





The great deceiver: a case series of ‘double fire’ atrioventricular nodal response

Sílvia Leão ^{1,2}, Justin Luermans^{1,3}, Kevin Vernooy ^{1,3}, Rachel ter Bekke¹, Dennis den Uijl¹, Dominik Linz ^{1,3,4}, and Sevasti-Maria Chaldoupi ^{1*}

¹Department of Cardiology, Maastricht University Medical Centre, P. Debyelaan 25, 6229 HX Maastricht, The Netherlands; ²Department of Cardiology, Centro Hospitalar de Trás-os-Montes e Alto Douro, Vila Real, Portugal; ³Department of Cardiology, Radboud University Medical Center and Radboud Institute for Health Sciences, Nijmegen, The Netherlands; and ⁴Department of Biomedical Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

Received 28 September 2022; first decision 26 October 2022; accepted 3 April 2023; online publish-ahead-of-print 21 April 2023

Background

The ‘double fire’ (DF) atrioventricular (AV) nodal response is a rare mechanism of two ventricular electrical activations following a single atrial beat due to dual AV node physiology. DF AV nodal response is often misdiagnosed and may lead to unnecessary invasive procedures.

Case summary

We describe a series of three cases with distinct clinical manifestations of DF AV nodal response: Patient 1 remained symptomatic after slow pathway modification for common AV nodal re-entry tachycardia. Patient 2 was misdiagnosed as having junctional bigeminy and developed heart failure with reduced left ventricle ejection fraction. Patient 3 was misdiagnosed as having atrial fibrillation (AF) and underwent two pulmonary vein isolation (PVI) procedures, without clinical improvement. All patients underwent an electrophysiological study (EPS) during which DF AV nodal response was confirmed and treated with radiofrequency ablation of the slow pathway. All patients were afterwards relieved from their symptoms.

Discussion and conclusion

DF AV nodal response is a rare electrophysiological phenomenon which can be clinically misinterpreted as other common arrhythmias, such as premature junctional bigeminy or AF and can contribute to tachycardia induced cardiomyopathy. Typical electrocardiogram- and EPS-derived findings can be indicative for DF AV nodal response. DF AV nodal response can be easily and effectively treated by slow pathway ablation.

Keywords

Double-fire AV nodal response • Slow-pathway ablation • ECG • supraventricular tachycardia • Heart failure • Catheter ablation • Case series

ESC Curriculum 5.5 Supraventricular tachycardia • 5.3 Atrial fibrillation • 6.2 Heart failure with reduced ejection fraction

Learning points

- ‘Double fire’ (DF) atrioventricular (AV) nodal response manifests with different clinical presentations and can be misdiagnosed as another arrhythmia.
- Sufficient symptom-rhythm correlation can be one of the most important tools to diagnose DF nodal AV response in the majority of the patients.
- Careful electrocardiogram analysis and electrophysiological study are the keys to an accurate diagnosis.
- Treatment by slow pathway ablation is effective and can prevent additional unnecessary and often risky interventions.

* Corresponding author. Tel: +31(0)43 3875093, Fax: 0031433877081, Email: marisevi.chaldoupi@mumc.nl

Handling Editor: David Duncker

Peer-reviewers: Henrike Aenne Katrin Hillmann; Carolina Schwab; Satoshi Higuchi; Paolo Gatti; Konstantinos Iliodromatis

Compliance Editor: Hikmet Kadioglu

Supplementary Material Editor: Siddhartha Mohan

© The Author(s) 2023. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

Introduction

A dual atrioventricular (AV) node physiology, which is common in the general population,¹ is mostly asymptomatic but can create a substrate for AV nodal re-entry tachycardia (AVNRT). AVNRT is the most frequently diagnosed and treated supraventricular tachycardia.² In addition to AVNRT, a so called ‘double fire’ (DF) AV node response is an electrophysiological mechanism that can occur in patients with a dual AV node physiology, where a single supraventricular beat is antegradely conducted over the fast and slow AV node pathways causing a double ventricular activation.³ DF AV node response has been well described,⁴ and according to the current European Society of Cardiology Guidelines for the management of patients with supraventricular tachycardia, DF AV node response is considered to be an extremely rare tachycardia with a risk of misdiagnosis and the development of tachycardia-induced cardiomyopathy.⁵ However, a systematic approach to its diagnosis and management is lacking. Herein, we report a case series of three patients with DF AV node response who presented with different clinical manifestations and who were misdiagnosed and incorrectly treated for a suspected different arrhythmia. We describe a systematic approach that may help to improve the diagnosis and treatment of DF AV node responses.

