CASE REPORT

Intermittent preexcitation indicates “a low-risk” accessory pathway: Time for a paradigm shift?

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We report three patients with intermittent loss of the preexcitation pattern in the ECG that had undergone an electrophysiological study. Despite apparently poorly conducting accessory pathway (AP), in each case a fast anterograde conduction, either during spontaneous atrial fibrillation or during incremental atrial pacing (on isoproterenol) was documented; shortest preexcited RR intervals of 200–240 ms were observed. We review the literature and conclude that intermittent preexcitation observed on resting 12-lead ECG lacks sufficient specificity for the diagnosis of an AP with long refractory period and cannot be considered a substitute for electrophysiological study in patients with this electrocardiographical phenomenon.

KEYWORDS

intermittent preexcitation, isoprenaline, sudden death, Wolff-Parikinson-White syndrome

1 | INTRODUCTION

It is commonly accepted that intermittent preexcitation detected during sinus rhythm is a specific finding indicating the presence of an accessory pathway (AP) that poorly conducts in the anterograde direction posing no risk of fast ventricular response during atrial fibrillation and subsequent development of ventricular fibrillation. However, such belief is mainly based on expert's opinions. Literature search does not reveal any large studies concerning intermittently conducting APs with regard to long-term risk of developing ventricular fibrillation. Only few small studies concerning electrophysiological properties of APs with intermittent conduction in surface ECG are available (Kiger et al., 2016; Klein & Gulamhusein, 1983; Mah et al., 2013; Wackel, Irving, Webber, Beerman, & Arora, 2012; Yamamoto, Yeh, Lin, & Wu, 1990). We have recently published a case of a 34-year-old man with third degree heart block, DDD pacemaker and no evidence of preexcitation during the block during slow ventricular escape rhythm, yet with fast antidromic tachycardia episodes via an adrenalin-dependent left lateral AP during emotions/exercise (Jastrzebski, Hart, & Czarnecka, 2016). This case clearly showed that a resting ECG can be occasionally

extremely misleading with regards to the presence of an AP with clinically significant anterograde conduction properties. The aim of this case series is to further elaborate on this subject.

2 | CASE 1

A 72-year-old woman with prior history of palpitations and syncope was urgently admitted due to preexcited atrial fibrillation with fast ventricular response. The shortest RR interval was 200–240 ms (Figure 1, upper panel). After cardioversion she was referred for ablation of the AP. Surprisingly, the electrophysiological study in a nonsedated, drug-free condition revealed an AP that was very barely conducting in the anterograde direction (Figure 1, lower panel). Since this was a left posterior pathway a mechanical trauma with catheters was not possible as the initial study was conducted from the right side. AP properties during isoprenaline administration were not assessed in this case. After ablation of the AP (guided by retrograde conduction) there were no further episodes of syncope nor preexcited atrial fibrillation events.

FIGURE 1 Upper panels: Fast preexcited atrial fibrillation with RR intervals of 200–240 ms. Lower panel: during electrophysiological study, 2:1 block in both the atrioventricular node and the accessory pathway (AP) during atrial pacing at 400 ms

3 | CASE 2

A 32-year-old man with vague symptoms of occasional chest discomfort was admitted for electrophysiological study due to intermittent preexcitation. Despite several ECGs and Holter monitoring documenting intermittent preexcitation both at rest and during moderate exercise, the electrophysiological study revealed, apart from orthodromic atrioventricular tachycardia, a left posterior AP that was able to conduct in a 1:1 anterograde direction at a rate of 250 bpm (during isoprenaline administration). The AP was successfully ablated with no recurrence of symptoms (Figure 2).

4 | CASE 3

A 13-year-old asymptomatic girl with an intermittent preexcitation on 12-lead ECG (Figure 3a) had undergone an electrophysiological study.

Surprisingly, during isoproterenol infusion the AP was able to conduct very fast with 1:1 anterograde conduction at a cycle length of 240 ms (Figure 3b). Orthodromic atrioventricular tachycardia was easily inducible. A left posterior AP was located and successfully ablated via retrograde aortic approach.

5 | COMMENTARY

This case series highlights a relevant clinical point: intermittent preexcitation does not necessary indicate poor anterograde conduction and long refractory periods. A literature search identified four similar cases of intermittent preexcitation and yet fast anterograde AP conduction (including one sudden death case) (Aleong, Singh, Levinson, & Milan, 2009; Easley, Sensecqua, Mann, & Reiter, 1988; Gemma, Steinberg, Prystowsky, & Padanilam, 2013; Medeiros, Iturralde, Guevara, Mendoza, & Colin, 2001). Moreover, one large study that

FIGURE 2 (a) Intermittent complete loss of preexcitation unmasking first degree atrioventricular block. (b) 1:1 anterograde conduction through the accessory pathway (AP) at a rate of 250 bpm (on isoproterenol)

investigated 1,007 patients with APs, reported that 7% of the 56 patients who experienced sudden cardiac arrest had intermittent preexcitation on resting ECG, however, no detailed electrophysiological data nor the value of using isoprenaline during EP studies were provided (Orczykowski et al., 2013).

