

CLINICAL EVALUATION OF CHILDREN WITH ELECTROCARDIOGRAPHIC PATTERN OF WOLFF-PARKINSON-WHITE AND PRESENTING OF SYMPTOMATIC CASES

WOLFF- PARKINSON-WHITE ELEKTROKARDİYOĞRAFİK PATERNİ SAPTANAN ÇOCUKLARDA KLİNİK DEĞERLENDİRME VE SEMPTOMATİK OLGULARIN SUNUMU

Filiz EKİCİ¹, İbrahim İlker ÇETİN¹, Leyla BİLGİN KARADENİZ²

¹ Ankara Çocuk Sağlığı ve Hastalıkları Hematoloji ve Onkoloji Eğitim ve Araştırma Hastanesi, Çocuk Kardiyoloji Kliniği

² Ankara Çocuk Sağlığı ve Hastalıkları Hematoloji ve Onkoloji Eğitim ve Araştırma Hastanesi, Yenidoğan Kliniği

ABSTRACT

Aims: To evaluate the children with electrocardiographic pattern of Wolff-Parkinson-White (WPW) and review their demographic features, presenting symptoms, electrocardiographic, echocardiographic findings, and management.

Methods: The study was conducted in a single tertiary research hospital from 2009 to 2011, retrospectively. Twenty-one children (1 day to 15 years) with a WPW pattern on surface ECG were included in this study. We classified patients into two groups as “Asymptomatic” and “Symptomatic Group”.

Results: Most children were asymptomatic (13 cases, mean age: 6.0 years) at the diagnosis and during the study period. Symptoms related to dysrhythmia were recognized in 8 cases (mean age: 9.1 years) and most common in school age children. There were no gender predominance between two groups. The symptoms were palpitations in 4 cases and syncope in one case. Three cases presented with attack of supraventricular tachycardia (SVT). They also had intermittent nature of WPW and male predominance. Echocardiography revealed mitral valve prolapsus in 7, hypertrophic cardiomyopathy in 3, aortic regurgitation in 1 and Ebstein abnormality in 1 case. SVT were successfully treated with Amiodoron or Adenosine. No patient died suddenly during the study period.

Conclusion: Children with electrocardiographic pattern of WPW should be recognized and managed properly.

Key words: Wolff-Parkinson-White, children, electrocardiography, echocardiography

Correspondence Address:

Uz. Dr. Filiz EKİCİ
Ankara Çocuk Sağlığı ve Hastalıkları
Hematoloji ve Onkoloji Eğitim
ve Araştırma Hastanesi, Çocuk
Kardiyoloji Kliniği
e-mail: ekicifiliz@gmail.com

ÖZET:

Amaç: Wolff –Parkinson- White (WPW) elektrokardiyografik paterni saptanan çocuk hastaların demografik özellikleri, başvuru yakınmaları, elektrokardiyografik ve ekokardiyografik özellikleri ve tedavi yöntemleri değerlendirilmiştir.

Materyal ve Yöntem: Bu çalışma tek bir merkezde ve üçüncü basamak araştırma hastanesinde 2009-2011 yılları arasında retrospektif olarak yapılmıştır. Yüzeysel EKG’ de WPW paterni saptanan 21 çocuk olgu (1 gün-15 yaş) çalışmaya dahil edildi. Hastalar asemptomatik veya Semptomatik olmak üzere iki gruba ayrıldı.

Bulgular: Olguların çoğu (13 olgu, ortalama yaş: 6.0 yıl) tanı anında ve çalışma süresince asemptomatikti. Disritmi ile ilişkili semptomlar 8 olguda (ortalama yaş: 9.1 yıl) belirlendi. Gruplar arasında cinsiyet bakımından fark saptanmadı. Başvuru semptomları: dört olguda çarpıntı ve bir olguda senkop idi. Üç olgu Supraventriküler taşikardi atağı ile başvurdu ve SVT’li olguların tümünde intermitten tipte WPW paterni ve erkek cinsiyet predominansı saptandı. Ekokardiyografi ile yedi olguda mitral kapak prolapsusu, üç olguda hipertrofik kardiyomiyopati, bir olguda aort yetersizliği ve bir olguda Ebstein anomalisi saptandı. SVT ataklarında Amiodoron veya Adenozin ile başarılı tedavi sağlandı. Çalışma süresince olguların hiçbirisinde ani ölüm gözlenmedi.

