Ablation of Nonautomatic Focal Atrial Tachycardia in Children and Adults with Congenital Heart Disease

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Ablation of NAFAT in Congenital Heart Disease. ***Introduction:*** **Nonautomatic focal atrial tachycardia (NAFAT) has been characterized in adults with structurally normal hearts. This article characterizes NAFAT in a population of patients with complex congenital heart disease.**

Methods and Results: **Electrophysiologic and electroanatomic mapping data and acute outcomes were reviewed in patients undergoing mapping and ablative procedures for atrial tachycardia at Children's Hospital, Boston, between January 1999 and December 2003. Twenty-two NAFAT foci were identified in 17 patients out of 216 patients studied. Fourteen of these 17 patients had congenital heart disease. The average age of the patients with a NAFAT mechanism was 27 years and there was no gender predilection. The presumptive diagnosis based on clinical grounds and surface ECG assessment in 11 of 17 patients with NAFAT was atrial flutter. None of the 17 patients were suspected of having a NAFAT mechanism by noninvasive assessment. Four of the 10 patients had both NAFAT and macroreentrant atrial tachycardias. NAFAT cycle lengths varied widely (200–680 ms) between patients. Sixteen of the 22 NAFAT foci were mapped to the anatomic right atrium (RA). Acute ablative success was achieved in 17 out of 22 foci (77%).**

Conclusion: **NAFAT is relatively uncommon in a pediatric tertiary care setting, and in that setting occurs most often in adults with congenital heart disease. NAFAT is indistinguishable from other forms of atrial tachycardia by noninvasive means and can mimic other forms of atrial tachycardia on electrocardiogram. The foci were predominantly found in the RA and were, in most cases, acutely amenable to catheter ablation therapy.** *(J Cardiovasc Electrophysiol, Vol. 17, pp. 359-365, April 2006)*

atrial tachycardia—focal, catheter ablation, heart defects—congenital, electrophysiology

Introduction

Atrial tachycardias can manifest as a macroreentrant circuit (e.g., atrial flutter) or emanate from a focal source. Focal atrial tachycardia can be further subdivided into nonautomatic and automatic forms. Automatic atrial tachycardia, as the name suggests, results from enhanced automaticity and, by definition, cannot be initiated or terminated by programmed electrical stimulation. In contrast, nonautomatic focal atrial tachycardia (NAFAT), by definition, emanates from an atrial point source and can be induced or terminated with pacing. NAFAT is a relatively recently described subform of focal atrial tachycardia. For the most part, NAFAT has been studied in adults with structurally normal hearts.[1-4] Even in adults, NAFAT appears to be a relatively uncommon arrhythmia mechanism. Kammeraad et al.[4] identified only 38 cases out of 1328 ablation procedures performed over a 6-year time frame at a single tertiary care center. The mean age at presentation was 31 years and most individuals coming for electrophysiology (EP) study had failed or had been intolerant to medical management. Overall ablation success in Kammeraad's series was 76%. The diagnosis of NAFAT generally requires formal EP study. Prior to EP study, patients with NAFAT are often presumptively diagnosed with supraventricular tachycardia, atrial tachycardia, or atrial flutter.[5] The mechanism underlying NAFAT is unknown, though both triggered and reentrant mechanisms have been implicated in clinical and experimental models.[1,2] In this article, we review our NAFAT experience to further our understanding of the nature and scope of this rare and incompletely understood arrhythmia in children and adults with congenital heart disease.

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Methods

We performed a retrospective review of clinical and electrophysiologic characteristics, as well as acute ablation outcome data for all patients meeting diagnostic criteria for NAFAT while undergoing electrophysiologic study at Children's Hospital, Boston, between January 1999 and December 2003. This time period was chosen because of the availability and utilization of the CARTO® (Biosense Webster, Diamond Bar, CA, USA) electroanatomic mapping system to localize and assist in characterizing these foci. Clinical data were reviewed with the approval of the Children's Hospital Institutional Review Board.

