Severity of Irukandji syndrome and nematocyst identification from skin scrapings

Truc T Huynh, Jamie Seymour, Peter Pereira, Richard Mulcahy, Paul Cullen, Teresa Carrette and Mark Little

ABSTRACT

Objectives: (1) To identify the causative jellyfish species by examining skin scrapings in patients presenting to Cairns Base Hospital with marine stings, and (2) to describe clinical outcomes of those with Irukandji syndrome and those in whom nematocysts were identified from skin scrapings.

Design and setting: (1) A retrospective case series of 128 patients, identified from Cairns Base Hospital emergency department records with discharge diagnoses of marine stings between 1 July 2001 and 30 June 2002. (2) A prospective study of skin scrapings from 50 patients presenting with marine stings from the same period.

Main outcome measures: Number of patients with Irukandji syndrome, their opioid requirements and cardiac findings (where available); identification of causative species from nematocysts isolated from skin scrapings.

Results: 116 patients retrospectively identified with marine stings had Irukandji syndrome. Of 50 patients who had skin scrapings, 39 had nematocysts consistent with *Carukia barnesi.* Symptoms experienced ranged from local pain alone to severe Irukandji syndrome with elevated troponin I levels, changes on electrocardiogram, cardiac dysfunction on echocardiography, and high opioid dose requirements. One patient had an unidentified cnidome on his skin scraping. He developed severe Irukandji syndrome and subsequently died from its complications.

Conclusion: This is the first published report of *Carukia barnesi* being successfully identified from skin scrapings. Most patients with identifiable cnidomes experiencing Irukandji syndrome were stung by *Carukia barnesi*, which we show causes a wide range of illness, including cardiac dysfunction. Our finding of a cnidome not consistent with *Carukia barnesi* in the setting of Irukandji syndrome makes it possible that other species of jellyfish may also cause this syndrome.

MJA 2003; 178: 38–41

JELLYFISH STINGS in northern Australia cause significant morbidity and mortality. Since early descriptions of Irukandji syndrome,[1,2] relatively little further knowledge has been gained about it. Although *Carukia barnesi* has been shown to cause the syndrome,[3] other species of jellyfish are also suspected to be responsible.[3-7]

We hypothesise, firstly, that many different cubozoans may produce Irukandji syndrome in Cairns, and secondly, that these different species of jellyfish may be responsible for different severities of this syndrome.

METHODS

Retrospective case series

All patients with a discharge diagnosis of "marine stings" (ICD-10 code T63.6)[8] after presenting to Cairns Base Hospital, Queensland, between 1 July 2001 and 30 June 2002 were retrospectively identified from the emergency department computer database, and epidemiological and clinical data were extracted and entered on a standardised form. Details collected included geographic location of sting, physiological parameters, analgesia required, biochemical abnormalities, electrocardiographic and echocardiographic findings.

We assessed the clinical severity of each patient's condition at presentation according to peak systolic blood pressure, total opioid dose administered, peak troponin I level, and length of hospital stay. As individual patients received either morphine, pethidine or fentanyl according to clinician preference, we arbitrarily converted their opioid dose to "morphine equivalents" (where 1 mg morphine = 10 mg pethidine = 10 μg fentanyl) to give a rough comparison of analgesic requirements between patients.

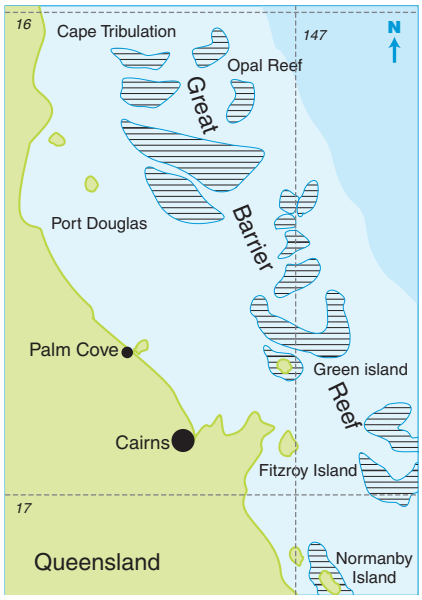
Prospective case series

Patients presenting with marine stings during this period were treated according to emergency department protocols, and additionally had skin scrapings of their sting site performed. Exceptions were distressed children, patients with stings to the face, women with stings to the breast region, and patients in whom an obvious sting site could not be identified; these patients did not have skin scrapings performed.

