CASE REPORT

Dermatological Progression of a Probable Box Jellyfish Sting

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This case report describes the typical features of the dermatological progression of a patient stung by a (probable) box jellyfish. The purpose is to guide clinicians and patients to an understanding of what to expect after such a sting using the clinical narrative and unique sequential photographs of the injury. With knowledgeable consultation from experienced physicians and meticulous care, this envenomation healed without the need for skin grafting.

Keywords: Cubozoa, *Chironex*, envenomation, Cambodia

Introduction

Jellyfish envenomations (stings) are a common affliction of ocean goers worldwide. Although many are of nuisance severity, some can be highly morbid or fatal.¹ The most severe nonanaphylactic envenomations are caused by jellyfish species that inhabit Indo-Pacific waters. Examples of species known to be clinically dangerous include the box jellyfish *Chironex fleckeri*, sea nettle *Chrysaora quinquecirrha*, and Irukandji (*Carukia barnesi*).

In this report, we provide written and visual details of the natural progression of a probable box jellyfish envenomation that originated in waters off Cambodia. We document a comprehensive visual demonstration of what patients and clinicians should expect after a severe sting by box jellyfish or similarly injurious species.

Case report

DAY 1

The last author was the patient, a 21-y-old woman in good health at the time of injury in early June. The patient was swimming with a friend 7.6 m off the coast of Koh Ta Kiev, Cambodia, in chest-deep water at approximately 1800 when she was stung. She did not see the jellyfish sufficiently well for positive identification at the time of

envenomation, but multiple species of box jellyfishes (class Cubozoa) are known to reside in these waters.^{2,3} The patient experienced immediate and intense (9/10) burning pain to her right lower extremity (RLE) that gradually subsided over the ensuing 10 h, bright red and swollen streaks where tentacles had contacted the skin of the right thigh (Figure 1), and lightheadedness with a brief 10-s syncopal episode after exiting the water within 20 min of the sting. The patient's friend assisted her in walking approximately 30 m back to the dining area of the hostel where they were staying. Once there, employees of the hostel provided the patient with vinegar to rinse the affected leg and then applied ice cubes directly to the affected skin within 30 min of the sting without any diminution in pain. The pain did not worsen, as is often precipitated by application of cool or cold water to a jellyfish sting. She then ingested ibuprofen 800 mg without pain relief. The wound was not covered with a dressing. At 2330 she vomited. After the initial burning pain subsided at 10 h, aside from discomfort caused by swelling and mild RLE soreness in the first few days after the sting, there was no further significant pain related to the sting for the entirety of the healing period.

Swelling immediately after the sting was limited to welt-like streaks where tentacles contacted the skin. The widths of the streaks were not measured acutely. There was no bleeding. Assessment of motor function and sensation was not formally performed, but the patient does not recollect loss of strength or sensation at the time of injury or at any time thereafter.

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Submitted for publication December 2018.

Accepted for publication May 2019.

Figure 1. Envenomation day 1.

Because of the remote location of the hostel and personal lack of knowledge about the situation, the patient did not seek further medical care immediately after the sting. The only means of emergency communication was a radio that could contact the Cambodian navy. When the patient's friends expressed concern to the staff that she might require additional medical care, the staff responded that they did not think it was a sufficiently severe situation to warrant contacting the navy.

DAY 2

Flat, dark purple coloration of the skin developed where the jellyfish tentacles had contacted the skin (Figure 2). There was no pain to touch, but the RLE was swollen and sore. Gait was irregular because of swelling and muscle pain. The patient felt weak and lightheaded. The patient self-prescribed medications, which were obtained at a local pharmacy: ibuprofen 400 mg plus paracetamol 333 mg in combination three times daily for 2 d then as needed; serratiopeptidase 10 mg twice. At 1700, the patient ate her first meal since the sting and boarded a night bus to Siem Reap.

DAY 3

The bus arrived at Siem Reap at 0430. The patient experienced a syncopal episode stepping off the bus and immediately was transported in a tuk tuk to the emergency department at Royal Angkor International Hospital, where she was admitted as an inpatient. Vital signs (the first noted since the sting) were blood pressure 119/69 mm Hg, heart rate 77 beats·min⁻¹, respirations 20 breaths·min⁻¹, and temperature 36°C. The RLE was noted to be swollen and warm, and skin lesions were noted on the right leg and less severely on both wrists and hands. Admission laboratory evaluation revealed white blood cell count 17.3/mm³ with 68% neutrophils,

Figure 2. Envenomation day 2.

