

Case Report: Unusual Bullous Reaction to *Physalia physalis* Venom after Recurrent Envenomation

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Abstract. *Physalia physalis*, often referred to colloquially as Portuguese man-of-war or bluebottle jellyfish, is a jellyfish-like organism found in tropical and subtropical areas of the Pacific, Atlantic, and Indian Oceans. Most often, envenomation by *P. physalis* tentacles results in painful but self-resolving epidermal stings. We report on two clinic visits of a patient who suffered from worsening reactions to recurrent *P. physalis* envenomation. The first clinical episode involved urticaria and severe pruritus that was worse than the pruritus the patient had experienced upon envenomation in the past. The second episode involved an unusual bullous reaction. Further study into the compounds present in *P. physalis* venom may help elucidate the mechanism of the present case and other abnormal reactions to envenomation. Patients and providers who care for patients at risk for recurrent stings (e.g., surfers, fishermen) should be cognizant of the potential for worsening reactions to envenomation. Further study into therapies such as oral antihistamines and *Aloe vera* gel may uncover additional appropriate treatments for symptomatic relief of *P. physalis* envenomation.

INTRODUCTION

Physalia physalis, often referred to colloquially as Portuguese man-of-war or bluebottle jellyfish, is a jellyfish-like organism and member of the order Siphonophorae (Figure 1).¹ As a colonial cnidarian, *P. physalis* consists of colonies of modified zooids that function together to feed and survive.² Some of those zooids form tentacles, which are used to paralyze and feed on fish and may also envenomate humans upon contact with human skin.² *Physalia physalis* organisms are generally found in tropical and subtropical areas of the Pacific, Atlantic, and Indian Oceans, most often from 55°N to 40°S.³

Most often, envenomation by *P. physalis* results in painful but self-resolving epidermal stings.⁴ Allergic, cardiac, gastrointestinal, muscular, neurological, and renal reactions have also been reported.^{3,5–9} Rarely, envenomation can result in death.^{10,11}

We report on two clinic visits of a patient who suffered from worsening reactions to recurrent *P. physalis* envenomation, the latter of which involved an unusual bullous reaction. We present images documenting the resolution of the lesions presented at those two visits and discuss the case in the context of relevant existing literature.

CASE PRESENTATION

The patient, a 24-year-old adult male, began surfing regularly in early 2021 at a beach located in the state of Hawaii, United States. That beach is known to be a site of frequent *P. physalis* stings. Since starting to surf, the patient recounted being stung at roughly 2- to 4-week intervals. Stings manifested as a linear collection of small, erythematous papules tracing the location at which *P. physalis* tentacles met the skin. Those skin lesions were accompanied by mild pruritus and did not require medical attention.

First clinical episode. The patient traveled away from Hawaii and did not enter the ocean for about 3 months. Upon returning in December 2021, the patient began surfing again at the same beach.

The patient presented to the outpatient clinic complaining of a 1-day history of severe pruritus at bilateral forearms. As a regular surfer in the area, the patient attested to being familiar with the appearance of *P. physalis* organisms and recalled seeing the organism come in contact with his skin upon envenomation. The pruritus during this episode was markedly more severe than that of previous episodes, leading the patient to seek medical attention. The pruritus was severe enough to interfere with sleep and was not relieved by application of topical triamcinolone cream. The patient did not present with any signs of anaphylaxis. The patient was 24 years old at the time of visit. Physical examination revealed bilateral urticaria on lower arms bilaterally (Figure 2).

A 5-day course of oral prednisone 40 mg once daily was prescribed to address the severe pruritus.

Progression of urticaria after the visit is depicted in Figure 2. After the visit, the patient reported that prednisone administration reduced the severity of pruritus enough to allow for sleep throughout the night. However, pruritus remained bothersome during the day for the duration of the prednisone course. The patient also reported brief symptomatic relief with topical application of commercially available *Aloe vera* gel.

Second clinical episode. After another 3-month period of not entering the ocean, the patient began surfing again at the same beach in December 2022. Now 25 years old, he presented with a 2-day history of blistering at the site of *P. physalis* envenomation at the posterior left ankle. The patient recalled seeing the organism come in contact with his skin upon envenomation. He reported that the site of envenomation originally appeared as a blanching plaque but progressed to bulla and diffuse ankle swelling. The patient reported pruritus of reduced severity compared with the first clinical episode. He did not present with any signs of anaphylaxis. Physical examination revealed diffuse left ankle swelling and series of roughly 2-cm bullae along the posterior aspect of the left ankle (Figure 3). Impetigo-like lesions were noted surrounding the bullae. The patient reported applying triamcinolone cream and commercially available lidocaine patches as an attempt to reduce swelling and prevent progression of the pruritus. Oral cetirizine 10 mg during the day and oral diphenhydramine 25 mg in the evening were recommended to prevent further pruritus.

