Effective Management of Atrioventricular Interval for Paroxysmal Atrial Fibrillation That Developed After DDDR Pacemaker Implantation in a Sick Sinus Syndrome Patient

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SUMMARY

A 68-year-old man with sick sinus syndrome (SSS) was referred to our department for pacemaker implantation. After implantation of a pacemaker with rate-responsive dual chamber (DDDR) mode and minimized ventricular pacing (MVP) functions, paroxysmal atrial fibrillation (PAF) repeatedly developed. Pacemaker memory showed that the intrinsic atrioventricular (AV) (atrial pacing-ventricular sensing [Ap-Vs]) interval was paradoxically prolonged during rate-responsive atrial single-chamber (AAIR) mode rapid pacing because of MVP. Accordingly, to eliminate the paradoxical prolongation of the AV interval during rapid atrial pacing, we changed MVP to medium AV hysteresis and conducted DDDR mode pacing with rate-dependent AV delay. PAF then sharply decreased without antiarrhythmic drugs. (Int Heart J 2015; 56: 558-563)

Key words: Minimized ventricular pacing, Intrinsic rhythm support plus, Medium AV hysteresis, Rate-response, Closed-loop stimulation, Intrinsic AV interval, Paradoxical AV prolongation, Rate-dependent AV delay

Development of paroxysmal atrial fibrillation (PAF) after pacemaker implantation (PMI) for sick-sinus syndrome (SSS) is an unresolved clinical issue. Several types of pacing properties, such as physiological pacing (atrial single chamber [AAI] or dual chamber [DDD]), minimized ventricular pacing (MVP), and some types of rate-response pacing such as closed-loop stimulation (CLS[®]), have been reported to be effective for prevention of PAF after PMI.¹⁻⁷⁾ However, there are few detailed reports concerning the effective management of atrioventricular (AV) interval for suppression of PAF which develops after implantation of a DDD pacemaker (PM) with the current standard functions of rate-response and MVP.

We implanted a DDD PM in an SSS patient and subsequently implemented the functions of rate-response and MVP at the same time. PAF then repeatedly developed after discharge. To suppress the PAF, we changed MVP to medium AV hysteresis and activated rate-dependent (Dynamic[®]) AV delay, while preserving the rate-response function. Thereafter, the repeated PAF sharply decreased without antiarrhythmic drugs or any additional therapy. We describe here the detailed clinical course of PAF, including PM memory, and assess the mechanism in this patient.

CASE REPORT

A 68-year-old man had been previously diagnosed with hypertension, sleep apnea syndrome, cardiomegaly, and sinus bradycardia. At the end of June 2010, he experienced syncope for the first time, when long pauses occurred during Holter monitoring which was performed to examine sinus bradycardia. Holter recording showed the development of PAF and consecutive pauses of 5.5, 3.5, and 3.45 seconds on its termination. In early July, he was admitted to our hospital for PMI with the diagnosis of SSS. Examination findings on admission were as follows: sinus bradycardia was 41 beats per minute (bpm) and the PQ interval was 150 milliseconds (ms) on a 12-lead electrocardiogram (ECG); the cardiothoracic ratio was 57% on chest X-ray; left atrial dimension (LAD) was 57 mm, left ventricular diastolic dimension was 59 mm, left ventricular ejection fraction was 75% on echocardiogram; and the serum B-type natriuretic peptide (BNP) level was 142.9 pg/mL.

In the middle of July, a DDD-mode PM (Entovis DR-T, Biotronik, Berlin, Germany) with 180 ms of AV delay on 60 bpm of lower-rate pacing was implanted (Figure 1). Leads were placed in the right atrial appendage and ventricular apex. Rate-dependent (Dynamic) AV delay was started on the date of PMI, although the function was virtually invalid because of DDD-mode back-up pacing with 180 ms of AV delay (Figure 1).