Sonuç: WPW elektrokardiyografik paterni tanısı alan çocuklara uygun tedavi uygulanmalıdır.

Anahtar Kelimeler: Wolff-Parkinson-White, çocuk, elektrokardiyografi, ekokardiyografi

INTRODUCTION

Wolff-Parkinson-White syndrome (WPWS) is a condition characterized by abnormal electrical pathways in the heart, which cause an arrhythmia. WPWS often occurs sporadically and familial cases reported rarely. The incidence of WPW pattern varies from 0.1 to 3 per 1000 electrocardiographies (ECGs), however it is not possible to determine the incidence of WPW pattern because of its intermittent nature (1-4). The presenting symptoms are dizziness, palpitations, syncope, discomfort of chest, and severe cardiopulmonary decompensation. In rare cases, arrhythmias associated with WPWS can lead to cardiac arrest and sudden death at initial presentation (1-4).

Patients with WPW have a risk for the development of both supraventricular and ventricular tachyarrhythmias. Supraventricular tachycardia (SVT) is typically orthodromic or rarely antidromic re-entrant tachycardia. AV reciprocating tachycardia, AV nodal re-entrant tachycardia, atrial flutter, and atrial fibrillation are common kinds of arrhythmias (1). Children with WPW have also some electrocardiographic differences than adult cases (5).

Here in, 21 infants and children with electrocardiographic pattern of WPW were reported and their demographic features, presenting symptoms, electrocardiographic, echocardiographic findings were evaluated. Management of children with WPW syndrome was also reviewed.

MATERIAL-METHODS

This study was conducted in a single research and training hospital from October 2009 to October 2011, retrospectively. Children with a WPW pattern on ECG were included in this study. Clinical, echocardiographic findings, the routine ECGs, and 24-hour-Holter monitoring records were all obtained within Pediatric Cardiology Department of our hospital. All ECGs were analyzed by two pediatric cardiologists. The criteria for the diagnosis of pre-excitation, based on the 12 lead surface ECG, were a shortened PR interval (for children <3 years less than 80 ms, 3-16 years less than 100 ms, and >16 years less than 120 ms) and a typical slurred upstroke of the initial QRS complex (delta wave) with a consequent widening of the QRS complex (QRS duration > 120 ms). We analyzed the polarity of the QRS complex and delta wave on the frontal plane of the conventional 12-lead electrocardiogram in all cases. Accessory pathway location was established by the use of ECG criteria according to Fitzpatrick's algorithm (6).

All patients were asked particularly about symptoms that could be related to episodes of tachycardia (including palpitations or syncope), cardioactive drugs, and previous attempts at surgical or transcatheter ablation. All patients underwent a careful physical examination. Surface ECG, 24 hour Holter ECG monitorization, and echocardiographic examination were performed in all cases. We classified patients into two groups as "Asymptomatic" and "Symptomatic Group". "Asymptomatic Group" consisted of cases having no symptoms related to dysrhythmia and no documented tachyarrhythmic event. Patients having symptoms related to dysrhythmia (palpitation or syncope) or documented tachyarrhythmic event were included in "Symptomatic Group". Children presented with episodes of tachycardia were evaluated by means of their ages, gender, clinical features, and associated cardiac diseases.

All cases were subsequently followed at 6 month intervals during the study period. Clinical examination, surface ECG, 24-hour Holter monitorization, and echocardiographic examination were repeated in every

6 months. When a patient had symptoms related to dysrhythmia (recurrent palpitation or syncope), documented tachyarrhythmic event or history of arrhythmogenic life threatening events, they referred for radiofrequency catheter ablation (RFA). Continuous variables are expressed as mean±standard deviation(SD) and analyzed by the 'Student t test'. Nominal findings were evaluated by the χ^2 test with Yates correction. A p value of < 0.05 was considered as significant.

RESULTS

The study population consisted of 21 children. Of all these cases, 14 (66%) were firstly diagnosed during study period. There were 10 male and 11 female (M/F ratio: 0.9) children. At diagnosis, the age of the children ranged from 1 day to 15 years and the mean age±SD was 7.2±4.3 years (Table 1). Electrocardiographic pattern of WPW was commonly recognized in children between 6 and 15 years old (14 cases, 65%). 13 children (61%) were included in asymptomatic group and 8 (38%) were included symptomatic group at diagnosis. The mean age of symptomatic cases was significantly higher than that of asymptomatic cases (9.1±5.0 years vs 6.0±3.5 years; $p<0.001$). The male to female ratio in symptomatic group did not significantly differ from asymptomatic group (1.0 vs 0.85; $p>0.05$) (Table 1).

