TEACHING CASES

Caterpillar-induced bleeding syndrome in a returning traveller

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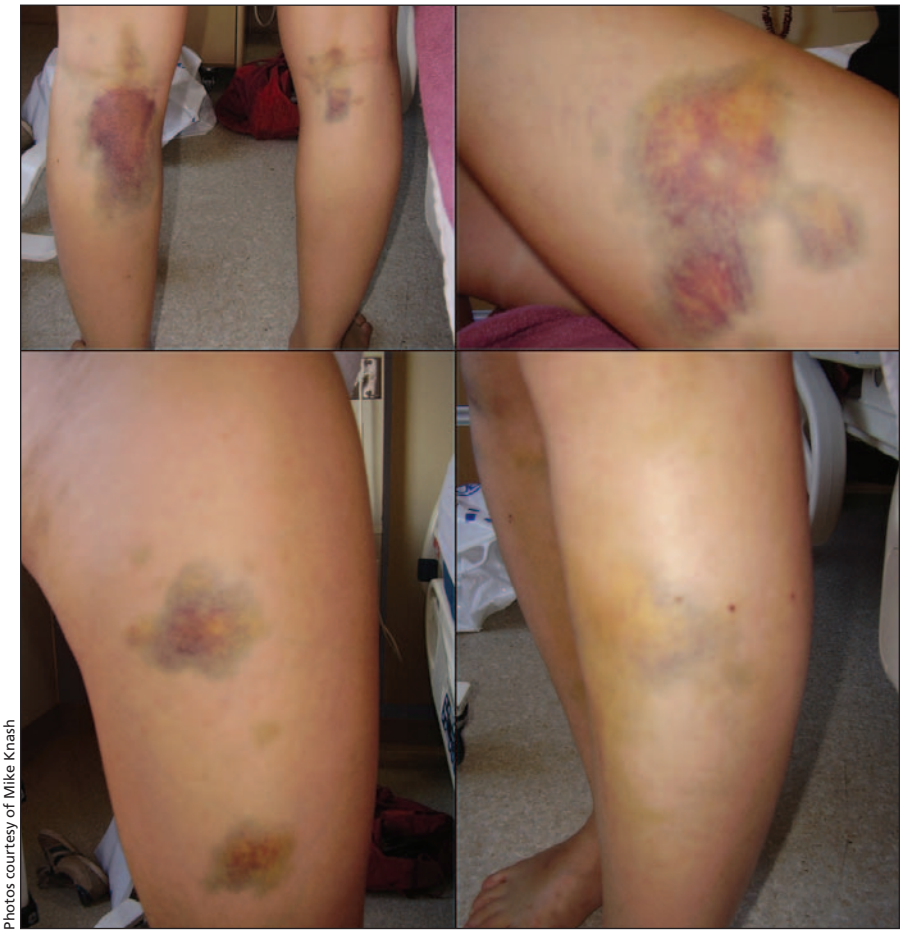
The case: A 22-year-old woman who was previously healthy presented with a 4-day history of expanding ecchymoses. She had no other bleeding manifestations and denied any constitutional symptoms, myalgias, arthralgias or rashes. Her medical history was unremarkable. She was not taking any medication, and she had no family history of bleeding problems or hematologic disorders. Her last normal menstrual period was 2 weeks before admission.

On examination, our patient was afebrile and had normal vital signs. She had no lymphadenopathy. Results of her cardiovascular, respiratory and abdominal examinations were unremarkable. There was no evidence of physical trauma, but she had extensive ecchymoses on both legs (Figure 1).

Seven days before admission our patient had returned from northeastern Peru, where she had stepped barefoot on 5 caterpillars. Immediately after contact with the caterpillars, she experienced burning pain in her foot, radiating proximally to her thigh. The pain worsened when she walked. A headache also developed. Both the foot pain and headache resolved over the subsequent 12 hours and she did not seek medical care at that time.



Photos courtesy of Mike Knash

Figure 1: Extensive ecchymoses on our patient's legs 2 days after admission.