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Figure 1. Clinical course in PMCs after PMI. After commencement of rate-response function (CLS) and MVP (IRS+), PAF frequently developed. After MVP (IRS+) was changed to medium AV hysteresis, PAF sharply decreased. Ap-Vs indicates atrial pacing-ventricular sensing; AT, atrial tachycardia; AV, atrioventricular; bpm, beats per minute; CLS, closed-loop stimulation; DDD, non-rate-responsive dual chamber mode; DDDR, rate-responsive dual chamber mode; IRS+, intrinsic rhythm support plus; ms, millisecond; MVP, minimized ventricular pacing; outpt, outpatient; PMC, pacemaker clinic; PMI, pacemaker implantation; V-pacing, ventricular pacing; and wk, week.

One week after PMI, intrinsic rhythm support plus (IRS+[®]), which is a type of MVP, and CLS, which is a type of rate-response function, were simultaneously activated. Both of these were expected to prevent development of PAF.³⁻⁶⁾ A lower rate was then set at 55 bpm (Figure 1). AV delay was set to the rate-dependent (Dynamic) AV delay again. However, the function was virtually concealed and canceled by MVP, an extreme type of AV hysteresis, regardless of sinus beats or atrial pacing beats (Figures 1, and 2A, B, C and D).

PAF had been documented only once before admission and was never documented on wireless ECG monitoring throughout hospitalization. However, during an approximately 10-month follow-up after discharge, atrial tachycardia events were repeatedly recorded in PM memory (Figures 1 and 3). The atrial tachycardia events were recorded by an originally installed program in PM and were recognized as PAF from an intra-atrial electrogram in the PM memory. These were obtained in outpatient pacemaker clinics (PMCs). Additionally, the PM memory obtained at the 1st outpatient PMC, which recorded the most frequent and longest PAFs under MVP (IRS+) setting (Figure 3), revealed that the circadian rhythm of occurrence time of PAF showed a peak in the daytime when the patient's activity was most augmented.

The intrinsic AV (atrial sensing-ventricular sensing [As-Vs]) intervals during sinus rhythm in PM memory from the first, second, and third outpatient PMCs showed that the AV conduction time was not prolonged much (Figure 2A, C and E), compared with the PQ time (150 ms) in the sinus-rhythm 12-lead ECG on admission. However, the intrinsic AV (atrial pacing-ventricular sensing [Ap-Vs]) intervals were prolonged up to approximately 250 ms during AAI-mode pacing at the

programmed lower rate (55 bpm) or rate-responsive atrial single-chamber (AAIR)-mode pacing at a slightly higher rate (up to 90 bpm) owing to the rate-response function (CLS) (Figure 2B and D). Moreover, when the atrial pacing rate became more rapid than 90 bpm during AAIR-mode pacing, AV (Ap-Vs) intervals were paradoxically prolonged to more than 250 ms (Figure 2B and D).

PAF had been frequently developing until the second outpatient PMC in early June 2011, although the LAD on the echocardiogram and serum BNP had already decreased to 39 mm and 20.6 pg/mL, respectively, at this time. We then changed MVP (IRS+) to medium AV hysteresis to eliminate the nonphysiological and paradoxical AV prolongation during AAIR rapid pacing exclusively over 90 bpm, while we preserved the rate-response function (CLS) (Figure 1). This medium AV hysteresis actually modified and eliminated the paradoxical prolongation during rapid atrial pacing and ultimately activated rate-dependent (Dynamic) AV delay (Figures 1 and 2F). That is to say, this process resulted in rate-responsive dual chamber (DDDR [CLS])-mode pacing with a rate-dependent stepwise-shortening AV sequence. As a result, the frequency and duration of PAF were rapidly decreased without antiarrhythmic drugs or any additional therapy except for anticoagulation (Figures 1 and 3).

Additionally, the medium AV hysteresis, which had moderately prolonged AV delay (Figure 2E and F), was able to maintain the ventricular pacing rate as low as 2–4%, which was almost the same rate as during MVP (Figure 1).

