Indian Pacing and Electrophysiology Journal 17 (2017) 176–179

Contents lists available at ScienceDirect

Indian Pacing and Electrophysiology Journal

journal homepage: www.elsevier.com/locate/IPEJ

Familial atrioventricular nodal re-entrant tachycardia: A case seriers and a systematic review

Muthiah Subramanian*, M.S. Harikrishnan, Mukund A. Prabhu, Praveen G. Pai, Saritha S. Shekhar, Kumaraswamy Natarajan

Department of Cardiology at Amrita Institute of Medical Sciences, Amrita Lane, Ponekkara, Kochi, Kerala 682041, India

ARTICLE INFO

Article history:
Received 14 April 2017
Received in revised form
7 June 2017
Accepted 8 July 2017
Available online 10 July 2017

Keywords:
Familial
AVNRT
Tachycardia

ABSTRACT

Multiple reports of familial clustering suggest that genetic factors may contribute in the pathogenesis of atrioventricular nodal re-entrant tachycardia (AVNRT). We report three cases of AVNRT in a father and his two sons along with a review of literature of other similar cases. Electrophysiological studies induced typical AVNRT, which was successfully eliminated by radiofrequency ablation in all of them. Of the 22 reported cases, 96% had typical (slow-fast) variant of AVNRT. The predominant pattern of inheritance appears to be autosomal dominant, though other patterns may exist. Further research is needed to understand the genetic influence of AVNRT and its pathophysiology.

1. Introduction

Although atrioventricular nodal re-entrant tachycardia (AVNRT) is the most common mechanism of paroxysmal supraventricular tachycardia, the precise anatomy of the re-entry circuit underlying AVNRT and the relative role of the AV node and extranodal atrial inputs remain controversial [1–4]. Recently, genetic loci have been identified for the pre-excitation syndrome and atrial fibrillation [5–9]. Although no specific putative gene has been associated with AVNRT, multiple reports of twins case studies and familial clustering suggest that genetic factors may play a role in the pathogenesis of AVNRT. We report three cases of typical (slow-fast AVNRT) in a father and his two sons along with a review of literature of other similar cases of familial AVNRT.

2. Methods

A systematic search through Medline archives accessed by PubMed (1950–2015) using search the terms 'AVNRT', 'Dual AV nodal physiology', 'Typical AVNRT', 'AV nodal re-entrant tachycardia' in combination with 'Familial', 'Twin studies', 'Familial clustering', and 'Genetic' was performed. Studies in the form of full-length articles, short reviews, and case reports both published and scheduled to be published were included in the search with "human" and "English" as limits.

Case reports from this search strategy were included if they demonstrated a fulfilment of the standard criteria for the diagnosis of AVNRT [1]. We found 5 case reports of twins studies and familial clustering of AVNRT (including this report). The corresponding authors were contacted for clarification, whenever there was missing or incomplete data.

3. Case report

3.1. Case 1 (1st generation - father, Fig. 1)

A 55-year-old male, with systemic hypertension and dyslipidaemia, presented with complaints of rapid palpitations for the 6 months associated with multiple episodes of presyncope. Electrocardiogram (ECG) documented narrow QRS tachycardia with a short RP interval. Two episodes were terminated with intravenous adenosine. Physical examination, resting 12 lead electrocardiogram, chest X-ray, and an echocardiogram was normal. Informed consent was obtained for an electrophysiological study and ablations which were performed in a non-sedated, fasting state.

* Corresponding author.
E-mail addresses: muthiah727@yahoo.com (M. Subramanian), harikrishnanms@aims.amrita.edu (M.S. Harikrishnan), mukundaprabhu@gmail.com (M.A. Prabhu), praveengpai@aims.amrita.edu (P.G. Pai), sarithasekhar@aims.amrita.edu (S.S. Shekhar), kunatarajan@gmail.com (K. Natarajan).

Peer review under responsibility of Indian Heart Rhythm Society.

http://dx.doi.org/10.1016/j.ipej.2017.07.005

Electrode catheters were introduced into the femoral veins bilaterally and positioned in the right atrium (RA), coronary sinus (CS), His – Bundle region, and right ventricle (RV). Baseline recordings showed normal AH and HV intervals (Table 1). Programmed ventricular stimulation with single extra stimulus showed concentric and decremental retrograde conduction. Sustained typical AVNRT (cycle length 390 msec) was induced by atrial burst pacing as well as single atrial stimulus protocol (Fig. 2). Using a standard curve EPT ablation catheter, radiofrequency ablation (RFA) was delivered at 40 W for 90 s. Post ablation, the dual AV nodal physiology was eliminated and AVNRT was no longer inducible with or without Isoprenaline infusion. A coronary angiogram revealed normal epicardial coronary artery with no flow-limiting disease. He has remained well without any symptoms for more than 9 years after the RF ablation.