Timeline

Patient 1 31-year-old woman

2014	Palpitations. Structural normal heart. Patient preferred not to undergo EPS.
2019	Typical AVNRT. EPS with slow pathway modification.
2018–2021	Occasional palpitations.
2021	Pregnancy. Worsening of symptoms. Suspicion of DF AV nodal response based on ECG documentation. EPS diagnostic for DF AV nodal response. Slow-pathway ablation. Symptom relief.

Patient 2 36-year-old man

2014	Incidental documentation of irregular pulse. On ECG bigeminy. Investigation leads to diagnosis of dilated cardiomyopathy (LVEF 30%, without LGE on MRI, genetic screening negative).
2016	Diagnostic EPS. Failure to induce sustained arrhythmias, revealed ‘junctional’ extra-systoles.
2016–2020	Persistent symptoms and reduced LVEF with optimal medical heart failure therapy.
2020	EPS diagnostic for DF AV nodal response. Slow-pathway ablation.
2021	LVEF normalized and symptom relief.

Patient 3 36-year-old man

2018	Palpitations, dizziness. Diagnosis of paroxysmal atrial fibrillation. LVEF 40%. Cryoballoon PVI. EPS excluded accessory pathway and failed to induce AVNRT.
2019 Feb	Radiofrequency re-do PVI without symptom improvement. Holter showing the same irregular heart rhythm.

Continued

Continued

2019 Aug	EPS with documentation of DF AV nodal response. Slow pathway ablation.
2020	LVEF improved to 54%. Symptom relief.

Table 1 Timeline. ECG, electrocardiogram; EPS, electrophysiological study; PAC, premature atrial contractions; LVEF, left ventricle ejection fraction; LGE, late gadolinium enhancement; PVI, pulmonary vein isolation; SVT, supraventricular tachycardia.

Patient 1

A 31-year-old woman was referred to our hospital for second opinion due to palpitations, which persisted despite a previous slow-pathway modification for common AVNRT. The patient had no history of syncope or chest pain; the physical examination was unremarkable, and the echocardiogram revealed a structurally normal heart. A two-lead electrocardiogram (ECG) during symptoms showed an irregular narrow complex tachycardia, with discernible and apparent sinus *P* waves with intermittent DF AV nodal response. The PR intervals were variable due to alternate antegrade conduction over the fast and slow pathways and frequent DF AV nodal response (Figure 1).

The patient consented to undergo an EPS that was performed under minimal sedation: a decapolar catheter was positioned in the proximal coronary sinus (CS), a hexapolar catheter was positioned in the His region, and a quadripolar catheter was positioned in the right ventricle apex (RVA) and was moved to the high right atrium (HRA) as needed. Intracardiac electrograms confirmed sinus rhythm with spontaneous conduction down both the fast and slow AV nodal pathways (Figure 2). During baseline, in sinus rhythm, the intervals between the local A (atrium) and the first and second His electrogram remained stable (A1H1 = 80–100 ms and A1H2 = 500–700 ms) with a stable HV of 50 ms. There was no retrograde conduction during right ventricular (RV) pacing. With programmed atrial pacing, AVNRT was not inducible. The slow pathway region was mapped, and ablation was performed with a 4-mm non-irrigated radiofrequency ablation catheter (45W) during continuous monitoring of the antegrade AV node conduction. This resulted in the complete abolishment of the slow pathway, and no DF AV node response was present any longer.

In this case, the presence of DF AV nodal response was most likely the result of the previous slow pathway modification, which increased the antegrade conduction delay of the slow pathway and abolished its retrograde conduction, creating the required conditions for a DF AV node response.

Patient 2

A 36-year-old man was referred because of frequent premature ‘atrial bigeminy’ and progressive dyspnoea on exertion. A cardiac MRI showed a dilated cardiomyopathy with reduced left ventricular ejection fraction (LVEF) of 30% without any late gadolinium enhancement (LGE). The patient developed typical symptoms of heart failure. Genetic screening was negative. Optimal medical heart failure treatment, including beta-blocker for arrhythmia control, was initiated but failed to improve symptoms, suppress ‘bigeminy’ or recover LVEF. Two years later, he underwent a diagnostic EPS that revealed ‘junctional’ extra-systoles which were suppressed with the administration of atropine, isoprenaline, and atrial burst pacing. As no sustained arrhythmias was inducible, no ablation was performed, and the patient remained symptomatic. Careful analysis of 12-lead ECG tracings revealed