Figure 2. Distribution of intrinsic AV intervals by HR obtained from the first, second, and third outpatient PMCs. The left panels (A, C, and E) show mean intrinsic AV (As–Vs) intervals by HR on sinus beats, and the right panels (B, D, and F) show mean intrinsic AV (Ap–Vs) intervals by HR on AAIR-mode pacing beats. The black bold lines in left and right panels show the rate-dependent (Dynamic) AV delay set for sinus beats and AAIR-mode pacing beats, respectively. The gray thin broken lines in panels A, B, C and D show MVP (IRS+), an extreme type of AV hysteresis, while those in panels E and F show medium AV hysteresis. PM memory from the first and second outpatient PMC revealed the intrinsic AV (Ap–Vs) intervals on AAIR-mode pacing beats were prolonged (B and D) compared with those on sinus beats (A and C). Moreover, paradoxical AV prolongation appeared when the atrial pacing rate increased to greater than 90 bpm (B and D; gray bold dotted-line arrows). The rate-dependent (Dynamic) AV delay had already been started on the date of PMI. However, MVP (A, B, C and D; gray thin broken lines) concealed the effect of the rate-dependent (Dynamic) AV delay (A, B, C, and D; black bold lines), and virtually canceled it out (B and D; gray bold dotted-line arrows). At the second outpatient PMC, MVP was changed to medium AV hysteresis (E and F; gray thin broken lines). This medium AV hysteresis (F; gray thin broken line) actually eliminated the paradoxical AV prolongation during AAIR-mode pacing exclusively at higher than 90 bpm (F; gray bold dashed-line arrow) and ultimately activated rate-dependent (Dynamic) AV delay, which led to DDDR pacing with a moderately prolonged but rate-dependent stepwise-shortening AV sequence. The black horizontal solid lines in panels B and D show the minimum level of distribution of mean intrinsic AV interval by HR in each panel for reference. The black horizontal dotted lines in panels A, C, E, and F show the maximum level of distribution of mean intrinsic AV interval by HR. AAIR indicates rate-responsive atrial single chamber mode; Ap–Vs, atrial pacing–ventricular sensing; As–Vs, atrial sensing–ventricular sensing; HR, heart rate. The other abbreviations are the same as in Figure 1.

DISCUSSION

In our SSS case, only one PAF event had been documented before PMI. The functions of rate-response (CLS) and MVP (IRS+) were simultaneously started 1 week after PMI (Figure 1). However, PAF repeatedly developed after the commencement of both functions.

Although the intrinsic AV (As–Vs) intervals during sinus rhythm were not prolonged (Figure 2A and C), the intrinsic AV (Ap–Vs) intervals during AAIR-mode pacing at the programmed lower rate or during AAIR-mode pacing at a slightly higher rate (up to 90 bpm) were prolonged to approximately 250 ms because of MVP (IRS+), that is, an extreme type of AV hysteresis (Figure 2B and D). Moreover, when the rate-response function (CLS) was fully activated by exercise or men-

tal stress, the heart rate (HR) increased to higher than 90 bpm and there was a paradoxical extension of the AV interval because of MVP (IRS+) (Figure 2B and D). The increase in HR and the extension of the AV interval were mutually paradoxical and nonphysiological.

Unlike in sinus rhythm, in cardiac electrophysiological studies, as the atrial pacing rate increases, a paradoxical prolongation of AV conduction time, decremental conduction, is observed in subjects with normal AV conduction.⁸⁾ The phenomenon can be explained by the status of intrinsic autonomic nerve, dominant vagal activity on the intrinsic AV conduction system. However, Sweeney, *et al*⁹⁾ also showed paradoxical AV interval behavior with an increase in HR, under the same settings of rate-response function and MVP as in our case, on DDDR-mode pacing in implantable cardioverter-defibrillator