Patients

Patients were identified by a database search of all ablation cases involving some form of atrial tachycardia done

at Children's Hospital, Boston, during the specified time period. To be included as a subject in the study, the patient must have at least 1 NAFAT focus. NAFAT was defined as a tachyarrhythmia initiated or terminated by programmed electrical stimulation having an atrial point source, defined by the radial spread of activation from an atrial focus. Other possible mechanisms of supraventricular tachycardia (SVT) including atrioventricular reciprocating tachycardia via accessory pathway or atrioventricular nodal reentrant tachycardia were excluded. For comparison of map and ablation times between NAFAT and intraatrial reentrant tachycardia (IART) targets, patients with IART matched by age, year of study, and anatomy were randomly selected and used as controls.

Electrophysiologic Study and Electroanatomic Mapping

Electrophysiologic study and electroanatomic mapping using the CARTO® mapping system were performed with the patient under general anesthesia, using standard techniques described previously.[6]

Data Collection

Medical record and database reviews were used to collect the following clinical and demographic data on patients meeting the diagnostic criteria for NAFAT: age, gender, cardiac anatomy, clinical arrhythmia history, and indication for EP study. In addition, procedural reports and original signal tracings were reviewed for NAFAT cycle length, location, entrainability, response to medications, and acute ablative success. To facilitate a comparison between NAFAT and IART ablation procedures, the following data were also collected: time to first ablation, ablation time until success, total ablation time, and total time to success. Acute ablative success was defined as noninducibility following application of radiofrequency (RF) energy using pacing maneuvers that had resulted in induction of the target arrhythmia preablation.

Results

During the specified study period, there were 216 patients diagnosed with an atrial tachycardia during an EP study and ablation procedure at our institution. Of these, 17 patients (8%) with an average age of 27 years (median 28, range 5–52 years) met criteria for the diagnosis of NAFAT (Table 1). There were 9 males and 8 females. Fourteen of the 17 had congenital heart disease and 13 of these 14 had undergone prior cardiac surgery.

Prior to undergoing EP study and attempted RF ablation, 14 of the 17 patients were receiving antiarrhythmic medical therapy; 9 patients were on multiple antiarrhythmic medications and the remaining 5 patients were on single drug therapy. The medications used included beta-blockers (n = 9), digoxin (n = 7), amiodarone (n = 3), sotalol (n = 2), flecainide (n = 1), procainamide (n = 1), dofetilide (n = 1), diltiazem (n = 1), and verapamil (n = 1).

Of the 17 patients found to have one or more NAFAT foci at EP study, none were presumptively suspected of having a NAFAT mechanism based on clinical features and noninvasive rhythm analysis. Eleven out of the 17 NAFAT patients had a presumptive diagnosis of atrial flutter. Figure 1 shows a representative 12-lead ECG during a NAFAT episode demonstrating an atrial flutter pattern with an undulating atrial signal without isoelectric time. As can be seen in Table 1, in this portion of our NAFAT population, all of the subjects had some form of congenital heart disease and 7 out of 11 had single ventricle physiology. Six out of the 17 NAFAT patients had a presumptive diagnosis of something other than atrial flutter

TABLE 1

Clinical and Anatomic Features of Patients with NAFAT

Patient No.	Age (Years)	Gender	Presumptive Arrhythmia Diagnosis	Arrhythmia Density	Anatomic Diagnosis	Surgical Intervention
1	41	M	Atrial flutter	Frequent, paroxysmal	TAPVR to CS	Repair
2	17	F	Atrial flutter	Infrequent, paroxysmal	PA/IVS	Fontan
3	52	F	Atrial flutter	Frequent, paroxysmal	TOF	Repair
4	40	F	Atrial flutter	Frequent, paroxysmal	DORV	Palliative systemic pulmonary shunts
5	41	M	Atrial flutter	Frequent, paroxysmal	DORV	Fontan
6	14	M	Atrial flutter	Frequent, paroxysmal	DORV, PS	None
7	35	F	Atrial flutter	Frequent, paroxysmal	Single left ventricle	Fontan
8	36	M	Atrial flutter	Incessant	Tricuspid atresia	Fontan
9	46	F	Atrial flutter	Infrequent, paroxysmal	TOF	Repair
10	16	M	Atrial flutter	Unknown	Tricuspid atresia	Fontan
11	15	M	Atrial flutter	Frequent, paroxysmal	TOF	Repair
12	28	M	Unspecified SVT	Infrequent, paroxysmal	PA/IVS	Repair
13	5	F	Concealed accessory pathway	Infrequent, paroxysmal	Normal	NA
14	17	M	Atypical AVNRT	Unknown	Normal	NA
15	11	F	EAT	Incessant	Normal	NA
16	13	F	Unspecified SVT	Frequent, paroxysmal	Shone syndrome	Coarct repair Cath MV dilation Device ASD closure
17	35	M	Unspecified SVT	Infrequent, paroxysmal	Tricuspid atresia	Palliative systemic pulmonary shunts