Presenting symptoms and clinical findings: Reasons for cardiac evaluation in asymptomatic cases were precordial murmur (n=3), attention deficiency-hyperactivity disorder (n=3), chest pain (n=2), motor and mental retardation (n=1), dyspnea (n=1), suspicion of metabolic disease (n=1), obesity (n=1), and growth retardation (n=1). Presenting symptoms in symptomatic group were palpitations in 4 and history of syncope in 1 case. Episodes of SVT were documented in 3 patients (14.7%) as the first arrhythmic event in all cases with a male predominance.

CASE 1; A one day old newborn baby referred to our hospital because of obvious tachydysrhythmia detected soon after prolonged labor. He was born at term with a

Table-1. Age and sex of cases with Wolff-Parkinson-White pattern / syndrome at the first diagnosis.

Clinical features	All cases	Symptomatic cases	Asymptomatic cases	P
Number of cases n (%)	21 (100)	8(38)	13(62)	
Mean Age (SD)(years)	7,2 (4,3)	9,1(5,0)*	6,0 (3,5)*	
Minimum-Maximum	1 day-15 years	1 day -15 years	1-13years	
0-5 years, n (%)	7(33)	2(25)	5(38)	<0,001
6-9 years, n (%)	9(42)	2 (25)	7(53)	
10-15 years, n (%)	5(23)	4(50)	1(7)	
Male/Female	10/11 (0,9)	4/4(1,0)**	6/7 (0,85)**	>0,05

*The mean age of symptomatic cases was significantly higher than that of asymptomatic cases (p<0.001).

** The male to female ratio in symptomatic group did not significantly differ from asymptomatic group (1.0 vs 0.85; p>0.05).

birth weight of 3400 g. Tachydysrhythmia with narrow QRS complex was managed with lidocain in local hospital (Figure-1A). Because of no response to lidocain infusion, Amiodoron (1 mgr/ kg/ min bolus) was given and then the patient was referred to our hospital. At the first examination in our hospital, he had electrocardiography showing heart rate of 240 beat/min with a regular RR interval and wide QRS complex and no cardiovascular instability (Figure -1B). Echocardiography revealed physiological patent ductus arteriosus and patent foramen ovale. Amiodoron infusion was continued in our hospital and SVT was terminated at the 4th hour of Amiodoron infusion (5mcgr/kg/min). ECG revealed a normal sinus rhythm (Heart rate: 160 beats/min) and no delta waves or short PR interval was observed in the surface ECG obtained after termination of SVT. On the first day of hospitalization, he was given digoxin for prophylaxis of SVT. After 2 days, ECG revealed short PR interval and delta waves in DI derivation andan intermittent nature of WPW was also observed (Figure-1C). Digoxin was stopped and propranolol prophylaxis was started.

CASE 2; A 10-year old boy admitted to our hospital because of palpitation during walking. ECG revealed a SVT (heart rate: 250/min) with a narrow QRS complex. He was treated with IV Adenosine (100 mcgr/kg). ECG revealed the characteristic findings for WPWS and the

right-sided accessory pathway (Figure-2A). Except for the first degree mitral regurgitation, he had no structural cardiac diseases revealed by echocardiography. Propranolol was started for prophylaxis of SVT. An intermittent nature of WPW was also observed in this patient during the study period (Figure-2B). He was offered for RFA.

CASE 3; A 15-year-old boy admitted to our hospital because of palpitation. He had had palpitations for two years. He had no cardiovascular instability and no clinical evidence of low cardiac output. ECG revealed a SVT (heart rate: 200/min) with a narrow QRS complex (Figure-3A). He was first treated with IV verapamil (0.1mgr/kg), whereas SVT was not terminated. Then, he was given IV Adenosine (100mcgr/kg) and SVT was terminated. ECG revealed normal sinus rhythm (heart rate: 160 beats/min) and there were no delta waves or short PR interval in the surface ECG obtained after termination of SVT (Figure-3B). He had no structural cardiac diseases revealed by echocardiography. Propranolol was started for prophylaxis of SVT. The characteristic surface ECG for WPWS and the right-sided accessory pathway was noticed at follow-up period (Figure-3C). He had also an intermittent nature of WPW. He was referred for RFA.

