TRACHEAL INTUBATION PREVENTED WITH ADMINISTRATION OF FAB ANTIVENOM AFTER SEVERE CROTALINE ENVENOMATION

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Abstract—Background: Crotaline snake envenomations are common, but severe crotaline envenomations are infrequent. Death from severe envenomation is usually from upper airway edema and respiratory failure. Published reports of severe respiratory compromise and anaphylactoid reactions are rare. Currently, FabAV (Crotalidae polyvalent immune Fab [Ovine]) [CroFab] is the mainstay of crotaline envenomation treatment; however, FabAV has been approved for only mild and moderate envenomations. Case report: We describe a case of a male with severe systemic effects and airway compromise after crotaline envenomation. The patient’s systemic effects and upper airway edema substantially improved after antivenom infusion and before epinephrine administration. Endotracheal intubation was averted, clinical deterioration was avoided, and improvement occurred after prompt FabAV use. Conclusion: Fab antivenom likely prevented endotracheal intubation in our case of severe crotaline envenomation. Published by Elsevier Inc.

Keywords—snakebite; crotaline; intubation; antivenom; severe envenomation

INTRODUCTION

Approximately 7000–8000 venomous snakebites occur per year in the United States; crotaline envenomations are the majority (1,2). Death, however, is rare, with typically five per year (3,4). Many of the deaths and severely ill patients are due to upper airway edema and obstruction or respiratory failure (1). Published reports of severe respiratory compromise and anaphylactoid reactions are rare.

Currently, FabAV (Crotalidae polyvalent immune Fab [Ovine]) (CroFab; Protherics Inc., Brentwood, TN) is the mainstay of crotaline envenomation treatment. It is effective and has fewer severe side effects than the Antivenin (Crotalidae) Polyvalent (ACP; Wyeth, Madison, NJ). Although currently the Food and Drug Administration has approved FabAV for only mild and moderate envenomations, use in severe cases is reported (2). Two reports have described FabAV with severe envenomation and airway compromise (5,6). The patient was intubated before receiving antivenom in both cases. We describe a case of a man with severe systemic effects and airway compromise after crotaline envenomation whose intubation was averted, clinical deterioration avoided, and improvement occurred after prompt use of FabAV.

CASE REPORT

A 40-year-old man was bitten twice on his right hand (on the thumb and index finger) by a native Western diamondback (Crotalus atrox). He had never been envenomed before this occurrence. He had progressive pain and swelling to the thumb and dorsum of his hand on
arrival in the Emergency Department (ED) 45 min after envenomation. He also had small ecchymoses on his thumb. He had placed a constriction band on his wrist immediately after the bite; it was removed on ED arrival. His initial vital signs were blood pressure 137/87 mm Hg, 98% pulse oximetry, heart rate 112 beats/min, and respiratory rate 24 breaths/min. He received 10 mg of intravenous morphine for his hand pain and 1 L normal saline on arrival. After consultation with the Medical Toxicology attending, six vials of FabAV were prepared for infusion. Approximately 30 min after ED arrival (75 min after envenomation) and before antivenom infusion, the patient developed diffuse urticaria and a hoarse voice. Diphenhydramine 50 mg and methylprednisolone 125 mg were administered intravenously, and nebulized epinephrine was started. The patient then developed edema of the face, lips, and uvula. The severe edema progressed quickly and the patient deteriorated to mild respiratory distress. The patient was wheezing and tachypneic; no fasciculations were present. The emergency physician anticipated the need for tracheal intubation. Repeat blood pressure was 153/88 mm Hg and heart rate was 96 beats/min. In consultation with Medical Toxicology, the FabAV was started, subcutaneous epinephrine was ordered, and airway devices and medications for a difficult endotracheal intubation were gathered.

Ten minutes after the antivenom was started, the facial (lips and eyelid) edema, oropharyngeal (uvula and posterior pharynx) edema, and respiratory symptoms improved substantially. Within 15 min of infusion, his hoarseness resolved, his uvular and lip edema continued to improve, and his mild respiratory distress abated. Epinephrine was available at that point and was administered subcutaneously (0.3 mL of 1:1000 solution). The epinephrine treatment was initially delayed because the treating nurse was unable to access the locked medicine cabinet where it was stored. The patient continued to have significant improvement of his facial and oropharyngeal edema with no recurrence of local or systemic symptoms. The initial partial thromboplastin time (PTT), prothrombin time (PT), fibrinogen, and platelets were normal. The initial hemoglobin was 14.4 grams/dL, creatine kinase 74 units/L, and creatinine normal.

The patient was admitted to the Intensive Care Unit for 14 h. He was then transferred to the surgical ward and used a patient-controlled analgesia morphine pump for pain. He received 22 vials of FabAV during admission: two boluses of six vials and one of four vials to obtain control of local and systemic effects, and then six vials for maintenance therapy. The PTT, PT, fibrinogen, and platelets remained normal throughout the hospitalization. His facial and oropharyngeal edema resolved completely 12 h after envenomation, and systemic effects did not recur. His extremity edema improved 14 h after envenomation. He was observed for 18 h after his last maintenance dose of FabAV and discharged home on hospital day 4. On scheduled follow-up 4 days later, the patient was readmitted for hand cellulitis and received intravenous antibiotics and local wound debridement. He had no recurrence of local or systemic effects.

