Old stuff still trending. Use of propafenone as a safety net until catheter ablation in a patient with documented pre-excited Atrial Fibrillation and Wolff-Parkinson-White syndrome - a classic case report.

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ABSTRACT

Background

Atrial Fibrillation in Wolff-Parkinson-White syndrome may result in life-threateningly rapid antegrade conduction over a bypass tract, manifested by an irregular broad-complex (pre-excited) tachycardia that can degenerate to ventricular fibrillation. Shortest pre-excited RR interval below 250msec during atrial fibrillation predicts increased risk of sudden cardiac death.

Case summary

We report a case of a 43-year-old man with unremarkable cardiac history who presented due to sudden-onset feeling of palpitations and pre-syncope after strenuous lifting. Electrocardiography depicted fast pre-excited atrial fibrillation. The shortest pre-excited RR interval was estimated at 160msec, indicating an accessory pathway with short antegrade refractory period at risk for mediating sudden cardiac death. Direct current cardioversion restored sinus rhythm unraveling delta-waves. The patient was put on propafenone 450mg/day having an uneventful clinical course. On day-10 post-admission, electrophysiological study induced rapid atrial fibrillation but the shortest pre-excited RR interval was substantially increased to 264msec. A left anterolateral accessory pathway was ablated. The patient remained symptom-free until his latest follow-up in the third month post-ablation without manifest pre-excitation on surface electrocardiogram.
Treatment options of pre-excited atrial fibrillation include anti-arrhythmic agents but mainly electrical cardioversion. Cardioversion can safely restore sinus rhythm, while use of anti-arrhythmics often requires ICU monitoring due to risk of QT prolongation.

Catheter ablation is the mainstay of therapy for symptomatic patients. Our rare report highlights the direct impact of propafenone on prolonging the refractoriness of the accessory pathway, effectively and safely, and reappraises propafenone's worthiness as a protective measure following pre-excited atrial fibrillation episode until ablation.

Keywords

Wolff-Parkinson-White syndrome, Pre-excited Atrial Fibrillation, Shortest pre-excited RR interval - SPERRI, Propafenone, Classic Case Report
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1 Learning points

1. Propafenone could be offered to patients with WPW syndrome after a documented episode of pre-excited AF with exceptionally short pre-excited RR interval as a bridge to ablation and safety net to avoid risk of ventricular fibrillation and sudden death.

2. Irregularly irregular wide-QRS complex tachycardia should set the diagnosis of pre-excited AF and emergency physicians should be capable of recognizing this unique ECG demonstration immediately.

3. Direct current cardioversion remains the gold standard therapy for fast broad irregular tachycardia in the acute phase followed by a pathway ablation in an experienced centre.
Acknowledgements: Dr Georgios Leventopoulos is a consult electrophysiologist at Patras University Hospital who reviewed and commented on focused points in the final draft.
### TIMELINE

<table>
<thead>
<tr>
<th>Day</th>
<th>Event</th>
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<tbody>
<tr>
<td><strong>Day 1</strong></td>
<td><strong>Hospital admission</strong>&lt;br&gt;Near syncope, Pre-excited AF with rapid ventricular response and SPERRI at 160msec, immediate transfer to the cardiac Intensive Care Unit (ICU).</td>
</tr>
<tr>
<td><strong>Cardiac ICU</strong></td>
<td>Light sedation with 5mg midazolam.&lt;br&gt;DC Cardioversion with 270 Joules restored sinus rhythm with manifest pre-excitation.&lt;br&gt;WPW syndrome diagnosed.&lt;br&gt;Uneventful recovery within several minutes.&lt;br&gt;Anticoagulation with enoxaparin 80mg b.i.d. (from day-1 to day-9).&lt;br&gt;</td>
</tr>
<tr>
<td><strong>Day 2</strong></td>
<td><strong>Cardiology ward</strong>&lt;br&gt;Complete blood count, cardiac troponin, d-dimers, Thyroid Stimulating Hormone (TSH): values within normal range.&lt;br&gt;Transthoracic echocardiography: normal left and right ventricular function and dimensions, no valvular lesions or septal defects.&lt;br&gt;X-ray imaging of the lungs: clear.&lt;br&gt;Start on propafenone 150mg t.i.d. (from day-2 to day-9).</td>
</tr>
<tr>
<td><strong>Day 3</strong></td>
<td>No QRS widening.</td>
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<td><strong>Day 8</strong></td>
<td>Transfer to a tertiary EP centre.</td>
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<tr>
<td><strong>Day 10</strong></td>
<td>Electrophysiological study with local anaesthesia (20mg of lidocaine subcutaneously) for sheath insertion; no sedation was required. SPERRI 264 msec. Catheter ablation of a left</td>
</tr>
<tr>
<td>Day 11</td>
<td>Discharged on rivaroxaban 20mg for a month.</td>
</tr>
<tr>
<td>1-month follow up</td>
<td>Symptom free, no pre-excitation on surface ECG, rivaroxaban stopped, family members screened for pre-excitation.</td>
</tr>
<tr>
<td>3-months follow up</td>
<td>Symptom free. Recommendation for periodic follow-up.</td>
</tr>
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MAIN TEXT