Echocardiographic examination; Nine cases (42.8%) had normal cardiac findings revealed by echo-



Figure-1:A; Ortodromic-reciprocal tachycardia with narrow QRS complex B; Antidromic reciprocal supraventricular arrhythmia during Amiodoron infusion C; Ten QRS complexes showing AV conduction over the AV node–His pathway only followed by 9 QRS complexes showing pre-excitation

cardiography. Coexisting cardiac disease was detected in 12 cases (61%). The most common cardiac abnormality was mild degree mitral regurgitation and mitral valve prolapsus and this abnormality was detected in 7 cases (33.3%). First degree aortic regurgitation was determined in one case. Hypertrophic cardiomyopathy was determined in 3 cases. Echocardiography revealed Ebstein abnormality in a 5-year-old boy.

Electrocardiographic examination; Prediction of accessory pathway from the resting surface ECG according to QRS polarity was left-lateral in 11 children (52%)

(Because of QRS polarity was positive on leads V1 and III). 7 cases (33.3%) had right-sided (because QRS polarity was negative on leads V1 and III) and 3 cases had posteroseptal accessory pathways. ECG of cases with Ebstein abnormality revealed a right-sided accessory pathway (Figure-4). Patients with syncope had a left anterior septally located accessory pathway (Figure-5). Intermittent nature of WPW was observed in 3 cases (14.2%) and all were presented with a SVT attack (Case 1, Case 2 and Case 3). A 24-hour Holter monitoring displayed no dysrhythmia except for WPW pattern in all cases.

