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ORIGINAL ARTICLE

A Multicenter, Long-Term Study on Arrhythmias in Children with Ebstein Anomaly

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Abstract To assess the prevalence, history, and treatment of arrhythmias, in particular preexcitation and Wolff–Parkinson–White (WPW) syndrome, in patients with Ebstein anomaly (EA) during childhood and adolescence, we performed a multicenter retrospective study of all consecutive live-born patients with EA, diagnosed, and followed by pediatric cardiologists between 1980 and 2005 in The Netherlands. During a follow-up after EA diagnosis of 13 years 3 months (range: 6 days to 28 years 2 months), 16 (17%) of the 93 pediatric EA patients exhibited rhythm disturbances. Nine patients showed arrhythmic events starting as of the neonatal period. Supraventricular tachycardia was noted in 11 patients. One patient died in the neonatal period due to intractable supraventricular tachycardia resulting in heart failure and one patient died at 5 weeks of age most probably due to an arrhythmic event. The 14 surviving patients all show preexcitation, albeit 4 of them intermittently, and all have a right-sided accessory pathway location. Nine patients underwent catheter ablation of an accessory pathway. Only four patients are currently on antiarrhythmic drugs. The 17% prevalence of rhythm disturbances in pediatric EA patients, most commonly supraventricular arrhythmias, is significantly lower than in adult EA patients. Life-threatening rhythm disturbances are not frequent early in life. Symptomatic patients are well treated with radiofrequency catheter ablation.

Keywords Ebstein anomaly · Cardiac arrhythmias · Preexcitation

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Introduction

Ebstein anomaly (EA) accounts for <1% of all congenital heart diseases and is characterized by apical displacement of the posterior and septal leaflets of the tricuspid valve [2, 21]. The downward displacement of the septal tricuspid valve leaflet is associated with discontinuity of the central fibrous body and septal atrioventricular ring and, hence, with direct muscular connections. Thus, a potential substrate for accessory atrioventricular connections and ventricular preexcitation is created [10]. This is reflected in the fact that preexcitation and Wolff–Parkinson–White (WPW) syndrome are more frequently associated with EA than with any other congenital heart defect [16], with a reported prevalence varying between 0 and 44% [2, 3, 6, 7, 9, 11, 13, 14, 17, 18, 24, 25, 27]. However, agreement on the prevalence in the young EA population is lacking. The objective of this retrospective study was to assess the prevalence, history, and treatment of arrhythmias, in particular preexcitation and

WPW syndrome, in patients with EA during childhood and adolescence.

Methods

All six Dutch pediatric heart centers granted access to the medical records of all consecutive live-born patients with EA, diagnosed, and followed by a pediatric cardiologist at one of these centers between January 1, 1980 (when echocardiography was routinely used) and March 30, 2005. An apical or downward displacement of the tricuspid valve from the atrioventricular valve ring $\geq$0.8 cm/m^2 body surface area was set as the criterion for EA. Excluded were only patients with congenitally corrected transposition of the great arteries. Medical records were examined for history of subjective and/or objective signs of arrhythmias. Resting 12-lead ECGs as well as 24-h ECGs were analyzed (by Tammo Delhaas) for preexcitation or arrhythmic events. In case of preexcitation, the most likely site of the accessory pathway was located by means of the QRS polarity in all ECG leads using both the pediatric algorithm devised by Boersma et al. [4] as well as the algorithm devised by d'Avila et al. [8] for adults. When possible, the pathways according to these algorithms were compared with the pathway as detected during invasive electrophysiology study and catheter ablation.

Results

For details on the results of this full cohort study on the perinatal and neonatal course along with the follow-up period during childhood and adolescence, we refer to the work by Kapusta et al. [15]. In short, 93 pediatric EA patients diagnosed, followed, and treated in one of the 6 Dutch pediatric heart centers were included in that study: 41 males and 52 females. Sixty (64.5%) patients were diagnosed with EA during the first 2 months of life, 6 (6.5%) between 3 and 12 months of age, and 27 (29%) beyond the first year of age.

