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BRIEF REPORT

Rebound Coagulopathy in Patients With Snakebite Presenting With Marked Initial Coagulopathy

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Objective.—An estimated 70% of patients with pit viper snakebites require antivenom to treat serious complications such as coagulopathy. Evidence-based guidance is limited for the appropriate administration of Crotalinae Polyvalent Immune Fab (FabAV) and the duration of laboratory follow-up. The objective of our study was to assess the incidence of marked and recurrent envenomation coagulopathy at our trauma center and identify practice patterns that may prevent serious complications.

Methods.—A retrospective case review was conducted over a 3-year period on patients treated for symptomatic snakebite injury. Case records were reviewed for the inclusion criteria of international normalized ratio (INR) greater than 2.0. The exclusion criterion was limited to patients receiving anticoagulant therapy.

Results.—In all, 61 patients were identified on retrospective chart review and 3 patients (4.9%) met inclusion criteria. Two of the 3 patients had marked rebound coagulopathy requiring readmission and additional treatment. In our small series, 2 patients presenting after crotaline envenomation with increased INR (>6.0), decreased fibrinogen (<60 mg/dL), and decreased platelet count (<100,000/mL) had recurrent coagulopathy and were asymptomatic, and recurrence was noted only with follow-up laboratory testing. All patients responded positively within a matter of hours to repeat FabAV administration, with resolution of rebound coagulopathy.

Conclusions.—We recommend periodic monitoring of patients with increased INR, decreased fibrinogen, and decreased platelet count. Patients should be monitored for 10 to 14 days after envenomation to identify asymptomatic rebound coagulopathy. Prompt readministration of FabAV appears to correct the coagulopathy.

Key words: coagulopathy, Crotalinae, envenomation, FabAV, hypersensitivity

Introduction

Most venomous snakebites in North America are inflicted by the Crotalinae subfamily of Viperidae, or vipers. The Crotalinae (crotalines) are commonly known as pit vipers and include species of rattlesnakes, copperheads, and cottonmouths.[1] Roughly 4000 to 6000 venomous snakebites occur each year in the United States. Although few are fatal, approximately 70% of victims require administration of antivenom.[2] Antivenom probably arrests the progression of some of the local effects of envenomation (eg, swelling, pain, ecchymosis, bruising), as well as the potentially serious systemic effects such as coagulopathy.[3]

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Pit viper envenomation often results in coagulopathy owing to disseminated intravascular coagulation (DIC), also referred to as consumptive coagulopathy.[4–6] Disseminated intravascular coagulation is a pathologic activation of coagulation mechanisms leading to the development of thrombocytopenia and prolongation of both prothrombin time (PT) and partial thromboplastin time (PTT), thus resulting in abnormal bleeding and usually accompanied by low fibrinogen levels.[7] Disseminated intravascular coagulation is associated with significant morbidity and can lead to end-organ damage.[4–6]

In a postmarketing, multicenter, retrospective chart review, 100% of 28 patients with severe envenomation showed improved severity scores for all venom effects, including coagulopathy/defibrination syndrome, thrombocytopenia, and significant/spontaneous bleeding.[3,5]

These same studies also showed that platelet counts may return to normal within hours after an initial control dose of Crotalinae Polyvalent Immune Fab (FabAV).[4] A significant number of patients did not normalize platelets 1 to 2 weeks after envenomation. None of these studies, however, have addressed the long-term consequences associated with snakebite envenomation. There is a paucity of data on the use of FabAV in the management of rebound coagulation, and there are few evidence-based protocols and algorithms available.[2,6] In a study by Seifert[7] in 2011, patients with normal hematology studies (fibrinogen, D-dimer, international normalized ratio [INR], PTT, and $<20\%$ increase in platelet counts) did not have late hematologic effects.

The development of recurrent coagulopathy or thrombocytopenia, which usually occurs after the patient has been stabilized and discharged, is recognized in the literature.[4] The underlying mechanism of recurrence remains to be fully elucidated; nonetheless, we have found that with modern therapies, control of envenomation is achieved earlier and hospitalization times have been shortened.[6] Unfortunately, we have learned that there is the potential that patients are not being monitored long enough to detect signs of rebound coagulopathy.

The objective of the present study was to determine the incidence of marked and recurrent envenomation coagulopathy at our trauma center with the intention of assessing the extent of the problem and identifying practice patterns that may improve outcomes for patients who receive a snakebite.

Methods

CLINICAL SETTING

Our facility at Texas Health Harris Methodist Hospital Fort Worth is a Level II Trauma Center. With an average of 3000 trauma admissions a year, approximately 20 patients are seen annually because of a snakebite injury. The majority of snakebite injury patients come from rural areas outside the suburban area of Fort Worth, Texas, and are transferred to our trauma center. All patients returned to the clinic 10 to 14 days after envenomation for laboratory testing of PT, INR, and platelet count to ensure there was no evidence of rebound coagulopathy.

STUDY DESIGN

A retrospective case review was conducted. This study was submitted to the Texas Health Institutional Review Board, which conducted an expedited review and assigned a status of exempt.

INCLUSION CRITERIA

All patient records over a 3-year period were searched for a diagnosis of snakebite. Case records were reviewed for the following: diagnosis, laboratory reports, procedures/treatments received, discharge summaries, dates related to course of treatment, and names of drugs and devices used as a part of treatment. Of all patient records identified, only patients with an INR greater than 2.0 were included in this study.

EXCLUSION CRITERION

Patients receiving anticoagulant therapy at presentation were excluded from this study.

PROTECTION OF PATIENT CONFIDENTIALITY

Appropriate steps were taken to ensure no breach of confidentiality. All identifying data were kept in the research coordinator's locked office, data were deidentified, and all computer files were password protected.

LABORATORY VALUES

The hospital's laboratory normal range values and a description of the scenario when a value is unable to be calculated are as follows: INR less than 1.2 normal; INR is a calculation based on the PT, and if the PT is beyond the measurable limit, the INR cannot be calculated (INR >22/PT >140 seconds); fibrinogen, 204 to 488 mg/dL (undetectable <60 mg/dL) by Clauss assay; PT, 11.9 to 14.7 seconds.

Case Reports

In all, 61 patients were identified on the initial chart review, and 4 met the inclusion criteria, with an INR greater than 2.0. One patient was receiving warfarin on admission and was excluded from further analysis. One patient did not have rebound coagulopathy and was not readmitted or retreated, and was also excluded from further analysis. The total patient cohort consisted of 2 patients presumed to have been bitten who presented with marked thrombocytopenia and clinical evidence of DIC. All patients underwent postdischarge laboratory evaluations 10 to 14 days after envenomation. The 2 patients had marked rebound coagulopathy requiring readmission and retreatment (Table 1). Neither patient had evidence of bleeding. The other 59 patients did not have rebound coagulopathy and did not require readmission and retreatment.