The sampling procedure was explained to patients and verbal consent was obtained. The sting site was scraped firmly with a sterile scalpel blade, which was then placed in a sterile specimen container containing 10% buffered formalin. The scalpel was shaken vigorously in the specimen container to cause adherent scrapings to fall off. The specimen was then centrifuged at 5000 revolutions per minute for 10 minutes, stained with eosin and distrib-

Emergency Department, Cairns Base Hospital, Cairns, QLD.
Truc T Huynh, MB BS, Emergency Registrar; **Peter Pereira,** FACEM, Director of Emergency; **Richard Mulcahy,** FACEM, Emergency Consultant; **Paul Cullen,** FACEM, Emergency Consultant.
School of Tropical Biology, James Cook University, Smithfield, QLD.
Jamie Seymour, PhD, Senior Lecturer; **Teresa Carrette,** BSc, Marine scientist.
Emergency Department, Sir Charles Gairdner Hospital, Perth, WA.
Mark Little, FACEM, Emergency Consultant.
Reprints will not be available from the authors. Correspondence: Dr Peter Pereira, Emergency Department, Cairns Base Hospital, PO Box 902, Cairns, QLD 4870. Peter_Pereira@health.qld.gov.au

1: Map showing the coastline, islands and reef where patients were stung



uted onto a Kova slide for microscopic examination.

Specimens were prepared and examined by one of the authors (J S), who was blinded to the source. Identification of jellyfish species was based on a cnidome database (a cnidome is a collection of nematocysts used to distinguish between species of jellyfish) being formulated by the examiner and due for publication in 2003.

The results of the species identification was then matched to the clinical data.

RESULTS

From 1 July 2001 to 30 June 2002, 128 patients at the Cairns Base Hospital emergency department had a discharge diagnosis of marine stings. Of these, 116 had symptoms consistent with Irukandji syndrome. Sixty-seven of the 116 patients (58%) were male and their average age was 26.5 years (range, 3–63 years).

Of the 116 patients with Irukandji syndrome, 89 (7%) were stung along the shore, 26 (22%) were stung offshore (Great Barrier Reef and islands; see Box 1), and one patient did not have the location recorded.

General clinical findings

Peak systolic blood pressure in the 94 adults with Irukandji syndrome ranged from 100 mmHg to 230 mmHg, with a mean of 145 mmHg. Nineteen of the 22 children had their blood pressures recorded. Seven had a systolic blood pressure 140 mmHg or above; the highest of these was 165/95 mmHg in a 12-year-old child.

Total analgesic requirements for adults during their hospital stay ranged from 0 to 255 mg of morphine equivalents (mean, 31 mg). Of the 10 children who had their weight recorded, analgesic dose ranged from 0 to 1.4 mg per kg morphine equivalents (mean, 0.29 mg per kg).

Cardiac findings

Troponin levels (cTnI) were measured in 103 patients whose pain did not settle with a single dose of parenteral opioid analgesia. Twenty five (22%) had elevated cTnI levels, ranging from 1.0 to 34.0 μg/L (reference range, < 0.7 μg/L). None of these patients had clinical or chest x-ray findings of pulmonary oedema. Eleven patients had non-specific electrocardiogram (ECG) abnormalities, most involving T-wave inversion and ST-segment depression. Echocardiograms were performed in 18 of the 25 patients with elevated cTnI levels, and abnormalities were found in six. Echocardiographic abnormalities ranged from mild impairment of systolic function to moderate dysfunction with segmental hypokinesis. One patient had global myocardial dysfunction. Two patients had serial echocardiographic studies showing normalisation of their systolic function over time (one within three months and the other over six months).

Among the 91 remaining patients only one had an abnormal ECG. He was a previously well 33-year-old man who developed paroxysmal atrial fibrillation (which resolved spontaneously over several hours); his echocardiogram was normal.

Hospital admissions

Average length of admission was 1.6 days and the longest was five days. Forty-two patients (36%) were discharged home directly from the emergency department within eight hours of presentation. Fifty-four patients (47%) were discharged from the emergency department observation ward the next day, eight were transferred to the coronary care unit (CCU), and 11 were transferred to the general medical or paediatric ward for ongoing analgesia. Additionally, one patient was transferred to the intensive care unit in Townsville General Hospital for neurosurgical care for an intracerebral haemorrhage.