Figure 3. Frequency and duration of PAF stored in PM memory. The vertical spikes show the frequency and duration of PAF. The downward arrows show PMCs during hospitalization and outpatient follow-up, where our patient underwent PM interrogation. The changes of PM settings at the PMC one week after PMI and the second outpatient PMC are indicated by the gray dotted and dashed arrows in the gray dotted and dashed boxes, respectively. The abbreviations are the same as in Figure 1.

patients. These cases lived ambulatory daily lives and HR increased in response to their activity or in proportion to their cardiac sympathetic activity. Therefore, the paradoxical prolongation of AV interval in these cases appeared different from the decremental conduction in electrophysiological study and might be associated with intra-atrial conduction time.¹⁰⁾

On the other hand, a previous report conducted at rest with an echocardiogram reported that diastolic mitral regurgitation occurred, when AV interval prolonged to more than 230 ms.¹¹⁾ Also in our case, if AV interval prolonged to longer than 250 ms under the IRS+ setting when HR increased to greater than 90 bpm according to CLS function due to physical or mental stress, it was expected that the same diastolic mitral regurgitation would occur and that the atrial volume and pressure overload could increase more dynamically than at rest. Under such physical or mental condition, conducting V-pacing because of DDDR (CLS)-mode with rate-dependent stepwise-shortening AV sequence, rather than preventing V-pacing, might have effectively reduced the atrial overload and improved the atrial vulnerability to AF exclusively during rapid pacing over 90 bpm in our case. Other population-based studies conducted under the condition of ambulatory daily life have shown that a PQ interval longer than 200 ms was associated with development of AF,¹²⁻¹⁴⁾ which also suggested that extreme AV prolongation along with diastolic mitral regurgitation might have resulted in atrial overload and be associated with atrial vulnerability to PAF.

Interestingly, while the LAD was 57 mm and serum BNP was 142.9 pg/mL on admission, PAF had been documented only once before admission. However, while the LAD and serum BNP decreased to 39 mm and 20.6 pg/mL, respectively, at the second outpatient PMC, PAF had most frequently developed since 1 week after PMI until the second outpatient PMC, when both functions of rate-response (CLS) and MVP (IRS+) had been available (Figures 1 and 3). This finding suggested that temporal, rather than persistent, atrial overload was more likely to occur and be a trigger for PAFs under IRS+ settings. Similar results were also obtained and discussed in a previous study.¹⁵⁾

Moreover, Nielsen, *et al*¹⁶⁾ compared single-lead AAIR pacing alone and DDDR pacing with a moderately prolonged AV interval in SSS patients, which were similar to DDDR pacing with MVP and that with medium AV hysteresis in our case, respectively. Interestingly, they reported that DDDR pacing with moderately prolonged AV interval might be associated with a lower incidence of PAF than AAIR pacing alone. In subanalysis of this study and another additional study, the superiority of DDDR pacing with a moderately prolonged AV interval over AAIR pacing alone in AF suppression was revealed among patients with a PQ interval longer than 180 ms, but not among those with a PQ interval shorter than 180 ms.^{16,17)} This finding suggested that DDDR pacing with the medium AV hysteresis in our case might suppress PAF more effectively than that with MVP.