Key points

- A complete history, including relevant travel history, is key to diagnosing the patient's condition.
- As adventure travel becomes more popular, more cases of exposure to exotic diseases will be encountered.
- Management strategies must include rapid recognition and collaboration with experienced clinicians to facilitate specialized treatment protocols.
- Online searches can be central to patient management.

Results of initial laboratory tests are summarized in Table 1. We diagnosed an atypical presentation of disseminated intravascular coagulation or primary fibrinolysis triggered by an unknown process. We started treatment with fresh frozen plasma, cryoprecipitate and fibrinogen concentrate. In view of her presenting signs and symptoms and travel history, we searched MEDLINE and Google Scholar, which revealed the possibility of caterpillar envenomation that could account for all her clinical symptoms and laboratory results.

Although our local poison control centre had no knowledge of caterpillar envenomation, they facilitated contact with clinicians from Brazil, who recommended immediate administration of a locally produced antivenin. They recommended that we avoid treatment with blood products (fresh frozen plasma and cryoprecipitate) because they felt these could worsen the coagulation abnormalities. We made arrangements to obtain the antivenin from Brazil, which took 48 hours to arrive.

Our patient's condition remained stable for the initial 48 hours. On her third day in hospital (10th day after envenomation), alveolar hemorrhage,

anuric acute kidney injury and hemodynamic instability developed. She received mechanical ventilation, vasoactive agents and continuous renal replacement therapy. Her hematologic and coagulation abnormalities worsened, and there was evidence of progressive microangiopathic hemolytic anemia, consumptive thrombocytopenia and disseminated intravascular coagulation. She was treated with fibrinogen concentrate, aprotinin and washed packed red blood cells and platelets. We received the antivenin from Brazil and administered it on the 10th day after envenomation (third day in hospital); however, our patient's organ dysfunction progressed, and she died of multiorgan failure later that day.

Caterpillar envenomation occurs after contact with the bristles of spiny caterpillars, which induces symptoms ranging from mild cutaneous reactions to severe systemic reactions.[1] Twelve families of caterpillars worldwide have been identified as potentially hazardous to humans. However, caterpillar-induced bleeding syndrome is a unique reaction specific to caterpillars of the *Lonomia* genus, a type of moth native to South America (Figure 2). In a 5-year period, there were 688 cases of caterpillar envenomation reported in the state of Rio Grande do Sul in Brazil.[2]

Caterpillar-induced bleeding syndrome is characterized by a consumption of clotting factors induced by the caterpillar's venom. Initial symptoms are usually mild, consisting of local burning pain, headache, nausea and vomiting.[1,3] As clotting factors are consumed through venom-induced activation of the coagulation system, bleeding manifestations, such as mucosal hemorrhages, hematuria and ecchymosis, become evident from 1 hour to 10 days after envenomation. Abnormal clotting parameters include prolonged prothrombin, partial thromboplastin and thrombin times, low to undetectable fibrinogen levels with increased fibrinogen degradation products, elevated D-dimer levels and absence of inhibitors.[1,3,4] Complications of *Lonomia* envenomation include alveolar hemorrhage, acute renal failure and intracranial hemorrhage.[5,6]

Table 1: Results of initial laboratory tests performed for a 22-year-old woman who presented with a 4-day history of expanding ecchymoses

Test	Result (reference range)
Hemoglobin, g/L	125 (120–160)
Platelet count, x 10^9/L	216 (140–450)
Leukocyte count, x 10^9/L	7.9 (4.0–11.0)
Haptoglobin, mg/L	610 (650–1900)
Total bilirubin, μmol/L	16 (< 20)
Lactate dehydrogenase, U/L	180 (100–225)
Creatinine, μmol/L	65 (40–115)
International normalized ratio	5.3 (0.8–1.2)
Partial thromboplastin time, s	105 (27–40)
Fibrinogen, g/L	< 0.20 (2.2–4.2)
D-dimer, ng/mL FEU	> 4000 (< 500)
1:1 mixing of patients plasma with normal pooled plasma	Showed correction, consistent with absence of an inhibitor
Coagulation factor II, U/mL	0.56 (0.50–1.50)
Coagulation factor V, U/mL	0.50 (0.50–1.50)
Coagulation factor XIII, U/mL	0.14 (0.60–1.69)
Peripheral blood smear	No morphologic evidence of hemolysis
Human chorionic gonadotropin, U/L	< 5 (< 5)
Pelvic ultrasound	Normal

Note: FEU = fibrinogen equivalent units.

