



Case report

Anaphylactic shock caused by sting of crown-of-thorns starfish (*Acanthaster planci*)



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ARTICLE INFO

Article history:

Received 4 July 2013

Accepted 3 January 2014

Available online 10 January 2014

Keywords:

Crown-of-thorns starfish

Marine dangerous animal

Anaphylactic shock

Venomous spine

Adrenaline for auto-injection

ABSTRACT

A 40s-year-old woman with previous history of injury due to contact with crown-of-thorns starfish, *Acanthaster planci*, was stung on the right middle finger. After immediately losing consciousness, she died 13 h after injury despite intensive medical treatment. Examination of the respiratory system revealed narrowing due to severe edema of the laryngopharynx, as well as alveolar hemorrhage, eosinophilic infiltration, and extensive neutrophil and eosinophil aggregation in the intravascular lumen of the lungs. Examination of the liver revealed severe diffuse hepatocellular necrosis and extremely high levels of liver transaminases, indicating severe liver damage. Based on these findings, we concluded that she had died from anaphylactic shock induced by circulation of crown-of-thorns starfish venom in the bloodstream. Injurious contact with the spine of the crown-of-thorns starfish can cause severe symptoms as well as systematic reactions, including anaphylaxis. To our knowledge, this is the first case of anaphylactic shock or death caused by human contact with the crown-of-thorns starfish reported in the English-language literature. Although rare, anaphylaxis due to injury by marine animals is potentially fatal. Saving lives requires providing education regarding prevention and enabling prompt response to possible anaphylaxis, including preparation of adrenaline for auto-injection.

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1. Introduction

The crown-of-thorns starfish, *Acanthaster planci*, widely inhabits tropical and subtropical coral reef systems ranging from the Red Sea to the Indo-Pacific Ocean. Due to recent changes in the marine environment, most notably global warming, the habitat of the crown-of-thorns starfish has extended even farther, leading to serious environmental issues, such as abnormal infestations of crown-of-thorns starfish in the Ryukyu Islands [1]. Crown-of-thorns starfish are notorious not only for eating coral but also for posing danger to other animals by injurious contact with the many venomous spines covering the surface of their body (Fig. 1) [1,2]. Although they do not attack other animals, primarily using their venomous spines for self-defense, crown-of-thorns starfish may inadvertently injure humans who make unintended contact with their venomous spines, such as by stepping on or touching them [2]. Injurious contact with their spines may result not only in extremely painful wounds, redness, and swelling but also serious

systemic reactions such as hemolysis, paralysis, and liver damage [1–3]. Moreover, as the venom within the spines contains a foreign peptide capable of causing anaphylactic shock, this rare but lethal reaction is a possible result of stinging by a crown-of-thorns starfish. Despite this deadly risk, to our knowledge, no report in the English-language literature describes a case of anaphylactic shock or death caused by contact with the spine of a crown-of-thorns starfish. Here, we present the first description of a fatal case of anaphylactic shock due to contact with the spine of a crown-of-thorns starfish.

2. Case report

A 40s-year-old female scuba-diving instructor in Okinawa had become involved in volunteer activity aimed at exterminating crown-of-thorns starfish from the Okinawa coral reef after abnormal infestations of the marine animals. While she was guiding scuba-diving students cognizant of her volunteer activity around the coral reef, a student handed her a crown-of-thorns starfish at a depth of 18 m so that she could exterminate it. Having no equipment for proper extermination, such as gloves and a knife, she attempted to kill the starfish by beating and crushing it with

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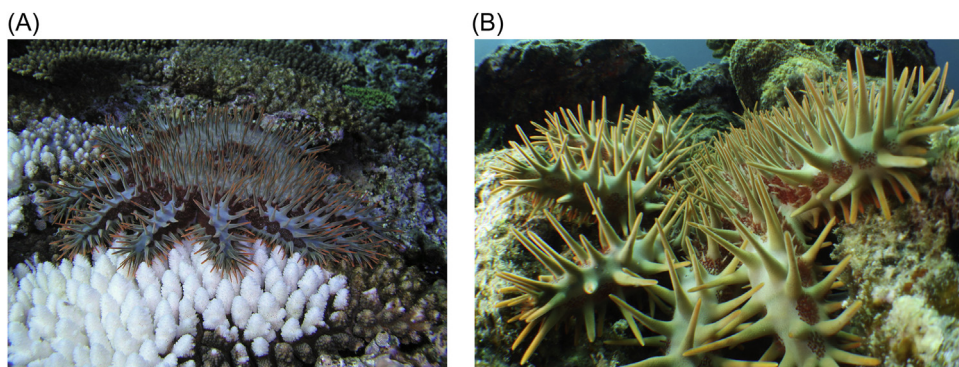


