

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⁺⁵ for IUGR
 - Mona Vale Hospital
- SVD
 - no instrumentation required
 - Birthweight 2.49kg, Apgars 9₁9₅
 - 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

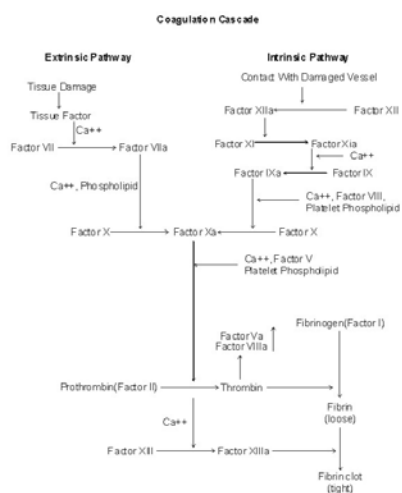
- 4/12
 - Factor X concentrate available in Australia
 - Switched to Factor XP
 - One vial(850-1000IU) weekly
- 11/12
 - Developed catheter infection with coag negative Staph. Aureus
 - One week of IV vancomycin, followed by daily vancomycin locks for 3 weeks
 - All further blood cultures negative
- 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