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Case Study

Administration of CroFab Antivenom by a Helicopter Emergency Medical Service Team

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A B S T R A C T

The case presented here highlights an unconventional use of a helicopter emergency medical service (HEMS) to provide a specialized medication to a critically ill patient when definitive transport was delayed. A 39-year-old man presented to a rural hospital 1 hour after sustaining a copperhead envenomation. He developed severe symptoms and was intubated. Arrangements were made for transfer to a tertiary referral center by HEMS, but because of incoming weather conditions, the team would not be able to make the return flight safely. The decision was made for the HEMS team to fly antivenom to the patient, administer the medication, and then transport the patient by ground to the tertiary medical center. This plan was executed, and the patient was safely transported to the accepting facility. Antivenom is most effective when administered early because this will halt the progression of edema and may reverse the systemic effects of envenomation. In this case, HEMS transport of antivenom to the patient with severe toxicity prevented a delay to administration and likely improved the patient's outcome. Although the traditional role of HEMS is to provide rapid transport to critically ill patients, HEMS teams can also function to deliver specialized medications to remote settings.

The traditional role of HEMS teams in the United States is to provide rapid transport to critically ill patients who would benefit from arrival at a center more promptly than they would by ground transport. Beyond that, HEMS teams often provide more experienced personnel with expanded capabilities than ground emergency medical service crews. Furthermore, in some cases, HEMS teams can facilitate expedited care through their ability to manage the clinical logistics of a complicated situation. We report a case in which an HEMS team was used to deliver a specialized medication to a patient's bedside for rapid administration when expeditious transport of the patient to the receiving center was not possible.

Case Report

A 39-year-old man presented to a rural community hospital by private vehicle approximately 1 hour after sustaining a copperhead snake envenomation to the left upper extremity. The incident occurred while the patient was removing debris behind his garage. The patient's wife stated that he had become progressively confused since the bite occurred.

His triage vital signs included an oral temperature of 98.3°F, blood pressure of 137/88 mm Hg, pulse of 85 beats per minute, and an oxygen saturation of 96% on room air. The patient initially appeared distressed but became progressively drowsy during his triage assessment. The patient was taken to an examination room where resuscitative efforts were begun. Calls were made at that time to locate the nearest facility that stocked the appropriate antivenom.

Fifteen minutes after arrival, the patient experienced rapidly worsening dyspnea, oral edema, and dysarthria. He was given 1 dose of subcutaneous (1:1,000) epinephrine. Thirty minutes after arrival, the patient's condition deteriorated further, and the decision was made to endotracheally intubate for airway protection.

Arrangements were made for the patient to be transferred to a tertiary referral center capable of administering CroFab antivenom

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(Protherics Ltd; London, UK). The hospital-based HEMS team was contacted for transport. Although the outgoing flight was predicted to be safe in terms of flying conditions, incoming weather was going to prevent the crew from returning safely with the patient. In collaboration with the medical toxicologist on call, a plan was made for the air medical crew to obtain the CroFab antivenom from the emergency department pharmacy and deliver it to the rural hospital for immediate administration. The HEMS team would then return to the accepting facility by ground with a plan for the pilot to return the helicopter to the hospital base upon resolution of the inclement weather.

After arrival of the air medical crew, the patient's airway, breathing, and hemodynamic stability were rapidly assessed. The CroFab antivenom medication was quickly reconstituted, and the loading bolus was initiated intravenously. The patient was subsequently transported by ground, under the care of the HEMS crew, with no deterioration of his status. On arrival at the accepting facility, the patient intermittently opened his eyes to verbal stimuli and began to follow simple commands. Care was immediately transferred to the awaiting critical care staff for further evaluation and management. The patient received the full treatment course of CroFab antivenom and did not require repeat dosing. He had improvement in his local tissue findings, was extubated without difficulty, and did not develop any coagulopathy or thrombocytopenia. The patient was discharged home without any long-term sequelae or recurrent systemic toxicity.

Discussion

We report this case to highlight the rapid delivery and administration of the *Crotalinae* species antivenom by a HEMS transport team in a case of a severe copperhead envenomation. HEMS teams have carried this drug in the past, particularly in the southwestern United States, but to the authors' knowledge, no case report of its administration by an HEMS team exists. Furthermore, we report this case as an example of an HEMS team being used to overcome difficult logistics, which represents a departure from the traditional role of rapid stabilization and transport.

