BAMP 2015

Haematology Case Studies

Coagulation Anomalies

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Brief Reminder:

- Coagulation is a complex physiological process involving Platelets, enzymes, inactivated factors, molecular “chaperones”, vascular endothelium in a co-ordinated process to form a stable fibrin clot at the site of vascular injury. Reactions carried out on the platelet surface.
- Fine balance maintained between pro-coagulant and pro-fibrinolytic systems.
- Still 'easier' to think of coagulation problems interms of the 'Intrinsic' and 'Extrinsic' pathways

- The PT: Prothrombin Time;classically measures the extrinsic and common pathway factors.
- VII,X,V,II and Fibrinogen.
- The PTT: Partial Thromboplastin Time; classically measures the 'intrinsic' and common pathway factors.
- XII,XI, IX,VIII,X,V,II and Fibrinogen
- Von Willebrand Factor: integral in platelet adhesion and 'chaperone' for factor VIII
- Platelets:provide a 'scaffolding' for coagulation and also secrete V,XIII(cross-links fibrin monomers) and vWF

CASE STUDIES
a) Myeloproliferative Disorders

- 1) Case ZP: Male age 18.
- Diagnosed CML in 2011; on Glivec treatment.

Hx : Variable compliance with Glivec and the

- disease is now in an Accelerated Phase.
- Oct: Hb 7.7 Wbc 227,**Plat 4,800.**
- **PTT 42.3secs; PT/INR: unrecordable.**
- Clinically severe muscle and joint pains

- Coagulopathy:consistent with Acquired vWD.
- Confirmation requires measurement of vWF antigen levels, activity levels and FVIII levels.
- Treatment: treat the underlying disease.
- High dose H/U started; platelets reduced to 2,387; after one week
- PT 21.6,INR 1.72
- Nov 12: Hb 8.6,Wbc 2.4,Plt 583; PT 16.6,PTT 38.3

- 2) MR age 63; female;
- Diabetic,Hypertensive;
- Recent Thalamic Infarct
- Referred to Haem Clinic with :
- Hb 20.0; HCT 60.9,Plt 737
- PT 18.1, PTT 30.2
- U/S: 'mild' hepatosplenomegaly.

- Abnormal PT due to the high HCT. This alters the blood:anticoagulant ratio in the Na-Citrate tube.
- Routine samples with normal HCT:
- Blood/anti-coagulant ratio is 9:1
- In high HCT: the volume of plasma is reduced which requires a reduction in the volume of the anticoagulant to be used
- C/w Spuriously raised PT value.

Case Studies
b) Congenital Disorders

- 1) RC:67yr ;female (2011)
- FH: 'father' was a 'bleeder'
- Hx of bleeding from teenager;
- Hx of Heavy menstrual cycles
- Bleeding with dental extractions
- 4 Children; all vaginal delivery;
- recalls that only one delivery had heavy
- post-partum bleed.

- vWD Screen results:
- Factor VIII function 50% (range 77-186%)
- vWF function: 58% (40% or >)
- vWF antigen : 101% (50%-168%)
- Finbrinogen 302.
- 2003: PTT 35.4secs;(21-37)
- 2015: PTT 29.2secs;(24.3-35)

- Son#1 JC: hx of bleeding as a child;
- In 2003: PTT 52.7secs; (range 21-37)
- Son #2 JC: no hx of bleeding
- In 2003: PTT 36.2 secs;(range 21-37)
- Daughter #1 JC:
- In 2003 (age 21) PTT 34.7secs;(21-37)
- Daughter #2 JC:
- In 2003 (age 20) PTT 30.4 secs; (21-37)
- Hx of heavy menses

- Son# 2: vWD screen results 2012
- Factor VIII Activity: 39% (50-150)
- vWF Ag: 71% (50-150)
- vWF Activity: 61% (50-170)

- Daughter #2 : vWD screen results 2012
- Factor VIII Activity: 28% (50-150)
- vWF Ag: 63% (50-150)
- vWF Activity : 62% (50-170)

- Son #1 Lives in the USA
- Daughter #1: screen results were all normal.

- Conclusion: as there is factor VIII def in both genders and history of bleeding in both genders
- a diagnosis of vWD Type 2N subtype is a very real possibility.
- The alternative option: Haem A with female members exhibiting X-chromosome lyonization.

- 2) Patient AS: age 7
- Referred by his primary care physician for
- investigation of bruising; no mucosal/joint
- bleed
- Hb 11.7,Plt 266,Wbc 6.3;N 2.11,L 3.4
- PT 14.4(Ctrl 13.9),INR 1.09
- PTT 32.9(Ctrl 30.4), range 24.3-35

Screen results for vWD:

- Patient AS: FVIII act.:43% (50-150)
- vWD act.:60% (>=40%)
- vWF ag.: 76.2%(44-144)
- Fibrinogen 240mg/dl (191-472)
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- Father ES: FVIII act.: 50%(50-150)
- vWF act.: 65% (>=40%)
- vWF ag.: 85% (50-168)
- Fibrinogen: 320mg/dl
- Mother MK: FVIII act.: 75%(50-150)
- vWF act.: 115%(>=40%)
- vWF ag.: 125%(50-168)
- Fibrinogen 298mg/dl

- Sister SS age 11
- FVIII act.: 81%
- vWF act.: 93%
- VWF ag.: 125%
- Fibrinogen 370mg/dl

- C/w likely Haem A, though cannot exclude completely vWD type 2N
- Requires FVIII gene analysis and possibly vWF multimer analysis.
- NB Father's boderline FVIII level.
- Both father and son have similar vWF act./ag ratio.
- Mother probably an obligate carrier; and could require gene analysis as well

- Paitent HH;age 73,MALE
- Referred by his urologist for a prolonged PT.
- No hx of any prior bleeding or bruising
- PT 18-19 secs that corrected on 50:50 mix
- FVII act. 61% (67-143)
- Mild FVII def..
- Underwent his prostatectomy with FFP cover.

- FVII def. Mild-severe.
- Has a variable clinical presentation.
- The patients with a bleeding phenotype require Recomb VII product.
- Extremely expensive: 1mg vial :at least $US1,500.00. Dose is based on weight.40ug/kg
- Given every two hours until bleeding stops!
- Also used in Haemophilias with inhibitors

- Conclusion:
- Coagulopathies need to considered :
- 1) when either the PT/PTT are altered
- 2) when neither the PT/PTT are altered
- 3) when there is a prominent thrombocytosis
- NB: effect of polycythaemia causing a 'spurious' effect on the PT.
- Most cases of prolonged PT are clinically insignifcant however any anomaly found should be repeated and discussed with the Haematology Lab.

.THANK YOU