



Case Report

Severe Lower Limb Ischemia after Bee Stings

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Bee stings entail allergic reactions that can be severe, sometimes even lethal. These reactions can occur immediately or several days after being stung. In this study, we report a case of severe ischemia of the left lower limb observed in a man, with no medical history, who was stung several times by bees.

CASE REPORT

A 40-year-old man, without any cardiovascular risks, and without any known or documented allergic history, was stung at the level of his neck and trunk by approximately 10 bees. On clinical examination, this patient was found to be afebrile. His blood pressure was 115/70 mm Hg with a regular cardiac rhythm (80 bpm).

He only presented pruriginous cutaneous reactions, which occurred at the sting sites, and was treated with antihistaminics in the emergency ward. The following night, he felt the sensation of the presence of pins and needles at the level of the toes of his left leg, which later developed into pain that affected the entire foot; then, in the next 24 hours, cyanosis appeared at level of the first and second left toes.

The patient was given analgesics and anti-inflammatory drugs by his practitioner because his magnetic resonance imaging scan showed a mild lumbar protrusion of the sacral lumbar spine. During the next 2 weeks, cyanosis at the level of the toes progressed into dry necrosis. A lower limb arterial duplex examination was performed along with an arteriography (Figs. 1, 2). Arteriography showed an occlusion of the three leg arteries at the upper one-third level with a well developed peroneal artery at the lower one-third of the left leg. At the level of the foot,

the collaterality of the pedal artery was weak. The patient was then transferred to our department.

He was a very healthy man. Clinical examination confirmed the necrosis of the distal part of the first two toes and a cyanosis of the other toes in association with an acute pain in the left foot and coldness experienced by the lower one-half of the leg; there was no motor or sensitive deficit. Peripheral pulses could be detected on the right side but not on the left side. The ankle–arm systolic pressure index (SPI) was found to be 0.5.

Biological tests performed on admission eliminated presence of autoimmune diseases (no circulating lupic anticoagulants, no anti- β 2-glycoprotein I antibodies, and no anticardiolipin antibodies) as well as hepatic or renal disorders. These tests also showed normal data for white blood cells and platelets, prothrombin time, activated cephalin time, serum creatinine, sedimentation rate, C-reactive protein, and homocysteine.

Cardiac echography showed that the systolic function of the left ventricle was preserved, without any vegetations or intracardiac thrombus. The electrocardiogram revealed sinus bradycardia without any signs of ischemia. Chest radiography was normal. Thrombogenic mutation research by polymerase chain reaction—sequence specific oligonucleotide showed a homozygote mutation (A1298C) in the methylenetetrahydrofolate reductase gene and a heterozygous mutation (G20210A) in the prothrombin gene (Table I).

A nonfractionated heparin treatment in association with intravenous prostaglandin E1, alprostadil (Prostava-sin[®], Schwarz Pharma, Monheim, Germany) was initiated. On the third day, the patient's clinical status improved. Prostaglandin treatment was continued for 3 weeks in association with repeated debridement of the necrosis.

On the 22nd day at the time of discharge from the hospital, the patient was asymptomatic with a SPI equal to 0.9. Antivitamin K treatment (warfarin) was started in association with an antiplatelet treatment (salicylic

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Fig. 1. Arteriography showing an occlusion of the three leg arteries at the higher one-third level of the leg, with development of the collaterality from the medial gastrocnemius artery.

acid). In the absence of any consensus, it was decided to keep an efficient anticoagulant treatment for 1 year and a lifelong platelet antiaggregation treatment.

The patient underwent regular follow-up. Arterial duplex scan at 1 year showed repermeabilization of the three arterial axes of the left leg with demodulated and weak flow. SIP was stable, equal to 0.9, and the patient was still asymptomatic with healing of toes.

DISCUSSION

Clinical manifestations of bee stings can be divided into the following three categories: localized reactions with pain and edema, immunological reactions that can lead to anaphylactic shock, and systemic toxic reactions caused by the release of toxins (hemolysis, coagulopathy, rhabdomyolysis, severe renal insufficiency, and hepatotoxicity).¹

Chen et al. presented a case of abdominal infrarenal aorta thrombosis that occurred 24 hours after multiple wasp stings.¹ Numerous cases of arterial thromboses secondary to wasp stings have been described in previously published data with a predilection for cerebral arteries.^{2,3}



Fig. 2. Arteriography centered on the lower one-third of the leg: reentry from the collaterality of a widely patent peroneal artery. Anterior tibial artery is narrow.

Bongo et al. reported a case of myocardial infarction without allergic reactions after three bee stings.⁴ Some authors consider that vasoconstriction secondary to inflammatory reactions and vasoactive amines should be held responsible for these cases.²⁻⁴ The exact component responsible for these manifestations is unknown and depends on the species that the bee causing the sting belongs to.