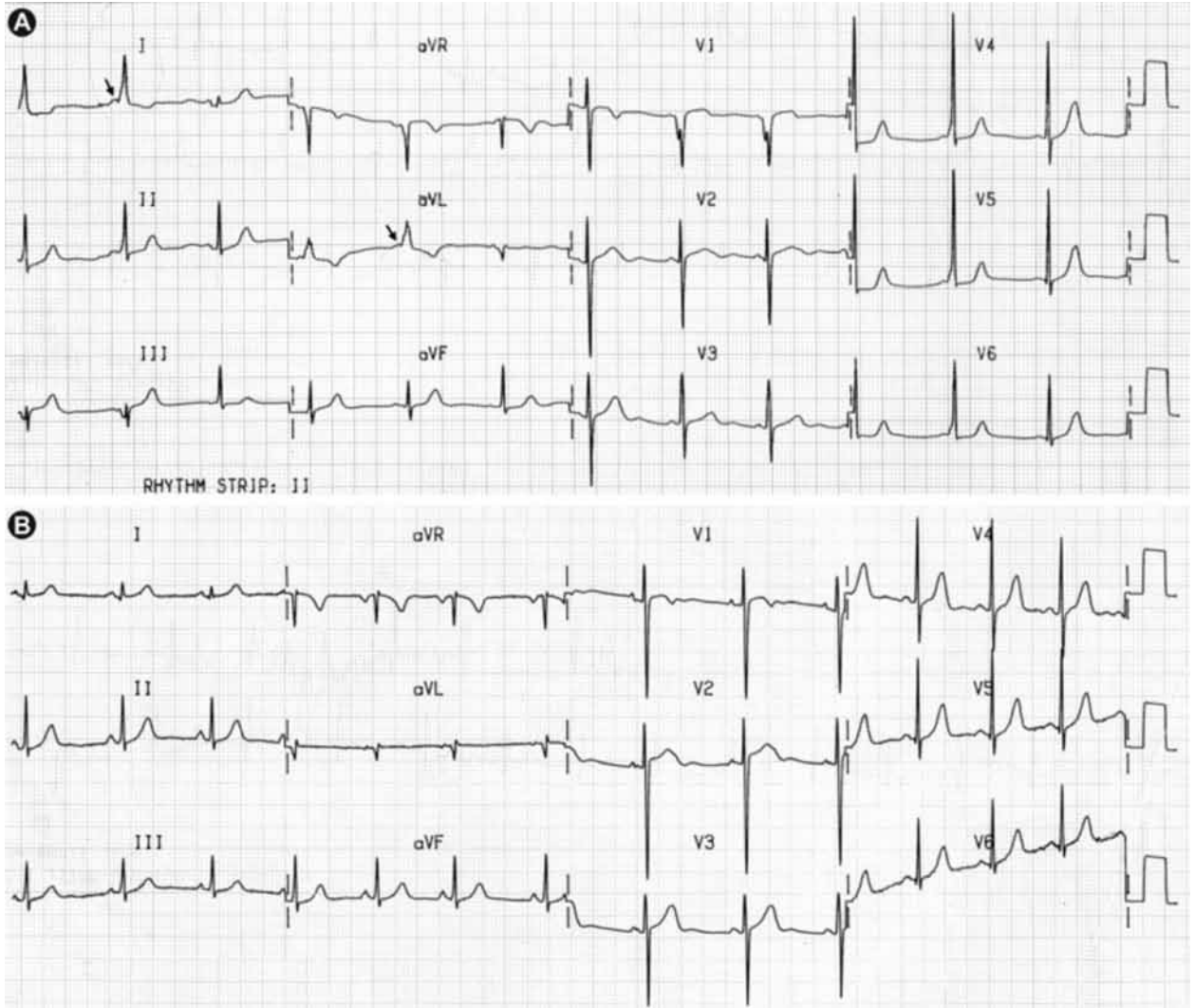


Figure-2; A; ECG revealed WPW (delta waves in DI and aVL derivations) and the right-sided accessory pathway. B; ECG in same patient; normal sinus rhythm and there was no delta waves in DI and AVL derivations.



Figure-3; A; Supraventricular tachycardia with a narrow QRS complex. B; no delta waves was observed in the surface ECG obtained after termination of SVT. C: The characteristic surface ECG for WPWS and the right-sided accessory pathway

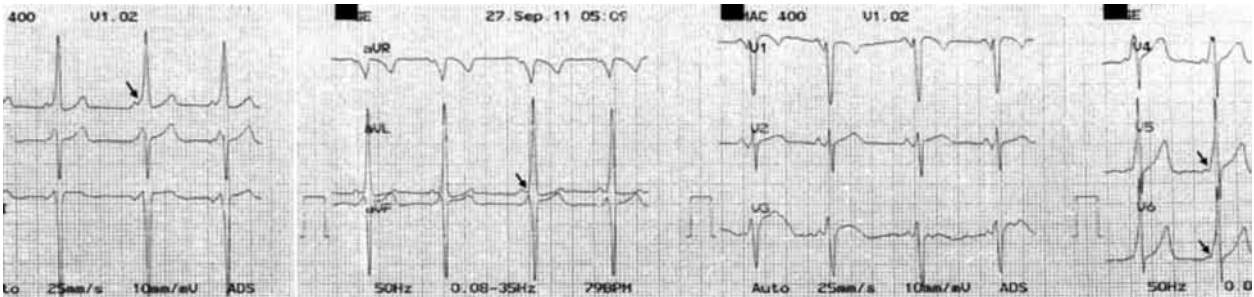


Figure-4; ECG of patient with Ebstein abnormality The S wave in lead V1 is downrigh, suggesting the presence of a right-sided accessory pathway.

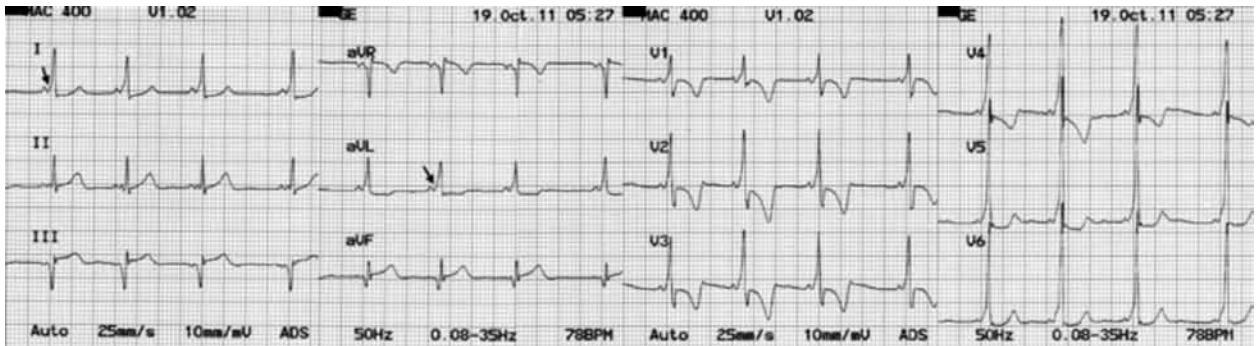


Figure-5; ECG revealed a left anterior septally located accessory pathway in patient who presented with syncope