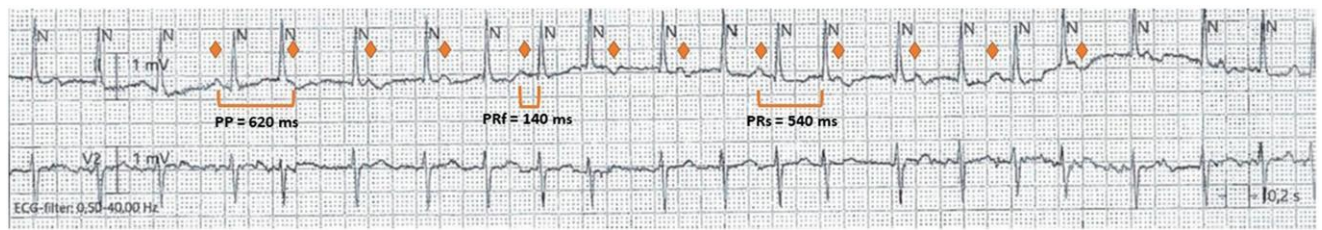


Figure 1 Two-lead electrocardiogram strip of patient 1: PP, PP interval; \diamond , P waves; PRf, PR interval of fast pathway; PRs, PR interval of slow pathway.



Figure 2 Patient 1: EP recording of double fire atrioventricular nodal response (speed 100 mm/s). Surface electrocardiogram, high right atrium distal: catheter on the right atrial appendage; HIS catheter, on His region with His 5–6 proximal electrodes and His 1–2 distal electrodes; dark filled arrow: conduction through fast pathway; dark dashed arrow: conduction through slow pathway; light filled arrow: proximal to distal His activation.

a sinus rhythm with P waves followed by two narrow QRS complexes which was highly suggestive of DF AV nodal response (Figure 3). The ECG pattern was intermittent and may have led to misdiagnosis of ‘junctional’ extrasystoles for the past years.

The patient gave informed consent to repeat the EPS. Under minimal sedation, a decapolar catheter was positioned in CS, a hexapolar catheter on the His region, and a quadripolar catheter on RVA and was moved to the HRA as needed. Intracardiac signals confirmed sinus rhythm with an AV conduction pattern in line with a dual ventricular response. Proximal to distal His activation was recorded with stable HV time of 48 ms during 1:2 conduction (A1H1 = 120–170 and A1H2 = 620–890 ms), that argues against His extrasystoles (Figure 4).

Isoprenaline and atropine administration as well as atrial burst pacing stimulation suppressed the extra systoles during the first EPS which made junctional extra systoles very unlikely. Atrial pacing manoeuvres confirmed dual AVN physiology. The slow pathway region was mapped and ablation was performed with a 4-mm non-irrigated ablation catheter and the double ventricular response disappeared during the radio-frequency application followed by slow junctional beats (Figure 5). Afterwards, with and without isoprenaline, a persistent 1:1 AV conduction via the fast pathway was documented without any indication of the presence of the slow pathway. Three months later the patient was asymptomatic, his LVEF improved to 56% and remained normal after 1 year.