CS = coronary sinus; DORV = double outlet right ventricle; PA/IVS = pulmonary atresia/intact ventricular septum; PS = pulmonary stenosis; TAPVR = total anomalous pulmonary venous return; TOF = tetralogy of Fallot.

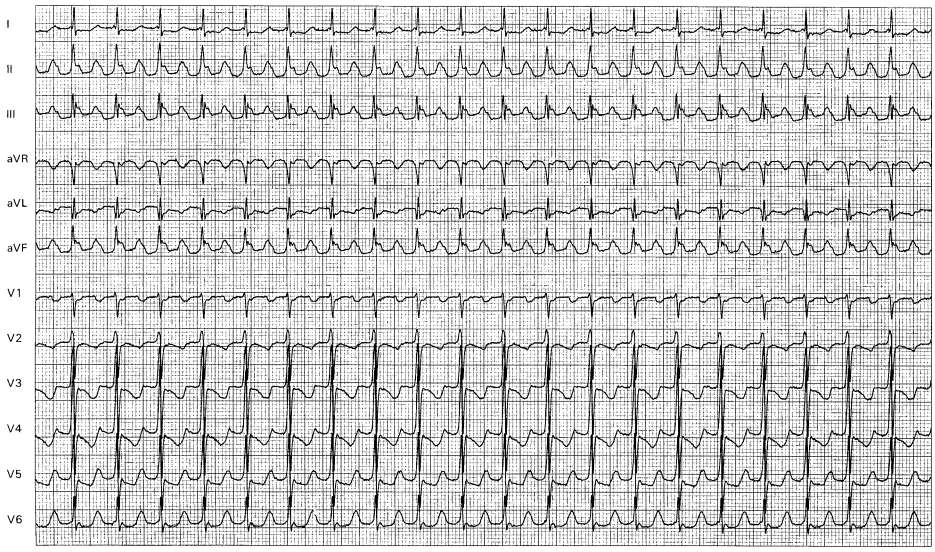

Figure 1. *Twelve-lead surface ECG of NAFAT mimicking atrial flutter.*

including unspecified SVT in 3, concealed accessory pathway in 1, ectopic atrial tachycardia (EAT) in 1, and atypical AVNRT in 1. A representative ECG during a NAFAT episode showing a long R-P tachycardia and discrete P wave with an abnormal P-wave axis characteristic of EAT is shown in Figure 2. In distinction with the NAFAT patients with presumed atrial flutter in which congenital heart disease was universally present, in patients in whom the presumptive diagnosis was something other than atrial flutter (e.g., SVT, EAT, AVNRT), only half had congenital heart disease and of those, only 1 patient had single ventricle physiology. These NAFAT patients tended to be younger than those with presumed atrial flutter (mean age 18 vs 32 years).

Twenty-two NAFAT foci were identified during 17 EP studies in the 17 patients, with 4 patients manifesting more than 1 NAFAT focus (Table 2). By definition, all of the NAFAT foci were pace-inducible (Fig. 3) or terminable and emanated from an atrial point source of activation (Fig. 4). NAFAT cycle lengths across the cohort varied considerably and ranged from 200 to 680 ms, with no correlation with age or cardiac anatomy. The tachycardia cycle length of several NAFAT foci showed considerable variation, changing by as much as 145 ms. Coexisting atrial arrhythmias were documented in 6 out of the 17 patients: 4 had coexisting macroreentrant atrial tachycardia circuits, 1 had AVNRT, and 1 had both macroreentrant atrial tachycardia and AVNRT. No consistent drug-testing strategy was employed during the EP study. Low-dose isoproterenol was used to sustain atrial tachycardia in 2 cases. In another, procainamide was used to stabilize the atrial tachycardia and prevent degeneration into atrial fibrillation. Lidocaine and verapamil were administered independently in a single case and had no effect on the atrial tachycardia cycle length, though verapamil did predictably increase atrioventricular conduction time. Adenosine (12 mg) was administered in one patient and resulted in abrupt termination of the tachycardia following a QRS complex. Entrainment mapping was not routinely performed, but successful entrainment was documented in one study.

