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Case Report

Recurrent Takotsubo syndrome in a boy with Duchenne muscular dystrophy: A case report

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ABSTRACT

Takotsubo syndrome is a rare cause of reversible ventricular dysfunction that imitate an acute coronary syndrome. The entity is unusual among pediatric populations and a recurrent episode is extremely rare. We report a case of recurrent takotsubo syndrome in an eight-year-old boy with Duchenne muscular dystrophy (DMD). His chest pain episodes were aggravated by a strong emotional stimuli. During episodes of chest pain, electrocardiograms (ECG) showed ST elevation while echocardiograms showed left ventricle apical ballooning; however, a coronary angiography was normal. Serial ECG and echocardiogram revealed a spontaneous resolution of ST elevation and normalized apical contraction which were compatible with the diagnosis of takotsubo syndrome. Interestingly, serial cardiac magnetic resonance imaging demonstrated increasing subepicardial enhancement which was compatible with progression of cardiac involvement in DMD.

<**Learning objective:** Takotsubo syndrome should be considered in pediatric patients with acute chest pain. A recurrent episode of takotsubo syndrome is rare but is possible in pediatric populations. Patients with inherited muscular dystrophy could also develop takotsubo cardiomyopathy. A growing awareness of this syndrome may help physicians to diagnose and provide an early appropriate management of children with chest pain.>

Introduction

Takotsubo syndrome (TTS) is an acute reversible apical ballooning of the left ventricle, named after its "octopus-trap like" left ventricle. The typical presentation is sudden onset of chest pain, which can mimic an acute coronary syndrome. Most of the reported cases were in post-menopausal women. Emotional or physical stresses are important trigger factors. Prognosis is typically good, as around 4% to 5% of patients would develop serious outcomes [1]. The true prevalence of TTS remains unknown; however, it seems to account for 2% of adult patients with suspected acute coronary syndrome. In children, TTS is extremely rare with only 38 reported patients worldwide who were under 20 years of age [2,3], and common predisposing factors were neurological or psychogenic disorders. In this article, we report a case of recurrent TTS in a boy with Duchenne muscular dystrophy (DMD). To the best of our knowledge, TTS with inherited muscular dystrophy has not been previously reported.

Case report

An 8-year-old boy was diagnosed with DMD with deletion of exon 45–50 in dystrophin gene. He had a progressive muscle weakness starting approximately 1.5 years before admission. His baseline creatine phosphokinase (CPK) at the diagnosis of DMD was 8859 Unit/L. He was referred to King Chulalongkorn Memorial Hospital with a history of non-radiating left-sided chest pain while

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watching television. An initial electrocardiography (ECG), which being done two hours after the onset of chest pain, showed a sinus rhythm with rate 80/min, ST elevation in lead II, III, aVF, V3–V6 (Fig. 1A). A chest X-ray revealed a normal heart size and normal pulmonary vasculature. Blood tests showed elevated CPK = 17,033 Unit/L, creatine kinase-MB (CK-MB) = 553 Unit/L, and troponin T = 0.93 ng/dL. Serial ECG showed progressive ST elevation, which turned to Q wave in lead V5–V6 in the next seven hours. His chest pain spontaneously resolved without any specific treatment. An initial echocardiogram demonstrated hypokinesia of the left ventricular (LV) apex without other structural abnormalities. The coronary angiography showed normal coronary arteries with hypokinesia of the LV apex and hypercontraction of the basal segment (Fig. 2). A cardiac magnetic resonance imaging (MRI) study done six days following his chest pain showed an impaired LV systolic function, hypokinesia, and hypersignal intensity on T2W images at mid anterior, all apical segments, and LV apex. Late gadolinium enhancement images showed subepicardial enhancement at basal-to-apical lateral wall, despite normokinesia and normal signal intensity on T2W images of basal-to-apical lateral wall (Fig. 3). He was completely asymptomatic during the admission and was discharged 10 days after his initial symptoms. Pre-discharge ECG showed the normalization of the ST segment, and Q wave in leads II, III, aVF, V5–V6 (Fig. 1B). An echocardiogram being taken at discharge was completely normal with LV ejection fraction 76%.

A follow-up cardiac MRI at two months after the illness showed an interval improvement of hypokinetic areas (midanterior, and all apical segments) as compared to his previous study with a markedly decreased hypersignal intensity on T2WI at mid anterior, all apical segments, and LV apex, representing resolved myocardial edema. An unchanged subepicardial enhancement at basal-to-apical lateral wall was seen, representing myocardial necrosis or scar which was found in muscular dystrophy. A follow-up echocardiogram showed good cardiac function. An ECG showed Q wave at leads II, III, aVF, V4–V6, and inverted T at leads II, III, aVF, V1–V5 (Fig. 1C).