CLINICAL COURSE AND TREATMENT

During the study period, symptoms related to dysrhythmia (palpitation) developed in 2 cases (15.3%) and they were asymptomatic at diagnosis. However, sudden death or unpredictable life-threatening arrhythmias did not occur in the asymptomatic WPW patients. Due to lacking of arrhythmogenic symptoms, patient with Ebstein abnormality and WPW pattern was not referred for electrophysiologic study. He was managed with beta-blocker (propranolol, 2 mgr/kg/day). We have followed him for 2 years with echocardiographic examinations and a 24-hour holter monitorization. He has been asymptomatic, yet. Propranolol (2 mgr/kg/day) was used by 7 symptomatic patients with frequent palpitation. Drugs used for SVT were Amiodoron in 1 case (Case-1) and adenosine in 2 cases (Case-2 and3). A newborn baby with a documented attack of SVT (Case-1) has been followed for 6 months and no dysrhythmia was observed during the study period. Six symptomatic patients referred to transcatheter ablation of the accessory connection using radiofrequency energy. The indication for the procedure was recurrent episodes of palpitation in 3 patients, attack of SVT in 2 patients, and syncope in 1 patient. No patient died suddenly. Another asymptomatic newborn baby referred to our department for metabolic disease suspicion had also WPW pattern and she died because of sepsis during follow up period.

DISCUSSION

Most of the patients in this study were asymptomatic at the first presentation and electrocardiographic pattern of WPW was most commonly recognized in children between 6-15 years old. Like previous studies, asymptomatic cases were significantly younger than symptomatic cases at first diagnosis (1). In previous studies, it was reported that the incidence of WPW was more than twice in males than in females but the reasons for male predominance are not known (4,7,8). In contrast to previous studies, there was no gender predominance in our study. Like our study, Sano et al reported a male to female ratio of 1:1 in Japanese school-children with ventricular pre-excitation (9).

Syncope in patients with WPWS may be related to either a rapid rate of SVT or rapid ventricular response over the APs (Atrial pacing) during atrial fibrillation (10). According to previous studies, syncope occurs in 9.5-19% of patients with WPWS and 67% of the patients with syncope had a septally located AP (1,4,10). Timmermans et al reported that the dense innervations of this area could cause extreme shortening of the refractory period of the APs leading to very fast ventricular response during atrial fibrillation (11). Syncope occurred in only one case in our study group and she had a left antero-septally located AP by ECG.

APs may be classified into three types: 1) Manifest APs are those that conduct more rapidly in the antegrade direction than the AV node, resulting in a discernible delta wave on the surface ECG. 2) Concealed APs conduct only in the retrograde direction and no delta wave is documented in the ECG. 3) Latent APs (intermittent) are those that have the capability to conduct in the antegrade direction. Latent pathways are most often far left lateral pathways where the conduction time to the AV node is much shorter than to the pathway. The incidence of intermittent WPW syndrome was higher in children and ranged from 11 to 15% (2, 5, 12). Some studies revealed that the case of WPW with intermittent pre-excitation at baseline revealed by exercise and isoproterenol administration with marked sensitivity to adrenergic stimulation (13). Delhaas et al reported that most cases with intermittent nature WPW had arrhythmic events, most commonly paroxysmal SVT (12). Mederius et al concluded that intermittent pre-excitation may not be used to identify patients who are at risk of sudden death (3). In our study, 3 patients with tachyarrhythmic attack also had intermittent nature of WPW. All of them had no manifest WPW pattern at the first diagnosis and it could be recognized after termination of SVT. The use of digoxin or verapamil for initial therapy of SVT is contraindicated for patients with WPW syndrome, because these medications may enhance antegrade conduction through the AP by increasing the refractory period in the AV node. In addition, digoxin may shorten the refractory period of the AP, further enhancing its antegrade conduction. The medications with beta-blockers should be preferred to treat SVT in the presence of pre-excitation.

Several algorithms have been developed to localize the site of APs from the surface ECG (1). These are usually based on delta wave amplitude, sum of delta wave polarities, R/S wave ratio, and QRS axis. Any obscuring in these components will reduce the accuracy of pathway localization. More than 50% of APs are located at the left free wall, 20-30% at the posteroseptum, 10-20% at the right free wall, and 5-10% at the anteroseptum (1). In this

study, the AP insertion site was localized most likely in the left lateral position in 52% of all patients.