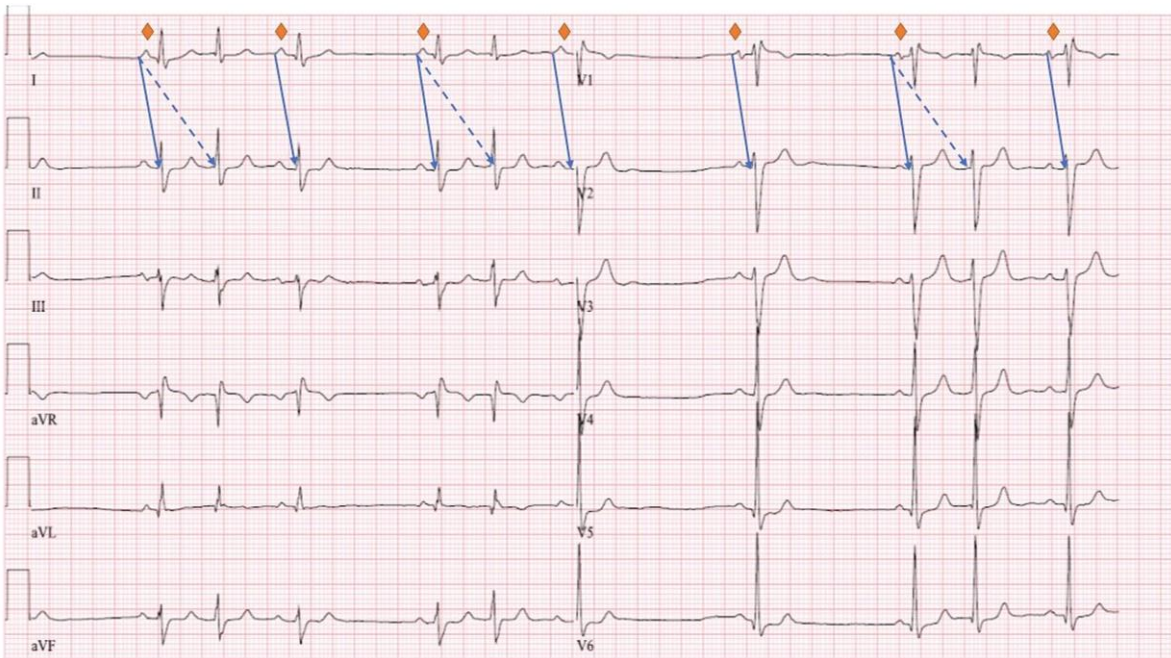


Figure 3 12-lead electrocardiogram patient 2. \diamond : P waves; dark filled arrow: conduction through fast pathway; dark dashed arrow: conduction through slow pathway.

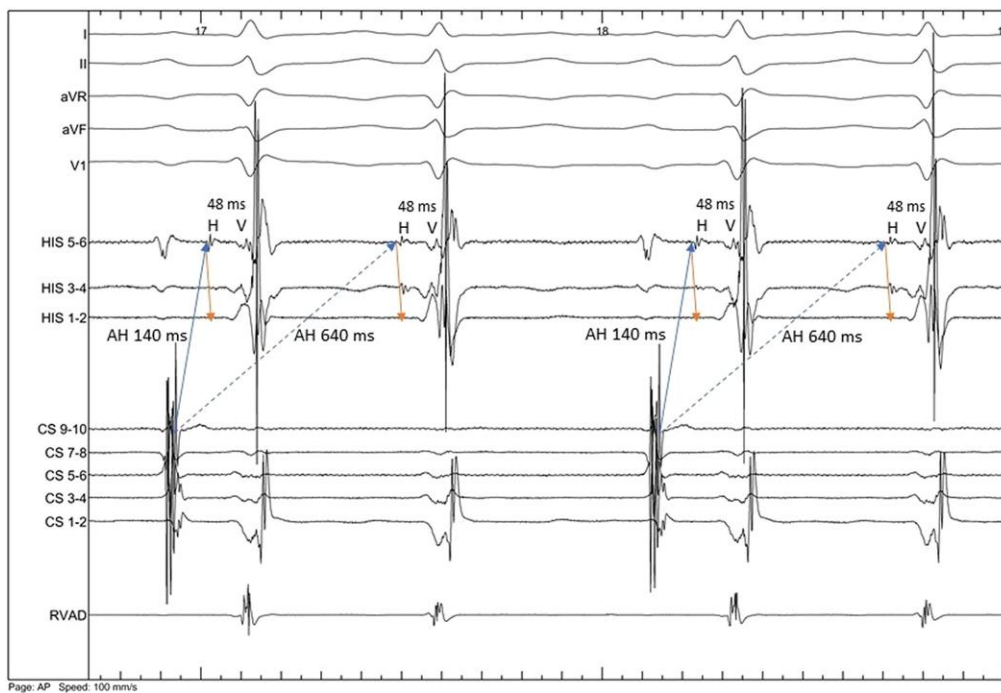


Figure 4 Patient 2: EP recording of the double fire atrioventricular nodal response (speed 100 mm/s). Surface electrocardiogram; HIS catheter, on His region with His 5–6 proximal electrodes and His 1–2 distal electrodes; coronary sinus, catheter in coronary sinus; right ventricle apex distal, catheter in right ventricular apex; dark filled arrow: conduction through fast pathway; dark dashed arrow: conduction through slow pathway; light filled arrow: proximal to distal His activation.



Figure 5 EP recording during ablation patient 2 (speed 25 mm/s). Double fire atrioventricular node response disappearing during ablation. HIS catheter on His region, CS catheter on coronary sinus, RF catheter on slow-pathway region (for abbreviation, see [Figure 4](#)).