Skin scrapings

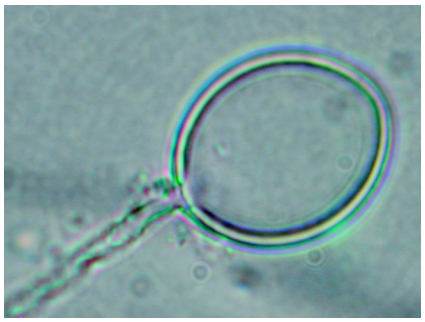
Skin scrapings were taken from 50 patients. Of these, four patients had local symptoms only, and the remainder had symptoms consistent with Irukandji syndrome. Forty patients (80%) had positive scrapings, while, in the remainder, either no nematocysts were found or the nematocysts were too damaged to be confidently identified (positive predictive value of 80%). Thirty-nine patients had a nematocyst cnidome identifiable as *Carukia barnesi*; two of these experienced only a mild sting at the site, and 37 had Irukandji syndrome. Of these 39 patients, 13 had a raised cTnI level; five of these had abnormal echocardiograms and seven had abnormal ECGs. Thirty-one patients with *Carukia barnesi* identified on skin scrapings (79%) were stung at local mainland beaches. The rest were stung at Fitzroy Island (4), Green Island (1), and Normanby Island (1) (see Box 1).

The patient with the most severe symptoms who had *Carukia barnesi* identified from skin scrapings was a 44-year-old man with a peak blood pressure of 160/100 mmHg and peak cTnI level of 30.8 μg/L, who required a total morphine equivalent dose of 255 mg over five days. He had widespread T-wave inversion and ST-segment depression on his ECG. His echocardiogram showed severe left ventricular dysfunction and anteroseptal hypokinesis, with an ejection fraction of 30%–35%. Six months later his echocardiogram was completely normal.

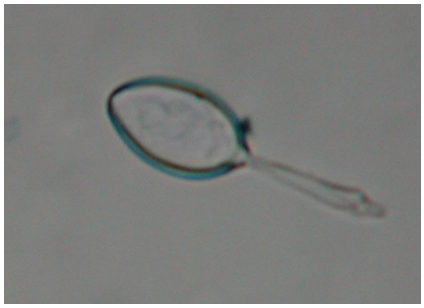
One 44-year-old man had an unidentified cnidome on skin scraping, which

2: Nematocysts from *Carukia barnesi* compared with unidentified nematocysts from a fatal envenomation

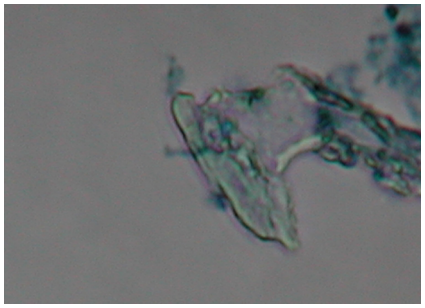
A: Discharged nematocyst from the tentacle of Carukia barnesi.



B: Discharged nematocyst from the bell of Carukia barnesi.



C: Discharged nematocyst from unidentified species of jellyfish (similar morphology to [A]).



D: Cigar-shaped nematocyst from unidentified species of jellyfish.

is of concern, as he was one of two patients reported to have died from Irukandji syndrome (the other having occurred in the Whitsundays).[9] Although some of the nematocysts identified were similar to those from *Carukia barnesi*, a morphologically different additional nematocyst was also present (Box 2). It is possible that this nematocyst was a "rogue" mastigmophore, and hence may be an incidental finding from another source. Alternatively, the cnidome may represent an unidentified jellyfish. The patient was stung at Opal Reef (see Box 1), had a peak blood pressure of 230/90 mmHg, peak cTnI level of 34 μg/L, and required 30 mg of morphine equivalents before being intubated for a depressed level of consciousness from an intracerebral haemorrhage.

DISCUSSION

In recent years a number of serious envenomations causing Irukandji syndrome have been described,[6,10-13] all associated with cardiac failure and pulmonary oedema. However, it has been observed that most stings in the Cairns region are, in fact, mild, without serious complications, and do not require admission to hospital.[4] Our study confirms this, as most patients were discharged within 24 hours of presentation.

Surprisingly, myocardial damage, as measured by an elevated cTnI level, was seen in 25 patients (22%) experiencing Irukandji syndrome. Six of these patients had echocardiographic evidence of myocardial dysfunction. It is evident that those with continuing pain and analgesic requirements are at risk of cardiac complications. Clinicians should therefore consider closely monitoring these patients with serial cTnI level measurements, and, if these are abnormal, consider echocardiographic evaluation.

