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CASE REPORT

Recombinant Factor VIIa for Treatment of Gastrointestinal Hemorrhage Following Rattlesnake Envenomation

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North American rattlesnakes possess venom with primarily cytotoxic and hemotoxic properties. When persons are envenomated by these snakes, thrombocytopenia and coagulopathy commonly occur, yet patients rarely develop severe bleeding. This report describes a 44-year-old Native American man bitten on the index finger by an unknown species of rattlesnake. The man developed massive gastrointestinal hemorrhage that was ultimately treated with recombinant factor VIIa. He presented to an emergency department with a depressed level of consciousness, a blood pressure of 60/20 mm Hg, and heart rate of 148 beats per minute. He was diaphoretic and vomiting bright red blood. Initial laboratory results revealed thrombocytopenia and coagulopathy. Despite aggressive fluid resuscitation and administration of blood and antivenom in the emergency department, the patient continued to have profuse upper gastrointestinal bleeding, with hemoglobin as low as 1.8 g/dL. He received fluids, antivenom, and multiple blood products, with cessation of bleeding after administration of recombinant factor VIIa. Esophagogastroduodenoscopy revealed a single Mallory-Weiss tear as the source of hemorrhage. The patient stabilized after 6 hours of aggressive resuscitation but over the next several days developed several complications, including acute renal failure and gram-negative sepsis. The patient died on hospital day 5. In cases of life-threatening hemorrhage after rattlesnake envenomation in which traditional therapy with antivenom and aggressive supportive measures fail, recombinant factor VIIa should be considered as an additional therapeutic option to achieve hemostasis.

Key words: rattlesnake, hemorrhage, recombinant factor VIIa

Introduction

North American rattlesnakes possess venom with primarily cytotoxic and hemotoxic properties. When persons are envenomated by these snakes, thrombocytopenia and/or coagulopathy commonly occur and are frequently associated with oozing of serosanguineous fluid from puncture wounds at the bite site. Extreme drops in both platelets and fibrinogen may occur. Yet even under these circumstances patients rarely develop severe bleeding.[1,2,3] The following report describes a patient with massive gastrointestinal hemorrhage after a bite to the index finger by an unknown species of rattlesnake. Resolution of bleeding was temporally associated with administration of recombinant factor VIIa.

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Case report

A 44-year-old Native American man was bitten on the right index finger by a rattlesnake while cleaning a chicken coop. His past medical history included alcohol-related liver disease, anemia, and thrombocytopenia, with a reported platelet count of 46 K/mm^3 1 month earlier. He presented within 15 minutes to a rural emergency department with a depressed level of consciousness, a blood pressure of 60/20 mm Hg, and heart rate of 148 bpm. He was diaphoretic and vomiting bright red blood. A puncture wound was present on the right index finger, and there was mild swelling of the hand.

He was initially treated with solumedrol 80 mg intra-

venously and 0.5 mg subcutaneous epinephrine, due to concern that he was having an anaphylactoid reaction to the venom. Two liters of normal saline were infused intravenously, which resulted in a transient improvement in systolic blood pressure to 106 mm Hg. A nasogastric tube was placed with output of 1 L of blood over the next 90 minutes. Initial laboratory studies revealed hemoglobin 13.1 g/dL, hematocrit 37.6%, platelets 10 K/mm^3, prothrombin time 56 seconds, and fibrin split products <5 μg/mL. There were no red blood cell fragments noted on peripheral smear. Fibrinogen level was not available.

Persistent hypotension developed, and he was administered normal saline, dopamine, and blood products. A total of 3 L of intravenous fluids, 2 units of packed red blood cells, 1 unit of fresh frozen plasma, and 4 vials of Crotalidae polyvalent immune Fab rattlesnake antivenom were administered in the emergency department. The hospital did not have additional antivenom or the capacity to manage this unstable patient. The patient was then transferred by fixed-wing aircraft to our toxicology center. At the time of transfer he was awake but drowsy. During transfer, the patient lost another 2 L of blood through the nasogastric tube. A norepinephrine infusion had been added, and an additional 2 L of intravenous fluids was given. Prochlorperazine 10 mg had been given intravenously for vomiting and diazepam, 10 mg was given intravenously for agitation.