Of the above-mentioned 93 EA patients, 16 (17%) exhibited rhythm disturbances. Patient characteristics of the latter 16 EA patients are described in Table 1. The median age at diagnosis of this subgroup of EA patients was 0 days (range: 0 days to 13 years 6 months). The median age at first ECG abnormality was 3 months (range: 0 days to 17 years 7 months). Follow-up after EA diagnosis was 13 years 3 months (range: 6 days to 28 years 2 months). Follow-up after first ECG abnormality was 9 years 7 months (range: 6 days to 18 years 4 months).

Five EA patients presented with a supraventricular tachycardia (SVT). One patient had an intractable SVT and he died at 6 days of age. The other four who could be conversed to sinus rhythm subsequently showed preexcitation. Three EA patients with preexcitation were detected on routine ECG at initial diagnosis of EA, whereas the other seven presented later in life with rhythm disturbances and were then found to have preexcitation. One patient was reported to have succumbed at 1 month 6 days of age most probably due to an arrhythmic event.

All of the 14 surviving patients show preexcitation, albeit 4 of them intermittently. Only one patient remained symptom-free. The most likely site of the accessory pathway was at the right side in all patients (8 right lateral, 5 right posteroseptal, 1 anteroseptal) when we located the pathway according to the QRS polarity-based pediatric algorithm as devised by Boersma et al. [4]. Using the adult d'Avila algorithm [8], the location of the pathway should be located in three patients on the left side. The location of the accessory pathway as detected during catheter ablation was always right-sided, even in one of the patients who would have had a left-sided pathway according to the adult algorithm. Only one patient had two pathways at different locations. In eight patients, periods with SVT led to catheter ablation of accessory pathways. In five patients, one accessory pathway was successfully ablated. Of the three patients who needed two ablation sessions, the one with the right-sided Mahaim fibers still has infrequent antidromic SVT. In one patient, catheter ablation was performed because the accessory pathway always conducted and the amount of preexcitated muscular tissue was so excessive that he had dyssynchrony-induced cardiomyopathy. In this patient, the anterograde conduction possibility of the AV node was tested before ablation. The first ablation was unsuccessful. Nine months later, this patient underwent a second, now successful ablation but showed a right bundle branch block since then. Because of mild heart failure, he is still on enalapril and metoprolol.

Of the nine patients who underwent catheter ablation of an accessory pathway, five were completely symptom-free after the procedure. One patient showed nonsustained right bundle branch block (RBBB) postablation, whereas another one showed persistent RBBB. The one patient with the Mahaim fibers still has infrequent antidromic SVT. The remaining one patient with persistent symptoms postablation had a short period of ectopic atrial tachycardia postablation and a persistently increased PR interval.

Only four patients are currently on antiarrhythmic drugs: one because of infrequent SVT while never ablated, one because of infrequent antidromic SVT despite two ablation sessions for Mahaim fibers, one because of ventricular fibrillation in the neonatal period, and the last one because of mild heart failure.

Three patients (19%) had been operated on for their EA, without any surgical antiarrhythmic procedure. Two

