**BRIEF COMMUNICATION**

# *Carybdea marsupialis* (Cubozoa) in the Mediterranean Sea: The first case of a sting causing cutaneous and systemic manifestations

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**Running title:** Systemic manifestations due to a *Carybdea marsupialis* sting

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Código de campo cambiado

**Abstract**

A woman stung by the box jellyfish *Carybdea marsupialis* (Cnidaria, Cubozoa) at a Spanish Mediterranean beach, showed systemic manifestations over several months (pain far from the inoculation point, arthralgia, paresthesia, hyperesthesia, increase of eosinophils and IgE ) in addition to the skin condition.

*Carybdea marsupialis* (Linnaeus, 1758) is the only box jellyfish found in the Mediterranean where it is occasionally observed in low densities. However, since 1980 high-density populations have been detected in the Adriatic Sea [1]. Since summer 2008, first aid services in Denia beaches recorded high numbers of stung people (year 2008: 3330 stung people; 2009: 3350; 2010: 1348; 2011: 2316 ; 2012: 3040; 2013: 1872). Those stings were mainly due to *C. marsupialis*. The density of *C. marsupialis* has been high since summer 2008[2] (at ~1m depth, mean density ~5 indvs 100 $m^{-2}$ with punctual maximums of more than 200 adult indvs 100 $m^{-2}$). The adult phase of *C. marsupialis* coincides with the summer months and thus the probability of this jellyfish stinging swimmers increases. Adults have an umbrella height of around 4 cm, and its shape resembles an “ice cube” with only four fine tentacles of between 5 and 15 cm .
The effects of the *C.marsupialis* sting on humans were described in the Adriatic in 1992[3], and 1997[4] where only dermatitis was described on patients. Here we present the first case of a *Carybdea marsupialis* sting that resulted in cutaneous and systemic manifestations.

**Case Report**

A 37-year-old Spanish Caucasian woman was accidentally stung by a jellyfish later identified with no doubt as *Carybdea marsupialis*. She was on holiday and while swimming at midday on 10 August 2012 at Les Marines beach in Denia (Spain) (38°51'29.73"N, 0° 4'17.44"E). The water depth was 0.8-1 m and the patient felt two stings simultaneously, one on the left side of her abdomen and one on her right thigh. The sting was not painful and no treatment was applied, but that night her toes swelled

up and became sore and itchy. The following day she observed the appearance of blisters on the contact area (Fig. 1). A topical treatment with a cream containing methylprednisolone was applied, leading to a slow and progressive improvement in the skin sores, which took 20 days to heal without skin sequelae.

Seven to ten days after the sting she developed arthralgia and paresthesia in her hands. The pain was intense and occasionally prevented her from sleeping. On other occasions, the pain woke her up and she found it difficult to move her hands, with hyperesthesia and cramps. She was treated with ibuprofen, without any clinical response.

The second set of symptoms appeared 20 days after the sting, when her inner right forearm around her elbow began to swell accompanied by a sensation of intense heat and burning. When touching the area, it was swollen but not painful. After 4-5 days similar swelling appeared on her right shoulder.

One month after the sting neither the pain nor the loss of strength in her hands had ceased. The paresthesia and the hyperesthesia prevented her from sleeping properly. As the symptoms persisted she visited a doctor, who took radiographies of her cervical spine and upper extremities, and an did an electromyography, and both were normal. The doctor also performed general analyses, which revealed a high degree of eosinophils (632 cells $\mu L^{-1}$) as the only significant finding. The patient continued treatment with non-steroidal anti-inflammatory drugs.

Two months after the sting the neurological symptoms as well as the articular and cutaneous manifestations were progressively decreasing, although she occasionally had macules and papules again on both her hands and abdomen (Fig. 2). The patient was sent to the Clinical Toxicology Unit of the Hospital Clinic de Barcelona where her immunological status was assessed. The assessment showed an increase in IgE (558 kU $L^{-1}$, reference value <100 kU $L^{-1}$) and an allergy to *Anisakis* (0.76 kU $L^{-1}$, reference

value < 0.35) and prawns (0.57 kU $L^{-1}$, reference value <0.35). The patient was advised to avoid these items because she had been found to be hypersensitive to them. Her clinical manifestations progressively improved.

**Discussion**

Purified venom of *C. marsupialis* from the Adriatic Sea[5] produced hemolytic activity in sheep red blood cells, but not in human or rabbit cells. The toxin was also heat labile and inactivated by proteases. Studies in the Caribbean[7] found a novel neurotoxin and three cytolysins with extremely powerful haemolytic activity on human red blood cells. These differences in toxicity between the two studies could be due to methodology or geographic differences or even because different species were used[6].

The systemic symptoms shown by our patient have been reported for other Cubozoan species but never for the Mediterranean *C. marsupialis*. In the Adriatic, symptoms of 41 patients were described as non-serious and of local toxicity[3,4] and after two weeks all symptoms had disappeared (swelling, soreness and burning sensation), but seven patients showed red-violet scars and one developed a keloid scar probably due to the use of ammonia. Symptoms were defined as irritant rather than allergic because none of the patients had ever had any previous contact with the jellyfish.

Arthralgias and paresthesias have been associated with *Chinorex fleckeri* (Fam. Chirodropidae) stings in Australia, and a few times with *Carybdea alata* (Fam. Carybdeidae) in Hawaii[7]. Hyperesthesia was described in a patient after a cubozoan sting, probably *Chinorex fleckeri* or *Carybdea sp.*[8] in Papua New Guinea. *C. alata* in Hawaii has produced paresthesia and cramps[9]. A high number of eosinophils have been

described after a sting of an unknown jellyfish in the Red Sea[10], probably a cubozoan due to the linear scar with small spots.

Considering the high IgE values in our patient several months after the sting, we believe that her clinical manifestations could be due to an allergic hypersensitivity to the cubozoan venom, although we cannot rule out the allergy to *Anisakis* and prawns. The patient did not have a personal or family history of atopy, bronchial asthma or allergies to medication, and she had never associated these clinical manifestations to food intake. The case presented here is the first one in which, after a *Carybdea marsupialis* sting, the patient showed a systemic reaction following the skin condition that lasted for months. This marks a turning point in terms of the toxicity of this species for humans. Beach managers should take the presence of this species in swimming areas seriously, particularly because the adult medusae are active swimmers that choose their habitat and do not simply drift with the current like other jellyfish (Scypozoa). If a high density of *C. marsupialis* adults is detected, the competent health and environmental authorities should take measures to reduce the risk of contact.

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200 **Figure legends**

201 **Figure 1** Erythematous lesions and blisters on the left side of the patient's abdomen 24
202 hours after the sting.

203 **Figure 2** Areas with edema and erythema on the abdominal region two months after
204 the sting.

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