Cardiology in the Young

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Takotsubo cardiomyopathy in a 4-year-old female with pneumococcal meningitis

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Brief Report

Cite this article: Munoz KJ, Feig CL, and Frandsen EL (2023) Takotsubo cardiomyopathy in a 4-year-old female with pneumococcal meningitis. *Cardiology in the Young* **33**: 1722–1725. doi: 10.1017/S1047951123000343

Received: 17 November 2022
Revised: 1 February 2023
Accepted: 19 February 2023
First published online: 15 March 2023

Keywords:
Cardiomyopathy; echocardiography; acute heart failure; reduced ejection fraction

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Abstract

A previously healthy 4-year-old female presented in cardiogenic shock with pneumococcal meningitis. Findings on echocardiogram raised suspicion for takotsubo cardiomyopathy. With supportive care, left ventricular systolic function normalised. Findings on cardiac imaging helped determine the aetiology and avoid further invasive studies or unnecessary treatment.

History of presentation

A previously healthy 4-year-old female presented to an outside hospital in status epilepticus. She was in her usual state of health until one day prior to admission when she developed poor appetite, back pain, and fever. She received rescue antiepileptic medications and was intubated before transfer. Empiric broad-spectrum antibiotics were started. On admission, blood pressure was 86/63 mmHg, heart rate 163, respiratory rate 18, oxygen saturation 100% while mechanically ventilated with FiO_2 0.45. Physical exam was notable for tachycardia and cold extremities peripherally.

Past medical history

The patient was born at term. Her medical history was notable for recurrent episodes of atypical pneumonia at 2 years of age, anaemia, and SARS-CoV-2 infection a year prior. Vaccinations were up to date. Growth and development were normal. There was no family history of early cardiovascular disease, sudden unexplained death, or cardiomyopathy.

Differential diagnosis

The initial differential diagnosis, considering cardiogenic shock in a child with fever and altered mental status, included myocarditis, sepsis-induced myocardial dysfunction, multisystem inflammatory syndrome in children, new presentation of dilated cardiomyopathy, and takotsubo cardiomyopathy.

Management

Shortly after admission, the patient suffered a rapid decompensation into cardiogenic shock, requiring escalating doses of multiple inotropic and vasopressor agents, but did not require chest compressions. An echocardiogram showed severe left ventricular systolic dysfunction (ejection fraction of 11%) with mid and apical hypokinesis/akinesis and relatively preserved basal myocardial thickening (Supplemental Video S1). Right ventricular systolic function was moderately diminished. Mild tricuspid and mitral valve regurgitation with bilateral ventricular dilation were appreciated. The electrocardiogram was notable for sinus tachycardia, ST depression in the anterior leads, and QTc prolongation (480 ms) (Fig 1). A head CT revealed diffuse cerebral oedema, early findings of anoxic brain injury, and mild tonsillar herniation. Laboratory studies were notable for minimally elevated high sensitivity troponin (145 ng/L (normal <= 13 ng/L)), elevated pro-BNP (9000 pg/mL (normal 30–125 pg/mL)), and elevated inflammatory markers (C-reactive protein 9.1 mg/dL (normal <0.8 mg/dL), procalcitonin 192.32 ug/L (normal <0.15 ug/L)). Viral respiratory panel including COVID-19 was negative; however, SARS-CoV-2 spike antibody was positive. Cerebral spinal fluid gram stain showed gram-positive cocci in pairs concerning for *Streptococcus pneumoniae* meningitis.

Due to concern for potential myocarditis, the patient received 2 g/kg intravenous immunoglobulin. Corticosteroids were deferred for concern of infection. One day later, the patient showed improvement in cardiac function with decreased inotropic support, down-trending cardiac markers, and gradual improvement in left ventricular function. A follow-up echocardiogram on the seventh day of hospitalisation off of all hemodynamic support showed complete recovery of left ventricular systolic function and no valvar regurgitation. Despite