He was later admitted with another episode of non-radiating chest pain while playing video game 14 months after the first attack. He presented to our hospital one day after the spontaneously resolved chest pain. His initial ECG showed the normal ST segment, Q wave at V4–V6. CPK = 6595 Unit/L, CK-MB = 536 Unit/L, troponin-I = 25,790 pg/mL. An echocardiogram showed mild hypokinesia of mid and the LV apex. Pre-discharge CK-MB, and troponin-I decreased to 169 Unit/L, and 21,046 pg/mL, respectively. On four-month follow-up visit, he experienced no further chest pain, CPK was 4244 Unit/L, CK-MB = 244 Unit/L, troponin-I = 39.8 pg/mL. An echocardiogram and a cardiac MRI showed a resolution of apical segments hypokinesia (Fig. 3). However, the extension of subepicardial delayed gadolinium enhancement at basal-to-apical lateral wall was increased. Three years after the second episode of TTS, the patient had no additional chest pain, but his muscle weakness was gradually worsening. CPK was 1586 Unit/L, troponin-I = 24.3 pg/mL. An ECG showed a normal ST segment with unchanged Q wave in lead V5-V6. An echocardiogram revealed a normal contraction at the LV apical segment.

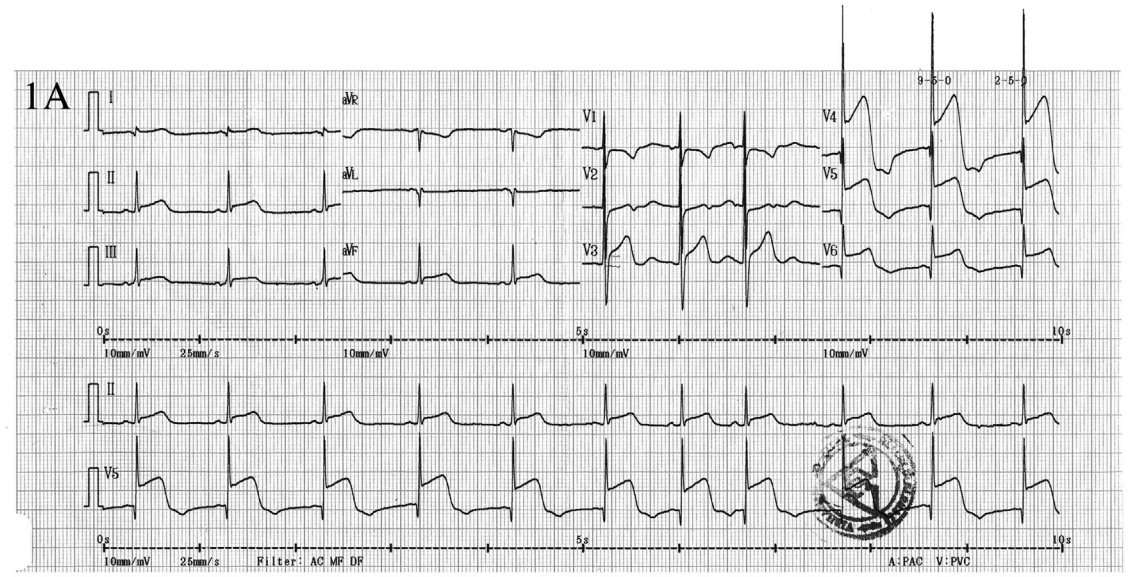
Discussion

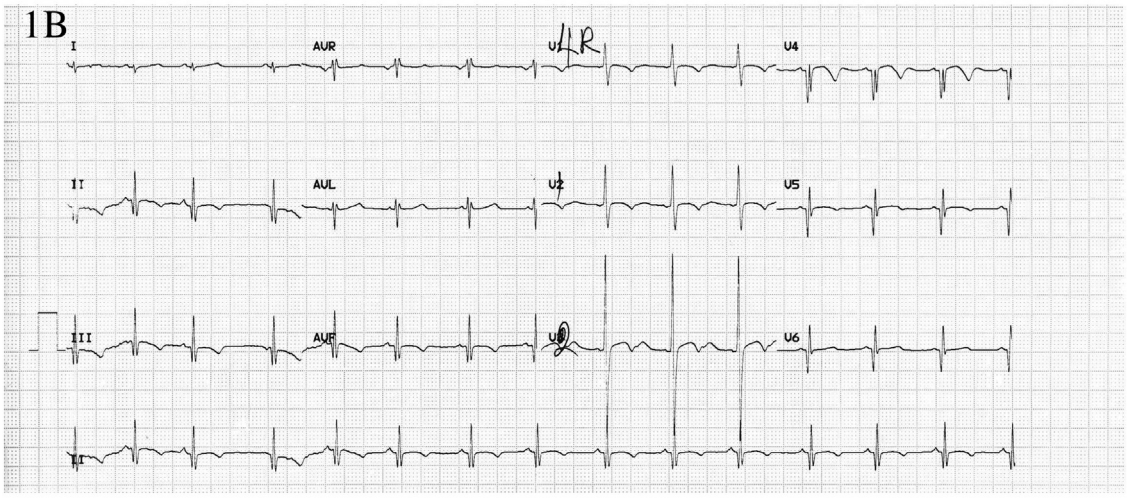
TTS, also known as takotsubo cardiomyopathy, is a rare disease of myocardium that mimics acute coronary syndrome [4]. Our patient developed chest pain with an extensive precordial ST segment elevation on initial ECG. The events were probably triggered by a stressful emotional event during watching TV and subsequently during playing video games. Initial angiogram showed normal coronary arteries. His echocardiogram showed transient hypokinesia of the LV apex with hyperkinesia at the basal segment which extended beyond a territory of a single coronary artery. Although his conditions were compatible with TTS, other possible etiologies including acute anterior myocardial infarction from transient coronary spasm or microvascular dysfunction need to be considered due to the rarity of TTS in the pediatric population [2]. A higher proportion of males is observed in pediatric TTS patients compared with predominant post-menopausal females in adults. Neurological and psychological disorders are common predisposing factors of TTS in both adults and children [2].