3.2. Case 2 (2nd generation–1st son)

A 27-year-old male first experienced episodic palpitation associated with presyncope and retrosternal chest pain at the age of 21. Despite treatment with oral atenolol, the frequency of the palpitations had increased over the previous 6 months. During tachycardia, the 12 lead ECG revealed a narrow regular QRS tachycardia (VR = 220/min) with a short RP interval. Physical examination and echocardiogram were normal.

During the EP study, baseline intervals (AH, HV) were normal and VA conduction was found to be concentric and decremental. Successful slow pathway radiofrequency ablation was delivered with a continuous junctional rhythm for 90 s. No complication occurred after the procedure and the patient was symptom-free at 3 years of follow-up.

3.3. Case 3 (2nd generation–2nd son)

A 33-year-old male presented with complaints of episodic palpitations accompanied by nausea, sweating, and retrosternal chest pain for 2 months in duration. These episodes were precipitated by stress and strenuous physical exercise. General examination, electrocardiogram, chest X-ray, and echocardiogram were normal and hence an EPS was performed.

Upon demonstration of dual AV nodal physiology and confirming a diagnosis of typical (slow-fast) AVNRT, radiofrequency ablation of the slow pathway was carried out in the M1-M2 region of Koch triangle at 50 W for 180 s resulting in a slow intermittent junctional rhythm. After ablation programmed atrial stimulation did not induce AVNRT despite isoprenaline infusion. At 3 months follow-up, he remained free of symptoms.

Table 1
Electrophysiological parameters of the three individuals.

	Father	1st Son	2nd Son
Mode of Induction	AH jump	AH jump	AH jump
Basic Cycle Length	714 ms	860 ms	805 ms
HV[a] interval during tachycardia	35 ms	30 ms	32 ms
Septal VA[b] interval	42 ms	45 ms	38 ms
Entrainment			
PPI[c] – TCL[d]	130 ms	150 ms	160 ms
SA[e] – VA	95 ms	102 ms	91 ms
Response post entrainment	VAHV	VAHV	VAHV
Location of ablation in Koch triangle	P1-P2	P1-P2	M1–M2

[a] HV = His-Ventricular.
[b] VA: Ventriculo-atrial.
[c] PPI: Post – pacing interval.
[d] TCL: Tachycadia cycle length.
[e] SA: Stimulus – atrial.

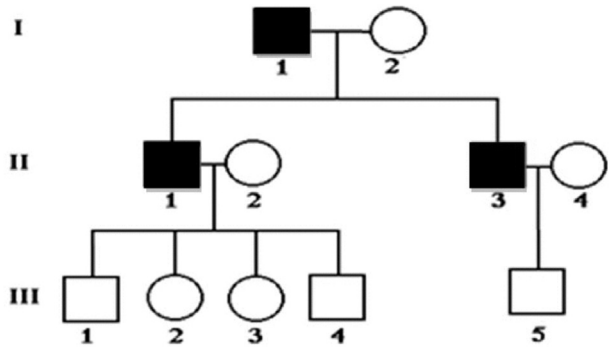

Fig. 1. Pedigree of one family with familial AVNRT. Circles denote female family members, squares male family members, and solid symbols affected family members.

4. Discussion

Until recently, paroxysmal supraventricular tachycardia caused by AV accessory pathways or dual AV nodal physiology were attributed to randomly occurring congenital anomalies of pathological substrates from birth [10].In this report, we describe three cases of typical slow – fast AVNRT in a father and his two sons along with a review of all previous reports of AVNRT based on familial clustering and twins case studies.

Although conclusive proof of a genetic basis is lacking, there is mounting evidence by multiple reports based on twins case studies and familial clustering of a significant hereditary contribution in the development of AVNRT (Table 2). It is of interest to note that there are only two occurrences of male-to-male transmission. However due to limited familial pedigree data available among affected individuals, further studies will be needed to elucidate the inheritance patterns of the disease. Of the 23 reported cases, 22 (96%) were diagnosed with the typical (slow-fast) variant of AVNRT; the exception being a 65 female who had both documented typical and atypical AVNRT pathophysiology. Radiofrequency ablation of the slow pathway was successful in all patients, although the difficulty in cannulation of a duodecapolar catheter into the coronary sinus was noted by Namgung et al.

Though there is a familial clustering, the age of onset is highly variable between the patients in all the studies. It is possible that though the substrate of dual AV nodal physiology is inherited, the triggering factor that marks the onset of AVNRT determines the age of manifestation. This may possibly explain the disparity in the age of manifestation within the families. There may be an underestimation of the prevalence of inherited dual AV nodal physiology as not all individuals may develop the clinical manifestations and thus remain undetected.