red blood cell count 5.7/mm³ with normal morphology and “adequate” platelets, hemoglobin 17.6 g·dL⁻¹, hematocrit 51%, sodium 125 (136–148) mEq·L⁻¹, potassium 3.9 (3.5–5.5) mEq·L⁻¹, chloride 96 (99–111) mEq·L⁻¹, total carbon dioxide 19.2 (22–29) mEq·L⁻¹, and C-reactive protein 31.92 (0–6) mg·L⁻¹. On day 2 of hospitalization, white blood cell count increased to 23.3/mm³ with 86% neutrophils. She was thought to be dehydrated, which was consistent with hemoconcentration. During the course of hospitalization, she was given an unspecified amount of IV normal saline and parenteral administration of ceftriaxone 2 g, chlorpheniramine 10 mg, dexamethasone 10 mg, metoclopramide 10 mg, and esomeprazole 40 mg, and topical silver sulfadiazine (SSD). Tissue compartment pressure was not measured.

DAY 4

The patient felt much better, and her weakness and dizziness resolved. She was discharged with prescriptions for etoricoxib 90 mg once daily (total of 3 doses taken); prednisolone 10 mg twice daily (total of 10 doses taken); and topical silver sulfadiazine cream (used once). The patient visited Angkor Wat at 1400 but cut the visit short because of irregular gait after walking 1200 m. She noted a significant increase in RLE swelling postambulation (Figure 3).

Figure 3. Envenomation day 4.

To the patient's knowledge, deep venous thrombosis was not considered by the first medical providers.

DAY 5

The patient flew to Bali. Upon arrival, she used a wheelchair to minimize mobilization, noted significant discomfort due to RLE-dependent edema, and performed neurovascular checks every 2 h due to concern for possible compartment syndrome. These checks were performed by ensuring that the foot and toes were warm to touch and had full sensation and adequate blood flow (capillary refill less than 2 s). Discomfort improved after RLE elevation.

DAY 6

Swelling was pronounced in the RLE and developed in the right lower abdominal compartment and groin when supine (Figure 4). The wounds began to form a crust with dark red, inflamed skin surrounding the wounds. The patient's mother contacted the first author via email on day 5. He telephoned the patient and advised her to return home immediately to receive the medical care necessary to attempt healing without complications. He provided the patient with the following instructions: cease taking the prednisone to avoid immunosuppression during a risk period for infection; keep the wound clean; apply an over-the-counter antiseptic or antibiotic cream or ointment; dress the wounds with gauze; take cephalexin 250 mg 4 times a day if the patient noted any sign of infection; keep the RLE elevated during the flight back home; take low-dose aspirin during air travel; and confirm tetanus immunization status. Cephalexin was recommended because the patient was out of the time window for an acute infection caused by *Vibrio* or *Aeromonas* species and would most likely have subsequently

Figure 4. Envenomation day 6.

experienced an infection by *Staphylococcus* or *Streptococcus*. No sign of infection was ever noted, and thus this antibiotic was never taken by the patient.

DAY 7

The patient flew to San Francisco via Taiwan with the RLE elevated. Additional wound crusts formed with small areas of blistering along the edges of some of the narrowest wounds (Figure 5). There was modest serous fluid discharge. Ambulation remained difficult because of discomfort and swelling of the entire RLE.

DAY 8

The wounds continued to darken, with some uncrusted shallow areas of the wound revealing beefy red granulation tissue (Figure 6). The RLE remained swollen and nontender to touch. There was no superficial sensation in the stung areas. The patient was seen by a dive medicine physician specialist in San Diego (third author). At that time, she was afebrile and vital signs were normal. Her RLE was significantly swollen, but all compartments in her leg were soft and there were no signs of cellulitis or compartment syndrome. Her wounds were crusting on the surface with underlying healthy granulation tissue and

Figure 5. Envenomation day 7.

Figure 6. Envenomation day 8.

clear serous drainage. There was no purulence or other sign of infection. She was instructed to wash the wound daily, continue to apply antiseptic ointment underneath a gauze dressing, and seek the advice of a plastic surgeon with burn care experience (second author).

DAYS 9–11

The RLE remained edematous and sore. The wounds continued to darken and form crusts with some scales, and there was persistent serous exudate (Figure 7). A macular, red, and pruritic rash on both wrists became more prominent.

DAY 12

The patient was examined by the plastic surgeon, who noted the evolving pruritic bilateral wrist rash. There was increasing exposure of the RLE wound tissue underneath the crusts, which appeared to be healthy, raised, and textured granulation tissue with scattered overlying scab formation (Figure 8). Initial consultation included considerations similar to those for a burn or chemical exposure injury—the extent and depth of the wound to guide treatment. Physical examination was consistent with superficial and deep partial thickness burns, possibly with near full

Figure 7. Envenomation day 10.