The diagnosis of TTS is based on clinical criteria from the Mayo Clinic which comprises classical regional wall motion abnormalities, normal coronary arteries, new onset of ECG abnormalities or elevation of cardiac enzyme, and absence of other specific causes that can mimic TTS. Several studies proposed ECG criteria to differentiate between TTS and acute anterior ST elevation myocardial infarction [5]. The presence of ST segment elevation in aVR, and absence of ST segment elevation in V1 favors the diagnosis of TTS with high sensitivity (91%) and specificity (96%). Therefore, ECG findings in this patient (Fig. 1A) supported the diagnosis of TTS. Cardiac biomarkers in TTS are mildly increased, and usually reach the peak at presentation followed by quicker normalization than in acute coronary syndrome [1]. However, cardiac enzymes in this patient seemed to be higher than typical TTS. Serial tests of his cardiac enzymes showed a decline but they did not reach their normal values. We postulated that this might be a result of his underlying muscular dystrophy. With conservative treatment alone, LV apical ballooning classically resolves within days to a few weeks (average of 18 days, range from 9 to 53 days) [6]. The duration to complete recovery of LV systolic function in reported children varied from 2 days to the longest duration of 4 months [7].The clinical course of TTS is not always benign with in-hospital mortality rate of approximately 4–5% in all age groups [2].Our patient was totally asymptomatic during both admissions and his serial echocardiogram showed complete resolution of cardiac dysfunction approximately three months after the chest pain.

In contrast with myocarditis and acute myocardial infarction, a cardiac MRI in an acute phase (within the first 5 days) of a patient with TTS did not demonstrate a delayed gadolinium enhancement of mid myocardium [8]. The cardiac MRI of our patient showed hypokinesia and hypersignal intensity on T2WI without late gadolinium enhancement at mid anterior and all apical LV segments, which were compatible with TTS. It also showed the subepicardial enhancement predominantly at the basal-to-mid lateral wall, which did not correspond to the hypokinetic area. The subepicardial enhancement was probably the result of his underlying DMD. In brief, DMD is an X-linked disorder in dystrophin gene which results in progressive myopathy. The incidence of cardiomyopathy in DMD increases with age, with about 59% of patients affected by the age of 10 years. The classic pathology of cardiomyopathy in DMD is subepicardial fibrosis especially inferolateral wall which is seen in a cardiac MRI as late gadolinium enhancement [9].

