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Venom-Induced Anemia: The Case of the Missing Red Blood Cells

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Introduction

Picture this: you're in a mid-1930s noir film. You're sitting behind your desk at your job as a private investigator smoking a comically large cigar and throwing back whisky shots as you contemplate your concerning lack of cases and your landlord's increasingly irate demands for the past-due rent payment. Suddenly, you hear a sharp knock on your frosted glass door. You ash your cigar and yell out for them to enter. In comes your next client, a snakebite victim. You ask who's missing, and that's when they tell you: their red blood cells.

NEWSLETTER HIGHLIGHTS

Various potential causes of anemia in rattlesnake bite patients

Image 1: Black-tailed Rattlesnake (*Crotalus molossus*)

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Alright, maybe the metaphor is a little silly, but hear me out: while much ado is made about the impact that rattlesnake venom has on the clotting cascade, anemia is a potential development that gets far less fanfare. In fact, venom-induced anemia is a phenomenon that has gone relatively unnoticed in the current scientific literature. It's not exceptionally rare either; between 2017-2022, about 5% of snakebite patients that AzPDIC was consulted on developed anemia during their treatment course. Given that a venom-induced drop in hemoglobin ≥ 2 g/dL is associated with delayed recovery rates, and anemia in general is associated with a laundry list of symptoms, it's worth investigating. But what causes the anemia in the first place? As an emergency physician, I am a relatively simple man and prefer problems to have simple answers, but unfortunately for me, the case of the missing RBCs may be somewhat complex. In this month's NFTP, we will do a deep dive into the various potential causes of anemia in rattlesnake victims.

Bleeding

Whenever I think about anemia, my next thought is always bleeding. Our bodies are relatively skilled at maintaining a stable level of red blood cells and can adjust production to maintain balance; however, this homeostasis can quickly be overcome in the event of acute bleeding. For snakebite patients in particular, bleeding can manifest in a variety of ways. The physical rattlesnake bite site typically doesn't cause enough trauma to lead to significant bleeding. In fact, some patients who suffer bites don't even realize they've been bitten at first since the bite site is so innocuous! However, patients occasionally suffer from trauma in conjunction with rattlesnake bites, such as falling after being bitten, which puts them at risk for significant bleeding that would only be compounded by the rattlesnake venom. The more insidious type of bleeding associated with rattlesnake bites is unprovoked bleeding, or bleeding without a clear cause. When a patient's clotting ability is sufficiently impaired, they begin to experience bleeding from the gums and other mucosal surfaces, even without an obvious traumatic injury. Reassuringly, data from AzPDIC has shown that the rates of significant bleeding, both provoked and spontaneous, are quite low for Arizona rattlesnake bites.

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Ecchymosis (Bruising)

In the same vein (get it?) as bleeding is bruising, given that it is just bleeding confined to the skin. Now, most people won't typically get anemia from a normal bruise in their day to day lives; however, the large bruises that form after a snakebite are a different beast entirely. They are caused by a variety of factors, but mainly are driven by damage to blood vessels, which cause leakage of blood into surrounding tissues, compounded by impairment of the clotting factors, which would otherwise stop continued leakage. As a result, patients develop extensive bruising after a rattlesnake bite that can extend past the bitten limb and even into the torso. It normally takes a few hundred milliliters of blood loss to drop a healthy person's hemoglobin by 1 g/dL, but some compartments of the body can hold significant amounts of blood (a single thigh can hold 2 liters of blood in serious trauma patients!). To this end, data from AzPDIC over the past few years found that significant bruising (extending at least halfway up the bitten limb) was strongly associated with eventual onset of anemia.

Destruction

Now, Arizona rattlesnake venom can wreak havoc with the body's clotting factors, but we typically don't think about it having a direct impact on red blood cells. However, various case studies and laboratory experiments have shown that rattlesnake venom does have the ability to lyse red blood cells, which could theoretically lead to anemia in significant envenomations. The other, more common route we consider for red blood cell destruction is indirect in nature. Pit viper venom in Arizona acts on the part of our blood that forms clots, causing all sorts of problems. In some patients, this results in the formation of small clots, or microthrombi, all over the body, a state referred to as Venom-Induced Consumptive Coagulopathy. When these microthrombi form, they may not completely block blood vessels because they are so small, but they can cause shearing forces on red blood cells, which tear apart the erythrocyte membranes and cause microangiopathic hemolytic anemia.

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Hemodilution

As every hardboiled PI knows, the first rule of a missing person case is determining whether they are actually missing (don't quote me on that). Are the RBCs missing, or is that decreased hemoglobin level just a red herring? To review, when a patient's hemoglobin is measured in the hospital, it is reported as a concentration, namely how many grams of hemoglobin per deciliter of blood is within a given sample of a patient's blood. It follows that giving someone saline intravenously should reduce a patient's hemoglobin concentration. Add in the fact that you basically get a liter of saline just for showing up at the ER, and you can see why this could cause hemoglobin values to drop!

Except, we now know that this is mostly a theoretical risk, and not one supported by actual data. Studies investigating the actual amount of hemodilution from saline administration showed the effect is marginal at best and not nearly pronounced enough to cause anemia in an otherwise healthy patient. While still a consideration, especially considering the amount of IV fluid a patient may receive from a multi-day hospital stay, the impact of hemodilution is likely minor for rattlesnake bite patients.

Conclusion

In all your years as a PI, you've never been stumped on a case like this before. You grab your fedora off the hat stand next to your door—the brim casts your face in deep shadows that reflect your innate cynicism—turn up the collar on your trench coat and step out into the cold night air. The case of the missing red blood cells might be one that you'll never truly solve.

Alright, perhaps that's a bit pessimistic, but the fact is that venom-induced anemia is likely multifactorial in nature and difficult to fully quantify. Further research is ongoing, but for now we will continue to measure a patient's hemoglobin and treat as the clinical picture dictates. There is one thing we know for sure: a mystery-loving toxicologist is always happy to take your call at 1-800-222-1222, whether for a rattlesnake bite or other interesting case!