Figure 8. Envenomation day 12.

thickness injury in larger, confluent tentacle contact areas. It was considered whether debridement was required to achieve a healthy wound bed and whether grafting might be needed vs allowing the wounds to heal by secondary intention. No debridement or grafting was indicated because the wounds were clean, not infected, and appeared to be improving. Wound care instructions were to continue washing the wounds with soap and water and to clean and dress the wounds twice a day, using SSD cream in the deeper areas and *Leptospermum* honey (Medihoney) or any antiseptic ointment of choice in the shallower areas, topped by gauze and gentle elastic bandage compression. Medihoney paste was chosen, applied twice a day thinly underneath a dressing. The immediate goals were to keep the wounds clean, prevent infection, maintain moisture to facilitate healing, and allow for serial examinations to determine the best method for wound closure. The patient would likely be fortunate and heal secondarily given the rapidity with which she was improving, allowing her to avoid the unsightly secondary donor site that would be necessary should deep dermal necrosis develop and require reconstructive surgery and a skin graft.¹ The risk of allowing healing by secondary intention alone was risk of hypertrophic scarring, particularly in the larger, deeper wound areas. Tetanus immunization status was confirmed.

DAYS 13–19

The wound continued to show increased granulation tissue as more of the superficial eschar continued to slough. The shallower areas were pink and clean; the deeper, larger, and confluent areas were white-yellow (similar to a deep, partial thickness second-degree burn) with a fibrinous appearance (Figure 9). At the end of this inter-

Figure 9. Envenomation day 15.

Figure 10. Envenomation day 19.

val, the wound edges began to re-epithelialize and contract in some areas where the wounds appeared more narrow and superficial. Bright pink edges surrounded areas of sloughed tissue (Figure 10) as the wound began to heal but not yet repigment. Swelling of the RLE decreased, particularly with rest.

DAY 24

Instructions were given to continue washing the wounds with soap and water and to continue application of SSD to white (deeper) areas of injury and Medihoney to red (shallower) areas of injury (Figure 11).

DAY 27

Wounds were a mixture of deep and superficial shallow with some lines of complete closure by secondary intention and re-epithelialization, overlaid by dry, shiny, and pink tissue that blanched with pressure. Pigment had not yet returned to the newly healed areas. Shrinking open wounds continued to demonstrate slow weeping of non-infected, serous fluid (Figure 12).

Figure 11. Envenomation day 24.

Figure 12. Envenomation day 27.

Figure 13. Envenomation day 29.

DAY 29

The closed areas of the wounds had begun to re-pigment and dry; other scabbed areas continued to weep serous fluid (Figure 13). Dry areas were at risk for cracking and opening, and frequent moisturizer and sunscreen application was recommended.

Figure 14. Envenomation day 32.

DAY 31–32

The narrowest lines of injury were nearly completely closed; healed areas were pruritic and dry, and deeper (white) areas of the wound showed improving granulation tissue (Figure 14).

DAYS 32–46

The patient took a road trip. Throughout the journey, she continued to follow wound care instructions to prevent

Figure 15. Envenomation day 33.

Figure 16. Envenomation day 46.

infection and maintain a moist wound-healing environment. The fibrinous tissue continued to slough, exposing pink or red granulation tissue (Figure 15). Healed areas were pruritic. The deepest areas continued to heal (Figure 16).

DAY 49

A very small area remained open and was not yet healed (Figure 17). The area of open wound was located in the proximal thigh. Pruritus was the predominant symptom in healed areas.

DAY 60

The wound was fully closed and healed with a small amount of residual scab (Figure 18); pruritus was resolved. Topical therapy was discontinued. Moisturizing lotion and sun protection measures were continued to optimize scar maturation (12–24 mo). The patient was counseled that she might be a candidate for elective scar revision, steroid treatment, and/or laser therapy in the future. The appearance of the wound 6 months after the initial injury is shown in Figure 19.

Figure 17. Envenomation day 49.

Figure 18. Envenomation day 60.

Discussion

“Jellyfish” are globally ubiquitous stinging ocean creatures. They include species of the phylum Cnidaria, subphylum Medusozoa. Their life cycle includes fertilized eggs that transform into free-swimming larvae (planulae). These attach to surfaces and transform into tentacled polyps, which can transform directly into medusae (the large jellyfish with which we are familiar). Alternatively, the planulae can divide into many plate-like segments (strobilae), which then transform into juvenile jellyfish (ephyrae) that then transform into medusae.⁴ Some tentacles can transform a tentacle fragment into a polyp and proceed from that point. Stinging forms include ephyrae and medusae.