The incidence of paroxysmal tachycardias in the young adult population is approximately 10% and increases with age up to 30% (8). Episodes of atrial fibrillation occur in as many as 20–30% of patients with the syndrome (1). The risk of sudden cardiac death due to WPW in the pediatric population is not known. The risk estimation have varied widely and range from 1% over a patient's lifetime to 0.0015 per patient-year (7,11). In our study, attack of SVT was observed in 14.2% of cases with a male predominance.

By electrophysiological study, children with WPW have some electrocardiographic differences than adult cases have (5). There was a higher occurrence of rapid AP needed to induce tachycardia in children. However, atrial fibrillation (AF) occurred more commonly in adult patients than pediatric patients (28% vs 16%). The pediatric patients had a higher incidence of multiple pathways (5% vs 1%). Both the onset and duration of symptoms were significantly shorter in the pediatric patients. The antegrade 1:1 AP conduction pacing cycle length (CL) and antegrade AP effective refractory period (ERP) in children were much shorter than those in adults with manifest WPW syndrome (5).

Patients with symptomatic arrhythmia can managed with catheter ablation of the accessory pathway by radiofrequency alternative current or, nowadays, by transvenous cryoablative catheter techniques (1). Ablation techniques provide the promise of a cure for WPW in as many as 90 to 100% of patients who undergo this procedure with relatively low risk (14-17). The most recent guidelines on the management of asymptomatic WPW patients suggest restricting catheter ablation of APs for high-risk occupations and professional athletes. Catheter ablation in asymptomatic pre-excitation patients was classified as an IIA indication with a B level of evidence (15). Prior studies suggesting that the prognosis of asymptomatic children with WPW is usually good, but some studies have shown that sudden death or unpredictable life-threatening arrhythmias can occur in the

asymptomatic WPW patients. Authors advocate that these patients should receive aggressive evaluation and interventional therapy (16,17). Tachyarrhythmia inducibility, short anterograde refractory period of APs and presence of multiple pathways were predictors of potentially life threatening arrhythmias. These findings will help to identify high-risk asymptomatic children with ventricular pre-excitation who may be candidates for AP ablation (1,16,17). Persistence of preexcitation during noninvasive stress and pharmacologic tests (with procainamide and propafenone) also showed good sensitivity to identify high-risk asymptomatic patients (18). During our study period, symptoms related to dysrhythmia (palpitation) developed in 2 cases (15.3%) who were asymptomatic at the first diagnosis. However, sudden death or unpredictable life-threatening arrhythmias did not occur in these asymptomatic patients.

In most cases, the cause of WPWS is unknown and occurs sporadically. A small percentage of cases with WPWS are caused by mutations in the PRKAG2 gene and it was responsible for the familial form of WPW syndrome (19). Some people with these mutations also have features of hypertrophic cardiomyopathy. WPWS often occurs with other structural abnormalities of the heart or underlying heart diseases (1). The most common heart defect associated with WPW is Ebstein abnormality (EA). At least 17% of patients with EA experience episodes of paroxysmal supraventricular tachycardia and most cases with EA had multiple APs (12). In our report, the most common cardiac abnormality associated with the WPW was mitral valve prolapsus and occurred in 33.3% of cases. EA was found in only one case. He had mild form of EA and no arrhythmogenic symptom. The accessory pathway in our patient with EA is at the right side as in a case reported previously (12).

Conclusion More than half of our patients were asymptomatic at the first presentation. Few cases had presented with obvious tachyarrhythmic attack and among these cases, a newborn baby with WPW first presented with a tachydysrhythmia. Remarkably, all cases with tachyarrhythmic attack also had intermittent nature

of WPW. Prolapsing of mitral valve was the most common associated cardiac abnormality. Every child with this electrocardiographic pattern should be recognized and managed properly.