Following three years of out-patient visits, our patient developed another episode of chest pain while playing video games. He had elevated cardiac enzymes and deterioration of the LV apex function, which was probably a recurrence of TTS with complete resolution of apical hypokinesia on the 4-month follow-up. In adults, a recurrent rate of TTS occurs in approximately 5–11% of patients with duration ranging from 3 months to 14 years after the previous episode [10]. In contrast, recurrent TTS is uncommon in children. Apart from our patient, only one pediatric patient has been reported to suffer two episodes of TTS triggered by status epilepticus [3].





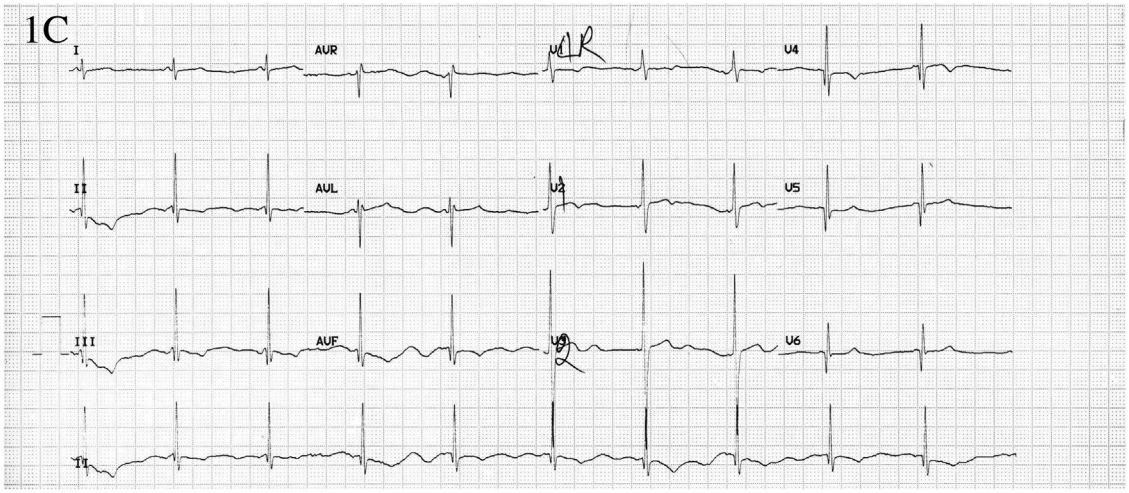
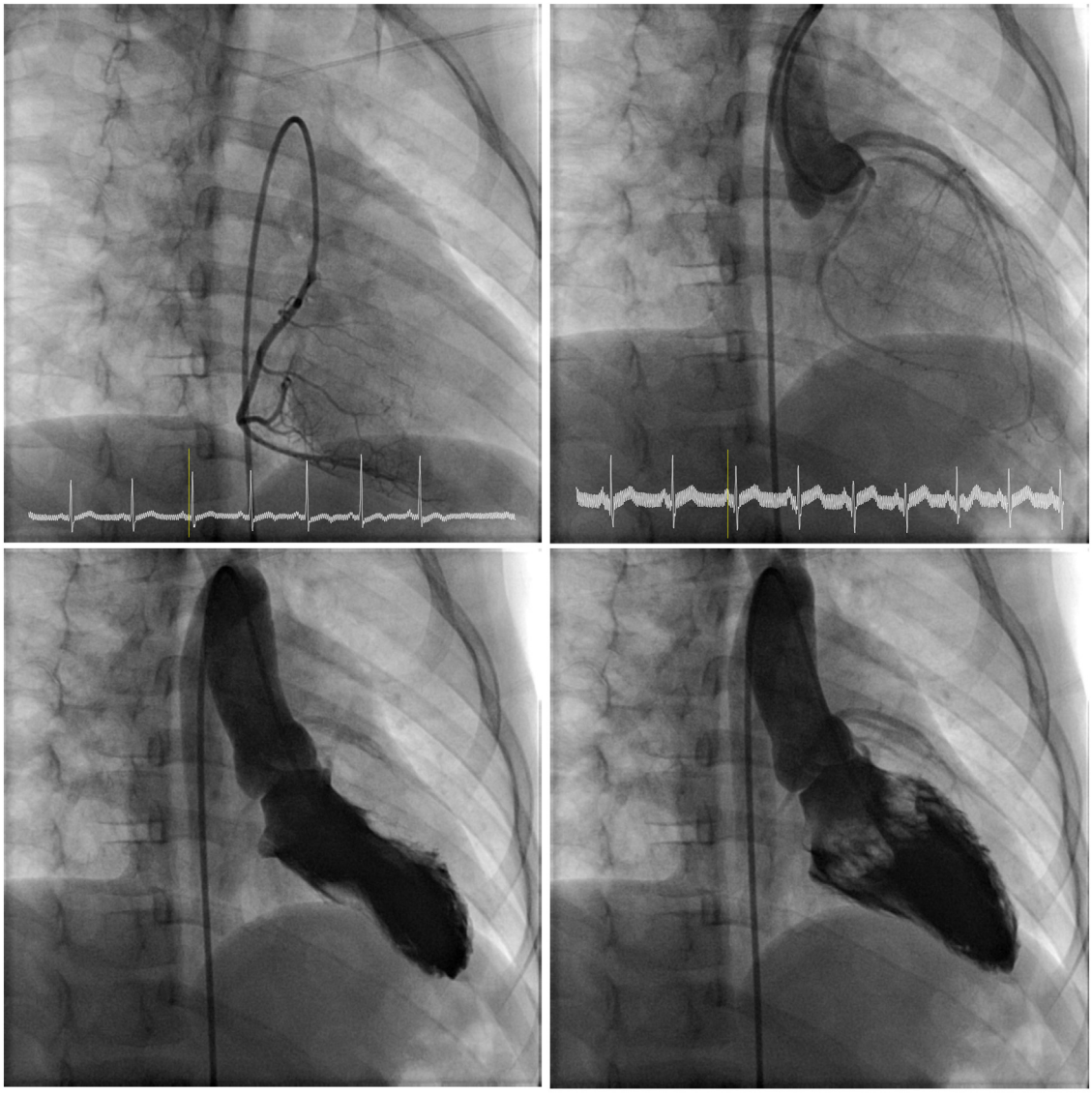
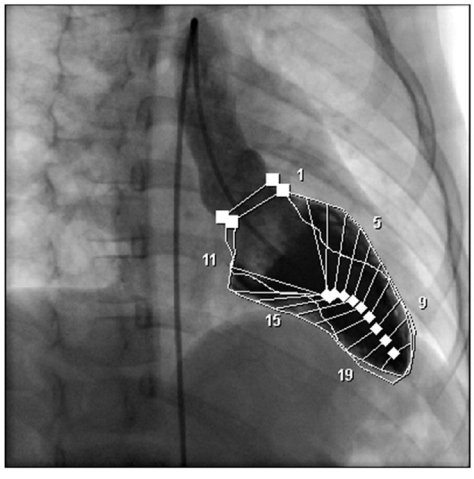