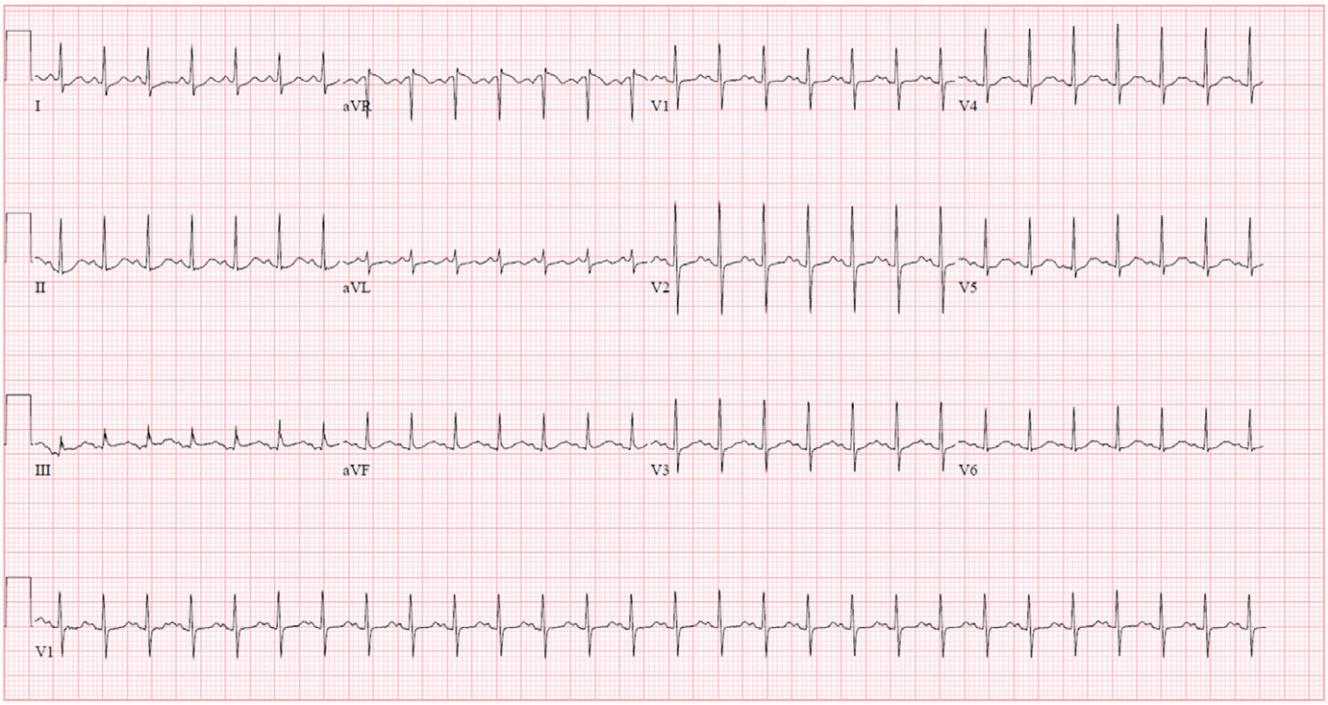

Figure 1. Electrocardiogram from day of hospitalisation 1 showing sinus tachycardia, ST depression in the anterior leads, and QTc prolongation (480 msec).

normalisation of cardiac function, the patient did not recover neurologic function and was declared brain dead.

Discussion

We report a young child presenting in cardiogenic shock with echocardiogram findings consistent with takotsubo cardiomyopathy secondary to severe anoxic brain injury related to pneumococcal meningitis.

Takotsubo cardiomyopathy, also known as stress-induced cardiomyopathy, is a form of severe, typically transient, left ventricular systolic dysfunction in the absence of coronary artery disease. It is mostly encountered in post-menopausal women following traumatic emotional or physical injury/stress; however, it has been described in all ages.

The revised Mayo Clinic Criteria for the diagnosis of takotsubo cardiomyopathy in adults include the following:

1. Transient hypokinesis, akinesis, or dyskinesis of the left ventricular mid-segments with or without apical involvement; the regional wall motion abnormalities extend beyond a single epicardial vascular distribution, and a stressful trigger is often, but not always, present.
2. Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture.
3. New electrocardiographic abnormalities (either ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin level.
4. Absence of pheochromocytoma and myocarditis.[1]

The findings on our patient's echocardiogram, particularly the pattern of dysfunction with relatively preserved basal myocardial contractility with mid and apical hypokinesis/akinesis, are typical of takotsubo cardiomyopathy.[1] Treatment is supportive, and recovery of left ventricular function is expected. Fulminant myocarditis was also considered, and the patient did receive treatment with intravenous immunoglobulin. However, troponin, which is typically pronounced in the setting of myocarditis, was only minimally elevated, and the electrocardiogram was quite unremarkable. Studies including endomyocardial biopsy and cardiac MRI, which can aid in diagnosing myocarditis, were not employed due to the increased risk of invasive/lengthy procedures in this unstable patient. In this instance, the specific findings on the echocardiogram made takotsubo cardiomyopathy the most likely diagnosis and further invasive studies or unnecessary treatment were deferred.

