Case Report

Obstetric Management of Copperhead Snake Envenomation in Pregnancy: A Case Report

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Keywords

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Abstract

Snakebites in pregnancy can result in significant maternal and fetal harm; however, the literature to guide management of this rare obstetric complication remains limited. We describe our approach to envenomation in pregnancy based on the currently available evidence. A 27-year-old G2P1 female presented at 27 weeks' gestation after suffering a copperhead snakebite. She received antivenom and antenatal steroids without adverse maternal or fetal event. Antenatal testing was reassuring throughout admission, and she was discharged home with plans for close outpatient surveillance. She later developed preterm premature rupture of membranes and preterm labor, with delivery of a live infant at 33 weeks' gestation. The risk of adverse maternal and fetal outcomes following snake envenomation in pregnancy may warrant closer antenatal surveillance than has been previously described.

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Introduction

Snakebites in pregnancy are uncommon, accounting for <1% of the ~5,000 cases of venomous snakebites reported in the US each year [1]. While rare, snake envenomation in pregnancy can result in significant maternal and fetal morbidity and mortality, with maternal death and/or fetal loss occurring in up to 10 and 43% of reported cases, respectively [2]. Due to the rarity of reported events and incomplete understanding of the pathophysiology of snake venom, evidence to guide the optimal management of even nonpregnant snakebite victims remains limited [3]. The management of pregnant snakebite victims is further compounded by the need to account for maternal physiological changes, judicious use of medications in pregnancy, and fetal wellbeing [4]. Here, we describe our approach to the medical and obstetric management of snake envenomation in pregnancy based on currently available evidence.

Case Presentation

A 27-year-old G2P1 female at 27 weeks' gestation was admitted to our tertiary care center approximately 3 h after sustaining a snakebite to her right foot. She initially presented to a local emergency room with acute-onset pain, swelling, and bruising after being bitten. The snake, collected by a family member, was identified as a copperhead snake (*Agkistrodon contortrix*) based on its characteristic light-tan coloration and cross-band patterning. The patient received six vials of Crotalidae polyvalent immune Fab (ovine) antivenom (CroFab; FabAV) for initial control of envenomation and oral opioids for pain before transfer to our facility for further care.

On arrival, the patient denied any systemic or obstetric complaints. She reported no significant medical history and an uncomplicated pregnancy thus far. She was afebrile and hemodynamically stable (heart rate 91 bpm, respiratory rate 18/min, blood pressure 144/73 mm Hg). Examination of the right lower extremity revealed two distinct puncture marks and ecchymosis extending to the mid-calf with associated tenderness to palpation; this area was marked to monitor spread. Admission labs revealed a normal electrolyte panel and no evidence of coagulopathy.

Initial obstetric evaluation revealed a category 1 fetal heart tracing, no contractions on external tocometer, and normal fetal fluid (amniotic fluid index 8.1 cm) and growth (1,167 g, 42nd percentile) on bedside ultrasound. The patient was managed by a multidisciplinary team that included medical toxicology and maternal-fetal medicine specialists for the remainder of her admission. She received three maintenance doses of CroFab antivenom without adverse effect. Regarding her right lower extremity, pain and ecchymosis initially progressed to the level of the knee before gradually receding (Fig. 1).

Given the increased risk of maternal coagulopathy, placental abruption, and stillbirth following snake envenomation, she underwent continuous electronic fetal monitoring throughout the remainder of her antivenom course. Additionally, in the event of emergent delivery, antenatal corticosteroids for fetal maturation were given. The fetal monitoring was category 1 throughout her antivenom course. After completion of her antivenom course, fetal nonstress tests were repeated nightly and remained appropriate for gestational age. Vital signs and laboratory data were followed closely during the patient's admission and remained stable

(Table 1). Given reassuring maternal and fetal status, she was discharged home on hospital day 4 with plans for close outpatient surveillance.

She was seen for an outpatient visit at 29 weeks' gestation. Labs repeated at that time remained stable with no evidence of coagulopathy (Table 1). A biophysical profile was reassuring, with a result of 8/8. She returned again at 31 weeks' gestation for a targeted ultrasound with Maternal-Fetal Medicine. This was performed due to increased risk of maternal and fetal coagulopathy and theoretical risk of fetal intracranial hemorrhage. Ultrasound showed normal amniotic fluid (amniotic fluid index 13.9) and fetal growth (1,692 g, 34th percentile). Anatomical survey was normal, with no evidence of intracranial hemorrhage.

