Contents lists available at ScienceDirect

Toxicon: X

journal homepage: www.journals.elsevier.com/toxicon-x

Rhabdomyolysis due to unidentified jellyfish envenomation in west Malaysian waters

Jia Shyi Loy^a, Chyi Chyi Khoo^a, Tilagavahti Arumugam^a, Geok Hoon Ngian^a, Ahmad Khaldun Ismail^{b, c,*}

^a Pediatric Department, Sultanah Fatimah Specialist Hospital, Muar, Johore, Malaysia

^b Department of Emergency Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Bandar Tun Razak, Kuala Lumpur, Malaysia

^c Hospital Canselor Tuanku Muhriz, Jalan Yaacob Latif, Bandar Tun Razak, Kuala Lumpur, Malaysia

ARTICLE INFO

Handling Editor: Dr. Denise Tambourgi

Keywords: Clinical toxinology Emergency Myotoxicity Pediatric envenomation

ABSTRACT

Jellyfish envenomation is a common marine injury. We report a case of a 9-year-old boy who developed muscle weakness and rhabdomyolysis after a jellyfish sting. He was stung on the face, hands, and feet. He sustained immediate pain and numbness; however no immediate action was taken. He was taken to a primary health clinic and discharged with syrup Paracetamol 15mg/kg/dose and syrup Chlorpheniramine maleate 0.1mg/kg/dose for symptomatic relief. Over the next several days, the pain became generalized involving upper and lower limbs, aggravated by movement, and not alleviated by analgesia nor antihistamine. His condition worsened with the development of weakness of upper and lower limbs and 'tea-colored' urine from day 3 of illness. He received treatment for rhabdomyolysis at a district hospital. Maintaining hydration and urine output and symptomatic relief are central to treatment. His muscle pain and weakness improved. He was discharged well and remained asymptomatic at follow up.

1. Introduction

Jellyfish are commonly found in Malaysian waters. Harmful jellyfish sting can be caused by Scyphozoan, Cubozoan and Hydrozoan. A study by Low mentioned nine scyphozoan jellyfish species found in peninsular Malaysia: *Chrysaora chinensis, Cyanea sp., Versuriga anadyomene, Rhopilema hispidum, Rhopilema esculentum, Phyllorhiza punctate, Acromitus flagellates, Lobonemoides robustus and Lychnorhiza malaynesis* (Low, 2017). Jellyfish in the Cubozoan family includes *Morbakka* sp and *Chiropsoides buitendijki* (Tan et al., 2019) There were also reports of box jellyfish belonging to the multi-tentacled *Chironex* species in Langkawi and Manjung. Stinging Hydrozoan found in Malaysian waters includes *Physalia physalis and Physalia utriculus* (Tan et al., 2019), however they are mainly confined to the east coast of peninsular Malaysia and East Malaysia. Currently there was no evidence of its presence in the Straits of Malacca.

Jellyfish sting is a commonest marine injury in Malaysia however, most cases are unidentified. There is inadequate documentation of harmful jellyfish species in Malaysian waters (Tan et al., 2019; Sivanasworn et al., 2023). A study at the west coast of Peninsular Malaysia showed that stings most often occur during clear weather, low average rainfall and high sea temperature (Mubarak et al., 2021). Common clinical features include immediate pain, rashes, headache, back pain, restlessness, profuse sweating, chest tightness, abdominal discomfort, vasospasm, hypertension, muscle cramps and nausea and vomiting (Sivanasworn et al., 2023; Mubarak et al., 2021; Mohd et al., 2016). There have been several deaths following multi-tentacled box jellyfish envenomation in Langkawi Island, Pangkor island and the coastal waters of Sabah. Rhabdomyolysis has been documented as a complication and may cause serious morbidity (Rengel et al., 2022). We present a case of rhabdomyolysis in a child stung by an unidentified jellyfish species in the west coast of peninsular Malaysia.

The characteristic and clinical features of a sting depend on the type of jellyfish. The sting may or may not result in significant signs and symptoms of envenomation. The severity also depends on the skin surface area in contact with the jellyfish. Most of the jellyfish stings in

https://doi.org/10.1016/j.toxcx.2023.100170

Received 21 September 2023; Received in revised form 10 October 2023; Accepted 11 October 2023 Available online 2 November 2023 2590-1210/© 2023 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC.

2590-1710/© 2023 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).



Case Report





^{*} Corresponding author.Department of Emergency Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latiff, Bandar Tun Razak, 56000 Kuala Lumpur, Malaysia

E-mail addresses: jiashyi.ljs@gmail.com (J.S. Loy), khoo_chyi@hotmail.com (C.C. Khoo), tilagavahti@gmail.com (T. Arumugam), geokhoonngian@yahoo.com (G.H. Ngian).