Takotsubo cardiomyopathy is a rare finding in children with favourable cardiac prognosis.[2] Several case reports have been published in children with similar echocardiogram findings in the setting of severe neurologic injury.[2–9] The included Table 1 outlines these cases. The median duration to recovery was 6.5 days, similar to our case. Of note, only three cases met three or more Mayo Clinical Criteria, highlighting the difficulty in applying adult criteria to children. All patients recovered with supportive care, in some cases requiring mechanical circulatory support.

In our case, the diagnosis of takotsubo cardiomyopathy was made in the setting of pneumococcal meningitis with severe anoxic brain injury. The pathogenesis of takotsubo cardiomyopathy has been ascribed to high levels of circulating catecholamines, oversaturating cardiac adrenergic receptors leading to increased oxygen demand and myocyte hypoxia. Subsequent metabolic changes during hypoxia include uncoupling of electron transport, affecting ATP synthesis. Release of oxygen-derived free radicals interferes with calcium and sodium transporters, compounding injury to the myocardium. It has been hypothesised that the regional differences in myocardial dysfunction may be explained by the differences in density of beta-1 and beta-2 adrenergic receptors in the apex versus the base of the heart.[10]

https://doi.org/10.1017/S1047951123000343 Published online by Cambridge University Press

Table 1. Case reports of children with takotsubo cardiomyopathy associated with brain injury. NR, not reported

Reference	Age (years)	Gender	Initial Presentation	Underlying Diagnosis	Brain Insult	Cardiac Symptoms/ Findings	ECG Findings	LVEF (%)	Other Echocardiogram Findings	Elevated Cardiac Enzymes	Inotrope/ Pressor Support	Days to Recovery	Mayo Clinic Criteria
Thomas, et al[3]	12	Male	Afebrile illness, jaw/mouth/throat pain	Unclear	Acute brainstem bleeding due to fistulous arteriovenous malformation	Hypotension Tachycardia Systolic murmur Weak peripheral pulses	ST depression II, III, aVF ST-elevation V1-4 T-wave inversion in leads V1, V2	30	Left ventricular dilation, moderate to severe mitral regurgitation	NT-proBNP Troponin	Norepinephrine Epinephrine Milrinone Levosimendan	7	4
Koyama, et al[4]	2	Female	Several-week vomiting and gait disturbance	Anaplastic Ependymoma	Obstructive hydrocephalus	Tachycardia	T-wave inversion in leads V4-V6	40	NR	Troponin	Epinephrine Milrinone	19	2
Serrano, et al[2]	0.6	Female	Unresponsive 4 hours after head trauma	Head trauma	Hypoxic ischaemic injury of the cerebral hemispheres and cerebellum with increased brain swelling	Cardiopulmonary arrest	Indeterminate QRS axis, Right ventricular hypertrophy	25	Restrictive diastolic dysfunction	Troponin	Epinephrine Milrinone	1.7	3
Shimbo, et al[5]	6	Male	Altered consciousness with fever	*L. monocytogenes* bacterial meningitis	Cerebral oedema	Cardiomegaly	NR	33	NR	Troponin Creatinine kinase	Milrinone	7	1
Pearson, et al[6]	12	Male	Loss of consciousness and apnoea	Trauma to posterior occipital area	Cervicomedullary contusion and subarachnoid haemorrhage with extension into the intraventricular space	Cardiogenic shock	NR	20	NR	NR	Epinephrine Norepinephrine	3	2
Krpata, et al[7]	15	Male	Unresponsive with normal vital signs	Motor vehicle accident trauma	Multiple skull fractures, severe intracranial trauma, elevated intracranial pressure	NR	T-wave inversions	15	NR	Troponin Creatine kinase	Norepinephrine Milrinone	7	3
De Rosa, et al[8]	12	Female	1 week history of headache, nausea, and recurrent vomiting	Intracranial astrocytoma	Obstructive hydrocephalus	Tachycardia Ventricular arrhythmias	Non-specific T-wave abnormalities QTc prolongation	30	Left ventricular non-compaction Severe mitral regurgitation Mild aortic insufficiency	Troponin Creatine kinase-MB	Dobutamine	15	2
Wittekind, et al[9]	13	Female	Unresponsive at home	Grade 1 pilocytic astrocytoma	Thalamic mass with severe mass effect and acute haemorrhage with cerebellar tonsillar herniation	Pulseless ventricular tachycardia	K-point depression and up-sloping ST segments in the inferior limb leads V4, V5. Isolated Q wave in lead aVL	23	Normal left ventricular size	Troponin	Epinephrine Phenylephrine	6	2
Wittekind, et al[9]	10	Female	Sudden headache followed by loss of consciousness and respiratory arrest	Ruptured cerebella arteriovenous fistula	Subarachnoid and parenchymal haemorrhage in left lobe of the cerebellum	Fluid-refractory shock	1-mm J-point depression in the inferior leads, V4, and V5 Isolated Q wave in lead aVL	25	NR	Troponin	Norepinephrine Dobutamine Milrinone	3	2