Fig. 1. (A) The crown-of-thorns starfish, *Acanthaster planci*, preys on reef coral polyps, as evidenced by the bleaching of the coral observable in the front of the photograph. (B) The upper surface of the crown-of-thorns starfish contains numerous sharp spines.

small coral stones held in her bare hands. While doing so, she injured her finger on a spine of the starfish, and within several minutes realized that her injury was serious. After writing “anaphylaxis” on her water board and ascending to the surface by herself, she was able to ask her co-worker on the boat for assistance before losing consciousness while gripping the ladder of the boat. Although she was immediately transported to the hospital, she died 13 h after the injury.

Review of her medical history revealed that she had no medical history of other allergic diseases such as bronchial asthma and had previously been stung 5 times by a crown-of-thorns starfish. After experiencing the most recent sting prior to the fatal sting, she had sought medical treatment including anti-allergic medication at a hospital to treat facial swelling and redness.

A medico-legal autopsy performed 28 h after her death revealed that her height and weight were 160 cm and 55 kg, respectively, and that she had been experiencing severe edema of the skin and conjunctiva of the face to the extent that the bulbar conjunctiva had become slightly jaundiced. A crown-of-thorns starfish sting on the top of the right middle finger had resulted in severe swelling and discoloration of the finger (Fig. 2), right-upper-extremity swelling, and hemoglobin permeation along blood vessels on the forearm and hand (Fig. 3). Examination of the respiratory system revealed severe edema of the laryngopharynx, which had caused the airway to narrow (Fig. 4); severe edema and congestion of the lungs, which both weighed 405/420 g; and the accumulation of a large amount of pleural effusion and ascites fluid. No congenital

abnormality of the heart, which weighed 290 g, was detected, nor was either stenosis of the coronary artery or ischemic lesion on the myocardium. Macroscopic examination of the liver revealed it to be 1400 g in weight, soft, and swollen, as well as blurring of the borders around the hepatic lobules. Microscopic examination revealed diffuse hepatocellular necrosis throughout the parenchyma and lobuli, sinusoidal dilatation caused by congestion, bile plugs in the canaliculi, and eosinophilic cytoplasm with pyknotic nuclei (Fig. 5). Microscopic examination of the lungs revealed not only alveolar hemorrhage and eosinophilic infiltration but also extensive neutrophil and eosinophil aggregation in the intravascular lumen, with the great extent of eosinophil aggregation

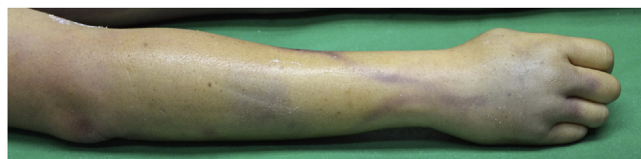


Fig. 3. Hemoglobin permeation along the blood vessel on the right forearm and hand.



Fig. 2. A sting on the top of right middle finger.



Fig. 4. Severe edema of the laryngopharynx caused the airway to narrow.

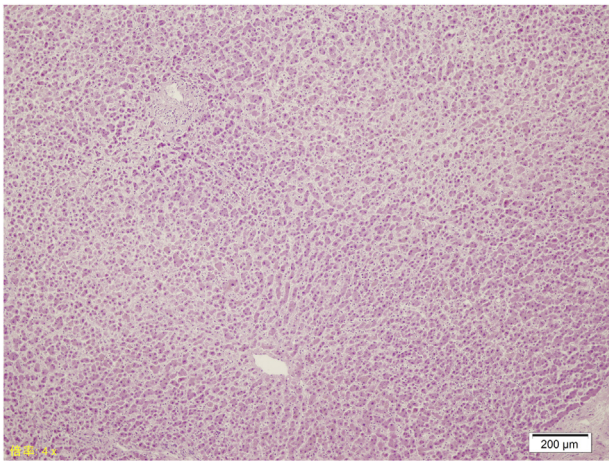


Fig. 5. Distribution of diffuse hepatocellular necrosis can be observed throughout the parenchyma ($\times 200$, hematoxylin-eosin).

around the bronchus and the extensive infiltration of the alveolus particularly notable.