Malaysia cause local effects such as pain, swelling, skin lesions, blisters, and rashes (Sivanasworn et al., 2023; Mubarak et al., 2021; Tan et al., 2022; Lippmann et al., 2011). However, some may result in systemic envenomation such as hypertension, vasospasm, myonecrosis or cardiac arrhythmias. Serious complications may include secondary bacterial infection, neurological and cardiorespiratory manifestations (Sivanasworn et al., 2023; Lippmann et al., 2011). Rhabdomyolysis is a delayed and rare presentation following a jellyfish sting (Rengel et al., 2022; Li et al., 2022).

2. Case report

Table 1

A 9-year-old child without a past medical history presented to the Emergency Department of a general hospital with a complaint of generalized weakness and pain. He had been stung by an unidentified jellyfish species that he picked up at a beach in the Southern region of West Malaysia seven days prior to presentation. He was stung on the face, hands, and feet. He sustained immediate pain and numbness; however no immediate action was taken. The jellyfish was described as having bluish tinge color, two palm-sized with several tentacles. However, no pictures of the specimen were taken. He was taken to a primary health clinic and discharged with syrup Paracetamol 15 mg/kg/dose and syrup Chlorpheniramine maleate 0.1 mg/kg/dose for symptomatic relief. Over the next several days, the pain became generalized involving upper and lower limbs, aggravated by movement, and not alleviated by analgesia nor antihistamine. His condition worsened with the development of weakness of upper and lower limbs and 'tea-colored' urine from day 3 of illness. His appetite was reduced but he was able to tolerate orally fluids. He had no complaint of chest pain, abdominal pain, vomiting or diarrhea.

On arrival at the emergency department, he was conscious with Glasgow coma scale (GCS) of 15/15 and afebrile. He complained of generalized muscle pain with a pain score of 4/10, which worsened with movement. His initial vital signs were blood pressure 107/68 mmHg, heart rate 100 beats/min, SpO₂ 98 % (on air) and respiratory rate 24 breaths/min. Examination of the cardiovascular, respiratory, and abdominal systems were normal. He had bilateral upper and lower limbs weakness with reduced muscle power at 3/5. He had normal muscles tone and deep tendon reflexes with intact sensation.

Initial biochemical investigation showed significantly raised muscle and liver enzymes (Table 1). The first urine myoglobin result on day eight after the incident was markedly high, $113,000 \mu g/L$. Renal function remained normal throughout. His management was mainly pain

Laboratory investigation of the patient from admission until outpatient follow-up.

control with oral Paracetamol 6 hourly and oral Ibuprofen whenever his pain score is more than 3/10. He was kept on intravenous 0.9% saline maintenance for 8 days, with furosemide given to achieve a urine output of >2mL/Kg/H. A drop in the muscle enzyme values was observed on the second day of treatment (Table 1). Following adequate rehydration and bed rest, his muscle pain and weakness improved. The urine myoglobin repeated at seven days was reduced to 154 µg/L. He was discharged and was asymptomatic when reviewed at outpatient clinic after a month.

3. Discussion

This case involved a child who was presented with rhabdomyolysis seven days after an unidentified jellyfish sting involving a large area of the body including the face, hands, and feet. However, there were minimal skin lesions. Rengel et al. reported a young adult woman who presented with rhabdomyolysis at 12 h following an unidentified jellyfish sting on the hip and torso. Both patients complained of generalized myalgia and muscle weakness. The parents of the child noted dark color urine on day 3 post incident meanwhile, the adult patient had similar finding at presentation. Both patients presented with significantly raised creatine kinase (CK) and raised liver enzymes and received intravenous fluid rehydration for several days. The child was given intravenous furosemide for several days. The adult patient was given sodium bicarbonate. It appears that the CK values reduction rate was faster in the adult patient compared to the child. However, the delay in the normalization of CK may have been influenced by the physiotherapy which was introduced at day two of admission. As a result, the child had a longer length of stay in the hospital compared to the adult patient. Neither patient developed acute kidney injury.