INTRODUCTION

Wolff-Parkinson-White (WPW) syndrome is a congenital condition referring to the Kent bundle; an accessory pathway (AP) providing direct cohesion between atrial and ventricular myocardium constructing a route for re-entrant tachycardia circuits [1]. It encompasses the combination of overt electrocardiographic pre-excitation [short PR, QRS with the delta wave, repolarization abnormalities] in the presence of sinus rhythm [1]. WPW’s unique characteristic is AP’s ability to conduct in a bidirectional fashion; either retrogradely resulting in atrioventricular reentry tachycardias (AVRT) of narrow QRS complexes or antegradely, originating wide QRS tachydysrhythmias like antidromic AVRT or pre-excited atrial fibrillation (AF) and atrial flutter. Malignant degeneration to ventricular fibrillation (VF) can emerge [2]. AP electrical properties and effects on atrial architecture along with increased atrial vulnerability and atrial myopathy constitute the underlying mechanisms in the pathogenesis of AF in these patients; spontaneous degeneration of AVRT may potentially trigger AF as well [3]. Advanced age with two peaks at the third and fifth decade of life, male sex, and prior history of syncope independently predispose WPW patients to AF [4].

Many studies distinguished the benefit of propafenone’s administration (or class Ic agents in general) in patients with WPW syndrome [5-8]. Although propafenone exerts unique prolonging effect on AP conduction and remarkable “anti-atriofibrillatory” activity [5-7], clinicians are usually reluctant to prescription due to proarrhythmic effects and non-negligible risk of converting AF to 1:1 atrial flutter [9].
In this report, we aim to communicate propafenone’s short-term favorable electrophysiological properties on AP refractoriness and reconsider its value in non-tertiary centers as a safety net for WPW patients documenting fast pre-excited AF, until electrophysiological study is performed.
CASE PRESENTATION

A 43-year-old man presented to the emergency department reporting sudden-onset feeling of palpitations and near-syncope after strenuous heavy lifting. He was pale and diaphoretic; blood pressure was measured 90/70mmHg, oxygen level 99%, heart-rate 210-230bpm and body temperature 36.6°C. Past medical history was clear for cardiac disease, syncope or presyncope. No history of sudden cardiac death (SCD) or cardiomyopathy into his family was stated. He denied recent flu-like symptoms, smoking, illicit drug use or excessive alcohol consumption. Physical examination was unremarkable. Initial electrocardiogram (ECG) depicted an irregularly irregular, broad QRS complex tachycardia (Figure 1). No previous ECG recordings were handed. Direct Current (DC) cardioversion restored sinus rhythm with manifest ventricular pre-excitation and clear “delta” waves (Figure 2) confirming our initial clinical suspicion for underlying WPW syndrome. Shortest Pre-Excited RR Interval (SPERRI) during AF was estimated at 160msec (Figure 1), indicating an AP with extremely short antegrade effective refractory period (ERP) at risk for mediating SCD. Echocardiography ruled out abnormalities associated with WPW, including Ebstein’s anomaly, valve lesions, cardiac hypertrophy, atrial aneurysms and septal defects [2]. Cardiac ischemia was also excluded on the basis of clinical, electrocardiographic, echocardiographic and laboratory data. The patient was put on enoxaparin 80mg b.i.d and propafenone 150mg t.i.d. and his clinical course remained uneventful. Electrophysiological Study (EPS) was performed at a tertiary centre on day-10 post-diagnosis; programmed atrial stimulation induced pre-excited AF with markedly increased SPERRI=264msec and a left anterolateral AP with antegrade only
conduction properties was ablated (Figures 3-5). The patient was scheduled for routine cardiologic follow-up and advised to abstain from intense physical activity for at least one month post-discharge [2]. In case of palpitations, ECG and 24-hour-holter monitoring were suggested. CHA₂DS₂-VASc Score was calculated zero, so one month of rivaroxaban 20mg daily was deemed sufficient post-ablation [10]. Family members were also screened for pre-excitation. The patient remained symptom-free without pre-excitation on surface ECG on his latest follow-up visit three months after the procedure.
DISCUSSION