Despite the many reports of familial AVNRT, it remains unclear whether it is secondary to a single gene defect or multifactorial inheritance. Given the estimated prevalence of AVNRT in the general population of 1.35/1000 persons, the calculated probability of a father and two sons having the disease merely by chance without any genetic predisposition is less than 0.001% [11]. It seems unlikely that the familial clustering of AVNRT is simply a fortuitous event or the result of ascertainment bias [12]. The coexistence of other inherited arrthymias such as Brugada syndrome in patients with AVNRT, provides further support to a possible underlying genetic locus [13]. Further epidemiological research and molecular analysis may be able to provide definitive evidence of the genetic influence of AVNRT and its pathophysiology. In addition, these studies may even suggest specific targets for therapy of AVNRT and other common arrhythmias.

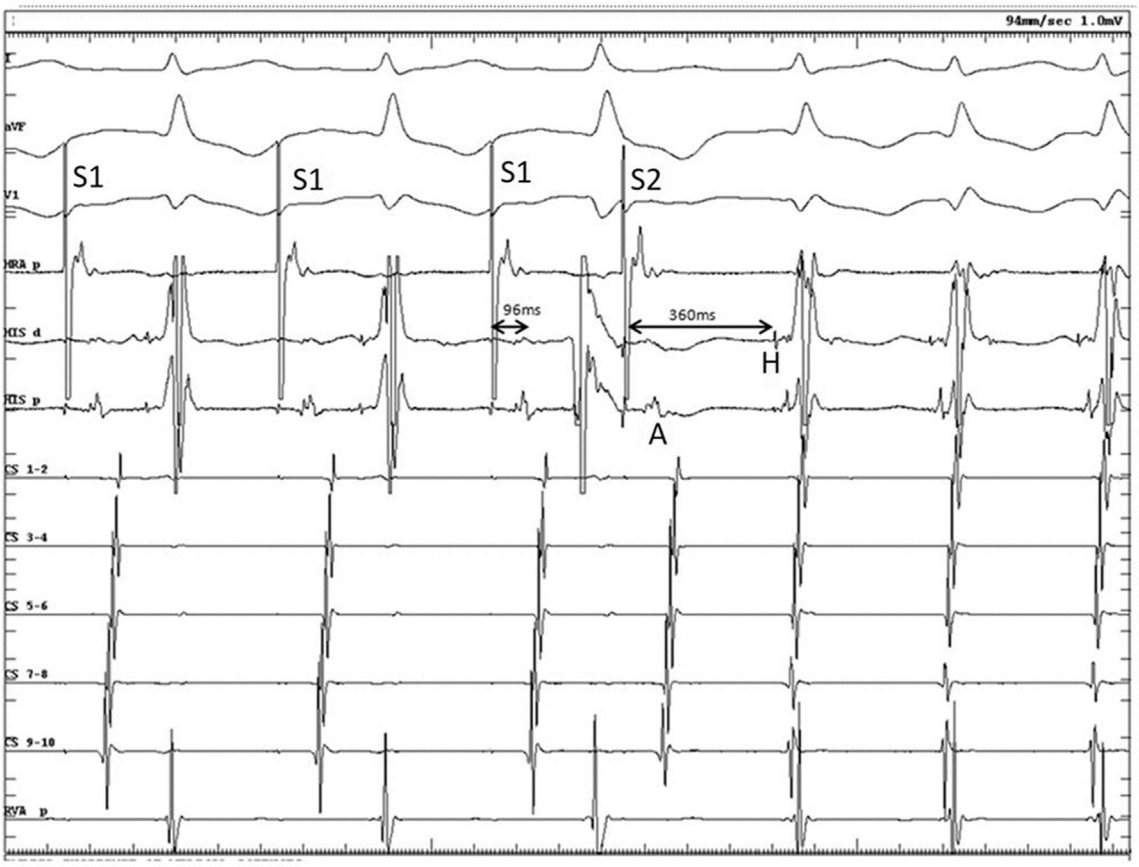

Fig. 2. The intracardiac tracing showing tachycardia induction in patient 1. From top to bottom are standard ECG leads I, aVL, V1 and electrograms from the high-right atrium (RA), distal and proximal His bundle area (HIS d and HIS p), distal and proximal CS (CS 1–10) and right ventricular apex (RVA). S1 and S2 represent the drive train and the premature stimulus of the PES sequence. The atrial electrogram is labelled as A whereas the HIS recording is marked H.

Table 2
Familial AVNRT: clinical and electrophysiological characteristics.