Five prior studies ($n = 11$ –41) have reported on electrophysiological properties of intermittent APs (Kiger et al., 2016; Klein & Gulamhusein, 1983; Mah et al., 2013; Wackel et al., 2012; Yamamoto et al., 1990). Klein and Gulamhusein studied 26 patients with intermittent preexcitation and found that four of them (15%) had shortest RR intervals between preexcited beats (SPRRI) <250 ms, however; the use of isoprenaline was not reported (Klein & Gulamhusein, 1983). Kiger et al. (2016) studied 26 children with intermittent APs and found two of them (8%) SPRRI ≤ 250 ms, both cases during isoprenaline infusion, however; only three cases out of these 26 patients were tested on isoprenaline. Mah et al. studied 41 children with intermittent preexcitation (17 with isoprenaline infusion) and

found that intermittent APs had longer AP refractory period than APs with persistent anterograde conduction, however; the difference in median value was not significant: only 15 ms on baseline testing and 30 ms when tested on isoprenaline. Moreover, four of these 41 patients had either SPRRI or AP effective refractory period ≤ 250 ms (Mah et al., 2013). Wackel et al. (2012) studied 24 patients with intermittent preexcitation either on ECG/holter or during exercise test and found that six of them (four during isoprenaline infusion) showed rapid conduction. Summarizing these studies, approximately 14% (16/117) of AP with intermittent conduction were capable of very fast anterograde conduction, perhaps more if all cases were tested during isoprenaline infusion. This percentage is not that much different from that seen in patients with persistent preexcitation. Since electrophysiological study is recommended for assessment of AP properties in asymptomatic patients with persistent preexcitation, should it be withheld from asymptomatic patients with intermittent preexcitation?

FIGURE 3 (a) 12-lead resting ECG with intermittent, alternating preexcitation via left posterior accessory pathway. (b) Leads V_1 – V_6 recorded during atrial pacing at a rate of 250 bpm showing 1:1 conduction (on isoproterenol)

We believe that fast anterograde conduction observed in cases of intermittent preexcitation, mostly reflect high catecholamine sensitivity of some APs. It is possible that the percentage of such APs is higher among intermittent APs than among APs with persistent anterograde conduction. Therefore, catecholamine sensitivity might be a major factor limiting usefulness of noninvasive tests in assessing AP properties. Exercise test considered useful in this regard (Refaat, Hotait, & Tseng, 2014), may not be specific enough to rule out risky APs with intermittent anterograde conduction in the resting

condition. Sudden loss of preexcitation during exercise test not always exclude fast AP conduction during isoprenaline administration or sudden death occurrence (Ali et al., 2016; Kiger et al., 2016; Sharma, Yee, Guiraudon, & Klein, 1987; Wackel et al., 2012). Perhaps isoprenaline test, similarly to adenosine test (Daubert et al., 1988), should be considered in selected WPW cases. Aside from catecholamine sensitivity, repetitive retrograde penetration of the AP (linking) can contribute to the presence of intermittent preexcitation despite short AP anterograde refractory period, this mechanism might act

synergistically with catecholamine sensitivity (prolongation of AP conduction time during low-adrenaline state might facilitate linking in these cases) (Castellanos, Portillo, Zaman, Luceri, & Myerburg, 1986; Middlekauff, Stevenson, & Klitzner, 1990; Prystowsky, Pritchett, & Gallagher, 1984).

6 | LIMITATIONS

The issue of prophylactic ablation of APs and significance of SPRRI values on and off isoproterenol with relation to the risk of sudden cardiac death are beyond the scope of the current short case series. We would like to avoid any impressions that we advocate routine prophylactic ablation of intermittent APs. However, the current guidelines recommend a SPRRI cutoff value of 250 ms without any provisions whether it should be assessed on or off isoproterenol (Page et al., 2016). SPRRI assessment on isoproterenol likely increases sensitivity (and decreases specificity) which might be desirable or not. We believe that decisions concerning ablation and isoproterenol use must take into account operator's ablation complications rate, degree of sedation/anesthesia and patient's preference rather than rely on a strict SPRRI cutoff value.

7 | CONCLUSIONS

Intermittent preexcitation observed on resting 12-lead ECG or during holter monitoring lacks sufficient specificity for the diagnosis of an AP with long refractory period and cannot be considered a substitute for electrophysiological study in patients with this electrocardiographical phenomenon.

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