REFERENCES

1. Lee KW, Badhwar N, Scheinman MM. Supraventricular tachycardia--part I. *Curr Probl Cardiol* 2008;33(9):467-46.
2. Kibos A, Deharo JC, Adoubi A, Assouan X, Djiane P. Clinical and electrophysiological study of asymptomatic Wolff-Parkinson-White syndrome. *Ann Cardiol Angeiol (Paris)* 2007;56(5):237-40.
3. Medeiros A, Iturralde P, Guevara M, Mendoza C, Colín L. Sudden death in intermittent Wolff Parkinson White syndrome. *Arch Cardiol Mex* 2001;71(1):59-65.
4. Goudevenos JA, Katsouras CS, Graekas G, Argiri O, Giogiakas V, Sideris DA. Ventricular pre-excitation in the general population: a study on the mode of presentation and clinical course. *Heart* 2000;83(1):29-34.
5. Lee PC, Hwang B, Chen YJ, Tai CT, Chen SA, Chiang CE. Electrophysiologic characteristics and radiofrequency catheter ablation in children with Wolff-Parkinson-White syndrome. *Pacing Clin Electrophysiol* 2006;29(5):490-95.
6. Fitzpatrick AP, Gonzales RP, Lesh MD, Modin GW, Lee RJ, Scheinman MM. New algorithm for the localization of accessory atrioventricular connections using a baseline electrocardiogram. *J Am Coll Cardiol* 1994;23(1):107-16.
7. Munger TM, Packer DL, Hammill SC, Feldman BJ, Bailey KR, Ballard DJ, et al. A population study of the natural history of Wolff-Parkinson-White syndrome in Olmsted County, Minnesota, 1953-1989. *Circulation* 1993;87(3):866-73.
8. Guize L, Soria R, Chaouat JC, Chrétien JM, Houe D, Le Heuzey JY. Prevalence and course of Wolff-Parkinson-White syndrome in population of 138,048 subjects. *Ann Med Interne (Paris)* 1985;136(6):474-8.
9. Sano S, Komori S, Amano T, Kohno I, Ishihara T, Sawanobori T, et al. Prevalence of ventricular preexcitation in Japanese schoolchildren. *Heart* 1998;79(4):374-8.
10. Paul T, Guccione P, Garson A Jr. Relation of syncope in young patients with Wolff-Parkinson-White syndrome to rapid ventricular response during atrial fibrillation. *Am J Cardiol* 1990;65(5):318-21.
11. Timmermans C, Smeets JL, Rodriguez LM, Vrouchos G, van den Dool A, Wellens HJ. Aborted sudden death in Wolff-Parkinson-White syndrome. *Am J Cardiol* 1995;76(7):492-4.
12. Delhaas T, Sarvaas GJ, Rijlaarsdam ME, Strengers JL, Eveleigh RM, Poulino SE, et al. A multicenter, long-term study on arrhythmias in children with Ebstein anomaly. *Pediatr Cardiol* 2010;31(2):229-33.
13. Aleong RG, Singh SM, Levinson JR, Milan DJ. Catecholamine challenge unmasking high-risk features in the Wolff-Parkinson-White syndrome. *Europace* 2009;11(10):1396-98.

14. Wellens HJ. Should catheter ablation be performed in asymptomatic patients with Wolff-Parkinson-White syndrome? When to perform catheter ablation in asymptomatic patients with a Wolff-Parkinson-White electrocardiogram. *Circulation* 2005;112(14):2201-7.
15. Blomström-Lundqvist C, Scheinman MM, Aliot EM, Alpert JS, Calkins H, Camm AJ, et al. ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Supraventricular Arrhythmias) *Circulation* 2003;108(15):1871-909.
16. Pappone C, Santinelli V. Should catheter ablation be performed in asymptomatic patients with Wolff-Parkinson-White syndrome? Catheter ablation should be performed in asymptomatic patients with Wolff-Parkinson-White syndrome. *Circulation* 2005;112(14):2207-15.
17. Pappone C, Santinelli V, Rosanio S, Vicedomini G, Nardi S, Pappone A, et al. Usefulness of invasive electrophysiologic testing to stratify the risk of arrhythmic events in asymptomatic patients with Wolff-Parkinson-White pattern: results from a large prospective long-term follow-up study. *J Am Coll Cardiol* 2003;41(2):239-44.
18. Gaita F, Giustetto C, Riccardi R, Mangiardi L, Brusca A. Stress and pharmacologic tests as methods to identify patients with Wolff-Parkinson-White syndrome at risk of sudden death. *Am J Cardiol* 1989;64(8):487-90.
19. Zhang LP, Hui B, Gao BR. High risk of sudden death associated with a PRKAG2-related familial Wolff-Parkinson-White syndrome. *J Electrocardiol* 2011;44(4):483-6.