The locations of the 22 NAFAT foci are shown in Figure 5. As can be seen, 16 (72%) of NAFAT foci were found in the right atrium (RA), with only 6 foci in 3 patients found in the

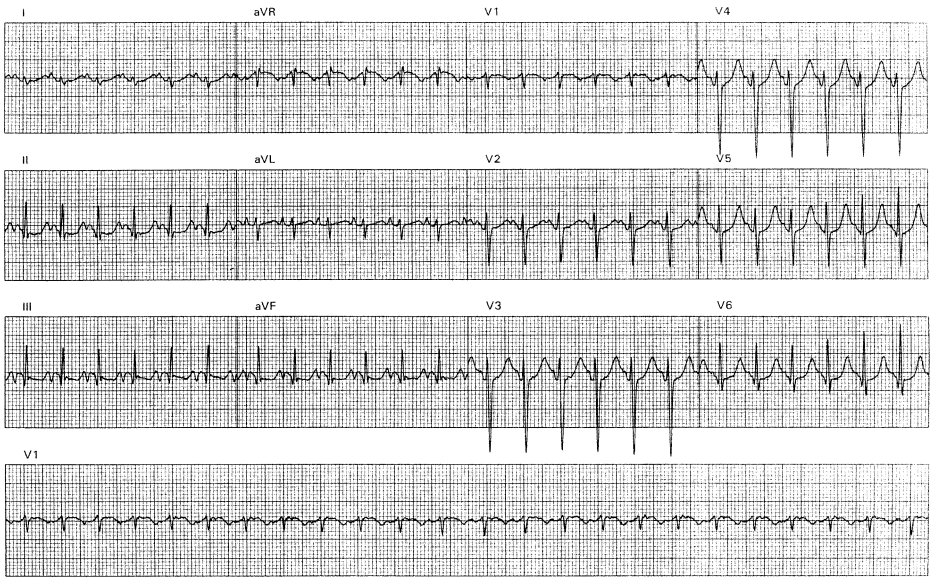

Figure 2. *Twelve-lead surface ECG of NAFAT mimicking EAT.*

TABLE 2
NAFAT Foci Characteristics

NAFAT No.	Patient No.	Cycle Length (ms)	Location	Acute Ablative Success
1	1	200	LA-RUPV	Yes
2	2	393–538	RA-crista terminalis	No*
3	3	320	RA-lateral free wall	Yes
4	4	320–370	RA-anterior septal	No†
5	5	680	RA-superior Fontan baffle	Yes
6	5	712	RA-posterior inferior Fontan baffle	Yes
7	6	235–270	RA-inferior anterior free wall	Yes
8	7	545	RA-inferior lateral free wall	Yes
9	8	290	RA-inferior lateral free wall	Yes
10	8	274	RA-inferior anterior free wall	Yes
11	9	430	RA-crista terminalis	Yes
12	10	244	RA-posterior junction with SVC	Yes
13	11	600	RA-anterior free wall	Yes
14	12	305–315	RA-cavo-tricuspid-isthmus	Yes
15	13	425	RA-inferior posterior	No†
16	14	376–399	RA-superior limbus of fossa ovalis	Yes
17	15	420	LA-mid septal	Yes
18	15	400	LA-LUPV	Yes
19	15	480	LA-orifice of LUPV	No†
20	16	420	RA-crista terminalis	Yes
21	17	245	LA-RUPV	Yes
22	17	237	LA-superior posterior septal	Yes

*Transient success with acute recurrence. †Limited or no RF attempted due to high-risk location (NAFAT No. 4—near His bundle electrogram; NAFAT No. 15—phrenic nerve twitch during RF; NAFAT No. 19—multiple prior RF applications in LUPV during ablation of NAFAT No. 18). LA = left atrium; LUPV = left upper pulmonary vein; RUPV = right upper pulmonary vein; SVC = superior vena cava.