Photo courtesy of Roberto Pinto Moraes (Butantan Institute)

Figure 2: Photograph of *Lonomia obliqua*. Note the aposematic coloration.

Generally, patients with this syndrome have normal platelet and hemoglobin levels, minimal hemolysis and red blood cell fragmentation, and normal levels of factors II, VII, IX, X, XI, XII and antithrombin. Rarely, clinically significant hemolysis has also been reported.[7] These characteristics, particularly the normal platelet count, are not consistent with classic disseminated intravascular coagulation and suggest a unique mechanism of clotting derangement, including fibrinolysis.

Two species of *Lonomia* caterpillars are known to cause this bleeding syndrome.[1,6] *L. obliqua* is native to southern Brazil, and *L. achelous* is more commonly found in Venezuela and northern Brazil. Both caterpillars induce a consumptive coagulopathy and bleeding syndrome that is similar in presentation. Although the pathophysiologic processes involved are not completely known, the mechanism by which this bleeding syndrome occurs is slightly different depending on which species caused it.

Two procoagulant toxins have been identified in the venom of *L. obliqua*.[1,6] Losac is an activator of factor X, and Lopap is an activator of prothrombin. The mechanism of *L. obliqua*-induced bleeding syndrome is a consequence of systemic intravascular activation of coagulation, which leads to a consumptive coagulopathy and secondary fibrinolysis in which the extent of fibrinogen depletion correlates with the severity of bleeding manifestations.

The procoagulant and anticoagulant activity[1,3,6] of the toxins identified in the

