ORIGINAL RESEARCH

Serum Sickness Following Administration of Antivenin (Crotalidae) Polyvalent in 181 Cases of Presumed Rattlesnake Envenomation

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Objective.—To describe the incidence and characteristics of serum sickness (SS) following administration of Wyeth Antivenin (Crotalidae) Polyvalent (ACP).

Methods.—A retrospective chart review was conducted involving presumed rattlesnake bite victims referred to our poison center. Serum sickness was defined as unexplained rash developing 3 to 21 days following the administration of ACP. Patients were monitored until complete resolution of all symptoms. Data collected included total number of ACP vials administered, associated signs and symptoms, duration of signs and symptoms, and medications used to treat SS.

Results.—Of the 181 cases included in our study, SS occurred in 102 (56%) patients. The frequency of SS in patients receiving fewer than 20, 20 to 29, 30 to 39, or 40 or more vials was 34%, 36%, 88%, and 100%, respectively. Duration of SS averaged 6.1 days (range, 1–21 days). Associated symptoms included subjective fever (49%), arthralgia (20%), and pruritus (40%). Reported medications used included prednisone (98%), antihistamines (92%), and histamine-2 blockers (3%).

Conclusions.—Serum sickness following administration of Wyeth ACP is common, with a strong correlation between ACP dosage and SS frequency.

Key words: rattlesnake, serum sickness, antivenin, envenomation, snakebite

Introduction

The incidence and characteristics of serum sickness (SS) following the administration of Wyeth Antivenin (Crotalidae) Polyvalent (ACP) have not been well described. The objective of this study was to describe the incidence and characteristics of SS following the administration of ACP in a statistically significant sample of snakebite victims, thereby providing physicians with a more dependable basis for estimating the risk of SS when faced with the clinical decision of administering ACP. Estimating this risk will become increasingly important with the advent of newer antivenoms for the treatment of rattlesnake bites.

Methods

We conducted a retrospective chart review of rattlesnake envenomations reported to our poison center during a 5-year period. The study population consisted of patients who were believed to have been envenomated by rattlesnakes, were treated with ACP, and either their physician or the patient called our regional poison center. The inclusion criteria were history of receiving ACP following a presumed rattlesnake bite and completion of the 21-day follow-up. Our study involved no new interventions, hence an expedited review was obtained from our institutional review board. We used descriptive statistics to describe our main outcomes of SS and associated signs and symptoms. Three reviewers were used, following 1 hour of instruction. Preidentified data were collected with the reviewers blinded to the exact purpose of the study. Another reviewer audited 10% of the charts to establish cohesiveness and a correlation coefficient.

Serum sickness was defined as unexplained rash de-

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veloping 3 to 21 days following the administration of ACP. Patients were monitored until complete resolution of all associated symptoms, which were defined as subjective fever, arthralgia, and pruritus.

Data were analyzed using descriptive statistics with stratification of data based on the number of vials of ACP received.

Results

A total of 414 patients were referred for presumed rattlesnake envenomation between January 1, 1996, and December 31, 2000. Of the 202 patients receiving ACP, 181 (90%) completed the required minimum 21-day follow-up period and were included in our study.

The mean number of ACP vials administered was 38 (range, 5–62). The number of patients receiving fewer than 20, 20 to 29, 30 to 39, or 40 or more vials was 5, 36, 78, and 62, respectively.

Serum sickness occurred in 102 (56%) patients. The frequency of SS in patients receiving fewer than 20, 20 to 29, 30 to 39, or 40 or more vials was 34%, 36%, 88%, and 100%, respectively, and this difference was statistically significant ($P < .001$).

Duration of SS averaged 6.1 days (range, 1–21 days). Associated symptoms included subjective fever (49%), arthralgia (20%), and pruritus (40%). Reported medications used included prednisone (98%), antihistamines (92%), and histamine-2 blockers (3%).

The κ value for interreviewer reliability was 0.69, with confidence intervals of 0.45 to 0.95. Statistics were calculated using Microsoft Access & Excel Programs 2002. A Student t test and χ^2 tests were used as appropriate.

Discussion

Antivenin (Crotalidae) Polyvalent is manufactured from hyperimmune horse serum in which antibodies have been raised against the venoms of 4 snake species, namely, *Crotalus adamanteus* (eastern diamondback rattlesnake), *Crotalus atrox* (western diamondback rattlesnake), *Crotalus durissus terrificus* (tropical rattlesnake), and *Bothrops atrox* (fer-de-lance), with albumin making up 6% W/W and IgG, 18.9% W/W.¹ Injection of such foreign proteins is known to trigger both acute and delayed allergic reactions in some people.

The retrospective study design eliminated our ability to confirm physical examination findings, medication use, and cause of the injury, including identification of the snakes involved. Nonetheless, our study represents a

significant sample of North American snakebite patients evaluated for SS following treatment with ACP.

These data should be considered when administration of ACP is contemplated and should be compared with the known incidence of SS associated with other antivenoms when choosing the most appropriate course of treatment. For example, CroFab has an SS incidence of less than 10%,² with a range of 3% to 16%.¹

The only prospective study of ACP reactions we were able to identify in the literature found that SS developed in 75% of patients ($n = 8$).³ Other retrospective series have shown increased SS with higher doses.^{4–6} Jurkovich et al⁵ found that 50% of snakebite patients treated with ACP and for whom follow-up data were available ($n = 20$) developed SS, although the authors point out that the sample size of their study did not yield statistical significance. Downey et al⁶ reported SS in 4 (18%) of 22 rattlesnake bite patients receiving ACP, but follow-up data for 8 of the 36 total patients were not available; the number of ACP-treated patients in this group is unclear.

In conclusion, based on our sample, the incidence of SS following administration of ACP can be expected to exceed 50% in the 30 to 39 vial dosage range, with the incidence of SS reaching 100% at dosages of 40 or more vials. When SS (characterized by unexplained urticaria) does occur, it can be expected to last approximately 6 days, with about half of the patients exhibiting subjective fever, 40% complaining of pruritus, and 20% complaining of arthralgias.

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