Fig. 1. (A) The electrocardiogram (ECG) at 2 hours after onset the of chest pain showed ST elevation in leads II, III, aVF, and V3–V6. (B) Pre-discharge ECG at 10 days after the onset of chest pain showed normalized ST segment, and presence of Q wave in leads II, III, aVF, and V5–V6. (C) The 2-month follow up ECG showed Q wave at leads II, III, aVF, and V4–V6, and inverted T at leads II, III, aVF, V1–V5.



Slager Wall Motion



Contribution of Regions to global EF (CREF)

Antero Basal	22.6 (%)
Antero Lateral	3.3 (%)
Apical	-1.7 (%)
Inferior	4.2 (%)
Postero Basal	24.0 (%)

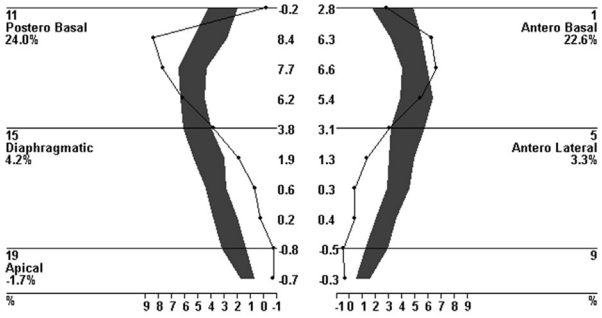


Fig. 2. Cardiac catheterization at the onset of chest pain showed normal coronary angiography and apical hypokinesia of left ventricularangiogram. CREF, Contribution of Regions to Global Ejection Fraction

