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Citation	Journal of Vascular Surgery Cases, 2016, v. 2 n. 1, p. 31-33
Issued Date	2016
URL	http://hdl.handle.net/10722/224953
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Successful treatment of jellyfish sting-induced severe digital ischemia with intravenous iloprost infusion

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Jellyfish sting-induced vasospasm and vasculitis is a rare complication that could lead to severe digital ischemia and gangrene. We report a 39-year-old woman with severe pain in her right middle, ring, and little fingers after being stung by a jellyfish. Therapy was initiated with a course of intravenous iloprost infusion and subcutaneous low-molecular-weight heparin, with successful revascularization. Our case illustrates that although emergency transfer to a vascular center is ideal, even in a delayed setting, patients can still benefit from specialist vascular care with a combination of medication and iloprost treatment, with acceptable functional outcome. (J Vasc Surg Cases 2016;2:31-3.)

Approximately 70 species of jellyfish are extremely toxic to humans, with stinging structures (nematocysts) that are used to sting their prey.[1] Contact with a jellyfish tentacle causes millions of nematocysts to pierce the skin and inject venom. The venom is a mixture of toxic and antigenic polypeptides and enzymes. There are three species of jellyfish commonly reported to cause fatalities. These fatal reactions may be caused by anaphylaxis or by the action of toxins in the venom on the heart, respiratory center, or kidneys.[2]

Other reported complications include cutaneous eruptions, motor-sensory neuropathy, vasospasm, and lymphocytic vasculitis, which are likely to be caused by the inflammatory mediators or vasoactive substances, such as bradykinin, histamine, proteases, prostaglandins, and serotonins, which are present in the venom. Toxic proteins obtained from tentacles of certain strains of jellyfish can also cause platelet aggregation in a concentration-dependent manner.[3] The spectrum of severity of jellyfish sting-induced vasospasm ranges from Raynaud phenomenon with cyanosis to finger necrosis and gangrene requiring amputation.[4] It is worth noting that most of the 9000 species of jellyfish are benign, and specific medical care is not required after an individual has been stung.

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Author conflict of interest: none.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2352-667X

http://dx.doi.org/10.1016/j.jvsc.2016.02.007

We describe a patient who presented with jellyfish sting-induced digital ischemia and was successfully treated with intravenous iloprost infusion and subcutaneous low-molecular-weight heparin. The patient gave written consent for the publication of this report.

CASE REPORT

A 39-year-old right-handed woman with no personal or family history of rheumatologic or vascular conditions was stung by a jellyfish on the right arm while swimming in the seas of Penang, Malaysia. She developed right middle, ring, and little finger numbness, and intense pain, together with immediate erythema and swelling over the right forearm. She flew home the next day and experienced progressively worsening pain, pallor, coldness, and numbness over the affected fingers.

She was seen by a dermatologist, who prescribed oral steroids but with no symptomatic improvement. She was seen in her local hospital 2 days later when her fingertips became pale and cyanotic. Emergency duplex imaging and a magnetic resonance angiogram showed significantly reduced flow in the right radial and ulnar artery distal to the wrist. She was subsequently referred to our tertiary vascular center for further management.

On presentation to us, the tips of her right middle, ring, and little fingers were pale and tender, and there was a diffuse erythematous vesiculopapular rash over her anterior forearm (Fig, *A*). She complained of coldness and numbness over the dorsal and palmar side of the affected fingers. There was no motor deficit or swelling, and she did not have any neurologic deficit in the median or ulnar nerve function to suggest forearm or hand compartment issues. The right brachial pulse was normal, but both radial and ulnar pulses were not palpable at the wrist. Doppler ultrasound imaging of the right radial and ulnar arteries at the wrist showed monophasic flow suggestive of peripheral digital vasospasm. Our local toxicology center advised that jellyfish sting could induce vascular insufficiency but did not recommend any specific treatment apart from keeping the hand warm.