Conclusion

Takotsubo cardiomyopathy should be considered in the setting of acute severe brain injury in a child with haemodynamic instability. The specific findings on cardiac imaging described in this report may help determine aetiology and aid in avoiding further invasive studies or unnecessary treatment.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/S1047951123000343

Acknowledgements. We thank Dr Sonia Voleti for her critical appraisal of the manuscript.

Financial support. This research received no specific grant from any funding agency, commercial, or not-for-profit sectors.

Conflicts of interest. None.

References

1. Medina de Chazal H, Del Buono MG, Keyser-Marcus L, et al. Stress cardiomyopathy diagnosis and treatment: JACC state-of-the-art review. J Am Coll Cardiol. 2018; 72: 1955–1971.
2. Serrano RM, Schamberger M, Parent JJ. Takotsubo cardiomyopathy secondary to non-accidental trauma presenting as an "unwitnessed" arrest. Cardiol Young. 2019; 29: 442–444.
3. Thomas C, Johler SM, Hermann M, et al. Takotsubo cardiomyopathy in a 12-year-old boy caused by acute brainstem bleeding - a case report. Transl Pediatr. 2021; 10: 3110–3117.
4. Koyama J, Akutsu N, Kawamura A. Pediatric takotsubo syndrome caused by hydrocephalus after posterior fossa tumor surgery. Childs Nerv Syst. 2021; 37: 3957–3961.
5. Shimbo A, Takasawa K, Nishioka M, Morio T, Shimohira M. Complications of Listeria meningitis in two immunocompetent children. Pediatr Int. 2018; 60: 491–492.
6. Pearson TE, Frizzola MA, Priest MA, Rochman MF, Froehlich CD. Pediatric extracorporeal cardiopulmonary resuscitation patient with traumatic subarachnoid hemorrhage and Takotsubo syndrome. Air Med J. 2018; 37: 64–66.
7. Krpata DM, Barksdale EM Jr. Trauma induced left ventricular apical ballooning syndrome in a 15 year old: a rare case of Tako-tsubo cardiomyopathy. J Pediatr Surg. 2013; 48: 876–879.
8. De Rosa G, Pardeo M, Di Rocco C, et al. Neurogenic stunned myocardium presenting as left ventricular hypertrabeculation in childhood: a variant of Takotsubo cardiomyopathy? Pediatr Crit Care Med J Soc Crit Care Med World Feder Pediatr Intens Crit Care Soc 2011; 12: e420–423.
9. Wittekind SG, Yanay O, Johnson EM, Gibbons EF. Two pediatric cases of variant neurogenic stress cardiomyopathy after intracranial hemorrhage. Pediatrics 2014; 134: e1211–1217.
10. Lyon AR, Rees PSC, Prasad S, Poole-Wilson PA, Harding SE. Stress (Takotsubo) cardiomyopathy—a novel pathophysiological hypothesis to explain catecholamine-induced acute myocardial stunning. Nat Rev Cardiol. 2008; 5: 22–29.