There are approximately 8,000 snake envenomations in the United States annually, resulting in about 5 to 6 deaths per year. The majority of these envenomations are from the *Crotalinae* family, which includes copperheads and rattlesnakes, among others.[1] These snakes possess infrared heat-sensing pits on their triangular-shaped heads that are used to direct strikes toward prey, hence the common name “pit viper.” Crotalids inhabiting the United States include the genera *Crotalus*, *Sistrurus*, and *Agkistrodon*. “Rattlesnake” is the common term for snakes of the *Crotalus* and *Sistrurus* genera, whereas “cottonmouths” or “water moccasins” and “copperheads” comprise the *Agkistrodon* genus.[2] Although copperhead venom is not used in the preparation of antivenom, CroFab antivenom has been successfully used in the treatment of copperhead (*Agkistrodon contortrix*) envenomations (Fig. 1), which are among the most common reptile envenomations in the United States.[3,4] Indications for antivenom use include progressive edema, coagulopathy with hypofibrinogenemia or increased prothrombin time, thrombocytopenia, and worsening hemodynamic status.[5] Studies of copperhead envenomations have found that clinically significant local effects (Fig. 2) requiring antivenom such as severe pain, edema, and ecchymosis occur in only 12% to 33% of copperhead snakebites.[6-9]

Crotalidae polyvalent immune Fab (FabAV), marketed as CroFab antivenom, was approved by the US Food and Drug Administration in October 2000, and is an ovine-derived antivenom formulated to treat *Crotalinae* snake envenomations.[10] FabAV has been found to be effective in the treatment of severe crotaline envenomation with rare treatment failure and with low risk of allergic and delayed hypersensitivity reactions.[11-15] Unfortunately, FabAV has a shorter half-life than traditional antivenom, so recurrent coagulopathy and thrombocytopenia can occur after the administration of FabAV, necessitating repeated dosing after administration.[14,16-18]

Figure 1. *Agkistrodon contortrix*, copperhead snake.

Figure 2. Local tissue effects from a copperhead envenomation.

CroFab antivenom can be administered under the direction of any physician, but consultation with a toxicologist or poison specialist can be helpful and is recommended. CroFab antivenom is lyophilized and packaged in glass vials. It must be reconstituted with 18 mL 0.9% saline by inversion and then further diluted in 250 mL 0.9% saline. Reconstitution by this method takes about 3 minutes.[19] The indications for use have not been rigorously defined but include progressive local edema, coagulopathy, and system effects.[1] Typical CroFab antivenom administration involves

an initial dose of 4 to 6 vials. If the control of both tissue effects and stabilization of thrombocytopenia and coagulopathy is obtained, maintenance dosing is given in 2 vials every 6 hours for 3 additional doses to complete the course of therapy.[16] The patient should be monitored for allergic reaction, and epinephrine, corticosteroids, and antihistamines should be available during administration.[5]

CroFab antivenom is most effective when administered early because this will halt the progression of edema and may reverse systemic effects of envenomation.[5,14,20] Sufficient stocking of antivenom is recommended for all hospital pharmacies in areas where crotaline species are found in order to prevent delay in administration.[21] In this case, HEMS transport of antivenom to the patient with severe toxicity prevented a delay in administration and likely improved the patient's outcome.

Conclusion

In summary, we present the case of a 39-year-old man who presented with severe toxicity from a copperhead envenomation. HEMS brought CroFab antivenom to this patient, treated him successfully, and then transported him to definitive care, showing the effective transport and administration of CroFab antivenom by HEMS. The presentation of this case raises the question of whether services should prepare for similar future situations with existing protocols.

In helicopter critical care transport, crew and patient safety must be prioritized when aeronautical decisions are made regarding adverse weather conditions. The consequences of inappropriate decisions can be disastrous. In the case of this critically ill envenomed patient, rapid helicopter transport to the receiving facility was not possible because of weather-related safety concerns. The decision to prioritize the rapid delivery of a critical antidote to the patient, as opposed to the typical use of HEMS in rapid patient retrieval, is an example of the flexibility in logistics that a HEMS team can provide.

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