We started our patient on oral aspirin, 1 mg/kg subcutaneous low-molecular-weight heparin (Clexane; Sanofi Aventis, Surrey, UK) every 12 hours, and topical glycerine trinitrate patch

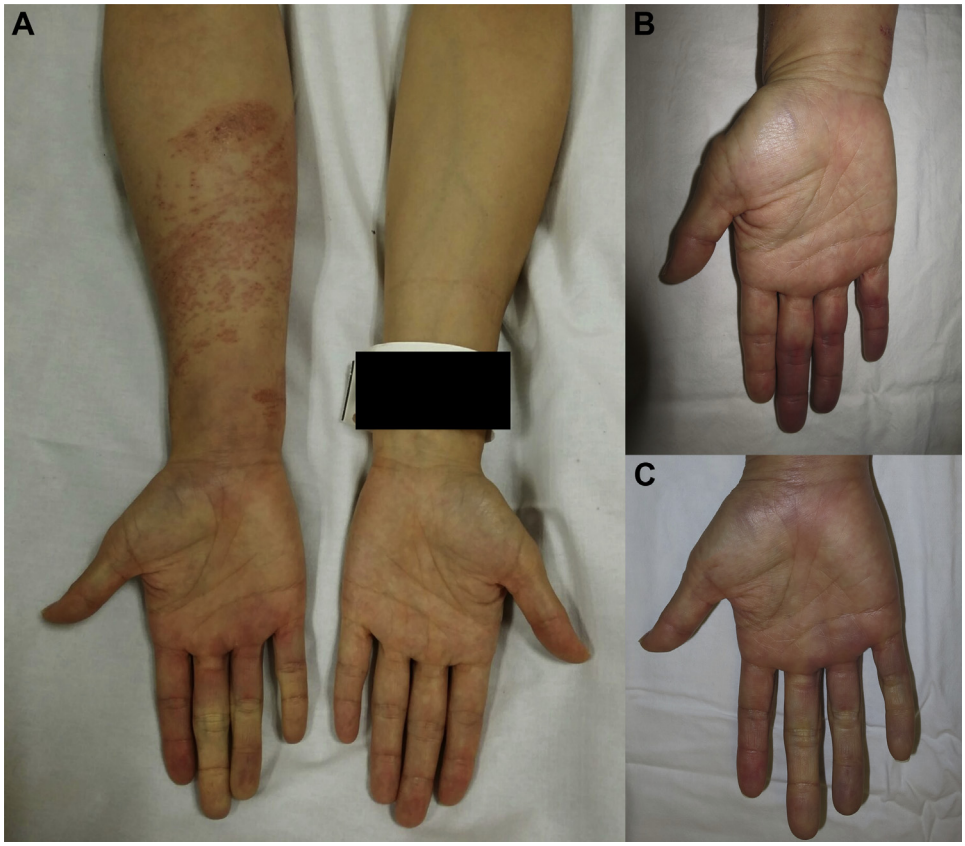

Fig. A, Initially the tips of the patient's right middle, ring, and little finger were pale and painful. There was diffuse erythematous vesiculopapular rash over her anterior forearm that showed progressive improvement after **(B)** 3 days and **(C)** 7 days of iloprost treatment.

(Nitroderm; Novartis, Macquarie Park, NSW, Australia), 10 mg/d, applied to the base of her wrist to promote vasodilatation. However, her symptoms were nonresolving, and the affected fingers were very painful and deeply cyanosed.

We decided to start her on a recommended increasing dosage of intravenous iloprost (Ilomedin20; Bayer Schering Pharma, Berlin, Germany) with an infusion pump. The infusion was administered after dilution as an intravenous infusion over 6 hours daily via a peripheral venous catheter with electrocardiography monitoring. The recommended dose of iloprost was adjusted according to her tolerability within the range of 0.5 to 2.0 ng/kg body weight/min. We diluted 20 μg iloprost in 100 mL normal saline, and with a body weight of 60 kg, she was given the infusion at 9 mL/h (30 ng/min) over 3 hours and then at 18 mL/h (60 ng/min) over another 3 hours on the first day. The next day the infusion was started at 18 mL/h for 3 hours, then at 27 mL/h (90 ng/min) for 3 hours, and on the third and subsequent days to 36 mL/h (120 ng/min) for 6 hours. The total cost of medication was ~U.S. $1041, excluding administration cost.

