Sheffield Teaching Hospitals NHS
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Managing the unpredictable: challenges in severe factor X (FX) deficiency

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Introduction

Factor X (FX) deficiency is a rare autosomal recessive bleeding disorder with an estimated prevalence of 1 in 10 million in the severe (homozygous) form. It is commoner in populations with a high incidence of consanguineous marriage.[1]

Those affected may suffer from umbilical stump bleeding, epistaxis, haemarthrosis, central nervous system and post-operative bleeding.[2] Affected women may also present with life threatening intra-abdominal bleeding associated with ovulation.

Reports of successful pregnancy and management of delivery are limited. Complications include recurrent miscarriage, uterine bleeding, premature labour and post-partum haemorrhage. Caesarean section may be recommended to minimise the risk of neonatal haemorrhage.[3]

We report the management of a woman with severe FX deficiency, including the outcome of a term pregnancy, and subsequent family studies.

History

Female patient, parents and grandparents on both sides are first cousins.

Neonatal surgery resulted in significant post-operative bleeding.

Severe FX deficiency (<0.01u/ml) diagnosed at 6 months of age following recurrent GI bleeding.

Ongoing epistaxis, muscle bleeds and menorrhagia.

Age 20 – 2 litre haemoperitoneum following ovulation (Hb 5.3 g/dl) necessitating emergency laparotomy and oopherectomy.

Age 21 – emergency laparotomy for intestinal obstruction (freeing of adhesions).

Age 23 – failed IVF attempt.

Age 30 – pregnancy resulting in live birth.

Age 38 and 39 – further intra-abdominal haemorrhages following ovulation.

Management

Treatment includes antifibrinolytics, virally-inactivated fresh frozen plasma (FFP) and the use of prothrombin complex concentrates (PCCs).

The United Kingdom Haemophilia Centre Doctors Organisation (UKHCDO) recommends the use of PCCs for severe bleeding and invasive procedures. Plasma FX levels of 15-30iu/ml are thought to be haemostatic.[2]

Thrombin generation measurement may have a role in monitoring therapy.[4]

Our patient:
Menorrhagia - treated at home with antifibrinolytics and PCCs.

Surgery – PCC daily to achieve FX levels of 1.0u/ml (based on daily measurement of FX levels) for 5-10 days.

Pregnancy – twice weekly prophylaxis with PCC.

Delivery – PCC to achieve levels of 1.0u/ml when in established labour. Daily PCC for 3 days post-partum. Epidural anaesthesia used (FX level 0.88u/ml).
Normal vaginal delivery of baby girl (using Ventouse - foetal distress).
Baby's cord FX level 0.26u/ml (prior to oral vitamin K).

Inheritance

Complex family tree (see below).

12 first cousin marriages in this family.

Genetic defect has been looked for by 4 different laboratories without success.

The gene sequence of the coding region of the FX gene was normal.

Therefore, in this family there may be either an intronic mutation resulting in abnormal splicing, or a deletion. Both would result in an abnormal FX protein.

Consequently asymptomatic heterozygous carriers with normal factor levels are currently undetectable.

In 2013 a male child with severe FX deficiency was born to cousins of our patient.

The baby was diagnosed at 4 weeks old when he bled for 5 days following circumcision.

His parents were unaware that they were carriers of FX deficiency.

Both had FX levels within the normal range, and no significant bleeding history.

Conclusion

- Treatment of this rare and potentially life-threatening condition is possible using PCC.
- However, the treatment is not without risks (arterial and venous thrombosis).[5]
- Accurate prediction of affected family members is dependent on genetic analysis.
- Management of severe factor X deficiency will continue to present significant therapeutic challenges.

References

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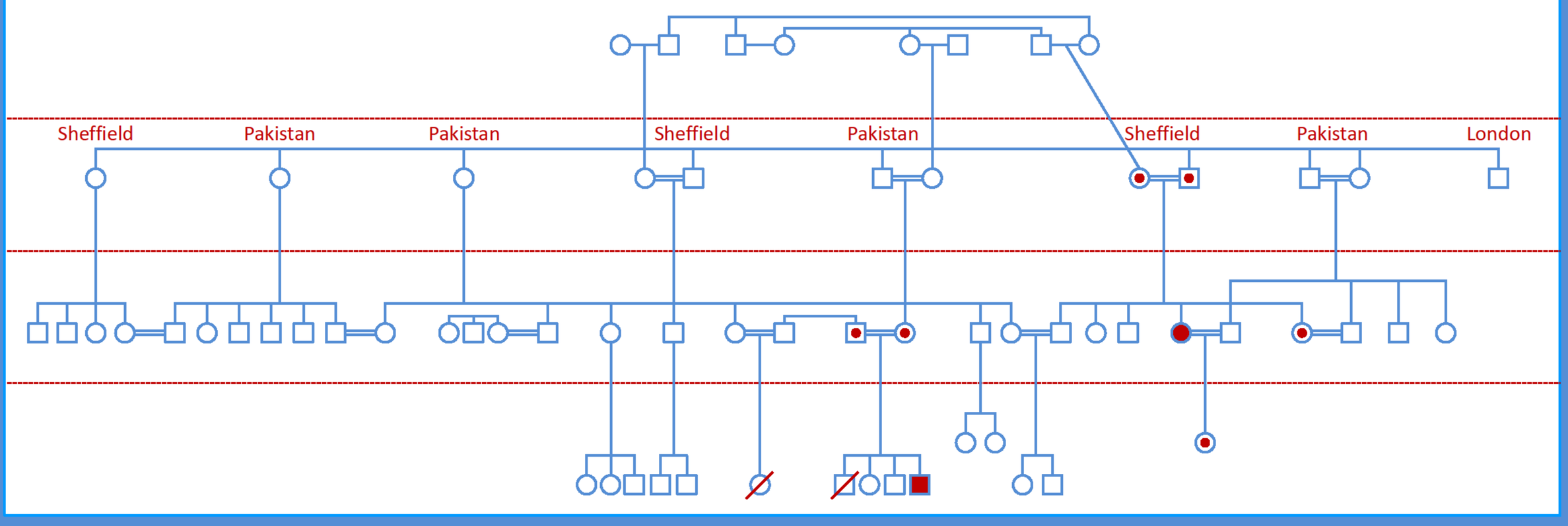
Family Tree

Key:
FX deficiency (male)
FX deficiency (female)
Carrier (male)
Carrier (female)



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