Patient 3

A 36-year-old man was referred to our hospital due to therapy resistant paroxysmal atrial fibrillation and sustained symptoms despite two PVI procedures elsewhere. He developed tachycardia-induced cardiomyopathy with heart failure with mildly reduced ejection fraction but he mainly complained of palpitations and dizziness, which did not improve after PVI. During the first PVI procedures, the presence of an accessory pathway was excluded, and no AVNRT was inducible. The echocardiography revealed a reduced LVEF of 40%, previously interpreted as tachycardia induced cardiomyopathy during AF. Careful analysis of the two-lead Holter tracings showed an irregular narrow complex tachycardia with group beating patterns ([Figure 6](#)). The ECG shows *P* waves at a rate of 75 bpm conducting through the fast pathway in the first 4 beats and later through the slow pathway for the next 10 beats. After that, an intermittent DF AV nodal response is observed and fast pathway conduction resumes on the last seven beats.

With those findings, a repeat EPS was proposed and the patient agreed. EPS was performed without sedation. A decapolar catheter was positioned in the CS, a quadripolar catheter on the His region, and a quadripolar catheter on RVA and was moved to the HRA as needed. During isoprenaline infusion, there was a retrograde conduction via the fast pathway. Programmed atrial stimulation revealed intermittent DF AV node response with stable Atrial his (AH) (A1H1 = 150–230 ms and A1H2 = 400–660 ms) and HV time (HV 54 ms), even during overdrive pacing ([Figure 7](#)), which could be repetitively induced and was very consistent with the clinical tachycardia documented on the Holter recordings. The slow pathway region was mapped and ablation was performed with a 4-mm non-irrigated ablation catheter. The above-described DF 1:2 response was no longer observed, even

during high dose isoprenaline infusion. At 1 year follow-up, the patient was asymptomatic and LVEF improved to 54%. Holter monitoring recorded sinus rhythm without any SVT.

Discussion

DF AV nodal response can present at any age³ with various symptoms. The most commonly reported symptoms are palpitations, but dizziness, syncope, dyspnoea, or fatigue may also occur.³ Herein, we present three cases of young patients (31–36 years old) with different clinical manifestations, which led to misdiagnosis of the underlying problem: patient 1 was referred mainly due to palpitations, patient 2 developed tachycardia induced cardiomyopathy with symptoms of heart failure. Finally, patient 3 developed heart failure with mildly reduced left ventricular ejection fraction and mainly complained of palpitations and dizziness. This variety in unspecific symptoms may have partially contributed to the misdiagnosis in the presented cases. Moreover, the 12-lead surface ECG is not always leading to the correct diagnosis as it sometimes mimics other arrhythmias. DF AV nodal response can be easily misdiagnosed as atrial fibrillation, atrial tachycardia, junctional ectopics, parasystoles, or even ventricular tachycardia, which may trigger unnecessary invasive procedures with higher complication rates than a slow-pathway ablation (i.e. left sided ablation with transeptal puncture). Patient 1 underwent previously a slow pathway modification for typical AVNRT and in this case the occurrence of the DF AV nodal response was most likely a result of an antegrade conduction delay and abolishment of the retrograde conduction properties of the slow pathway. To our knowledge, this is the first description of DF AV nodal response after successful slow pathway modification for AVNRT