The stinging apparatus (an organelle known as a cnidocyte or nematocyte) resides in the explosive cells (known as cnidocytes or nematocytes) found predominantly for most species on the tentacles and exclusively on the tentacles for *C fleckeri*. Cnidocyst activity is one of the most elaborate wounding mechanisms in nature. Within the ovoid or round stinging organelle is a coiled thread (tubule) that terminates in a dart-like structure.⁵ This thread is a double helical structure of venom granules that are released after the thread anchors to the victim by the

dart. This act occurs when the cnidocyst is stimulated to activate by chemical or mechanical stimulation, which causes the thread to be exocytosed explosively in milliseconds with acceleration of more than 40,000 g, with an estimated skin striking force of 2 to 5 psi.⁶

Pelagic jellyfish sometimes are visible to ocean goers, such as when they swarm at the surface or land on the beach, and can be avoided. At other times, particularly when the creatures are swimming solo and submerged beneath the surface, they are not detected until a person is envenomed.

To serve as an example, one species of box jellyfish (the dreaded *C fleckeri*) is found throughout Indo-Pacific waters, including those adjacent to Cambodia.⁷ The diameter of the bell ranges from 2 to 30 cm.⁸ The severity of the sting is somewhat correlated with the size of the creatures, with small jellyfish (5–7 cm diameter bell) causing less severe stings than larger jellyfish (more than 15 cm diameter bell). Each adult *Chironex* carries up to 15 tentacles in each corner of its bell, each tentacle with a length of up to 3 m.^{9,10} Clinical manifestations of *C fleckeri* envenomation include significant pain, acute cutaneous inflammation, dermonecrosis and permanent scarring, dyspnea, pulmonary edema, hypertension followed by hypotension, cardiovascular

Figure 19. Envenomation day 120.

collapse, and death. In severe cases, cardiovascular collapse and death can occur within minutes.

The venom of *C fleckeri* contained in the nematocyst has been isolated, but only a few individual toxins have been identified.^{11,12} Recent studies have identified the potential structure of these proteins.¹³ *C fleckeri* venom includes CfTX-like proteins (CfTX-A, CfTX-B, CfTX-1, and CfTX-2), proteases, hemolysins, cytolysins, and protease inhibitors. The most abundant protein toxins are CfTX-1 and CfTX-2. The type I cardiotoxins CfTX-1 and -2 are thought to have a direct cardiotoxic effect on the myocardium, causing cardiovascular collapse that can lead to death.¹⁴ CfTX-1 and -2 proteins are also thought to be responsible for skin inflammation and necrosis.

Most envenomations from *C fleckeri* do not cause death but rather a significant skin reaction. The sting is immediately painful, and skin blistering appears in the first few hours, followed by superficial necrosis in 12 to 18 h.⁸ The vast majority of stings are identified by immediate intense pain and the skin lesion pattern that appears after human contact; the creature is rarely seen in open ocean water by the victim. The broad-banded configuration of each tentacle enables prompt identification of a box jellyfish sting from its cutaneous imprint. By virtue of the appearance of the skin lesions, the patient in this

case report was likely stung by a box jellyfish, which might have been *C fleckeri*. Although nematocyst recovery from the envenomed skin was not performed for definitive identification of *C fleckeri*, the sting pattern and skin reaction were classic for this species. The dark and dusky, purplish skin discoloration was followed by wheals, blistering of epithelium, and broad, deep partial-to-full thickness necrosis in a whip-like pattern.

Recommendations for field therapy for a *C fleckeri* or other potent jellyfish envenomation are based on observations of empiric therapy rather than controlled trials.¹⁵ Current consensus, with some dissenting opinions, is to immediately flood the affected skin with household vinegar (acetic acid 5%). This often provides some pain relief by an unknown mechanism of action. It has been proposed that the nematocysts might be rendered inactive or the venom somehow made less provocative of pain. After immersion of the stung area in vinegar, tentacles or fragments are removed by grasping and lifting if possible or using a sharp edge as a second choice, avoiding disturbing the tentacles, rubbing, or compression. Improper removal technique may result in further nematocyst-mediated injury.¹⁶ Other topical therapies reported to be effective, ineffective, or deleterious include nonscalding hot water,¹⁷ ice packs,¹⁸ lemon and oil emulsion,¹⁹ and seawater rinsing. Hot water is the most likely of these to be effective. In vitro studies demonstrate that cardiocytotoxic activity of *C fleckeri* venom is significantly decreased when it is heated to 44°C.²⁰ Caution should be exercised to not burn skin during treatment with hot water. In our opinion, ice water immersion should be avoided because it is a potent vasoconstrictor and may cause further ischemia of the wound and delayed wound healing, or even frostbite. Furthermore, melting ice cubes become unheated fresh water, which may worsen the envenomation. Lukewarm water applied during the healing phase increases blood flow to the area, which might accelerate healing. Maintaining appropriate core temperature reduces vasoconstriction of the skin capillary beds and allows appropriate blood flow to the injured areas.