Yang et al.⁵ described a protein, magnifin, which was purified from the venom of the wasp *Vespa magnifica* (Smith). This protein has an activity similar to phospholipase A1 and it generates platelet aggregation associated with *in vivo* thrombosis.⁵ In comparison with bee venom, wasp venom contains more phospholipase A1 than phospholipase A2.⁶

Ouyang et al.⁷ concluded that phospholipase A2 generates platelet aggregation as a result of an enzymatic activity chain that leads to thromboxane A2 formation. Cerebral and cardiac complications described in the published data appear *a priori* after several stings.^{1,2,4,8} Stings at the level of neck or face

Table I. Research of thrombogenic mutation by PCR-SSO

Studied gene	Searched mutations	Result
Factor V	G1691A Leiden	No mutation
	H1299R	No mutation
Prothrombin	G20210A	Heterozygote
Factor XIII	V34L	No mutation
Fibrinogen	G455A	No mutation
Methylenetetrahydrofolate reductase	C677T	No mutation
	A1298C	Homozygote
Apo B	R3500Q	No mutation

PCR-SSO, polymerase chain reaction—sequence specific oligonucleotide.

result in cerebral ischemia homolateral to the stings by vascular occlusion.^{2,8} Although a relation between sting localization and symptomatology has not been studied, it seems that the location of the sting plays an important part in the occurrence of complications.

The case described in this study represents, as far as we know, the first case of lower limb severe arterial ischemia secondary to bee stings. Vasoactive amine secretion, such as thromboxane, leukotriene, or thrombogenic substances contained in bee toxins, could be respectively responsible for vasospasm and diffuse thrombosis.⁴ The presence of underlying thrombogenic genetic mutations was certainly a predisposing key factor to thrombus occurrence. Up to now, in the case of arterial thrombosis associated with bee stings, no mutation research studies involving polymerase chain reaction—sequence specific oligonucleotide have been published.

Initially, platelet antiaggregants were not prescribed for the patient of this study because there was no underlying atherosclerosis predisposition and also there was a 3-week delay between the occurrence of symptoms and the patient's transfer to our department. A 1-year efficient anticoagulation treatment in association with a lifelong platelet antiaggregant treatment was proposed for this patient so as to escape potentially severe cerebral or cardiac complications, should he be exposed to bee stings in the future.

Intravenous E1 prostaglandin was used as a therapeutic option because of its vasodilator effect that counterbalances the vasoconstrictor effect of the inflammatory mediators. After the severe phase is overcome, there is no need for corticotherapy and plasmapheresis.

In practice, in presence of arterial occlusion secondary to insect stings, we advise to systematically search for thrombogenic genetic mutations. In case of lesions occurring rapidly after stings, plasmapheresis has a potential but also a questionable role.¹

In the presence of systemic symptoms, corticotherapy is a good option. The role of intravenous prostaglandins has still not been codified. At an initial stage, a platelet antiaggregant treatment should be considered in association with an anticoagulant treatment. In case of underlying thrombogenic genetic mutation, an anticoagulant is indeed considered a major advantage.

Lifelong platelet antiaggregant treatment can be considered to reduce potential complications risks, should the patient be exposed to more bee stings in the future.⁷ The patient should also be informed about the major risks of future sting exposition. It is obvious that every risky situation should be avoided. Because there is no consensus or defined advice available, such a patient should always carry an emergency kit with a low-molecular-weight heparin dose, corticoids, and platelet antiaggregant to be used after contacting a practitioner. This behavior should be seriously considered because multiple stings do occur.

REFERENCES

1. Chen DM, Lee PT, Chou KJ, Fang HC, Chung HM. Descending aortic thrombosis and cerebral infarction after massive wasp stings. *Am J Med* 2004;116:567-569.
2. Sachdev A, Mahapatra M, D'Cruz S, Kumar A, Singh R, Lehl SS. Wasp sting induced neurological manifestations. *Neurol India* 2002;50:319-321.
3. Crawley F, Schon F, Brown MM. Cerebral infarction: a rare complication of wasp sting. *J Neurol Neurosurg Psychiatry* 1999;66:550-551.
4. Bongo AS, Fornaro G, Sansa M, Maccio S, Rognoni A. Acute myocardial infarction after wasp sting without anaphylactic reaction. *Ital Heart J Suppl* 2005;6:178-182.
5. Yang H, Xu X, Ma D, Zhang K, Lai R. A phospholipase A1 platelet activator from the wasp venom of *Vespa magnifica* (Smith). *Toxicon* 2008;51:289-296.
6. Binder M, Fierlbeck G, King T, Valent P, Bühring HJ. Individual hymenoptera venom compounds induce upregulation of the basophil activation marker ectonucleotide pyrophosphatase/phosphodiesterase 3 (CD203c) in sensitized patients. *Int Arch Allergy Immunol* 2002;129:160-168.
7. Ouyang C, Huang TF. Effect of the purified phospholipases A2 from snake and bee venoms on rabbit platelet function. *Toxicon* 1984;22:705-718.
8. Riggs JE, Ketonen LM, Bodensteiner JB, Benesch CG. Wasp sting-associated cerebral infarction: a role for cerebrovascular sympathetic innervation. *Clin Neuropharmacol* 1993;16:362-365.