The remainder of her pregnancy course remained unremarkable until 32 weeks' gestation, when she was readmitted for preterm premature rupture of membranes. She received a 10-day course of antibiotics to prolong latency and a second course of antenatal corticosteroids. Her pregnancy was managed expectantly until 33 weeks' gestation, when she developed preterm labor. She had an uncomplicated labor and delivery course, birthing a live male infant weighing 2,110 g via uncomplicated spontaneous vaginal delivery. Apgar scores were 8 and 9 at 1 and 5 min, respectively. Her postpartum course was uneventful and she was discharged home on postpartum day 2.

The infant's course was complicated by respiratory distress requiring continuous positive airway pressure, microcephaly (head circumference 28.5 cm, 9th percentile), anemia (hematocrit 60%), thrombocytopenia (platelets 49,000/ μ L), and hyperbilirubinemia (peak bilirubin 13.6 mg/dL). Neonatal head ultrasound showed no abnormalities. At the time of submission, the infant had been discharged home with plans for outpatient pediatric follow-up and evaluation of microcephaly.

Discussion

Pregnant victims account for <1% of the approximately 5,000 cases of venomous snakebites reported to US poison centers each year [1, 4]. Though a rare obstetric complication, snake envenomation leads to maternal and fetal mortality in up to 10 and 43% of reported cases, respectively, and likely warrants closer antenatal surveillance than has been previously described [2].

The various inflammatory, cytotoxic, neurotoxic, and hemotoxic components of snake venom help snakes immobilize and digest prey. The toxic components in snake venom – and thus patient manifestations and outcomes after snake envenomation – depend on the type of snake involved [2, 5].

The three main families of venomous snakes – Hydrophidae, Elapidae, and Viperidae – differ in appearance, geographic distribution, and venom profiles. The Viperidae family (pit vipers) is the one most commonly implicated in reported snakebite cases and is the subject of the presented case. Pit vipers have wide triangular heads, elliptical pupils, ridged scales, and long, movable, and canalized fangs. In the US, the Viperidae family includes North American rattlesnakes, cottonmouths, and copperheads. The Elapidae family – which worldwide includes cobras and mambas – is represented in the US by coral snakes. These snakes have commensurate head-neck width, large smooth scales, round pupils, and short, fixed, grooved fangs covered by a mucous membrane [2, 5, 6].

Both Elapidae and Viperidae venoms contain enzymes that can deplete clotting factors and cause subsequent consumptive coagulopathy as well as enzymes that can damage the endothelial lining of blood vessels and cause local and systemic hemorrhage [7]. Despite these potential sequelae, the most common manifestations of snake envenomation are local erythema, swelling, and tenderness at the puncture site, occurring in up to 90% of patients [6].

The basic principles of managing snakebites include (1) first aid and supportive measures, (2) serial physical exams and laboratory evaluations, and (3) prompt treatment with antivenom when indicated [2, 5, 6]. The initial management of snakebite victims should include arranging expedited transfer to an appropriate medical facility. The victim should be assessed for airway compromise, breathing, and circulation. If possible, obtaining a photograph from a safe distance may be valuable later for species identification. The affected extremity should be immobilized. The puncture site, leading edge of erythema, as well as limb circumference above and below the snakebite should be examined and marked every 15–30 min until the swelling stabilizes.

Laboratory studies (i.e., complete blood count, basic metabolic panel, liver function panel, coagulation studies, fibrinogen, D-dimer, total creatine kinase, and urinalysis) are of little value in diagnosing envenomation, but abnormalities can reveal cytopenia, coagulopathies, and rhabdomyolysis. Thus, they can be useful for evaluating the severity and in guiding decision-making about specific interventions. Laboratory studies should be repeated as indicated by the severity of envenomation [5, 6].

Antivenom is the only effective antidote to snake venom, and current guidelines recommend antivenom administration for any snakebite victim with progressive signs or symptoms [5, 6]. Antivenoms are animal serum-derived immunoglobulins that function by binding and neutralizing venom in the intravascular space as well as by diffusing into the interstitial space to halt the progression of local tissue injury. The ovine-derived Crotalidae polyvalent immune Fab antivenom (CroFab; FabAV), which our patient received, was approved by the US Food and Drug Administration in 2000 and causes fewer adverse reactions than previous products [5, 6]. Administration within 4 h of the bite is recommended, but antivenom has proved its effectiveness even when given within 24 h of the bite [5]. Patients should be observed for at least 24 h after administration of the last dose, as hypersensitivity reactions and serum sickness develop in 8 and 13% of patients treated with CroFab, respectively. If these reactions do occur, they should be treated with epinephrine, steroids, antihistamines, and emergency airway management as needed [5, 6]. Importantly, as soon as any adverse reactions are controlled, it is imperative to resume treatment with antivenom to continue reversing the effects of the venom. Patients who receive antivenom should undergo repeat laboratory evaluation after receiving the last dose to evaluate for delayed onset of recurrent coagulopathy [6].

