SURREPTITIOUS SUPERWAFARIN INGESTION & ITS CLINICAL MANIFESTATIONS IN A 25-YEAR-OLD POSTPARTUM CHINESE LADY

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HISTORY

- Mrs LPL, 25-year-old Chinese lady
- c/o ecchymosis of Rt leg and hematuria X 2/7
- 9 months postpartum of 2\textsuperscript{nd} child
- History of ingesting some leaves bought from the Chinese Herb Store in Bentong, Malaysia
Figure 1: Large ecchymosis at right flank and right leg
INVESTIGATIONS

- Hb of 7 g/dl
- WBC 10.4
- Plt 317

- PT 120 sec, aPTT 180 sec

- -> Tx with 2 pint PC & 4 unit FFP
- -> IV Vit K 10mg x 3 days
IMPRESSION

- ? Warfarin poisoning
- TRO Acquired haemophilia
FURTHER HISTORY

- No similar problem in the past
- Denied any renal, hepatic or gastrointestinal problems
- No history of excessive alcohol ingestion
- Diet - adequate intake of vitamin K
- No other medications – denied warfarin usage
- No exposure to rodenticides/pesticides
FURTHER HISTORY

- No family history of bleeding diathesis
- Live in a terrace house in a village in Bentong
- Water from tap, not from well
- Husband is a farmer
FURTHER INVESTIGATIONS

- PT 21.3 sec (12.0 - 15.0 sec)
- aPTT 56.4 sec (32.0 - 44.9 sec)
- Mixing test (PT, aPTT) corrected
- INR 10
- D Dimer 423 mg/dL (0.00 - 0.50)
- Thrombin time (TT) and fibrinogen were normal
FURTHER INVESTIGATIONS

- Coagulation factor:
  - II = 24.9 % (50.0 - 150.0)
  - VII = 8.5% (70.0 - 130.0)
  - IX = 48.1% (60.0 - 150.0)
  - X = 20.7 % (70.0 - 120.0)

- Protein C = 5% (70 - 142)
- Protein S = Activity 5% (70 - 142)
- Protein S = Free 12% (50 - 150)
FURTHER INVESTIGATIONS

- Coagulation Factor VIII Activity 81.9% (50.0-200.0)
- Von Willebrand Factor Antigen (VWF) 60.5% (60.0-150.0)
- Von Willebrand Factor Activity (VWF) 59.8% (60.0-150.0)
- LA neg

- RP, Liver enzymes were normal
- No evidence of DIVC
MANAGEMENT

- Impression:
  TRO Superwarfarin poisoning/exposure

- Oral vitamin K 5 mg od
- Iberet 1 dly
- Tranexamic acid 500 mg 6hrly
PATIENT PROGRESS

- Oct 2012 to Feb 2014 – 4x relapse
- spontaneous bruises
- menorrhagia
- oral vitamin K 10mg daily up to 40mg od
■ Mac 2014 had MVA
■ Lt hand and Rt knee hematoma
■ ROM limited due to swelling
■ Hb 10.5 Wbc 12 Platelet 452
■ PT 23.4/ APTT 73.4/ INR 2.28

■ IV Vit K 25mg QID x2/52
■ 1 episode of PC + FFP transfusion
■ discharge with oral vitamin K 20mg TDS
Serum & leaves for toxicology – normal gas chromatography

- high PIVKA-II (undercarboxylated prothrombin) detected in serum (Oct 2013)
- suspected brodifacoum but negative

- Normal psychiatric assessment
High levels of vitamin K1 (due to treatment with the vitamin) were detected. We also detected much higher than normal vitamin K1 2,3-epoxide levels indicating the presence of an antagonist. In this sample the PIVKA-II (undercarboxylated prothrombin) levels were also grossly raised to a level that I would associate with a highly prolonged PT or INR, consistent with the presence of a vitamin K antagonist.
Figure 1. Vitamin K is converted to vitamin K epoxide (inactive) in the liver. Brodifacoum (a superwarfarin) interferes with vitamin K metabolism by inhibiting the 2,3-epoxide reductase enzyme, which increases levels of vitamin K epoxide (inactive vitamin K) and inhibits the synthesis of active factors II, VII, IX, and X.

Reference:
**LATEST RESULTS (09/2018)**

- WBC 9.5, Hb 10.5, plt 360
- PT 13.2 (11.7 - 14.0)
- aPTT 41.9 (33.0 - 44.5)
- INR 1.05
- FII 99.1% (50 - 150)
- FVII 92.7% (70 - 130)
- FIX 132.65% (60 - 150)
- FX 93.7% (70 - 120)
- Protein C 120 (90 – 142)

Manage to taper down oral vitamin K and off in Nov 2015
TAKE HOME MESSAGE

■ SUPERWARFARIN EXPOSURE/POISONING
■ unexplained acquired bleeding + coagulopathy + vitamin K dependent factor deficient
  – absence of detectable warfarin
■ Cases of surreptitious warfarin or superwarfarin -> psychiatric evaluation
  – TRO Munchausen syndrome, depression
■ High vitamin K1 epoxide–reduced vitamin K1 ratio + PIVKA
CONCLUSIONS

- New entity
- Acquired inhibitor to Vitamin K epoxide reductase (VKOR) enzyme
- The cause of superwarfarin effect remains unclear
ACKNOWLEDGEMENT
THANK YOU
Q & A