Laboratory examination on admission and autopsy revealed severe hemolysis, hemoconcentration, and abnormal hemostasis (Table 1). Extremely high levels of liver transaminases including aspartate transaminase, alanine aminotransferase, and lactate dehydrogenase indicated severe liver damage from the early stage after injury. Levels of tryptase, histamine, and non-specific IgE in the autopsy sample were also abnormal at 6.7 µg/mL (normal <13.5 mg/mL), 1030 ng/mL (normal, 0.15–1.23 ng/mL), and 95.6 IU/mL (normal <170 IU/mL), respectively. Ethanol was not detected in the blood, and the results of drug testing using a drug-abuse screening kit (Triage®) were negative.

3. Discussion

The crown-of-thorns starfish, *Acanthaster planci*, is the second largest sea star on earth. Reaching a diameter up to 60 cm, the adult crown-of-thorns starfish is a carnivorous predator that typically preys on reef coral polyps [1]. The upper surface of this marine animal contains numerous sharp spines approximately 2–3 cm in length covered with a thin skin containing 2 types of glands that produce venom and mucus (Fig. 1(B)). Most injuries due to contact with crown-of-thorns starfish are the results of accidents, such as those that occur when divers or swimmers step on the starfish or marine volunteers make injurious contact with the spines during attempts at extermination [2]. According to the Okinawa Prefectural Institute of Health and Environment, 91 victims, including 37 divers and 24 swimmers, were reported to have

been injured by contact with the spines of crown-of-thorns starfish between 1998 and 2011 in Okinawa prefecture [4].

Stinging by the crown-of-thorns starfish may have serious consequences, resulting in not only severe topical pain and swelling but also serious systemic reactions, including hemolysis, liver damage, and, although rare, potentially lethal anaphylaxis [1,2]. Due to these risks, extermination of infestations of crown-of-thorn starfish has become a very important task for not only maintenance of the marine environment but also protection of the tourism industry. As the incidence of abnormal infestation of crown-of-thorns starfish in major diving spots has increased, the opportunity for human contact with them has increased accordingly, resulting in an increasing number of reports of stinging and injuries [2]. In the case described here, the victim had been stung on the right middle finger while attempting to kill a crown-of-thorn starfish with her bare hands, as manifested by a sting wound on the right middle finger and severe swelling and discoloration of the upper-right extremity. Although the spine of the crown-of-thorn starfish had not been left in the sting wound, only contact with a spine could have resulted in her injury.

The venom of crown-of-thorns starfish exerts various biological activities, including hepatotoxic, hemolytic, capillary permeability-increasing, and histamine-releasing activity from mast cells [3]. The lethal components of the venom have been identified as plancitoxin I/II, which are slow-acting hepatotoxic factors [2,3]. In the case described here, elevation of liver transaminase levels was noted at hospitalization, and diffuse hepatocellular necrosis was observed on microscopic examination of the liver. As no necrosis was observed on any internal organs other than the liver, the severe liver damage could only have been caused by hepatotoxicity induced by injection of crown-of-thorns starfish venom. Extrapolating from the LD₅₀ of plancitoxin I/II for mice, which is 0.17 mg/kg [5], the LD₅₀ for a human weighing 55 kg is 9.35 mg. However, Shiomi [3] reported that only 3 mg and 0.04 mg of plancitoxin I and II can be extracted from 100 g of adult crown-of-thorns starfish spines, respectively, as the amount of plancitoxin I and II contained in a spine that weighs about 10 g is only 0.3 and 0.004 mg, respectively. Moreover, we argue that in cases of accidental stinging, the lethal components of the venom cannot reach levels fatal to humans, even if all the venom from a spine is injected. Furthermore, as it is known that the lethal components induce hepatotoxicity very slowly, having been reported to occur in mice between 72 and 96 h at LD₅₀ doses [5], we argue that induction of hepatotoxicity by the venom could not have resulted in the victim's cardiopulmonary arrest within several minutes of stinging. Based on our arguments, we hypothesize that her death was not directly due to induction of hepatotoxicity by the lethal factors contained in the venom of the crown-of-thorns starfish spine. Based on review of her medical history and autopsy findings, we instead propose that she died from induction of anaphylactic

Table 1
Results of laboratory examination on hospital admission and autopsy.