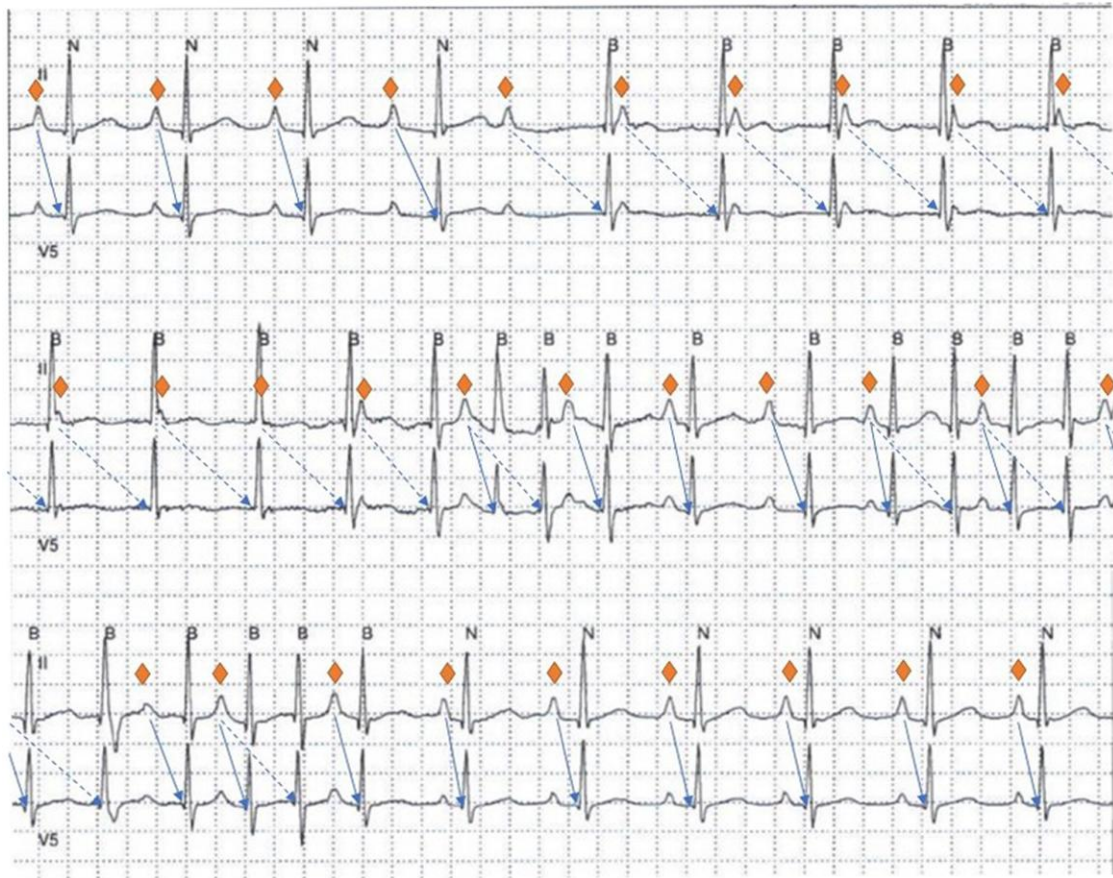


Figure 6 Two-lead Holter recording patient 3. Intermittent dual ventricular response. \diamond , P waves; dark filled arrow: conduction through fast pathway; dark dashed arrow, conduction through slow pathway.

treatment, and it should warn for this possible outcome while treating AVNRT. Two of the three patients developed tachycardia induced cardiomyopathy and were followed for many years with misleading diagnoses. Patient 2 was on heart failure medication for 7 years until the LVEF quickly recovered after slow-pathway ablation. Patient 3, who complained mainly of symptoms of arrhythmia, underwent two unnecessary PVI procedures before the correct diagnosis was made and the problem was solved by slow-pathway ablation. There are also reports of inappropriate ICD implantation and shocks when DF AV nodal response is misdiagnosed as ventricular tachycardia.^{6,7}

In patients with DF AV nodal response, misdiagnoses are common (approximately 70%), and the average time for the final diagnosis is often longer than 1 year.⁸ A careful ECG analysis and considering DF AV nodal response as a differential diagnosis can prevent unnecessary and potentially harmful interventions. The most significant finding in the ECG, which is indicative for DF AV nodal response, is a P wave followed by two narrow QRS complexes.³ Dual AV nodal conduction may occur intermittently and may be misclassified as atrial premature beats, junctional extrasystoles, or paroxysmal atrial fibrillation even in young patients. However, atrial fibrillation is rather uncommon in young patients without structural heart disease; other arrhythmias, such as DF AV nodal response, should be considered as differential diagnosis. Other ECG findings described to be associated with DF AV nodal response are R-R alternans during continuous 1:2 AV conduction, aberrant conduction of the second QRS complex mimicking premature

ventricular complexes, pseudo-T wave alternans and/or pseudo-giant P waves due to superimposition of the P and T waves, QRS alternans, and QRS linking. In the absence of 1:2 AV conduction and tachycardia, the presence of two different PR intervals during 1:1 AV conduction also suggests the presence of dual AV nodal physiology and perhaps the ability to sustain DF AV nodal response in physiologic conditions.⁹