Therefore, we hypothesized that the nonphysiological and paradoxical prolongation of the intrinsic AV interval, which derived from MVP and was exclusively observed during AAIR-mode rapid pacing at a HR higher than 90 bpm (Figure 2B and D), was an etiology of the repeatedly developed PAF after PMI. Then, at the second outpatient PMC, we changed MVP, an extreme type of AV hysteresis, to medium AV hysteresis, while preserving the rate-response function (CLS) (Figure 1). This medium AV hysteresis activated rate-dependent (Dynamic) AV delay, which led to a moderately prolonged, but not too long or too short, and rate-dependent stepwise-shortening AV delay (Figures 1 and 2F). The effect of rate-dependent (Dynamic) AV delay had been virtually concealed and canceled by MVP until this time since 1 week after PMI (Figures 1, 2B and D). This activation of rate-dependent (Dynamic) AV delay by introducing medium AV hysteresis actually eliminated the paradoxical prolongation of the intrinsic AV (Ap-Vs) interval exclusively during rapid atrial pacing at greater than 90 bpm (Figure 2F). That is, this process resulted in DDDR (CLS)-mode pacing with a moderately prolonged and rate-dependent stepwise-shortening AV (Ap-Vs) interval (ie, DDDR [CLS]-mode pacing with medium AV hysteresis and activated rate-dependent [Dynamic] AV delay) (Figures 1 and 2F). As a result, the repeated PAFs sharply decreased in frequency and length without antiarrhythmic drugs or any additional therapy (Figures 1 and 3). Accordingly, modification of AV hysteresis and elimination of the paradoxical and nonphysiological prolongation of the AV (Ap-Vs) interval might have reduced the hemodynamic atrial overload exclusively during rapid pacing in ambulatory states, and thus could have had a suppressive effect on PAF in our SSS case.

In reality, the duration in a day when HR increased to greater than 90 bpm due to rate-response (CLS) function was very short. Accordingly, after the change from MVP (IRS+) to medium AV hysteresis, even though V-pacing came to be conducted at higher HR than 90 bpm, the duration of V-pacing in a day would also be very short; it might be several hundred beats in a day, which would hardly change the V-pacing rate (2-4%) any further. However, we hypothesized that such several hundred beats of paradoxical AV prolongation and the expected atrial pressure or volume overload during rapid pacing over 90 bpm in an ambulatory state under the IRS+ setting could be a cause of atrial vulnerability to PAF,¹⁸⁾ and that even one pacing or premature beat under such a condition could be a trigger to induce PAF. Interestingly, the PM memory obtained at the 1st outpatient PMC revealed that the circadian rhythm of occurrence time of PAF showed a peak in the daytime when the patient's activity was probably most augmented, which also seemed to support our hypothesis.

Therefore, we inferred that the modification of the several hundreds of non-physiological AV prolongations by V-pacing (DDDR-mode pacing with rate-dependent stepwise-shortening AV-sequence) at a rate higher than 90 bpm must have resulted in suppression of PAF. Actually, after the change from MVP (IRS+) to medium AV hysteresis, the AV interval became rate-dependently and stepwise short because of DDDR (CLS)-mode pacing with medium AV hysteresis along with rate-dependent (Dynamic) AV delay (Figure 2F). Then the repetitive PAFs after PMI sharply decreased (Figures 1 and 3).

Additionally, the ventricular pacing rate did not change, and remained as low as 2-4% before and after the manage-

ment of AV interval at the second outpatient PMC (Figure 1). This finding suggests that the decrease in PAF was not attributed to a change in ventricular pacing rate.

Regarding limitations of this case report, we cannot exclude the possibility that the PAFs, including postoperative PAF, developed accidentally and concurrently with PM-mode changes in this patient's clinical course. Additionally, the AV interval management in this case might be effective for specific cases in which PAFs did not develop before PMI but in which PAFs repeatedly developed after PMI. Crossover testing or a randomized controlled trial is necessary to examine this further.

In conclusion, the elimination of paradoxical prolongation of the AV (Ap-Vs) interval exclusively during rapid atrial pacing, by changing MVP to medium AV hysteresis and thus activating rate-dependent (Dynamic) AV delay, might have played an important role in preventing PAF in our case. This assessment might be applicable only to this specific PM algorithm in this patient's individual electrophysiological and hemodynamic conditions. However, when PAFs come to repeatedly develop after implantation of a DDD-PM with the current standard functions of rate-response and MVP in an SSS patient, if the paradoxical prolongation of Ap-Vs intervals due to MVP is recognized in PM memory, the elimination of paradoxical prolongation mentioned above might be an available option for managing PAFs.

DISCLOSURE

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