Jellyfish envenomation with delayed hypersensitivity and concurrent SARS-CoV-2 infection

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Keywords: Cnidaria, concurrent viral infection, COVID-19, delayed hypersensitivity, envenomation, jellyfish, nematocysts, SARS-CoV-2, Waikiki, Hawaii

To the Editor:

Jellyfish are medusal and gelatinous aquatic invertebrates of the Cnidaria phylum, which spans over 9000 species [1]. There are approximately 100 species of jellyfish known to cause potentially fatal outcomes, which occur via stinging envenomation [2]. Notably, populations of cnidaria are typically greater in higher temperature climates and higher incidences of jellyfish stings are also reported in these environments; tropical regions, in particular, report the highest rate of stings among cnidaria [3].

When a patient is stung by a jellyfish, the treatment of choice may vary based on the specific species of cnidaria, the extent of trauma sustained, and the incidence of patient comorbidities such as a viral infection [2,4].

Herein, we report a patient stung by a jellyfish along the coast of Hawaii. Although the species of jellyfish that stung the patient is unknown, the likely culprit is the *Alatina moseri* or *Carybdea alata*, otherwise commonly known as the box jellyfish; these are prevalent in Hawaii and they possess lethal toxins [5]. Importantly, the patient experienced both an immediate and a delayed hypersensitivity reaction, which was likely exacerbated by a concurrent SARS-CoV-2 infection.

A healthy 22-year-old woman presented to a Waikiki emergency hospital with numerous well-demarcated erythematous and edematous papules confined to her right posterior leg. The eruption developed from a jellyfish sting, which caused immediate sharp pain, followed by subsequent localized swelling and itchiness along the affected leg. While on-scene and at the hospital, venomous stingers from the jellyfish were removed from the patient's leg. The patient was prescribed topical lidocaine to reduce pain, along with oral diphenhydramine to reduce inflammation. Over the following week, the patient noted near full resolution of symptoms.

Two weeks after the initial sting, the patient's symptoms recurred. Following an infection with SARS-CoV-2, she presented to an urgent care clinic with numerous erythematous papules along her right leg, positioned in the same manner as in the original eruption (**Figure 1**). The patient noted tenderness, swelling, sharp pain, and itchiness, all of which were reported to be more intense than the symptoms presented shortly after the sting. Fever, nasal congestion, and memory fog were also noted, but these were more likely attributed to the viral infection. She was diagnosed with a delayed hypersensitivity reaction; the patient was prescribed topical clobetasol 0.05% ointment, twice daily, along with oral cetirizine 10mg, once per day, until resolution of symptoms.

Envenomation by jellyfish involves the self-defense activation of nematoblast-synthesized capsules known as nematocysts. Thousands of these are

densely arranged along the epithelial surface of the organism's tentacles, oral arms, and bell [2]. Upon physical contact with a person, a jellyfish may activate its nematocysts, which release serrated and barbed spine-laden tubules carrying proteinaceous venom made of polysaccharides, glycoproteins, and mini-collagens; depending on the species of cnidaria, this venom may be toxic [2]. Deposition of jellyfish venom may reach different depths in the skin, depending on the amount of toxins released and the time-sensitive distribution of venom exposure along a patient's skin [2]. Additionally, the severity of a cnidarian sting can influence whether venom remains in the patient for several days to several weeks [2].

Symptoms of jellyfish stings may be localized or systemic, and immediate or delayed. These can be recurrent or persistent and in more severe cases, jellyfish stings can cause fatal outcomes [1]. Typically, initial symptoms include immediate pain, erythema, and burning. Subsequent symptoms of a jellyfish sting may consist of papulovesicular cutaneous eruptions that can vary in appearance and these are susceptible to long-term skin discoloration or hyperpigmentation. In some cases, stings may also lead to flagellated and edematous purpuras, which can evolve into bullae [6].

In more severe cases, structural jellyfish carbohydrates such as chitin may cause immune-mediated respiratory inflammation or failure [2]. Additionally, toxic Cnidaria venom can circulate through the blood, causing cardiovascular failure. In some instances, circulating jellyfish toxins may form erythrocytic pores and compromise the cells' plasma membranes, therefore leading to possible tissue damage as a result of necroptotic or apoptotic effects [7].

Figure 1. *A delayed hypersensitivity reaction showcasing reappearance of erythematous and edematous papules confined to the patient's posterior lower thigh and upper calf.*

Treatment of choice for jellyfish envenomation depends on the severity of the incident. After addressing a patient's vital signs, the priority may involve alleviating effects of local venom poisoning and reducing further penetration of toxic discharge. In more severe cases, treatment may involve treating shock, sepsis, or localized organ damage [8]. Regardless of the severity of a jellyfish sting, nematocysts should immediately be removed using gloves and tweezers. After removal of nematocysts, topical lidocaine gel or heat packs may be used for analgesia [9]. Topical or oral corticosteroids may be recommended for the immediate inflammation caused by the toxins as well as the delayed hypersensitivity reaction that can follow [10]. Contrary to the myth, acetic acid (vinegar) is not recommended, given that its effectiveness is noted only against particular species of jellyfish, including the *Carybdea marsupialis*. In some cases, vinegar may promote further nematocyst discharge and subsequent exacerbation of symptoms [11]. Notably, certain cases of jellyfish stings may require even more invasive or tailored intervention than the aforementioned and these should be evaluated on a case-by-case basis.

For our patient, it is plausible that the deposited jellyfish venom remained in the system for long enough to trigger an antigenic reaction following re-activation of the immune system by SARS-CoV-2. Although the pathogenesis of skin manifestations arising from COVID-19 is not yet fully understood, it is known that the receptor-mediated interactions between angiotensin converting enzyme-2 (ACE-2) receptors and the SARS-CoV-2 virus increase the level of pro-inflammatory cytokines responsible for exacerbation of pre-existing dermatitis [12,13].

The patient was prescribed topical corticosteroids given the limited body surface area involved and her symptoms resolved fully within two weeks.

Given that changing environmental conditions have led to the recent abundance of jellyfish and higher rates of associated cnidarian stings, healthcare

workers should recognize the envenomation's clinical presentation, along with particular therapeutic options available to treat both the immediate and delayed symptoms. Early detection and effective intervention in the event of jellyfish stings may lower associated complication rates and shorten recovery periods. Furthermore, effective preparation and exposure to the clinical manifestations of jellyfish-induced immune and hypersensitivity reactions may enable clinicians and researchers alike to better understand the interactions between cnidarian venom and the immune system.

Potential conflicts of interest

The authors declare no conflicts of interest.

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