A carefully structured baseline EPS, even in patients referred for PVI, may prevent some misdiagnosis.¹⁰ During the EPS, a multi-electrode diagnostic His catheter helps to visualize the proximal and distal part of the bundle of His. RV pacing should be performed to evaluate the retrograde conduction. Dual AV node physiology should be evaluated with programmed right atrial pacing; however keeping in mind that the pacing protocol can be challenging due to interruption arising from the AV double response. Additionally, a 'jump' is not reported for all patients with DF AV nodal response. Dual AV nodal antegrade conduction in DF AV nodal response can also be characterized by discontinuous AV conduction, or it may be implied by a single atrial complex followed by two His signals and two related ventricular complexes with rather stable A1H1, A1H2, and HV time.³ Some minor variability can be observed in A1H2 intervals, as shown for patients 2 (A1H2 = 620–890 ms) and patient 3 (A1H2 = 400–660 ms). This may be due to decremental properties of both, the fast and slow pathway. We also hypothesize that penetration of fast-pathway wavefronts may result in a concealed distal part of the slow-pathway or of the lower common pathway. However, this theory could not be proven in the

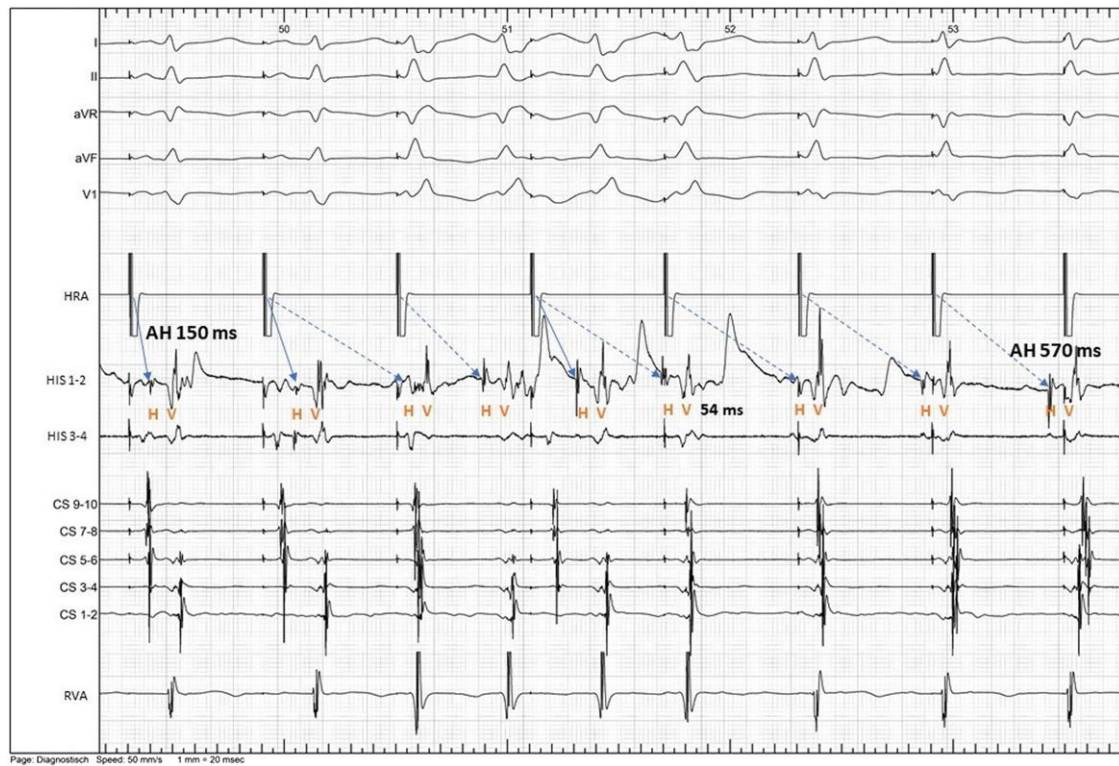


Figure 7 EP recording patient 3. Intermittent double fire atrioventricular nodal response during atrial pacing (speed 100 mm/s). Surface electrocardiogram; high right atrium catheter on the right atrial appendage; HIS catheter, on His region with His 5–6 proximal electrodes and His 1–2 distal electrodes; coronary sinus, catheter in coronary sinus; right ventricle apex distal, catheter in right ventricular apex; dark filled arrow: conduction through fast pathway. Dark dashed arrow: conduction through slow pathway. The third atrial-paced beat shows a marked shortening as compared to the other slow pathway conduction; this variation of AH interval in the slow pathway can be due retrograde concealment of the fast pathway; a conducted fast pathway impulse exhibited an influence on the distal slow pathway through its retrograde penetration of the slow pathway which is gone for this beat.

respective EPSs. To date, the success rate of slow pathway modulation/ablation for DF AV nodal response treatment seems to be comparable but slightly lower than for AVNRT.³ In our three cases, RF ablation targeting the slow pathway was successful, leading to significant clinical improvement and medication discontinuation. In some instances, cryoablation of slow-pathway may also be considered as an alternative. This technique has been proven to be safe and effective for slow-pathway ablation mainly in paediatric population in context of AVNRT.¹¹ To our knowledge, there are no reports on cryoablation for the treatment of DF AV nodal response.