The patient tolerated the infusion well, with no adverse effects of headache or dizziness. There was gradual and progressive subjective improvement of her symptoms. Clinically, there was better perfusion of the fingers, and her radial and ulnar pulses were progressively stronger after 3 days of infusion (Fig, *B*). The infusion was continued for 7 days.

The patient was discharged with minimal symptoms. Her fingertips had full sensation and were hyperemic (Fig, *C*). The patient was happy to be discharged and to return to work. She was discharged on aspirin only. She was last seen 1 week after discharge, and her right hand had nearly returned to normality.

DISCUSSION

This is a report of an adult patient who had severe jellyfish sting-induced digital vasospasm and was successfully treated with iloprost and low-molecular-weight heparin, thereby preventing debilitating surgery or irreversible finger ischemia. Iloprost is a synthetic analogue of epoprostenol (prostacyclin [PGI2]; a potent but short-lived prostanoid mainly produced in the vascular endothelium), which has vasodilatory effects and has been used by vascular surgeons for >20 years for the treatment of patients with unreconstructable critical leg ischemia, thromboangiitis obliterans, vasculitis, or severe Raynaud phenomenon. Apart from a potent but short-lived vasodilatory effect, iloprost also inhibits platelet aggregation and improves abnormal vascular reactivity.

Although rare, jellyfish sting-induced severe digital vasospasm can result in permanent disability if treatment is delayed. Five cases have been reported worldwide. Williamson et al[5] reported three cases of jellyfish sting in

the Indian Ocean and the Andaman Sea, resulting in upper limb ischemia and gangrene. Two of the patients underwent surgical fasciotomy, and surgical exploration was performed on the third patient. Major debilitation occurred in all three patients. Lam et al[6] reported a man who had ischemia and gangrene of his hand and required fasciotomy and repeated surgical débridement.

Binnetoglu et al[7] reported a boy with bilateral bluish discoloration of the fingers and areas of necrosis over the pulps of the index fingers after contact with jellyfish. He was treated with low-molecular-weight heparin, aspirin, nifedipine, and sildenafil for 5 days, without clinical improvement, and was then started on intravenous iloprost, intravenous steroid, and hyperbaric oxygen. The iloprost was continued for 4 weeks, and gradually the necrotic finger tips autoamputated.[7]

Major differences in outcomes could be explained by different toxicity of the jellyfish, although the species were not usually identified in real-life situations. In addition, prompt iloprost infusion in our patient and in the patient reported by Binnetoglu et al[7] also improved the final results.

In a systematic review and meta-analysis of 332 patients in seven randomized controlled trials comparing prostaglandin analogues (iloprost or Cisaprost) vs placebo, Pope et al[8] showed benefit in patients with secondary Raynaud phenomenon associated with scleroderma, with evidence for decreasing the severity and frequency of acute attacks and for preventing or healing digital ulcers. In most of the studies in the current literature reviews, the use of iloprost was also shown to be effective in treating Raynaud phenomenon and, in particular, those secondary to systemic sclerosis in a multicenter, placebo-controlled, double-blind study.[9] Iloprost can be used intra-arterially,[10] but we have no experience with this and have only used it intravenously. Even in the Iloprost in Acute Ischemia of Lower Limbs (ILAILL) Study, intra-arterial iloprost was followed by a few days of intravenous use, so we do not think it would likely be more cost-effective.[10]

CONCLUSIONS

This is a case of successful treatment of jellyfish sting-induced digital ischemia with iloprost infusion, low-molecular-weight heparin, and aspirin. The vasodilatory effect of iloprost was apparent by improvement of symptoms and progressive return of the patient's radial and ulnar pulses after 3 days of infusion. Our case illustrated that although emergent transfer to vascular center is ideal, even in delayed setting, patients can still benefit from specialist vascular care with a combination of medication and iloprost treatment, with acceptable functional outcome.

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Submitted Oct 14, 2015; accepted Feb 2, 2016.