The patient arrived at our intensive care unit approximately 5 hours after the bite occurred. His blood pressure was 87/44 mm Hg, heart rate 133 bpm, respiratory rate 21 bpm, and core temperature 91°F. Ventilatory effort was poor, and pulse oximetry was 94% on an oxygen nonrebreather facemask. The patient was comatose and without purposeful movement, and there was continued profuse loss of bright red blood via his nasogastric tube. Heart sounds were normal and lungs were clear to auscultation. Swelling of the hand was moderate and had progressed to involve the forearm. The right arm was ecchymotic with soft compartments, and a small hemorrhagic bleb was forming on the finger at the site of fang entry. There was some blood oozing from other puncture sites on the extremities. There was no evidence of tissue infarction on the skin or extremities. A Foley catheter was placed without return of urine.

The patient was orotracheally intubated after administration of vecuronium and midazolam intravenously. Simultaneous treatment with packed red blood cells and fresh frozen plasma, antivenom, sodium bicarbonate boluses, intravenous fluids, vasopressors (including epinephrine, norepinephrine, and dopamine), and thiamine was instituted immediately. A detailed account of blood products, fluid boluses, and antivenom administration over the first 30 hours is presented in the Table. Octreotide 50 mcg was given intravenously. Arterial blood gases showed pH 6.85, pCO_2 62 mm Hg, pO_2 272 mm Hg, bicarbonate 10 mEq/L, and base deficit 21 mEq/L on FIO_2 1.0. Other laboratory values on arrival to the intensive care unit included hemoglobin 3.9 g/dL, platelets 7 K/mm^3, prothrombin time 46.7 seconds, partial thromboplastin time >150 seconds, fibrinogen 35 mg/dL, sodium 145 mmol/L, potassium 4.2 mmol/L, blood urea nitrogen 4 mg/dL, creatinine 1.1 mg/dL, lactic acid 21 meq/L, creatinine kinase 66 U/L, ammonia 160 μmol/L, and ethanol 104 mg/dL. Initial studies included a chest radiograph that was negative for effusions or infiltrates. Electrocardiogram was significant for a sinus tachycardia at a rate of 134 bpm, inferior Q waves, QRS 92 msec, and QTc 460 ms. An echocardiogram was negative for cardiac tamponade, pericardial effusion, or thrombus and showed normal contractility with an ejection fraction of 65%.

Within 1 hour of arrival, the patient had lost an additional 6 L of blood through his nasogastric tube. Repeat laboratory studies at this time revealed Hg of 1.8 g/dL and hematocrit of 5%. Platelets had risen to 57 K/mm^3. Three more liters of blood were lost over the next two hours. Over the first 4 hours of intensive care unit resuscitation, the patient received 5 L of intravenous fluids, 350 meq of intravenous sodium bicarbonate, 20 vials of Crotalidae polyvalent immune Fab rattlesnake antivenom, 12 units of packed red blood cells, 8 units of fresh frozen plasma, 2 units of platelets, and 10 units of cryoprecipitate (Table).

Because severe hemorrhage continued from the upper gastrointestinal tract despite the above therapy, the patient was treated with 7.2 mg recombinant factor VIIa intravenously, after which bleeding ceased almost immediately. He then stabilized with a heart rate of 60 bpm, systolic blood pressure of 110 mm Hg off vasopressors, and hemoglobin oxygen saturation of 99% on 1.0 FIO_2, and he began making clear urine and following simple commands.

Computed tomography scan of the brain was obtained and was negative for the presence of blood but positive for fluid in the sinuses. Esophagogastroduodenoscopy revealed a Mallory-Weiss tear responsible for the bleeding and was negative for esophageal varices, which had originally been suspected to be present.

In the first 36 hours after initial stabilization and cessation of hemorrhage, there was no further bleeding noted, but the coagulopathy and thrombocytopenia persisted. It was unclear if these were due to venom, the large volume resuscitation and acidosis the patient had experienced, or both. Additional blood products were given in an attempt to completely reverse coagulopathy and keep hemoglobin