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FIGURE 1. *Physalia physalis*, often referred to colloquially as Portuguese man-of-war or bluebottle jellyfish, is a jellyfish-like organism found in tropical and subtropical areas of the Pacific, Atlantic, and Indian Oceans. Most often, envenomation by *P. physalis* tentacles results in painful but self-resolving epidermal stings.

One of the bullae was accidentally ruptured during the visit, and a culture was collected. A 7-day course of 500 mg oral cephalexin once daily was prescribed out of clinical suspicion of infection. Gram stain of the culture revealed 3+ epithelial cells, no leukocytes, and no organisms. The culture was later found negative for growth at 2 days.

Progression of the bullous lesion is depicted in Figure 3. After the visit, the patient reported relief of pruritus with the use of recommended oral antihistamines.

DISCUSSION

We present a patient who suffered from worsening reactions to recurrent *P. physalis* envenomation over time, the most recent episode of which involved a rare bullous reaction. Our review of the literature did not uncover any other reports of a bullous reaction to envenomation by *P. physalis*.

The exact composition of *P. physalis* venom has not been completely elucidated. A review by D'Ambra and Lauritano summarized the components of the venom that are currently known.⁴ Phospholipase A2 is noted to be present in venom and likely contributes to the manifestation of pruritus upon envenomation.⁴ Phospholipase A2 breaks down plasma membrane phospholipid to arachidonic acid; arachidonic acid may be converted to either prostaglandins or to leukotrienes which, in turn, may induce the release of histamine and result in pruritus. Histamine itself is also present in the venom, which may cause pruritus directly.⁴ Of note, collagenases and elastases are present in *P. physalis* venom, which are known to cause blisters.⁴

However, the patient's history of worsening reactions to recurrent exposure and the fact that his bullous reaction is a rare presentation of *P. physalis* envenomation potentially suggest an abnormal immune etiology of the patient's bullous lesion. Bulla formation may be caused by autoantibodies to hemidesmosomes, as is the case in the development of bullous pemphigoid.¹² As such, cross-reactivity of antibodies to a component of *P. physalis* venom and dermal hemidesmosomes

	Right arm	Left arm
1 day after initial visit		
5 days after initial visit		

FIGURE 2. The patient presented in December 2021 with severe pruritus and urticaria at the bilateral forearms corresponding to the site of *Physalia physalis* envenomation. The patient was prescribed a 5-day course of oral prednisone 40 mg once daily to address the severe pruritus. The progression of the urticaria after the patient visit is depicted.



FIGURE 3. The patient presented in December 2022 with a 2-day history of blistering at the site of *Physalia physalis* envenomation at the posterior left ankle. Culture of a ruptured bulla was negative for growth at 2 days and Gram stain revealed no leukocytes and no organisms. The progression of the lesion is depicted.

may have caused the patient's bullae. Bulla formation may also be caused by destruction of desmoglein-1 complex, similar to the etiology of bullous impetigo.¹² As such, cross-reactivity of antibodies to a component of *P. physalis* venom and desmoglein-1 complexes or direct insult to the desmoglein-1 complex by a component of *P. physalis* venom may result in bullae as well. It is also possible that a confluence of toxicologic and immunologic factors contributed to the patient's bullous reaction. Given those potential immunological considerations, our case suggests that patients and providers who care for patients at risk for recurrent stings (e.g., surfers, fishermen) should be cognizant of the potential for worsening reactions to envenomation.

There are currently no widely accepted guidelines regarding the best way to treat the symptoms of *P. physalis* envenomation because there is currently a paucity of literature on this matter. Current literature suggests that heat application to the site of envenomation via hot-water immersion is effective for pain relief, although evidence is scarce.^{13,14} Other proposed therapies for symptom relief include vinegar or cold pack/ice application to the site of envenomation, but empirical evidence for their efficacy is lacking.^{13,15,16} After his first clinical episode, our patient reported that topical application of commercially available *Aloe vera* provided brief symptomatic relief of his severe pruritus. Topical application of *Aloe vera* extract has been shown to effectively treat symptoms of skin inflammation.¹⁷ However, our review of the literature failed to uncover any study into the use of topical *Aloe vera* in the context of envenomation specifically. After his second clinical episode, our patient reported that oral antihistamines provided reliable relief of his pruritus. The use of antihistamine medications to treat *P. physalis* envenomation has been reported previously, but those studies failed to provide conclusive evidence on their efficacy in the context of such stings.^{18,19} Further study into the use of topical *Aloe vera* gel and oral antihistamines in the context of *P. physalis* envenomation may give providers additional and potentially more reliable options for the symptomatic treatment of this condition.

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