**DISCUSSION**

A severe systemic reaction from crotaline envenomation rarely occurs. Anaphylactoid response, anaphylaxis, and severe envenomation have caused airway compromise, and have been treated with ACP and FabAV (5,7,8). However, in these reports, FabAV was used after intubation to treat systemic effects. Our report is unique in that FabAV was administered for the upper airway edema and other systemic effects, and it prevented intubation by halting the edema progression and reducing the patient’s symptoms.

FabAV for airway compromise after crotaline envenomation has been reported in two cases that we found. In one, a child was envenomated in the face and developed progressive facial and oropharyngeal edema and stridor (6). She was intubated and then administered FabAV. Her systemic effects were hypofibrinogenemia, prolonged PT and PTT, and mild anemia that required transfusion of red blood cells. In the second case, Camilleri and Offerman described a young male with a right elbow envenomation. Immediately after removal of the restriction band, the patient rapidly developed face and neck edema and dyspnea (5). The patient was intubated, intravenous epinephrine was infused, and FabAV was then administered. Our case is similar to Camilleri and Offerman’s, but in our case, FabAV was infused before intubation. The subsequent facial and upper airway edema resolved, and intubation was avoided.

Our case demonstrated oropharyngeal edema after systemic envenomation from a crotaline extremity snakebite. His effects could also have been from anaphylaxis or an anaphylactoid response to the venom (9). The FabAV may have bound the venom antigen responsible for his symptoms, thereby quelling its effects. His rash is suggestive of an immunogenic reaction. Differentiating the three possible etiologies is difficult without additional immunologic testing because clinical presentations overlap (10). Our patient did not demonstrate hypotension, bronchospasm, or vomiting. The initial clinical management for the three entities is the same (7).

The FabAV was being reconstituted when the patient developed upper airway symptoms; therefore, it was infused shortly after his systemic symptoms began. Although the antivenom was promptly administered, the appropriate preparation to manage a difficult airway and to treat anaphylaxis or an anaphylactoid reaction was initiated. The patient received an intravenous H1 antag-
onist, a steroid, nebulized racemic epinephrine, and intravenous fluids. Delivery of the subcutaneous epinephrine was inadvertently delayed, due to a systems error, but was administered shortly after the antivenom. This pharmacy systems error was corrected.

Antivenom will reverse systemic effects. In addition, it is thought to halt local edema progression and hasten its recovery (2). Although FabAV may not reverse local edema at the bite site, systemic edema did resolve in our case during FabAV infusion and before the subcutaneous epinephrine. The patient refused pictures, which would have helped demonstrate the severity of his symptoms and the rapid regression after antivenom.

The patient did receive an H1 blocker and a steroid before the antivenom; however, these medications are not expected to reverse edema and improve symptoms as quickly as in this patient (9). Nebulized epinephrine was also administered; however, the dramatic resolution of the patient’s edema would not be expected on his nonmucosal surfaces. However, because the patient received intravenous diphenhydramine and nebulized epinephrine with the FabAV, the antivenom cannot conclusively be considered the sole agent for his symptom abatement. Finally, morphine allergy is an unlikely cause for his severe symptoms. He denied history of an opioid allergy and tolerated morphine through a patient-controlled analgesia pump during his 4-day hospital stay.

Although intubation was not performed in this case, management of crotaline envenomation-induced upper airway edema requires a predetermined Emergency Medicine approach to a difficult airway. This approach includes early intubation for obstructive laryngeal edema and adeptness with rescue airway techniques, including “awake intubation,” fiberoptic bronchoscopy, use of a smaller endotracheal tube, and cricothyrotomy. Intubating laryngeal mask airway and blind nasotracheal intubation are important approaches to the difficult airway, but these blind approaches can be perilous in severe supraglottic edema (11,12). The physician should be facile with these techniques and have a prepared algorithm for these patients because envenomated patients with systemic effects can precipitously deteriorate (2,5). Preparation for both an oral intubation and surgical airway (“double setup”) is preferred (11). Parenteral (subcutaneous, intramuscular, or intravenous) epinephrine can control and improve edema, and should be administered promptly (9). In our case, subcutaneous epinephrine was given in this normotensive patient. H1- and H2-histamine receptor antagonists are secondary agents that should also be used (9). Lastly, a parenteral steroid should be administered to prevent rebound of symptoms (9).

Intravenous FabAV likely prevented endotracheal intubation in our case. However, if the patient had not had immediate and significant clinical improvement after FabAV, he would have been intubated early, before the upper airway edema worsened. In addition, epinephrine would have been administered before the FabAV if the epinephrine had been readily available and the antivenom had not already been prepared for infusion. Based on this case, FabAV is still an adjuvant treatment of allergic symptoms induced by crotaline envenomation; traditional treatments for anaphylaxis (early tracheal intubation, parenteral epinephrine, and histamine blockers) should be used first. Occasionally, prophylactic intubation should be performed before life-threatening upper airway edema occurs.

CONCLUSION

Rattlesnakes can rarely cause severe envenomation, including upper airway and facial edema. In our case, intravenous administration of FabAV halted upper airway edema, reduced respiratory distress, and averted tracheal intubation. Although FabAV was useful in this severe, systemically ill crotaline-envenomated patient, preparation also should be made to manage a difficult tracheal intubation and treat refractory hypotension.

REFERENCES