Title: A coagulopathic dilemma: snakes or genes.

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A 66 year old male presented in March 2013 to a small hospital in south-west Queensland-Australia, after a snakebite to his index finger. He had a history of haemochromatosis and was on no regular medications. He reported no local or systemic symptoms. Bloods were collected 45min post-bite and he was transferred to a larger hospital. Initial international normalised ratio (INR) and fibrinogen were normal, qualitative D-Dimer was positive but the activated partial thromboplastin time (aPTT) was unrecordable (Figure 1). In the context of an asymptomatic patient with a normal INR, and the D-dimer assumed to be a possible false positive , the elevated aPTT was interpreted as a sampling error.

Six hours post-bite, repeat aPTT was >200sec and INR was normal. A commercial snake venom detection kit from a bite site swab and urine sample were positive for brown snake (*Pseudonaja* spp.) venom. A clinical toxicologist from the Poisons Centre advised not to give antivenom and to observe and repeat pathology investigations given the patient was asymptomatic and laboratory investigations were inconsistent with snakebite coagulopathy. An isolated raised aPTT was not consistent with brown snake venom induced consumptive coagulopathy (VICC),[1] where both INR and aPTT are abnormal. A moderately raised aPTT can occur in black snake (*Pseudechis* spp.) envenoming, but the patient would have symptoms.[2]

Eleven hours post-bite the patient reported nausea and vomited. Repeat aPTT remained >200sec, butand the INR was 1.4 (Reference range[RR]:0.9-1.2) and fibrinogen 1.6g/L (RR:1.7-4.5). His creatinine doubled from 78μmol/L to 141μmol/L. Further discussion with the toxicologist again raised the possibility of brown snake envenoming with mild VICC, but the unrecordable aPTT and mildly abnormal INR were inconsistent. Black snake envenoming was also unlikely despite the abnormal aPTT, because of mild symptoms and normal creatine kinase. An undiagnosed clotting factor deficiency was considered possible. Antivenom was not given because of the delay post-bite and the fact that it was unclear if the patient was envenomed and by what snake.

At 24 hours post-bite, the quantitative D-dimer was >20mg/L (RR:<0.40), but his INR and creatinine had normalised, consistent with envenoming., Howeverhis aPTT remained >200sec. He was discharged with follow up for possible undiagnosed factor deficiency. Factor studies done two weeks later were all normal except factor XII levels were <0.01U/mL (RR:0.5-1.5). Venom specific enzyme immunoassays were performed on serum collected as part of the Australian snakebite project, which found 1ng/mL of brown snake venom.[1]

This is an unusual case of brown snake envenoming in a patient with undiagnosed factor XII deficiency. The unrecordable aPTT and only slightly abnormal INR made the diagnosis difficult, as brown snake envenoming causes VICC due to a prothrombin activator toxin with low factor I, II, V and VIII levels, resulting in equally abnormal INR and aPTT.[3] In contrast, black snake envenoming causes an isolated elevated aPTT due to an anticoagulant toxin, but the aPTT is rarely >100sec and patients are systemically unwell.[2] In this patient the elevated aPTT was due to factor XII deficiency, and the transient mild elevation in INR was due to partial VICC.[1, 3] The abnormal creatinine was consistent with renal toxicity from brown snake envenoming.[1] Antivenom was not administered in the case because the diagnosis only became clear when it was too late to be administered.

Factor XII deficiency is usually an incidental finding and only detected if the patient has coagulation studies. The incidence of severe factor XII deficiency is 0.3%,[4] and despite the prolonged aPTT it is not associated with spontaneous or major bleeding.[5] This case demonstrates the interesting complexities of coagulation studies in snake envenoming, and the difficulty with diagnosis which was only made by measuring venom concentrations and clotting factor levels.

Authors Contribution: AC and GI wrote the case report and were involved in the management of the patient.

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