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Sudden Cardiac Death in Pre-Excitation and Wolff-Parkinson-White

Demographic and Clinical Features

The prevalence of the Wolff-Parkinson-White (WPW) electrocardiogram (ECG) pattern is estimated between 0.1% and 0.3% (1). The risk of malignant arrhythmias in asymptomatic individuals is low and ablation of the accessory pathway can abolish the risk of sudden cardiac death (SCD) (2). Autopsy reports on SCD victims with a previously recognized WPW ECG pattern are anecdotal (3). This study sought to describe the clinical and pathological features of SCD cases with a premorbid diagnosis of WPW.

The Cardiac Risk in the Young center for cardiac pathology at St. George's University of London receives >400 cases of SCD annually. We reviewed a database of 3,684 consecutive cases of SCD referred to our institute between 1994 and 2014 and identified a subgroup of 19 cases (0.5%) with a recognized WPW ECG pattern before death. Clinical information was obtained from referring coroners that were asked to complete a questionnaire inquiring about the demographics of the deceased, past medical history, family history, cardiac symptoms, and circumstances of death. All subjects underwent detailed autopsy evaluation of the heart by an expert cardiac pathologist including histological analysis conducted. The heart weight was recorded in grams and ventricular wall thickness and internal cavity dimensions were measured at the midventricular level excluding the papillary muscles and fat. A minimum of 10 blocks of tissue were taken for histological analysis as reported previously. Sections of myocardium were fixed in formalin, embedded in paraffin, and stained with hematoxylin and eosin, as well as elastic Van Gieson stain to highlight myocardial fibrosis. SCD was defined as a death within 12 h of apparent well-being. Results are expressed as mean ± SD for continuous variables or as number of cases and percentage for categorical variables.

The vast majority of patients were men (n = 16; 84%) and white Europeans (n = 17; 89%) (Table 1). The mean age at death was 31 ± 15 years. Five cases (26%) were asymptomatic. Of the 14 symptomatic patients, 13 (68%) had reported palpitation, 1 (5%) experienced syncope and 2 had documented supraventricular

TABLE 1 Characteristics of the Study Population

Age (yrs)	Sex	Symptoms and Medical History	Circumstances of Death	HW (g)	MWT (mm)	LV Fibrosis	RV Fibrosis	Autopsy Diagnosis
Asymptomatic								
7	M	–	Unknown	200		No	No	Normal heart
48	M	–	At rest	526	20	Yes	No	HCM, mild CAD
50	F	–	During sleep	384	18	No	No	HCM
26	M	–	During exertion	510	20	Yes	No	HCM
18	M	–	At rest	390	19	No	No	Normal heart
Symptomatic								
20	M	Palpitation, on flecainide	At rest	237	9	No	No	Normal heart
26	M	Palpitation	At rest	361	16	No	No	Normal heart
20	M	Palpitation	At rest	444	14	No	No	Normal heart
20	F	Palpitation	At rest	311		No	No	Normal heart
46	M	Palpitation, on beta-blocker	At rest	474	16	No	No	Cardiac sarcoid
33	M	Palpitation	At rest	532	21	No	No	Enlarged LV
16	M	Palpitation	At rest	366	25	No	No	HCM
36	M	Syncope	At rest	498		Yes	No	Idiopathic fibrosis
55	F	Palpitation, on beta-blocker	At rest	385	13	No	No	Normal heart
Previous Ablation								
28	M	Palpitation	During sleep	316	19	No	No	LVH, mild CAD
27	M	Asymptomatic	During exertion	426	21	No	No	Normal heart
24	M	Asymptomatic	At rest	578		No	No	ILVH
65	M	Palpitation	At rest	486	12	No	No	Normal heart
28	M	Palpitation	During sleep	302	12	No	No	Normal heart

CAD = coronary artery disease; HCM = hypertrophic cardiomyopathy; HW = heart weight; ILVH = idiopathic left ventricular hypertrophy; LV = left ventricle; LVH = left ventricular hypertrophy; MWT = maximal wall thickness; RV = right ventricle.

tachycardia at hospital admission. Five individuals (26%) had a previous ablation, 4 of which were associated with successful resolution of the WPW pattern on the ECG. In the majority of cases (n = 16; 84%), SCD occurred at rest. The mean heart weight was 408 ± 105 g. In 10 patients (53%), the autopsy revealed a normal heart, 5 cases showed definitive cardiac pathology (4 cases of hypertrophic cardiomyopathy [HCM] and 1 case of cardiac sarcoid), and 4 cases demonstrated autopsy findings of uncertain significance (2 cases of idiopathic left ventricular hypertrophy, 1 with idiopathic fibrosis, and 1 with an enlarged left ventricle). Of the 5 asymptomatic patients, the postmortem revealed HCM in 3 and a normal heart in 2 cases. Two of the 4 patients with HCM showed myocardial fibrosis in the interventricular septum. All deaths attributed to HCM were characterized by left ventricular hypertrophy associated with myocyte disarray. None showed intracellular vacuolization characteristic of glycogen storage diseases associated with pre-excitation. None of the cases in this cohort showed significant valvular abnormalities. Among patients who underwent ablation, 3 showed a normal heart and 2 showed idiopathic left ventricular hypertrophy. Based on our pathologic series, the proportion of WPW cases with structural abnormalities at autopsy was similar to cases without the reported WPW ECG pattern (n = 1,870; 51%).

In conclusion, our findings suggest the following: 1) a proportion of cases with the WPW ECG pattern may die suddenly in the absence of symptoms; 2) many die at rest; 3) deaths may occur after the fourth decade; and 4) a substantial proportion of individuals have concomitant pathology that may contribute to atrial fibrillation. Previous prospective studies have showed that the presence of symptoms is not useful in the risk stratification of WPW patients (2,4,5). In addition, accessory pathway ablation did not seem to eliminate the risk of SCD, because 5 of the SCD cases were subjected to an ablation procedure. This is possibly due to the presence of multiple pathways or of other coexisting substrates for fatal arrhythmias. Finally, pre-excitation was associated with additional structural abnormalities in almost 50% of cases, underscoring the importance of performing baseline echocardiography and possibly cardiovascular magnetic resonance in all individuals with WPW and suggesting that the combination of pre-excitation with additional cardiac pathology may render individuals at higher risk of SCD.

Our study has some limitations. Although all the clinical information relating to the deceased was gathered in a meticulous fashion, only a small percentage of the entire cohort in our SCD registry was investigated with an ECG, therefore the true prevalence of SCD from WPW cannot be ascertained from this study. Our data suggest that WPW causes death in asymptomatic individuals and deaths may occur following ablation; however, this study cannot ascertain the prevalence of fatal events in these circumstances because our information relied on secondary reports and we did not have adequate details about the electrophysiological studies, including the refractory period or the number of pathways, respectively. Finally, the cardiac autopsy did not include a standardized demonstration of accessory pathways at the histological assessment.

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Diastolic Blood Pressure and Myocardial Damage

What About Coronary Perfusion Time?

In a recent issue, McEvoy et al. (1) examined the relationship between diastolic blood pressure (DBP) with subclinical myocardial damage (using