Wounds should be frequently (2 to 3 times a day) debrided of blistered skin to expose the wound base and allow proper cleansing and wound care. For very large affected areas (>10% total body surface area), the risk for significant insensible fluid loss is high, so fluid resuscitation and urine output monitoring should be considered. Titrate urine output to appropriate color (light or straw-colored) if precise urine output measurement is not available. As soon as is feasible, a burn center or tertiary care facility with plastic surgery consultation should be consulted for large areas of necrosis. In these instances, a systemic inflammatory response should be

anticipated and supportive care provided. Measures should be taken to prevent dehydration and reduce risk of infection that may cause progression of illness to sepsis. If there are signs of anaphylaxis, administration of epinephrine by the intramuscular route is recommended. It is important to note that different species of jellyfish may respond differently to each of the various individual topical agents recommended by locals and experts for therapy, and no field therapy has been definitively confirmed from bench to bedside.¹⁶

Regardless of the field therapy and its efficacy, subsequent treatment is directed at systemic manifestations (eg, supportive care of hypotension, respiratory failure, cardiac arrest) of envenomation and the destructive local tissue reaction, which can be necrosis to the point of gangrene and wound infection.^{21,22} Regarding the former, if the stinging species is known to be *C fleckeri*, a sheep-derived antivenom available from Commonwealth Serum Laboratories in Australia is indicated for treatment if it can be administered promptly after the initial event (immediately if possible; effectiveness diminishes rapidly postenvenomation and is likely negligible after 12 h).²³ The initial dosage is 2 ampules (40,000 units), which may be repeated in part or in whole after a few hours if there are persistent systemic derangements. Box jellyfish antivenom is thought also to reduce the severity of the tissue reaction and scarring, but this has not been quantified by any human clinical study with a control group.²⁴ The timing and dose are the same; these parameters to determine efficacy for all indications are under review.²⁵ Had it been available in a timely fashion and had the care provider thought that a *C fleckeri* envenomation had occurred, it would have been reasonable to administer in this case.

Other syndromes that are seen after jellyfish envenomation include vasospasm and vasculitis,²⁶ digital ischemia,²⁷ local skin necrosis, and hyper- or hypopigmentation. The long-term sequelae may involve months of intermittent skin desquamation, discolored striae, and pruritus.⁸ Those of higher Fitzpatrick skin type may be prone to hypertrophic scarring, keloid formation, chronic pain, and the secondary disabilities and deformities that accompany these conditions. Treatment of these secondary conditions may require specialist consultation and a staged approach over the course of several years.

LIMITATIONS

The obvious limitation is the inability to precisely identify the stinging jellyfish because it was not directly visualized by the victim, which is very often the case in such incidents. It has been noted that attributing jellyfish stings to a particular species can be problematic.²⁸ The

only certain ways to identify a jellyfish are by visualization or recognition of cnidocysts from skin scrapings observed under the microscope. In this case, our designation of “box jellyfish” was made by a classic clinical presentation, predominately the physical configuration of the skin lesions in combination with the systemic symptoms and pain. It is possible, but somewhat less likely based upon the clinical presentation, that a species of jellyfish of the class Cubozoa other than *Chironex*, such as of the genus *Carybdea*, might have caused the sting. Other jellyfish families of the class Cubozoa that reside in the Gulf of Thailand, which are the waters in which the patient was stung, include Chirodropidae and Chiropsalmidae.^{2,3} However, *Carybdea marsupialis* and all other species found in the coastal waters of Cambodia do not as commonly cause a severe necrotic stinging skin reaction in a pattern similar to that caused by *Chironex*. A possibility is that the jellyfish was *Chironex yamaguchi*, although this species has been mostly observed in Japanese and Philippine waters.

Author Contributions: Drafting of the manuscript (PA, DG, KVH, AZ); critical revision of the manuscript (PA, AZ); approval of final manuscript (PA, DG, KVH, AZ).

Financial/Material Support: None.

Disclosures: None.

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