Data on hospital admission							
WBC	16,600 μ L	Seg	41.0%	Na	148 mEq/L	AST	285 U/L
RBC	494×10^4 μ L	Lym	48.0%	K	7.0 mEq/L	ALT	201 U/L
Hb	16.0 g/dL	Stab	6.0%	Cl	111 mEq/L	LDH	828 U/L
Ht	51.3%	Monocyte	3.0%	Ca	9.7 mEq/L	ALP	327 U/L
Plt	34.4×10^4 μ L	Eosinophil	2.0%	Mg	2.5 mEq/L	γ -GTP	53 U/L
CRP	<0.05 mg/dL			BUN	8.1 mg/dL	CPK	350 U/L
PT	18.2 sec			Cr	0.8 mg/dL	T-bil	0.3 mg/dL
PT(%)	43.6%					D-bil	0.1 mg/dL
APTT	54.7 sec						
Histamine							1030 ng/mL
Tryptase							6.7 μ g/mL
Ig E							95.6 IU/mL

shock by injection of crown-of-thorns starfish venom. Our hypothesis is supported by the fact that she had written “anaphylaxis” at the scene, perhaps because she had felt the same symptoms that she had experienced after a sting 3 months prior.

Anaphylaxis is a serious, potentially fatal systemic allergic reaction that occurs immediately after contact with an allergy-causing substance [6]. The venom injected during stinging by insects, such as bees and ants, is a very common allergy-causing substance, as evidenced by the attribution of 79 fatalities per year to sting by hymenoptera in the United States [7]. Although the venom of the crown-of-thorns starfish contains foreign substances with the potential to induce anaphylaxis, to our knowledge, no case of anaphylaxis has been directly attributed to stinging by crown-of-thorns starfish. Such lack of reporting may be due to the relative rarity of stinging by crown-of-thorns starfish compared to that by bees and ants. Postmortem diagnosis of anaphylaxis is very difficult and most often performed by exclusion, as evidenced by the paucity of autopsy findings suggesting anaphylactic death [8]. Previous reports have shown that while measurement of postmortem histamine level in blood is not useful for diagnosis of anaphylaxis because of histamine release from other cells, especially basophils, during sample processing, measurement of tryptase level may be useful [8,9]. However, because of the short $T_{1/2}$ of tryptase, approximately 2 h, measurement of tryptase level was not useful in diagnosis of anaphylactic shock in the present case [9].

Symptoms suggesting allergic reaction, generally erythematous skin rash and edema, laryngeal edema, mucous plugging in the airways, and eosinophilia infiltration in the mucosa and submucosa of the respiratory tract, have been observed in a limited number of anaphylactic deaths [10]. While acknowledging that several symptoms might have been enhanced by 13 h of intensive medical care, including transfusion, several symptoms suggesting anaphylaxis, including skin, laryngopharynx, and lung edema and lung congestion were observed in this case. This observation, as well as the fact that there is no other plausible cause, led us to hypothesize that her cardiopulmonary arrest had been caused by anaphylactic shock induced by injection of venom by the crown-of-thorns starfish.

As this case demonstrates, avoidance of contact with the crown-of-thorns starfish is important to avoid injury. Divers and swimmer should thus always wear gloves and boots to avoid accidental contact with dangerous marine animals including crown-of-thorns starfish. In the event of stinging, first-aid treatment is removal of the spine as soon as possible and warming of the lesion to relieve

local severe pain [1]. However, most cases of anaphylaxis, including those resulting in death, occur suddenly in unexpected situations. As, according to previous reports [6], the median time from stinging to cardiac arrest in fatal cases attributed to anaphylactic shock is 15 min, preparation for and diagnosis of anaphylaxis are essential for saving lives. In patients with a history or those who face the risk of anaphylactic reactions, such as the patient in this case, preparation for anaphylaxis includes preparation of adrenaline for auto-injection, which can significantly increase chances of survival if performed within 30 min of stinging [6]. To ensure that such preparation is possible, since September in 2011, authorized doctors in Japan have been permitted to prophylactically prescribe adrenaline for auto-injection to patients with a history of anaphylaxis. We believe that such an enlightened understanding of prevention and appropriate response to current conditions is important.

Acknowledgment

We would like to special thanks Mr. Yamagata, Japan Coast Guard, 11th Regional Coast Guard Headquarters, for beautiful pictures of crown-of-thorn starfish.

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