In this report of WPW syndrome manifested by life-threatening pre-excited AF, we wish to highlight old-school medicine knowledge of using propafenone as a short-term protective measure in preventing relapses of pre-excited arrhythmias/AF and/or SCD until ablation. In our specific patient, propafenone prolonged SPERRI from 160msec on presentation, indicating increased risk for SCD, to 264msec during EPS, surpassing borderline safety limit (250msec) within only 10 days [2]. This remark seems important underlining rapid and drastic modification of AP refractoriness. No AF relapses or atrial flutter episodes [9] were recorded, emphasizing propafenone’s short-term “anti-atriofibrillatory” effects without adverse impact on atrioventricular nodal (AVN) conduction. In this respect, administration of propafenone could be encouraged, especially in non-tertiary care facilities, as a safety net until EPS. Pre-defined connecting pathways for patient transfer to experienced EP centers should be established.

In our case, ECG upon presentation (Figure 1) depicted a grossly irregular, wide QRS complex tachycardia with atypical RBBB morphology [2]. Differential diagnosis of this bizarre-looking tachycardia should include AF with anterograde conduction over an AP, polymorphic ventricular tachycardia (VT) or atrial tachycardia with variable degree block and aberrancy. Pre-excited AF demonstrates irregularity, a greater beat-to-beat variability and erratic QRS morphology due to alternate degrees of fusion and activation over both the AP and the AVN; however, unlike polymorphic VT or torsades de pointes, it maintains a stable axis without twisting. If still in doubt about clarification, electrocardioversion should be opted [2].
Paroxysmal AF accounts for approximately 50% of WPW patients with fateful events [11]. These patients are typically young without structural heart disease and usually present with hemodynamic instability, requiring urgent cardioversion and early AP ablation [12]. The AP is of primary importance in the induction of spontaneous AF and decreased incidence of AF recurrence is reported after successful AP elimination [3]. In this respect, AP over pulmonary veins ablation was prioritized in our relatively-young patient with low 10-year Atherosclerotic Cardiovascular Disease Risk (ASCVD) Score (1.2%) and zero CHA₂DS₂-VASc Score [2,3]. Risk of SCD in WPW syndrome is increased if multiple APs are present, short AP ERP (<240msec) is measured, AF and atrial flutter are established, or a family history of premature SCD is mentioned. However, SCD occurs as the first and only symptom in only <1% of WPW patients [11-13]. On admission, DC cardioversion (preferred over ibutilide or procainamide necessitating complex hemodynamic/ICU monitoring) resumed sinus rhythm, unveiling an overt (manifest) left anterolateral AP according to St George’s algorithm [2]. APs may be located in the left (most commonly) or right free wall or septum; in 5-10% of patients, multiple pathways are present [2]. In our specific patient, left-sided AP position and intact tricuspid valve (TV) apparatus on echocardiography ruled out Ebstein’s anomaly as this entity is commonly associated with right-sided APs and TV abnormalities. In up to 50% of WPW cases, APs are electrocardiographically silent (concealed), as they conduct only retrogradely perpetuating an orthodromic AVRT [2]; in this setting, propafenone can increase antegrade ERP, widening the tachycardia zone thus making macro-reentry more likely. Instead, APs propagating impulses only in the anterograde direction, like in
our case, are quite uncommon (≤10%) [2]; in this specific subset, we can ex
juvantibus postulate that propafenone is safe and propitious, especially when
ablation is not feasible.
Propafenone has been reported to minimize AF induction or prevent pre-excited AF
by SPERRI elongation, resume sinus rhythm or decrease markedly peak ventricular
rate during AF and terminate or slow ventricular response of inducible AVRT [5-7]. Its
unique “anti-atriofibrillatory” effect along with its prolonging action on AP
refractoriness slowing or blocking conduction in both antegrade and retrograde
direction [5-7], qualified administration. Possibly, Ic agents in general could have also
functioned well in our patient as they share similar electrophysiological effects on
normal conduction system and APs [14]. Although our data may suggest a significant
short-term impact of propafenone on SPERRI prolongation, sympathetic over-
discharge upon presentation may have underestimated initial SPERRI
measurements. In addition, sedative protocols and parasympathetic stimulation may
influence EPS SPERRI calculations and overrate propafenone’s effect, however in our
case no sedative agents were administered. During the acute phase, nodal blocking
agents were sidestepped because of imminent degeneration to VF, facilitating
conduction via the AP [12]. Following stabilization, propafenone’s additional b-
blocker effect (compared with other Ic agents) may have prevented adverse
arrhythmic events, including 1:1 atrial flutter [14,15]. Although not confirmed in our
specific patient, oral use has been associated with long-term benefits, by preventing
symptomatic arrhythmias or modifying recurrent ones, making them rarer, slower or
prone to self-termination [5,6]. Validated data render propafenone fairly safe
overall; significant electrophysiological side effects and proarrhythmia with
enduring use have been reported in 1.9%, while SCD in 0.6% with underlying WPW syndrome or structural heart disease [16].
CONCLUSION