It is still unknown which jellyfish species cause rhabdomyolysis. However, a recent study reported that jellyfish *Nemopilema nomurai* causes myotoxicity through the metalloprotease component of venom (Li et al., 2022). *Nemopilema nomurai* is a large rhizostome jellyfish, in the same size class as the lion's mane jellyfish *Cyanea capillata*, the largest cnidarian in the world. Neither species are present in the tropics. However, there are large jellyfish probably belonging to the genus *Cyanea* present in Malaysian waters. Another group of jellyfish that is frequently encountered in the west coast of peninsular Malaysia is *Chrysaora* species. These have been suggested to cause significant envenomation and probably have myotoxic venom (Rengel et al., 2022). Lie et al., 2022). The Portuguese man o' war, *Physalia physalis* is not known to be present in the west coast of peninsula Malaysia (Tan et al., 2019;

Investigation	Unit	Reference range	Days after jellyfish sting incident								
			7	8	9	10	11	12	14	16	32
White blood cell	X10	4–10	10.4	-	-	-	-	-	-	-	_
Haemoglobin	d/dL	13–17	13.1	-	-	-	-	-	-	-	-
Haematocrit	%	40–50	37.9	-	-	-	-	-	-	-	-
Platelet	X10	150-410	334	-	-	-	-	-	-	-	-
Urea	mmol/L	1.8-6.4	5.2	4.1	4.5	4.5	5.1	5.2	4.5	6.1	4.2
Creatinine	umol/L	23-68	29	24	23	17	16	17	19	21	27
Sodium	mmol/L	136-145	134	136	138	137	135	134	136	137	-
Potassium	mmol/L	3.5-5.1	5.2	4.1	4.7	4.3	4.3	4.1	4.0	4.4	_
Calcium	mmol/L	2.2 - 2.7	2.36	-	2.36	-	-	-	_	2.43	_
Phosphate	mmol/L	1.29-2.26	1.56	-	2.02	-	-	-	_	2.23	_
Magnesium	mmol/L	0.73-1.06	0.81	-	0.82	-	-	-	_	0.89	_
Albumin	g/L	35–52	37	34	-	-	31	-	37	37	_
Total protein	g/L	57-80	72	65	-	-	64	-	74	73	_
Bilirubin	umol/L	5-21	4	7	-	-	4	-	6	3	-
ALP	U/L	42-390	139	104	-	-	118	110	130	123	140
ALT	U/L	<50	621	552	-	-	994	1412	1224	884	35
CK	U/L	<171	71463	57687	65860	70396	83822	82329	51588	23533	99
LDH	U/L	<248	2688	2423	3278	3304	4291	4746	4334	2758	_
AST	U/L	<50	2493	1910	2361	2667	2707	2838	1994	907	34

ALP, alkaline phosphatase; ALT, alanine transaminase; CK, creatine kinase; LDH, lactate dehydrogenase; AST, aspartate aminotransferase.

Low, 2017).

Rhabdomyolysis can be caused by envenomation from venomous species, including jellyfish (Maldonado et al., 2017; Li et al., 2022; Rengel et al., 2022). Rhabdomyolysis is a result of damaged skeletal muscle. The release of intracellular contents into the extracellular circulation during muscle injury is responsible for the clinical manifestations. Presentation may vary from asymptomatic with isolated raised creatinine kinase (CK) levels to life-threatening conditions associated with acute kidney injury, electrolyte imbalance, compartment syndrome, hypovolemia, and coagulopathy (Elsayed and Reilly, 2010). It is important to closely monitor renal profile in order to detect serious complications such as renal tubular necrosis and renal ischemia (Mizuno, 2016).

The child in this case report received hydration and diuretic agent as the primary management for rhabdomyolysis. There was no development of acute kidney injury and the urine output was within normal rate throughout the hospital stay. Szugye HS reviewed the available literature for rhabdomyolysis in children and suggested the general approach that involves addressing the underlying cause, managing complications, and promoting recovery (Szugye, 2020). Maintaining good hydration is essential to prevent kidney damage and promote the elimination of muscle breakdown products. The rate of intravenous fluids administration can be adjusted based on the urine output. There are no urine output goals published for pediatric age groups, but one recommendation is to maintain at three to four times of normal output (Elsayed and Reilly, 2010; Szugye, 2020). Close serial monitoring for hyperkalemia, hyperphosphatemia, and hypocalcemia is recommended. Alkalinization of urine with sodium bicarbonate has been suggested to help prevent the formation of myoglobin casts and uric acid crystals in the renal tubules which may cause further damage (Mannix et al., 2006; Elsayed and Reilly, 2010; Szugye, 2020). While medications like mannitol and loop diuretics have been suggested for forced diuresis, the clinical evidence of these are still lacking (Mannix et al., 2006; Elsayed and Reilly, 2010; Rupert, 2002). In cases with acute kidney injury, prompt consultation with a nephrologist is important. Adequate rest is also essential to promote muscle recovery and avoid further damage.

