - Brown snake bite in 2004
    - 14 week hospitalisation with severe coagulopathy, renal failure requiring dialysis and catheter-related thrombosis
  - Dental extractions and arthroscopic surgery with no abnormal bleeding

## Examination

- Clinically well
- Bruises on all limbs from venepunctures and heel-pricks
- Swollen bruised left hand and bruise right side of lower back
- Active and moving all four limbs
- Anterior fontanelle soft and flat

## Investigations

- Coags
  - PT>200s
  - INR>14
  - APTT>150s
- FBP
  - Hb initially 103g/L, fell to 75g/L some hours later
- Imaging
  - Cranial and abdominal US showed no internal bleeding

## Investigations

- Factor assays
  - FX <1%
  - Other factors normal for age

## Management

- FFP 20ml/kg on day 3 and day 6
  - Complete correction of coagulopathy
- Packed cells 20ml/kg

## Progress

- Neonatal
  - Represented at 11 and 24 days with mucocutaneous bleeding(periumbilical and oral)
  - Hb 50g/L
  - Treated with Prothrombinex(50U/kg) and oral iron
  - Hickman catheter inserted and prophylaxis commenced with twice weekly Prothrombinex
  - Ongoing anaemia and FX survival shorter than expected
    - FX 7% at 48/24 post infusion
  - Dosage increased to 80-90U/kg

## Progress

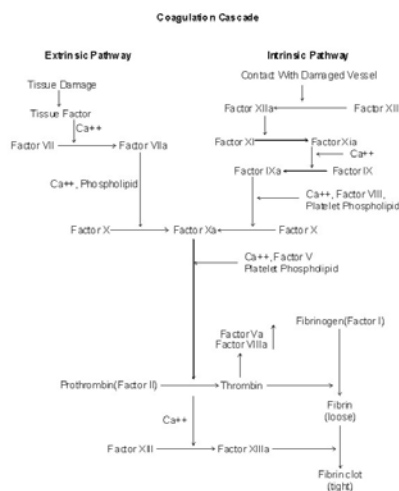
- 4/12
  - Factor X concentrate available in Australia
  - Switched to Factor XP
    - One vial(850-1000IU) weekly
- 11/12
  - Developed catheter infection with coag negative Staph. Aureus
  - One week of IV vancomycin, followed by daily vancomycin locks for 3 weeks
  - All further blood cultures negative
- 12/12
  - Family moved to Perth
- 15/12
  - Hickman line removed and infusaport inserted
  - FX 163% one hour post Factor XP infusion

## Progress

- Well, no further bleeding episodes
  - Factor XP increased to twice weekly at 21/12 as pre-dose FX assay 2%
  - Remains on 1 vial twice weekly (~50-100IU/dose)
- Genetic testing confirmed carrier status in both parents
- Baby brother born September 2010
  - Precautions for delivery
    - No instrumentation
    - Factor studies and coags on cord blood
    - IM injections withheld pending results
  - FX at birth 27%(normal for age)

## Factor X

- Vitamin-K dependent clotting factor
- First factor in common coagulation pathway
- First identified in 1950s



## Factor X deficiency

- Autosomal recessive
- Rare, 1:1,000,000
- Males and females equally affected
- Heterozygotes 1:500
  - Very rarely symptomatic carriers
- Factor X gene
  - Long arm of chromosome 13, downstream from FVII gene
  - Both point mutations and gene deletions identified

## Clinical features

- Spectrum of severity
  - Factor levels do not correlate well with clinical presentation
- Umbilical stump bleeding common
- May present with mucosal bleeding, including GI
- Easy bruising and menorrhagia common in less severely affected patients
- Haemarthroses and muscle bleeds less common than in Haemophilia A and B

## WA experience in severe factor X deficiency.

4 patients - all presented early.  
2 with intracranial bleeding.  
Prothrombinex prophylaxis in older 2 girls. No significant bleeds on therapy.

## Acquired Factor X deficiency

- Liver disease/Vitamin K deficiency
  - Other Vitamin-K dependent factors also affected
- Amyloidosis
  - Functional defect; FX adsorbs onto amyloid fibrils
- Myeloma
  - Rarely reported; ?binding of FX to excess light chains
- Malignancy
  - Spindle cell thymoma, renal carcinoma, gastric carcinoma, AML
- Infections
  - Transient FX deficiency reported with Mycoplasma infection
- Drugs
  - Sodium valproate
- Acquired inhibitors
  - Reported with burns, leprosy and exposure to topical thrombin



## Management

- Need for management is guided by clinical symptoms, not FX level
- On-demand vs prophylaxis

## Prothrombinex

- Freeze-dried prothrombin complex concentrate prepared from pooled donated plasma
- Contains Factors II, IX, X; low levels of V and VII
- Risk of thrombosis
  - Case 1; Factors IX and II both >190% while on Prothrombinex

## Factor XP

- Plasma-derived Factor concentrate
- Available in Australia under TGA SAS
  - Approved for FX deficiency and FIX deficiency
- Vials contain
  - Factor X 600-1200IU
  - Factor IX 600IU