Investigation of Catecholaminergic Polymorphic Ventricular Tachycardia Children in China: Clinical Characteristics, Delay to Diagnosis, and Misdiagnosis

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To the Editor: Catecholaminergic polymorphic ventricular tachycardia (CPVT) often occurs in children or adolescents without organic heart diseases. It is a rare malignant arrhythmic disorder with hereditary features characterized by exercise- or emotional stress-induced ventricular arrhythmias, especially bidirectional/polymorphic ventricular tachycardia (VT), syncope, or sudden death.[1] The mortality rate of symptomatic CPVT patients before 30 years of age is 31%,[2] and an early treatment with beta-blockers could effectively improve their prognosis.[3] Therefore, getting a confirmed diagnosis of CPVT in time is of utmost importance. On this context, this study summarizes the clinical characteristics and diagnosis of pediatric cases with CPVT. This study was approved by the Ethics Committee of The First Hospital of Tsinghua University (No. HX200901) and was conducted in accordance with the 1964 *Declaration of Helsinki*.

The study involves 12 CPVT cases [Table 1], including eight males and four females, in which ten cases had a history of recurrent syncope after emotional distress or exercise. Except for two cases whose CPVT were confirmed by HOLTER monitoring, the remaining ten cases underwent treadmill exercise tests. Bidirectional VT or polymorphic VT was induced in all these cases during treadmill exercise test in which three of them showed concurrent atrial arrhythmias. Genetic test was performed in 11 cases and positive results were identified in all of them (*RYR2* gene mutation in nine cases and *CASQ2* gene mutation in the remaining two cases). Among the 12 CPVT cases, nine cases were given long-term oral propranolol therapy, whereas for the remaining three cases, long-term oral metoprolol was given. During the follow-up period of 0.92 ± 0.80 years (0.08–2.42 years), seven patients were observed to be free from symptoms or discomforts such as syncope, and three patients had significantly decreased the frequency of syncope, whereas one patient died suddenly during the course of oral metoprolol therapy while he was playing.

The mean age at the onset of CPVT symptoms for the 12 cases was 8.4 ± 3.2 years (4.0–13.7 years). The mean age at diagnosis for these 12 cases was 10.7 ± 2.3 years (7.0–14.0 years). Mean duration between the onset of symptoms and diagnosis was 2.4 ± 1.7 years (0.04–5.0 years) [Figure 1]. Among the 12 cases diagnosed in our center, nine cases were presented typical CPVT clinical manifestations. However, only two cases were suspected as CPVT when diagnosed in other hospitals. All other cases were misdiagnosed in other hospitals in which three cases were misdiagnosed as syncope with cause to be determined, five cases were misdiagnosed as complex arrhythmias, and two cases were misdiagnosed as epilepsy.

Delayed diagnosis and even misdiagnosis for CPVT are not uncommon. A multicenter study reported that the mean duration between the first clinical episode and diagnosis for 226 CPVT cases under 19 years was 0.5 year.[4] Among them, 38% had more than 1-year delay for diagnosis, whereas 56% was initially misdiagnosed. For some of the Chinese pediatric CPVT patients (35 cases from the relevant studies or reports in the CNKI database published from 2004 to 2017), the delay of diagnosis is 3.0 years (0.1–36.0 years). Only 19.5% was diagnosed within one year.

Severe delay of diagnosis and misdiagnosis exist for CPVT, and the possible reasons are as follows. The foremost cause could be due to the lack of knowledge and inadequate recognition of CPVT. A study in the form of questionnaire survey was accomplished to investigate the level of understanding for etiologies of sudden death in the young among 614 Canadian medical students and recent graduates (within 5 years of graduation). The results showed that only 30% answered had adequate understanding and recognition of CPVT.[5] Second, some patients have quite concealed symptoms and it is quite difficult to get electrocardiogram recording during the syncope episode. Patients usually have normal resting electrocardiogram, echocardiogram, and intracardiac electrophysiologic study. These might contribute to misdiagnosis or no confirmed diagnosis of CPVT. Third, due to the low prevalence of CPVT and its most common symptom,

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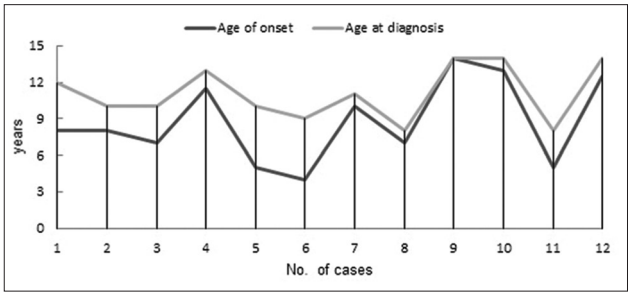

Figure 1: Distribution for the age of onset of symptoms (dark gray line) and the age at diagnosis (light gray line) for 12 cases of CPVT. Delay of diagnosis occurred in most of the pediatric CPVT patients. CPVT: Catecholaminergic polymorphic ventricular tachycardia.

Table 1: Characteristics of CPVT cases in the series (n = 12)

Characteristics	*n*
Number of males	8
Syncope as first symptom	9
Number with SSS	6
Number with atrial arrhythmias	5
Treadmill exercise test	10
Treadmill exercise test positive	10
Genetic test	11
Genotype positive	11
Drug therapy (β-blocker)	12
Propranolol	9
Metoprolol	3
PM therapy	1

CPVT: Catecholaminergic polymorphic ventricular tachycardia; SSS: Sick sinus syndrome; PM: Pacemaker.

i.e., syncope, tends to be diagnosed as epilepsy or vasovagal syncope which has a higher prevalence.

Severe delay of diagnosis and even misdiagnosis of CPVT are not uncommon due to some reasons. Improving the understanding of CPVT, paying more attention to explore the relationship between syncope and exercise or emotional stress, and performing treadmill exercise test might help to confirm the diagnosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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