Skin-scraping methods have been described for a number of jellyfish species,[14-17] but, to date, there are no published data on successful identification of *Carukia barnesi* nematocysts in patients with Irukandji syndrome. While acknowledging some limitations, it is reasonable in this setting to equate the species identified through cnidome assessment with causation. Therefore, we can, with reasonable confidence, assert that *Carukia barnesi* was causative in 39 patients. We can also deduce that envenomation by this species produces a wide range in severity of illness, and that it was the only identifiable causative cuboidal jellyfish in patients stung on the Cairns beaches. We can less confidently claim that a single victim may have been stung by an unknown species of box jellyfish, ultimately leading to his death. The cnidome in this case was similar to, but with distinct differences from that of, *Carukia barnesi* (Box 2). We acknowledge that *Carukia barnesi* may have been causative in this instance, as the mastigophore isolated from this patient may have been an incidental finding. A further possibility is that the *Carukia barnesi* cnidome may change to include mastigophores as the animal ages or grows (as is seen with *Chironex fleckeri*). We are ignorant of the life cycle of *Carukia barnesi,* and therefore can only speculate.

There are obvious serious implications if the cnidome is that of an unidentified cuboidal jellyfish. It has long been suspected that jellyfish species other than *Carukia barnesi* can cause Irukandji syndrome.[3-7] Case reports include a patient with severe Irukandji syndrome in whom a 2 mm length of tentacle not from *Carukia barnesi* was found in a skin scraping of the sting site,[6] and where tentacles isolated resembled, but were distinctly different from, those of *Carukia barnesi*.[7] Our results provide further supportive evidence that species other than *Carukia barnesi* may be linked to Irukandji syndrome.

Interestingly, two patients with cnidomes consistent with *Carukia barnesi* did not develop Irukandji syndrome. These patients had mild local symptoms only. Thus, a sting by *Carukia barnesi* does not necessarily result in Irukandji syndrome. Factors affecting venom load, such as thickness of the keratinised skin, presence of hair, length of tentacle involved, duration and pressure of the contact between tentacle and skin have been proposed by other authors.[3,17]

As only a single cnidome suggestive of a different jellyfish species was found, we can make no statistical inferences about the severity of Irukandji syndrome and the jellyfish species identified from skin scrapings. Additionally, patients were not randomly selected in terms of whether or not they would have skin scrapings performed. Thus, it is possible that more seriously affected patients would have attracted more interest and were more likely to have skin scrapings performed.

Our interpretation of these findings is based on a number of assumptions. Our conversion of "equivalent doses" of narcotics has not taken into account the differences in their duration of action. Finally, we have assumed that jellyfish (indicated by their cnidome) caused the patients' symptoms.

In conclusion, we can infer that, in patients with Irukandji syndrome, the causative jellyfish can usually be successfully identified from skin scrapings on the basis of known cnidomes. Most patients with Irukandji syndrome in the Cairns region were stung by *Carukia barnesi*, which has now been shown to cause illness ranging from local symptoms to severe Irukandji syndrome with cardiac dysfunction. Our finding of a cnidome that was not that of *Carukia barnesi* suggests that other species of jellyfish may cause Irukandji syndrome.

COMPETING INTERESTS

None identified

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(Received 23 Sep 2002, accepted 1 Nov 2002) ❑

book review

Stoking the fires of drug controversy

Modernising Australia's drug policy. Alex D Wodak and Timothy Moore. Sydney: UNSW Press, 2002 (103pp, $19.95). ISBN 0 86840 482 9.

THE DISCUSSION OF ILLICIT drugs policy is littered with controversy, stoked by strong feelings on both sides and full of assertions that fundamental morality is at stake. Those who support prohibition and have a clear view of law enforcement as the answer need not read this book, as they will find little to relate to.

The authors have a long record of challenging the current international philosophy of prohibition, stemming as it does from the muscular nationalism of Teddy Roosevelt, who convened the Shanghai Conference in 1909. That policy has been honed and developed with US leadership in successive international treaties of 1912, 1926, 1961, 1971 and 1988. Richard Nixon's invention of the politically potent "War on Drugs" in 1972 is given attention in its Australian incarnation "Tough on Drugs". The book is readable, rather than scholarly, and tells of the folly of this ideological commitment in terms of failed outcomes. Its assertions are not referenced, but the authors speak from a position of authority after years of contributing to the debate. It is an easy read.

The book urges the separation of cannabis markets from heroin and cocaine, but is critical of half-hearted decriminalisation when legalisation, with regulation, taxation and health advice about cannabis, would be far more appropriate. The rationale is compelling. It argues clearly that the major problems for society from illicit drugs — crime, corruption, disease and overdose deaths — are primarily the consequences of prohibition rather than the drugs.

Misleading advocacy and misuse of naltrexone are well discussed. There is little coverage of cocaine and amphetamines. Although occasionally repetitive, it is worthwhile reading for all concerned citizens, including politicians, medical practitioners and parents. It is good value as a paperback entry to a difficult area of public policy.

David G Penington
Emeritus Professor, and Past Chairman
Victorian Premier's Drug Advisory Council
Melbourne, VIC