Table 1 Characteristics of the patients with EA and arrhythmia

Gender	Date of birth	Age at diagnosis EA	Age at first ECG abnormality	Current age	Pathway location			Age at EPS	Ablation # of AP's	Arhythmic events		Current drug
					Pediatric	Adult	EPS			Past	Current	
M	16-2-1999	0 days	0 days	9 years 5 months	RL (AS)	RL			–	Infrequent SVT	Infrequent SVT	Sotalol
M	13-11-1996	0 days	0 days	11 years 8 months	RL (AS)	RL	RPS	7 years 10 months	1	LBBB	RBBB post abl	Enalapril
							RPS	8 years 7 months	1			Metoprolol
F	7-9-1995	0 days	0 days	12 years 10 months	RPS (MS)	RL (PS)	RPS	8 years 10 months	1		AVB1 EAT	–
M	30-1-2000	0 days	0 days	8 years 6 months	RPS (MS)	RPS	RPS	1 years 1 months	1	SVT		–
F	8-6-1992	0 days	0 days	16 years 1 months	AS (PH)	LL	RPS	13 years 4 months	1	SVT		–
										EAT post abl		
M	10-1-1991	0 days	0 days	6 days†						SVT		
M	4-10-2000	0 days	1 days	7 years 9 months	RPS (MS)	LL			–	VF (neonatal)		Sotalol
F	18-10-1987	0 days	0 days	1 months 6 days†						?		
F	10-4-1997	0 days	3 years 7 months	11 years 3 months	RL (AS)	RL			–	Infrequent SVT	Infrequent SVT	–
F	3-11-2001	22 days	22 days	6 years 8 months	RPS (MS)	RL			–	–	–	–
F	20-9-1989	6 months	6 months	18 years 10 months	RPS (RL)	RPS (RL)	RPL	16 years 3 months	1	SVT		–
F	21-2-1991	1 years 5 months	9 years 3 months	17 years 5 months	RL	RL	RL	9 years 4 months	1	SVT JET AVNRT		–
							Inf. AV	16 years 10 months	1			
F	14-6-1995	6 years 2 months	6 years 2 months	13 years 1 months	RL (AS)	RL	2 × RPS	12 years 3 months	2	SVT	RBBB post abl	–
							RPS	12 years 4 months	1	SVT		
F	27-4-1984	9 years 9 months	9 years 9 months	24 years 3 months	RL (PH)	AS	Rt Mah	9 years 9 months	1	Antidromic SVT	Antidromic SVT	Sotalol
							Rt Mah	13 years 9 months	1			
F	19-5-1980	11 years 9 months	11 years 9 months	28 years 2 months	RL (AS)	RL (PS)	AS	15 years 8 months	1	SVT		–
M	4-1-1982	13 years 6 months	17 years 7 months	26 years 6 months	RL (PH)	LL			–		AVB1 RBBB	–

AP accessory pathway, *AS* anteroseptal, *AVB1* first-degree atrioventricular block, *AVNRT* atrioventricular nodal reentry tachycardia, *EA* Ebstein's anomaly, *EAT* ectopic atrial tachycardia, *EPS* electrophysiology study, *Inf. AV* inferior to atrioventricular node, *JET* junctional ectopic tachycardia, *LBBB* left bundle branch block, *LL* left lateral, *MS* mid-septal, *PH* parahisian, *RBBB* right bundle branch block, *RL* right lateral, *RPS* right posteroseptal, *Rt Mah* right-sided mahaim fibers, *SVT* supraventricular tachycardia, *VF* ventricular fibrillation

underwent a tricuspid valve repair and atrial septal defect closure, one also with plication of the right ventricle. The latter had a spontaneously subsiding junctional ectopic tachycardia rhythm disturbance in the immediate postoperative period. The other patient underwent a series of operations resulting in a Fontan procedure.

Discussion

This retrospective study of all consecutive live-born EA patients referred to one of the six Dutch pediatric heart centers over a 25-year period shows that 16 out of 93 pediatric EA patients exhibited rhythm disturbances during childhood or adolescence. Two died in the neonatal period: one because of a suspected arrhythmic event and one due to incessant SVT. The 14 patients still alive all showed (intermittently) preexcitation and all but one had arrhythmic events, most commonly paroxysmal SVT. In nine patients, arrhythmic events urged catheter ablation of accessory pathways that were successful in eight patients.

