Successful Use of Plasma Exchange for Profound Hemolysis in a Child With Loxoscelism

abstract

We describe a 6-year-old boy who presented with massive hemolysis, shock, disseminated intravascular coagulopathy, and acute renal failure after loxosceles envenomation. In this patient, plasma exchange therapy (PEX) successfully cleared the plasma from an initial hemolytic index of 2000 (equivalent to 2 g/dL hemoglobin, where optometric laboratory evaluation is impossible) to an index of <50 (no detectable hemolysis). This allowed the PICU team to correct his coagulopathy, assess his degree of organ dysfunction, and provide routine laboratory assessments during continuous venovenous hemodiafiltration. After 9 single volume PEX sessions, his hemolysis and coagulopathy had resolved and his plasma had cleared sufficiently to permit routine laboratory assessments without difficulty. Multigang system support with an aggressive transfusion strategy, mechanical ventilation, inotropes, and continuous venovenous hemodiafiltration resulted in complete recovery. We conclude that in the presence of overwhelming hemolysis, plasma can become so icteric that optometric laboratory evaluation is impossible. In this setting, PEX can be used to clear the plasma, restoring the ability to perform routine laboratory assessments. Pediatrics 2014;134:e1464–e1467

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ABBREVIATIONS

ABG—arterial blood gas
CVVH—continuous venovenous hemodiafiltration
FFP—fresh-frozen plasma
PEX—plasma exchange therapy
RBC—red blood cell

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Loxoscelism is considered the most common spider envenomation in North America. *Loxosceles reclusa* is the best known of 13 *Loxosceles* species found in North America and is responsible for most American envenomations. Although most of the reported clinical manifestations are limited to dermo-necrotic effects, severe systemic loxoscelism has been reported with fulminant intravascular hemolysis, disseminated intravascular coagulopathy, and multiorgan system failure. In almost all cases, supportive care with red blood cell (RBC) transfusions, intravenous fluids, and local wound care are sufficient to provide full recovery. In more severe cases, hyperbaric oxygen, dapsone, and antivenom have been used with variable success. Although overwhelming hemolysis has long been understood by laboratory professionals to interfere with laboratory tests that depend on optimetric analysis, this phenomenon remains poorly understood by clinicians. To our knowledge, this is the first case to describe the clinical presentation of a patient with systemic loxoscelism and fulminant intravascular hemolysis that resulted in an inability to obtain optimetric-based routine laboratory tests. In this report, we describe the case, review how hemolysis interferes with many common laboratory tests, and present the novel use of plasma exchange therapy (PEX) to clear the plasma of a 6-year-old boy with systemic loxoscelism complicated by fulminant intravascular hemolysis. In this child, daily PEX sessions cleared the RBC breakdown products, reestablishing our ability to obtain accurate laboratory data and provide complex, multisystem support.

This article adheres to the standards for publication established by the Washington University institutional review board. Informed, written consent for this report was obtained.

**CASE REPORT**

Our patient is a previously healthy 6-year-old African American boy who presented with a 1-day history of abdominal pain, nausea, vomiting, and intermittent fever. That morning, his mother had found a dead spider in his bed, and suspected that a spider bite might explain his symptoms. In our emergency department, his physical examination was notable for a temperature of 36.9°C, heart rate 96 beats per minute, blood pressure 77/47 mm Hg, respiratory rate 31 breaths per minute, and oxygen saturation 88% in room air. He was obtunded, had abdominal distention, erythoderma, and 2 large, bullous lesions with ecchymotic and erythematous bases on his left lower abdomen. Laboratory evaluation revealed a white blood cell count of 18 000/µL, a hemoglobin (Hb) concentration of 6.4 g/dL, and a platelet count of 121 000/µL. In the first few hours after his presentation, his initial serum chemistries were within normal limits except for an elevated lactate (3.6 mmol/L). His presenting coagulation profile was also abnormal (prothrombin time, 50.1; partial thromboplastin time, 65.6; and international normalized ratio, 2.96). Urinalysis was notable for cola-colored urine that was positive for Hb and myoglobin but negative for RBCs. Immediate resuscitation included emergent intubation, volume resuscitation, and RBC transfusion. PICU admission was requested with concern for systemic loxoscelism complicated by hypotensive shock and hemolysis.

On arrival in the PICU, central venous and peripheral arterial catheters were placed. An arterial blood gas (ABG) revealed a pH 7.22, *PaO₂* 41, *PaCO₂* 293, calculated carbon dioxide 16, and base deficit of −10.4. Whole blood lactate was 5.8. Due to persistent hypotension, infusions of both dopamine and epinephrine were started. Bright red blood was suctioned from his endotracheal tube, and a unit of fresh-frozen plasma (FFP) was given. A multisystem laboratory assessment was ordered. Shortly after his blood samples arrived in the laboratory, we received notification that all tests requiring optimetric analysis for determination (renal function, liver function tests, ammonia) were impossible to perform due to profound hemolysis (initial H index was >2000, where 0 = no hemolysis and >2000 = fulminant intravascular hemolysis).