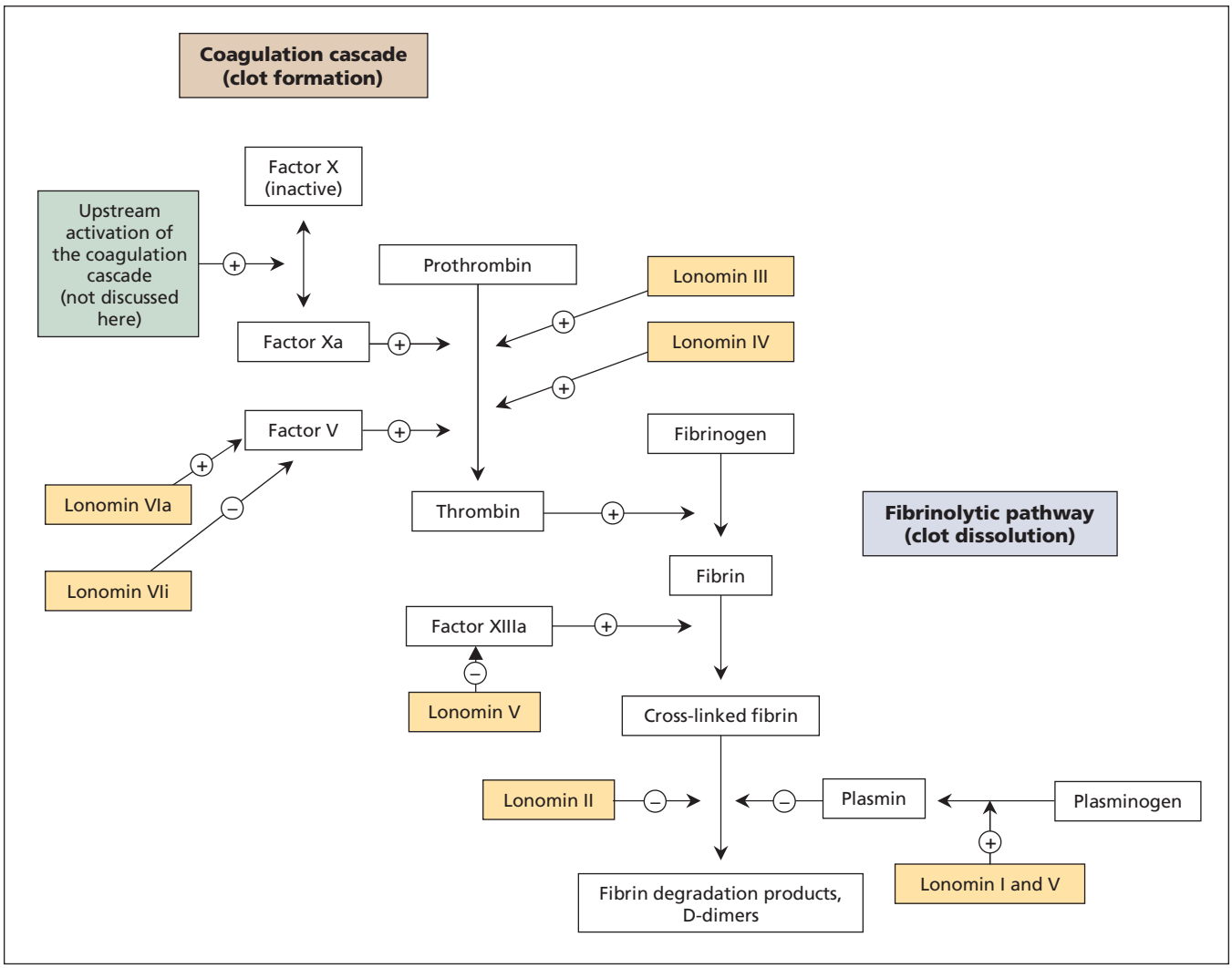


Figure 3: Caterpillar-induced bleeding syndrome results from exposure to the venom of the *Lonomia* genus caterpillars. Toxins (lonomins) in the venom of *Lonomia achelous* caterpillars cause an activation of the coagulation system. This ultimately consumes clotting factors and leads to systemic bleeding manifestations and abnormal clotting parameters, low fibrinogen levels and increased fibrin degradation. + = promotion of activity, – = inhibition of activity/degradation.

venom of *L. achelous* is described in Figure 3. Lonomin II and lonomin I activate fibrinolysis, and lonomin V is a factor XIII protease. There is also a mild disseminated intravascular coagulation with *L. achelous* envenomation that is attributable to procoagulant activity of lonomin IV (factor Xa-like activator) and lonomin III (direct prothrombin activator). However, the main mechanism of *L. achelous* envenomation is intense fibrinolysis, as suggested by the prolonged euglobulin lysis time seen in almost all patients.

After envenomation from either *L. achelous* or *L. obliqua*, it is common to see decreased levels of factors V, VIII and XIII. Decreased levels of factor XIII are more common with *L. achelous* than with *L. obliqua*.[1,6] Decreased plasminogen, α2-antiplasmin and protein C levels have also been documented.[1]

Traditionally, patients were treated with fresh frozen plasma and cryoprecipitate. However, management has evolved since it has been recognized that such treatment may worsen the patients' conditions.[1,3] Owing to increasing numbers of caterpillar envenomations in southern Brazil, the Butantan Institute in Sao Paulo has produced an equine-derived antivenin against *L. obliqua* toxins.[6] It has proven very effective if administered within 12–24 hours after envenomation. The antivenin prevents further complications of bleeding and acute renal failure. Current recommendations include treatment with purified fibrinogen concentrates, antifibrinolytics and timely administration of the antivenin.[1,3,6] This course of action usually results in rapid clinical recovery, with a slower improvement of hypofibrinogenemia. The effectiveness of this antivenin against *L. achelous* toxins has been postulated by researchers and clinicians in South America but remains unproven.

As adventure travel becomes more popular, we can expect to see more cases in Canada of exposure to exotic diseases. Management strategies must include rapid recognition in order to facilitate specialized treatment protocols.

The role of poison control centres and online searches are central to the diagnosis and management of patients with this syndrome.

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