Finally, the present case series provides a systematic analysis of ECG and EPS recordings of a rather rare AV node response. Although the number of patients included here is rather limited, our cases present the diversity of clinical manifestations and risk of misinterpretation that can complicate the management of patients with DF AV nodal response. DF AV nodal response is a relatively rare EP phenomenon but should be considered as a differential diagnosis.

Conclusions

Identification of DF AV nodal response remains challenging and can be easily misinterpreted as more common arrhythmias such as premature atrial bigeminy and AF. DF AV nodal response is a rare but important differential diagnosis for other more common arrhythmias and should be systematically excluded, particularly if arrhythmias and suspected

tachycardia-induced cardiomyopathy remain after invasive treatment procedures and initiation of heart failure medication in otherwise healthy and relatively young patients. Typical ECG- and EPS-derived findings can be indicative for DF AV nodal response, and its treatment with slow pathway ablation is effective.

Lead author biography



Sílvia Leão (1986) is a Cardiologist from CHTMAD—Vila Real, Portugal. She graduated in Medicine at ICBAS (Universidade do Porto) in 2010. At the present, she is working as Invasive Electrophysiology Fellow at UMC + Maastricht.

Acknowledgements

None.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: All patients gave informed consent, in accordance with the COPE guidelines, to be included in this case series report.

Conflict of interest: None declared.

Funding: None declared.

Data availability

The data underlying this article are available in the article and in its online [supplementary material](#).

References

- Mani BC, Pavri BB. Dual atrioventricular nodal pathways physiology: a review of relevant anatomy, electrophysiology, and electrocardiographic manifestations. *Indian Pacing Electrophysiol J* 2014;**14**:12–25.
- Markowitz SM, Lerman B. A contemporary view of atrioventricular nodal physiology. *J Interv Card Electrophysiol* 2018;**52**:271–279.
- Peiker C, Pott C, Eckardt L, Kelm M, Shin DI, Willems S, et al. Dual atrioventricular nodal non-re-entrant tachycardia. *Europace* 2016;**18**:332–339.
- Wu D, Denes P, Dhingra R, Pietras R, Rosen K. New manifestations of dual A-V nodal pathways. *Eur J Cardiol* 1975;**2**:459–466.
- Brugada J, Katritsis DG, Arbelo E, Arribas F, Bax JJ, Blomström-Lundqvist C, et al. 2019 ESC guidelines for the management of patients with supraventricular tachycardia. *Eur Heart J* 2020;**41**:655–720.
- Karnik AA, Hematpour K, Bhatt AG, Mazzini MJ. Dual AV nodal nonreentrant tachycardia resulting in inappropriate ICD therapy in a patient with cardiac sarcoidosis. *Indian Pacing Electrophysiol J* 2014;**14**:44–48.
- Türkmen Y. Misinterpretation of dual atrioventricular nodal non-reentrant tachycardia as ventricular tachycardia and implantation of implantable cardioverter-defibrillator followed by inappropriate shocks. *Anatol J Cardiol* 2020;**24**:117–120.
- Hartmann J, Jungen C, Stec S, Klatt N, Willems S, Makimoto H, et al. Outcomes in patients with dual antegrade conduction in the atrioventricular node: insights from a multi-centre observational study. *Clin Res Cardiol* 2020;**109**:1025–1034.
- Wang N. Dual atrioventricular nodal nonreentrant tachycardia: a systematic review. *Pacing Clin Electrophysiol* 2011;**34**:1671–1681.
- Mansour M, Marrouche N, Ruskin J, Natale A, Keane D. Incessant nonreentrant tachycardia due to simultaneous conduction over dual atrioventricular nodal pathways mimicking atrial fibrillation in patients referred for pulmonary vein isolation. *J Cardiovasc Electrophysiol* 2003;**14**:752–755.
- Zook N, DeBruler K, Ceresnak S, Motonaga K, Goodyer W, Trela A, et al. Identifying an appropriate endpoint for cryoablation in children with atrioventricular nodal reentrant tachycardia: is residual slow pathway conduction associated with recurrence? *Heart Rhythm* 2022;**19**:262–269.