Worsening lactic acidosis, hemodynamic instability, and renal dysfunction progressing to anuric renal failure complicated his course over the next 24 hours. He demonstrated signs of disseminated intravascular coagulopathy, with hemolysis, thrombocytopenia, elevated D dimer (12 572 ng/mL), hypofibrinogenemia (164 mg/dL), moderate anisocytosis, and a positive direct Coombs test. Hemolysis persisted, with hematocrits ranging between 18.5 and 23.7 despite frequent RBC transfusions (total of 25 mL/kg). Repeated attempts to measure serum chemistries, renal and liver function failed using our standard laboratory instruments (Cobas 6000, Roche Diagnostics, Indianapolis, IN), due to persistently elevated H indices. Serial ABGs demonstrated appropriate gas exchange and persistent metabolic acidosis. Chemistry data available from the ABG samples revealed eunatremia and progressive hyperkalemia (peak serum potassium = 7.2). Because of the anuria, acidosis, hyperkalemia, and significant blood product volume requirements, we decided to initiate continuous venovenous hemodiafiltration (CVVH). We also discussed the utility of adding PEX therapy to correct his coagulopathy and clear the plasma, permitting more accurate laboratory evaluation.

That morning, a hemodialysis catheter (Mahurkar 11.5 French dual lumen dialysis catheter, Covidien, Mansfield, MA) was placed and a 1.5-volume PEX session with 100% FFP replacement was performed, followed by CVVH. He tolerated the procedure well with removal of
profoundly hemolyzed plasma (Fig 1). Throughout the next several days, we were able to routinely obtain complete blood cell counts, coagulation assessment, and blood gas analyses. Additional laboratory assessments were obtained once each day after his PEX sessions, when his H-index was at its nadir. Additional assessments were made on whole blood by using ABG samples. By PICU day 4, his H indices had dropped to <50 and routine assessment of renal and liver function became possible (Fig 2).

Over the next several weeks, our patient slowly improved. With multiple RBC transfusions (total of 64 mL/kg), we were able to stabilize his hemodynamics and oxygen delivery. By PICU day 8, his lactate had normalized, he had weaned off all inotropes, and had a normal neurologic examination. The hemolysis gradually cleared, and PEX was continued through PICU day 9. As his urine output improved, CVVH was weaned, then discontinued on PICU day 11. He was successfully extubated on PICU day 12. After a 21-day PICU admission, our patient was transferred to the ward with normal cardiovascular and mental status, normal coagulation profile, normal liver function, and improving renal function. He was discharged from the hospital on hospital day 28 on maintenance amlodipine with a normal physical examination and normal renal function.

DISCUSSION

Although fulminant intravascular hemolysis is a known, rare complication of loxosceles envenomation, we are the first to present a case of hemolysis so profound that severe hemoglobinemia prohibited routine laboratory measurements. In this setting, PEX was successfully used to treat the coagulopathy and clear the plasma, allowing us to reestablish frequent laboratory monitoring. Even with the assistance of PEX, clearing the plasma took several days, requiring us to clinically manage a child with uncompensated shock and multi-organ failure with limited availability to assess organ function. Without the use of PEX, the interval to plasma clearing and accurate laboratory valuation would likely have been much longer, putting the child at even greater risk of complications and poor outcome.

Routine tests of organ function performed in clinical laboratories often depend on optimetric analysis. These tests include measurements of renal function, liver function, and serum glucose, as well as many drug levels (including vancomycin and gentamicin). A subset of these tests, including electrolytes and serum glucose, can alternatively be ascertained via electrical detection, which relies on the production of electrical current, rather than light absorption. When a sample first arrives in the laboratory, the degree to which standard testing is impaired due to free Hb (hemoglobinemia) is usually measured first, and the hemoglobinemia is quantified as the H index. For reference, the H index is a scan of diluted plasma at 540 nm, and its value correlates with free Hb concentrations in mg/dL (for example, an H index of 100 is roughly equivalent to a Hb concentration of 100 mg/dL). Interestingly, the H index is often not reported to clinicians. However, staff caring for patients with massive hemolysis can ask to have the H index reported and are encouraged to inquire about the availability of electric current-based assays that would permit some laboratory measurements until hemolysis can be controlled.
Clinicians should also be aware that complete blood cell count results usually report a total Hb level, which does not discriminate Hb present in RBCs from free Hb that has already been released into the blood stream due to hemolysis. As a result, the measured Hb, in isolation, is a poor surrogate for RBC volume and oxygen delivery. In contrast, HCT, if directly measured using RBC volume and oxygen delivery, is a much more accurate measure of circulating RBC number. Unfortunately, some laboratories do not directly measure HCT, and instead calculate it from total Hb measurements. In this setting, neither Hb nor HCT will accurately reflect the degree of ongoing hemolysis. It is critical that clinicians familiarize themselves with their own laboratory practices so they know how to best interpret their laboratory data.

CONCLUSIONS

When patients have overwhelming hemolysis, plasma can become so opaque that optometric laboratory testing becomes impossible. In this setting, PEX can be used to clear the plasma, restoring the ability to perform routine laboratory assessments. In our case, PEX served a dual purpose, as it was also therapeutic in correcting coagulopathy. We encourage clinicians to familiarize themselves with their laboratory’s procedures so safe and effective care can be provided when routine laboratory testing is unavailable.

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