The Mystery of Asymptomatic Wolff-Parkinson-White Syndrome

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It is exactly 80 years since L. Wolff, J. Parkinson and P.D. White described the syndrome bearing their name (August 1930) [1]. Since then a large volume of literature has accumulated, mainly because of the ease with which the macro-reentry mechanism of the arrhythmia in patients with Wolff-Parkinson-White syndrome is understood. Although the number of patients with WPW is relatively large and there are important clinical problems imposed by WPW, the approach to asymptomatic subjects with WPW-type electrocardiogram is still under debate. In contrast to symptomatic patients, the risk in asymptomatic patients is not well established. As a result, there is no standard accepted approach to both determine risk and devise prophylactic treatment [2].

In this issue of *IMAJ* [3] the invasive approach to both risk stratification and prophylactic treatment is exemplified. A 12 year old boy was referred for electrophysiological evaluation because an ECG recorded as a prerequisite for league volleyball playing showed ventricular preexcitation. Although the child was asymptomatic, electrophysiology testing showed short refractoriness of the accessory pathway. Rapid conduction on the pathway resulted in 1:1 conduction at a rate of 200/min. Atrial fibrillation was induced with rapid atrial pacing, which subsequently degenerated to ventricular fibrillation. During the same procedure the accessory pathway was successfully ablated and the boy could resume his intensive sporting activity.

This case illustrates a possible high risk condition, but what is the chance of clinical occurrence of this arrhythmia and could this arrhythmia endanger the life of this young patient? This question was hotly debated in the last decade. The debate is based on unanimously accepted facts and arguable assumptions based on surrogates. First described in the early 1940s [4], ventricular fibrillation complicating WPW is well known. In 1971, for the first time, ventricular fibrillation was shown by Dreifus et al. [5] to be clearly linked with atrial fibrillation. Wellens and Durrer [6] elegantly demonstrated that the accessory pathway refractory period determines the ventricular rate during atrial fibrillation in WPW and this relationship is linear. The classic work on ventricular fibrillation in patients with WPW was published in 1979 by Klein at al. [7]. These researchers compared 31 patients with WPW and documented ventricular fibrillation with 73 patients who also had WPW but did not have a history of ventricular fibrillation. Significantly more patients in the VF group had a history of atrial fibrillation. Electrophysiologically, 16% of the patients in the VF group had multiple pathways compared to 5% in the other patients. The accessory pathway refractory period was significantly shorter in the VF group and had the shortest RR interval, and the mean RR interval during atrial fibrillation was shorter in the VF group. Based on these findings the surrogates for high risk in WPW are multiple pathways, short accessory pathway refractory period, and short RR interval during atrial fibrillation. However, in three young patients the VF was the first and only presentation of WPW.

It became abundantly clear that we need reliable risk stratification in asymptomatic patients with WPW. This test may be based on the three surrogates mentioned above. The invasive test is electrophysiology testing. Of note, the first electrophysiologic test was performed 50 years ago in patients with WPW, at that time for academic purposes.

In a relatively small study [8], the inducibility of atrioventricular reentrant tachycardia in asymptomatic patients with WPW was very low due to lack of retrograde conduction on the pathway and long AV nodal refractoriness. The follow-up was short and no adverse events were recorded in the patients with high risk defined during the electrophysiology study. In this study no isoproterenol or atropine challenge was performed [8]. A second study with a larger population (including the population from the previous study) showed that the inducibility was still very limited and the refractory period of the pathway was relatively long. Although the follow-up was much longer the well-being of these patients was still not affected [9]. If an electrophysiologic test is repeated after a mean of 54 months,
up to 31% will lose the preexcitation, and this may be the reason for the favorable follow-up [10]. The inducibility was low also in a subsequent study [11]. In more recent studies the inducibility was higher and the risk could be predicted by means of electrophysiology study [12-14]. Based on these studies, it has become accepted practice to use the electrophysiology study as a reliable risk-assessment tool. However, the test is not always accepted because it is invasive. As a result, several non-invasive tests have been used but they have not achieved wide acceptance because their predictability is uncertain [15].

One of the main reasons for a change in approach to the invasive test was the development of a unanimously accepted procedure – catheter ablation of the accessory pathway [16,17]. Very recently, the impact of catheter ablation on the mortality and morbidity of asymptomatic patients with WPW was evaluated [18,19]. Not only was an invasive test accepted, but the possibility of a definitive treatment was seen as a promising step for these patients. However, three major questions should be considered before such a step can be implemented:

- Does the accessory pathway bear high risk-predicting properties (short refractoriness, short RR during atrial fibrillation with wide QRS, multiple pathways with possible short refractoriness, at least in one of them)?
- Is the location of the pathway associated with increased risk for complications?
- Is the subject involved in a high risk occupation or hobby (pilot, bus driver, ambulance driver, firefighter, policeman/woman, competitive sportsmen/ women or similar)?

These three issues must be addressed when we suggest radiofrequency catheter ablation to a patient with asymptomatic WPW. The patient presented in this issue of the journal had an accessory pathway with short refractoriness, and the inadvertently induced atrial fibrillation degenerated into ventricular fibrillation. The accessory pathway was located far from the conduction system and the boy returned to his volleyball team.

Finally, it should be mentioned that a strong electrophysiology group [20] opposes the invasive approach. This fact must be taken into account too. However, most of us will tend to refer asymptomatic patients to catheter ablation if the cases comply with the three questions stated above, as illustrated by the case presented in this issue of IMAJ.

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References

“"It is not necessarily true that averaging the averages of different populations gives the average of the combined population (Simpson’s paradox)”

Edward H. Simpson (b. 1922), British statistician. The above paradox is widely used in mathematical statistics teaching in order to illustrate the care statisticians need to take when interpreting data.