Specific ECG morphology should set the diagnosis of pre-excited AF. DC cardioversion is preferred over antiarrhythmic drugs. Propafenone could come back in trend out of our armamentarium and be used at least for short term as a bridge to the EP lab. Its remarkable effects prolonging AP ERP and SPERRI, depressing atrial arrhythmias, along with sympathoplegic and b-blocking action, establish it as an old but gold agent in interim prevention of AF recurrences and SCD. Ablation, though, remains the ultimate therapy.
Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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List of figure legends

- **Figure 1.** Electrocardiogram upon presentation demonstrating an irregular, wide QRS complex tachycardia consistent with Wolff-Parkinson-White syndrome with pre-excited atrial fibrillation, with the shortest pre-excited RR interval (SPERRI) measured at 160 msec.

- **Figure 2.** Electrocardiogram immediately after direct current cardioversion illustrating classic Wolff-Parkinson-White findings: short PR interval (<120 msec), wide QRS complex (>120 msec) with slurred onset of the QRS waveform (*delta* wave); and secondary ST-T wave changes of abnormal repolarization directed opposite the major *delta* wave and QRS complex. By using the stepwise approach proposed by the St George’s algorithm (absence of negative QRS in both III and V1 leads (Step 1); positive QRS complex in aVL (Step 2); and positive QRS complex in V1 (Step 3)), a left anterolateral AP was tracked [2].

- **Figure 3.** Atrial stimulation (S1=600msec) during the electrophysiological study performed on day-10 post-diagnosis, illustrating that (A) the antegrade earliest ventricular activation site was at CS1-2 dipole, indicating a left anterolateral location of the accessory pathway, and (B) the antegrade accessory pathway effective refractory period was 300 msec.

- **Figure 4.** Pre-excited atrial fibrillation induced during the electrophysiological study [rapid atrial pacing with drive train (S1) at 600msec followed by an
extrastimulus (S2) at a coupling interval of 280msec. The shortest pre-excited RR interval (SPERRI) was calculated at 264msec.

- **Figure 5.** Intracardiac electrograms during accessory pathway ablation with 40W radio-frequency lesion targeted at the earliest activation (fused atrial and ventricular signals) at the lateral mitral annulus (transeptal approach); rapid loss of pre-excitation (please observe the fourth and fifth QRS complexes) immediately after initiation of ablation is clearly depicted. (b) Post-ablation surface electrocardiogram also illustrating loss of pre-excitation (absence of “delta” waves).