Rhabdomyolysis is a rare complication of jellyfish envenomation. This case was probably due to myotoxic envenomation caused by an unidentified Scyphozoan jellyfish in the west coast of peninsula Malaysia. Investigation for rhabdomyolysis should be considered for patients with any features of myalgia, weakness, and dark colored urine. Timely and appropriate treatment is required to prevent acute kidney injury. As jellyfish envenomation is a common presentation in Malaysia, the public need to be aware of the potential dangers and should seek treatment and closely monitored in a medical facility.

Ethical statement

Written consent to publish this case report was taken from the guardian of the patient. This case report has obtained approval from the National Medical Research Register (NMRR), Ministry of Health Malaysia: NMRR ID-23-01672-XSC.

Source of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Jia Shyi Loy: Writing – original draft, Project administration, Formal analysis, Data curation. **Chyi Chyi Khoo:** Writing – original draft, Formal analysis, Data curation. **Tilagavahti Arumugam:** Writing – original draft, Formal analysis, Data curation. **Geok Hoon Ngian:** Writing – original draft, Supervision, Formal analysis, Data curation. **Ahmad Khaldun Ismail:** Writing – review & editing, Validation, Supervision, Formal analysis, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

Acknowledgments

The authors would like to thank Professor Colin Robertson (Edinburgh) for reviewing this manuscript.

References

- Elsayed, E.F., Reilly, R.F., 2010. Rhabdomyolysis: a review, with emphasis on the pediatric population. Pediatr. Nephrol. 25, 7–18.
- Li, A., Yu, H., Li, R., Yue, Y., Yu, C., Geng, H., Liu, S., Xing, R., Li, P., 2022. Jellyfish Nemopilema nomurai causes myotoxicity through the metalloprotease component of venom. Biomed. Pharmacother. 151, 113192. Jul 1.
- Lippmann, J.M., Fenner, P.J., Winkel, K., Gershwin, L.A., 2011. Fatal and severe box jellyfish stings, including Irukandji stings, in Malaysia, 2000–2010. J. Trav. Med. 18 (4), 275–281.
- Low, LB, 2017. Morphological Characterisation of Selected Scyphozoan Jellyfish Species and Geometric Morphometric Analysis of Chrysaora Chinensis in Peninsular Malaysia/Low Liang, Boon (Doctoral dissertation, University of, Malaya.
- Maldonado, E., Maillaud, C., Barguil, Y., Labadie, M., 2017. Rhabdomyolysis during envenomation by Physalia sp envenomation in new caldonia. Medecine et Sante Tropicales 27 (1), 105–108.
- Mannix, R., Tan, M.L., Wright, R., Baskin, M., 2006. Acute pediatric rhabdomyolysis: causes and rates of renal failure. Pediatrics 118 (5), 2119–2125.
- Mizuno, M., 2016. Envenomation by cnidarians and renal injuries. The Cnidaria, Past, Present and Future: The World of Medusa and Her Sisters 623–635.
- Mohd, A., Tan, W., Shahrul, A.S., Cheng, H., Munirah, O., 2016. Jellyfish stings on Langkawi island, Malaysia. Med. J. Malaysia 71 (4), 161–165.
- Mubarak, A.I., Shukri, W.N., Ismail, A.K., 2021. Estimation of local incidence of jellyfish envenomation in developed marine coastal areas and large populated island on the western coast of Peninsular Malaysia using case surveillance of government health facilities in Manjung, Perak and Langkawi Island. Int. Marit. Health 72 (2), 93–165.
- Rengel, A.C., Davel, S., O'Connor, S., Medcraft, N., 2022. Rhabdomyolysis due to jellyfish envenomation in Western Australian waters. Med. J. Aust. 216 (8), 397–399.
- Rupert, S.A., 2002. Pathogenesis and treatment of rhabdomyolysis. J. Am. Acad. Nurse Pract. 14 (2), 82–87.
- Sivanasworn, N.K., Anantham, G., Jamal, S.M., Hatta, M.M., Ismail, A.K., 2023. Managing an unidentified jellyfish sting with mixed envenomation syndrome at a noncoastal hospital: is this a new form of jellyfish envenomation? Wilderness Environ. Med. 34 (2), 225–230.
- Szugye, H.S., 2020. Pediatric rhabdomyolysis. Pediatr. Rev. 41 (6), 265–275.
- Tan, A.T.S., Peng, C.T.C., Nilamani, N., Yasin, Z., 2019. Harmful Jellyfish Country Report in Western Pacific. Penang. Malaysia. Universiti Sains Malaysia, Centre for Marine and Coastal Studies.
- Tan, A.T.S., Ismail, A.K., Miyake, H., 2022. Penang. Kuala Lumpur. In: General Management Guide for Harmful Jellyfish Stings in the Western Pacific and Adjacent Areas. Malaysia Society on Toxinology, Malaysia.