The prevalence of 17% of arrhythmic events in our EA population of children and adolescents is significantly lower than the prevalence reported in adult EA patients [2]. Adult EA patients have a higher prevalence of arrhythmic events because they not only show preexcitation but also can show prolonged PR interval, ectopic atrial tachycardia, atrial flutter, and atrial fibrillation. These arrhythmic events are caused by tricuspid regurgitation-induced right atrial enlargement, or due to secondary alterations of the right atrial myocardium from previous cardiac surgery, or occur postoperatively as a result of incisional atrial tachycardia. Surprisingly, all surviving pediatric EA patients with arrhythmic events also had (intermittently) preexcitation, rendering a preexcitation prevalence of 15% in this pediatric population of EA patients. This prevalence is not different from the ones reported in populations of EA patients of all ages, ranging from 10% to 21% [2, 3, 6, 7, 9, 11, 13, 14, 17, 18, 24, 25, 27]. As EA is a malformation of the right side of the heart, it is not surprising that in our study, as in others [2, 3, 6, 7, 9, 11, 13, 14, 17, 18, 24, 25, 27], only right-sided accessory pathways are found. The pediatric algorithm to predict the location of the accessory pathway based on QRS polarity in all ECG leads as devised by Boersma et al. [4] appeared to be more congruent with the results during catheter ablation than the adult algorithm as developed by d'Avila [8].

Little is known about the prevalence of preexcitation in neonates with EA. Starnes et al. [24] and Knott-Craig et al. [18] reported no preexcitation in their patients, yet the number of neonates studied was very limited (five and three, respectively). Celermajer et al. [7] found a prevalence of 10% (5 out of 50 neonates). This is in accordance with the current study with a prevalence of 10% in neonates (6/58).

The estimated prevalence of the WPW pattern in the general population is reported to be 0.01–0.3%. However, this might be an underestimation because an intermittent type of WPW pattern is common [23]. The prevalence of WPW increases in a population with congenital heart defects, in particular EA [16].

Five of the EA patients with preexcitation were detected during follow-up because of arrhythmia-related symptoms. Most probably, preexcitation was not detected at the time of EA diagnosis because of the intermittent nature of the WPW pattern, as already demonstrated by Munger et al. [19] and Goudevenos et al. [12]. The clinical presentation and natural history of patients with accessory pathways is highly variable. Cardiac arrhythmias, most frequently paroxysmal supraventricular tachycardia, occur in approximately 50% of individuals who have ventricular preexcitation [1, 12, 19]. Furthermore, only half of the patients with accessory pathways have their first tachycardia at <20 years of age [22].

Treatment of patients with WPW pattern depends on the existence of arrhythmias and their frequency and severity. Patients with symptomatic arrhythmia might be managed in the long term with antiarrhythmic drugs or with catheter ablation of the accessory pathway. Al-Khatib et al. [1] concluded that if the patients' paroxysmal supraventricular tachycardia is satisfactorily controlled by a beta-blocker, no additional evaluation or therapy is required. In our patient population, which includes patients over a long follow-up time span, 6 of the 11 symptomatic patients had undergone catheter ablation, 2 patients planned to undergo catheter ablation in the near future, and 5 patients were controlled satisfactorily with antiarrhythmic drugs. None of the asymptomatic patients in this study received antiarrhythmic treatment nor were they evaluated electrophysiologically. At present, the consensus in The Netherlands is that patients with symptomatic WPW should undergo electrophysiology study and catheter ablation of the accessory pathways. A consensus had not yet been reached concerning the treatment of patients with asymptomatic WPW. Pappone et al. [20] suggested evaluating the risk of arrhythmias by means of electrophysiology study and ablating the high-risk patients. However, the definition of these high-risk patients remains unclear [26].

It has been suggested that in children with EA, catheter ablation has a lower success rate and the risk of recurrence is higher [5].) These observations could not be confirmed in our study.

The authors believe that for EA children with symptomatic WPW, the treatment of choice should be radiofrequency catheter ablation. Whether asymptomatic patients with EA and WPW pattern need to be treated is still controversial.

Study Limitations

This is a retrospective study of all 93 patients referred to six pediatric heart centers over a 25-year period. As such, all limitations of retrospective studies apply.

Conclusions

In our study of the pediatric EA patients, rhythm disturbances were present in 17%. All but one of these patients with arrhythmias showed (intermittently) preexcitation. This prevalence of rhythm disturbances in childhood and adolescence is significantly lower than reported in adult patients with the same cardiac malformation. Supraventricular arrhythmias are the most common disturbances in the pediatric EA population; these symptomatic patients are well treated with radio-frequency catheter ablation. Life-threatening rhythm disturbances are not frequent early in life.

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