Given the rarity of snake envenomation in pregnancy, the pathophysiology leading to adverse maternal and fetal outcomes remains poorly understood. It remains unclear whether snake venom crosses the placenta, though indirect evidence of placental transfer has been previously described in cases where adverse fetal effects occurred in the absence of adverse maternal effects [2, 4]. The proposed mechanisms of perinatal morbidity and mortality include direct effects on the fetus, maternal coagulopathy (causing placental abruption or acute maternal and/or fetal anemia), uterotonic effects (causing preterm labor and/or delivery), cytokine release after tissue damage, and maternal anaphylaxis and/or shock in response to either venom or antivenom [2, 4, 8].

Close clinical collaboration between medical toxicologists and obstetric specialists is recommended in managing gravid snakebite victims. Pregnant patients should receive the same supportive measures and serial laboratory evaluations as their nonpregnant counterparts supplemented with appropriate antenatal testing to evaluate fetal status [4, 6]. In the present case, our patient underwent continuous electronic fetal monitoring until completion of her antivenom course, nightly fetal nonstress tests until hospital discharge, ultrasound evaluation with biophysical profile at the time of outpatient laboratory testing, and targeted ultrasound with a maternal-fetal medicine specialist 4 weeks after the inciting event, given the theoretical risk of fetal intracranial hemorrhage after potential fetal coagulopathy.

Regarding the administration of snake antivenom in pregnancy, the effect of antivenom on fetal wellbeing is unclear. In a 2010 literature review examining 213 cases of snakebite in pregnancy, 96 patients received antivenom [9]. Of these, maternal death and fetal loss occurred in 2 (2.1%) and 29 (30.2%) of cases, respectively. However, administration of antivenom is not necessarily an independent risk factor for adverse fetal outcomes; rather, poor fetal outcomes are thought to be associated with more significant systemic maternal envenomation [2]. In fact, the current thought is that Fab antivenoms, at molecular weights of ~50,000 Da, cannot cross the placenta [4]. Given likely placental transfer of snake venom without transfer of antivenom, there remains a risk of persistent fetal coagulopathy even after administration of antivenom.

Antivenom is effective in preventing maternal death [2]. High morbidity and mortality rates have been associated with delayed treatment in low-resource, rural areas of developing countries where antivenoms are often scarce and expensive [7]. Conversely, no maternal deaths and only two fetal deaths have been reported after envenomation of gravid patients by native US species of snakes; this may be due to both increased access to hospital care and increased availability of antivenom [2]. Given that the risks of withholding treatment likely outweigh the risks of antivenom administration, current guidelines recommend that pregnant snakebite victims receive antivenom as would be indicated in nonpregnant patients [6].

In conclusion, snakebites are extremely rare complications of pregnancy, which has limited the current literature in informing a clear understanding of the pathophysiology of adverse outcomes and in guiding treatment and monitoring recommendations. Our presented case resulted in minimal adverse maternal outcomes, largely secondary to management within an optimal healthcare setting and timing to treatment. For future cases, we recommend focusing on three primary points in the care of envenomated gravid patients: (1) interdisciplinary shared clinical management by obstetric and toxicology specialists, (2) decreased time to antivenom treatment when indicated, and (3) serial laboratory, antenatal, and antepartum evaluation for the signs of maternal coagulopathy, nonreassuring fetal status, or preterm labor.

Statement of Ethics

This research complies with guidelines for human studies. The patient gave written informed consent for publication of her case, including publication of images.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All authors contributed to the clinical management of the patient, the gathering of data, the review of the existing literature, and the writing and editing of the manuscript.

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Fig. 1. Lateral dorsum of the right foot 4 days after post snakebite envenomation showing mild edema and erythema, with visible puncture sites lateral to the area of erythema. The oval around the area of erythema with parallel dotted lines demarcates any changes in edema at different time intervals.

Table 1. Maternal vital signs and laboratory data

Gestational age	Heart rate	Blood pressure	Hemoglobin	Platelets	INR	Fibrinogen
27 ⁺³	78	103/59	11.8	236	0.98	421
27 ⁺⁴	86	107/66	11.8	240	1.01	533
27 ⁺⁵	75	101/64	10.8	250	0.98	498
28 ⁺²	90	117/72	11.8	272	0.94	477
32 ⁺⁰	79	114/58	10.6	202	–	–
33 ⁺³	81	105/75	11.2	177	–	–
33 ⁺⁴	86	122/79	10.9	–	–	–

–, value not available.