Study	Proband/Relationship	Age[a]/Sex	Electrophysiology	Associated structural heart disease	Outcome
Hayes et al. [12]	Six families with at least 14 affected first-degree relatives. Most common relationship mother – daughter. One family with themale-male transmission. Two families with three affected first- degree relatives.	32; Of the 14 familial cases, ii (79%) were female.	12 of 13 patients who underwent EP testing had inducible slow – fast (typical) AVNRT.[b]	Mitral valve prolapsed was present in all three affected individuals in one family.	RFA[c] of the slow AVN pathway was curative in all 13 cases.
Namgung et al. [14]	Mother and Son	29 and 14 years	Slow- Fast (typical) AVNRT in both patients	None	RFA of the slow AVN pathway was successful in both patients
Frisch et al. [15]	Brother and Sister (both diagnosed with Wolfram syndrome)	14 and 23 years	Slow- Fast (typical AVNRT in both patients)	None	RFA of the slow AVN pathway was successful in both patients
Barake et al. [16]	Identical female twins	12 and 11 years	Slow – Fast (typical) AVNRT in both patients	None	RFA of the slow AVN pathway was successful in both patients
Present study	Father and both sons	55, 15 and 31 years	Slow – Fast (typical AVNRT) in all three patients	None	RFA of the slow AVN pathway was successful in all patients.

[a] Age: Age at onset of symptoms of supraventricular tachycardia.
[b] AVNRT: Atrioventricular nodal re-entrant tachycardia.
[c] RFA: Radiofrequency Ablation.

Funding

No sources of funding.

Author contributions

Muthiah Subramanian: Contributed in the design of the study, data collection, analysis, and drafting of the article.

M.S. Harikrishnan: Contributed in the design of the study, data collection, drafting and critical revision of the article.

Mukund A. Prabhu: Contributed in the design of the study, drafting and critical revision of the article.

Praveen G. Pai: Contributed in drafting and critical revision of the article.

Saritha S. Sekhar: Contributed in drafting and critical revision of the article.

K.U. Natarajan: Contributed in drafting and critical revision of the article.

Conflict of interest

The authors declare that there is no conflict of interest.

References

[1] Katritsis DG, Camm AJ. Classification and differential diagnosis of atrioventricular nodal re-entrant tachycardia. Europace 2006;8:29–36.
[2] Kwaku KF, Josephson ME. Typical AVNRT—an update on mechanisms and therapy. Card Electrophysiol Rev 2002;6:414–21.
[3] Patterson E, Scherlag BJ. Anatomic and functional fast atrioventricular conduction pathway. J Cardiovasc Electrophysiol 2002;13:945–9.
[4] Wu D, Yeh SJ, Wang CC, et al. Nature of dual atrioventricular node pathways and the tachycardia circuit as defined by radiofrequency ablation technique. J Am Coll Cardiol 1992;20:884–95.
[5] Gollob MH, Green MS, Tang AS, et al. Identification of a gene responsible for familial Wolff-Parkinson-white syndrome. N Engl J Med 2001;344:1823–31.
[6] Gollob MH, Seger JJ, Gollob TN, et al. Novel PRKAG2 mutation responsible for the genetic syndrome of ventricular preexcitation and conduction system disease with childhood onset and absence of cardiac hypertrophy. Circulation 2001;104:3030–3.
[7] Tan HL, van der Wal AC, Campian ME, et al. Nodoventricular accessory pathways in PRKAG2-dependent familial preexcitation syndrome reveal a disorder in cardiac development. Circ Arrhythm Electrophysiol 2008;1:276–81.
[8] Brugada R, Tapscott T, Czernuszewicz GZ, et al. Identification of a genetic locus for familial atrial fibrillation. N Engl J Med 1997;336:905–11.
[9] Chen YH, Xu SJ, Bendahhou S, et al. KCNQ1 gain-of-function mutation in familial atrial fibrillation. Science 2003;299:251–4.
[10] Prystowsky EN, Klein GJ. Cardiac arrhythmias: an integrated approach for the clinician. New York: McGraw-Hill, Health Professions Division; 1994.
[11] Orejarena LA, Vidaillet Jr H, DeStefano F, et al. Paroxysmal supraventricular tachycardia in the general population. J Am Coll Cardiol 1998;31:150–7.
[12] Hayes JJ, Sharma PP, Smith PN, et al. Familial atrioventricular nodal reentry tachycardia. Pacing Clin Electrophysiol 2004;27:73–6.
[13] Hasdemir C, Payzin S, Kocabas U, et al. High prevalence of concealed Brugada syndrome in patients with atrioventricular nodal reentrant tachycardia. Heart rhythm 2015;12:1584–94.
[14] Namgung J, Kwak JJ, Choe H, et al. Familial occurrence of atrioventricular nodal reentrant tachycardia in a mother and her son. Korean Circ J 2012;42:718–21.
[15] Frisch DR, Kwaku KF, Allocco DJ, et al. Atrioventricular nodal reentrant tachycardia in two siblings with Wolfram syndrome. J Cardiovasc Electrophysiol 2006;17:1029–31.
[16] Barake W, Caldwell J, Baranchuk A. Atrioventricular nodal re-entry tachycardia in identical twins: a case report and literature review. Indian Pacing Electrophysiol J 2013;13:45–51.