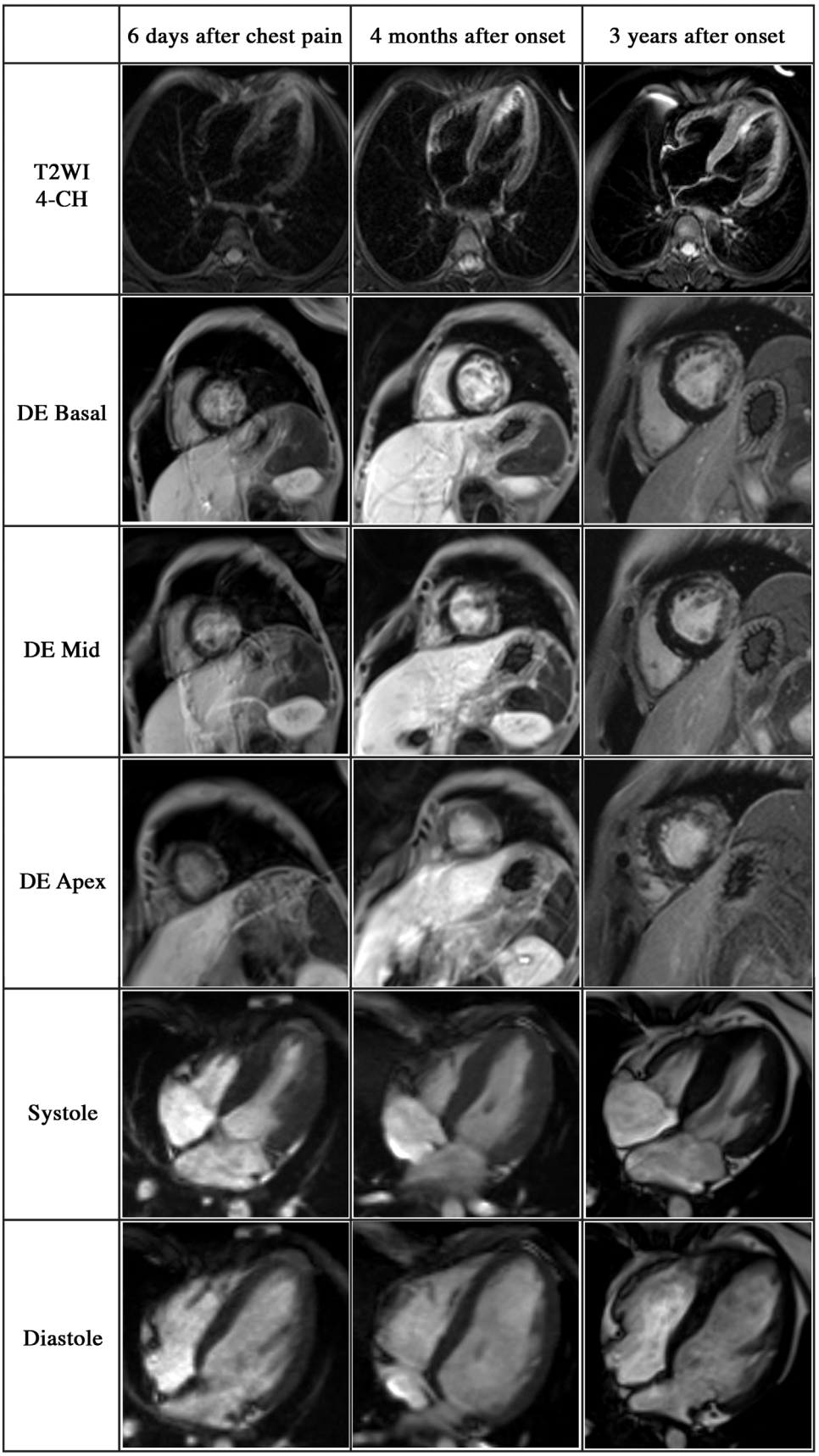


Fig. 3. The cardiac magnetic resonance imaging with gadolinium at the onset of chest pain showed impaired left ventricular systolic function, hypokinesia at mid anterior, all apical segments and left ventricular apex, together with subepicardial enhancement at lateral wall. The follow-up cardiac magnetic resonance imaging revealed resolution of hypokinesia, but increase of subepicardial enhancement.
4-CH, 4-chamber view; DE, delayed enhancement; T2WI, T_2 weighted image.

Conclusion

We report the first case of TTS in a child with DMD. It is emphasized that TTS could occur in pediatric patients with underlying muscular dystrophy. This patient experienced the second episode of chest pain followed by LV apical ballooning, which was probably a recurrence of TTS.

Statement of consent

The authors confirm that the written consent for submission and publication of this case report including images and associated texts has been obtained from the patient in line with COPE guidance.

Conflict of interest

The authors declare that there is no conflict of interest.

Acknowledgment

None.

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