left atrium. The CARTO® mapping system was used in all but 3 cases. Acute ablative success was achieved in 17 out of 22 foci (77%). In 3 of the 5 cases in which ablative success was not achieved, no or limited attempts at RF ablation were made due to the high-risk location of the NAFAT foci. For example, in patient number 4 the NAFAT focus was mapped to near the His bundle electrogram (see Table 2). Five of the 22 foci demonstrated gradual slowing prior to tachycardia termination during RF ablation. In the remainder, there was abrupt termination during the RF application. No acute complications resulted from the EP study in any of the 17 patients.

A comparison of mapping and ablation with respect to time to first ablation (mapping time), ablation time until success, total ablation time, and total time to success between NAFAT and IART was performed. The small sample size

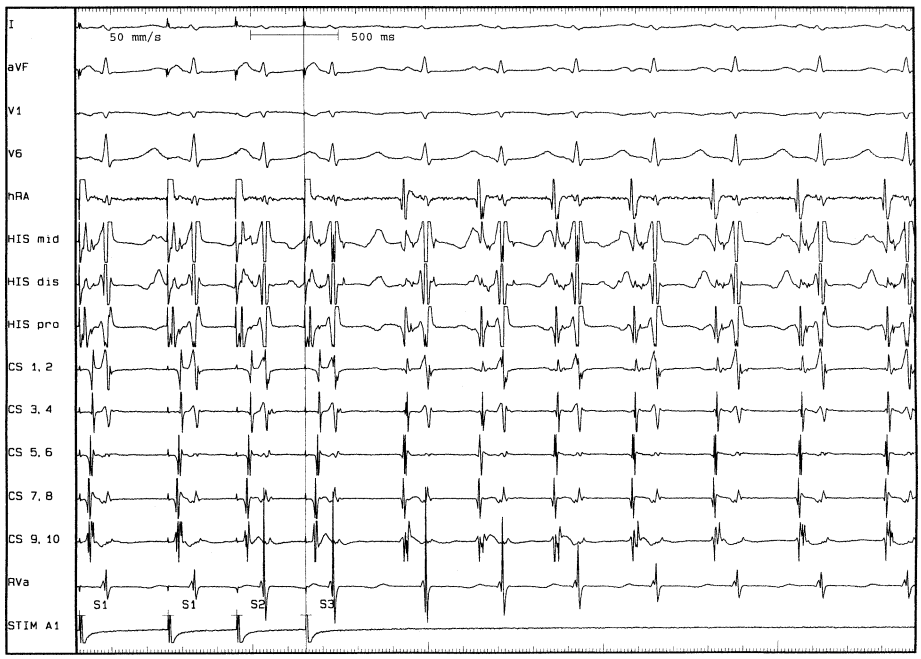

Figure 3. *Induction of NAFAT with programmed electrical stimulation.*

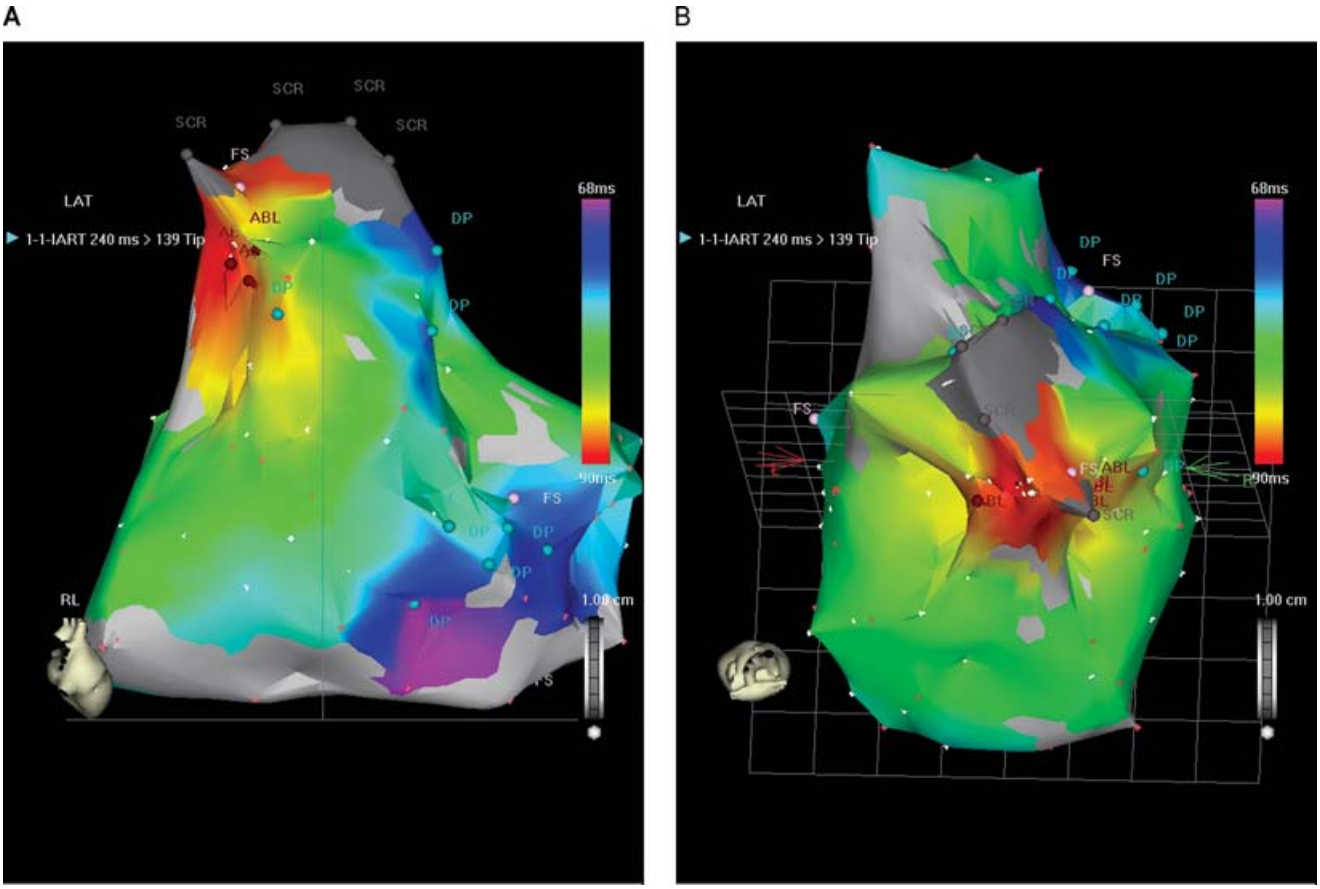

Figure 4. *Electroanatomic map of a nonautomatic focal atrial tachycardia focus. Red is the earliest activation and purple is the latest. Earliest activation can be seen emanating from the SVC with radial spread to the remainder of the atrium. A: Right lateral view. B: Superior view.*

precluded meaningful statistical analysis, though we did note a trend toward less total ablation time and shorter overall time to success in the NAFAT group compared to the IART (Table 3).

Discussion

We identified 17 patients with one or more NAFAT foci out of 216 cases of atrial tachycardia. Consistent with previous reports,[2,4] NAFAT was predominantly (though not exclusively) found in adults. Acute ablative success rates when RF was attempted were high. The comingling of NAFAT and congenital heart disease in our series likely reflects the biased population of adult patients cared for in our institution rather than any specific association between NAFAT and congenital heart disease. Our incidence of NAFAT was considerably lower than that reported by Kammeraad et al.[4] where 38 patients with NAFAT were identified out of 98 patients with atrial tachycardia. This might be due to the relatively large proportion of children relative to adults in our study population. Unlike that series, but similar to Chen et al.[2] we did not observe any gender predilection.

Consistent with prior reports, we found the majority of NAFAT foci in the RA.[4,7–9] The reasons behind this laterality are unknown, but several hypotheses have been put forth including enhanced susceptibility of micro-reentry due to normal right atrial anatomic or functional barriers such as the crista terminalis.[7] Interestingly, when present on the LA side, NAFAT foci seemed to cluster near or within the pulmonary veins similar to areas where EAT foci are commonly found.[10] Apart from areas deemed high-risk due to proximity to

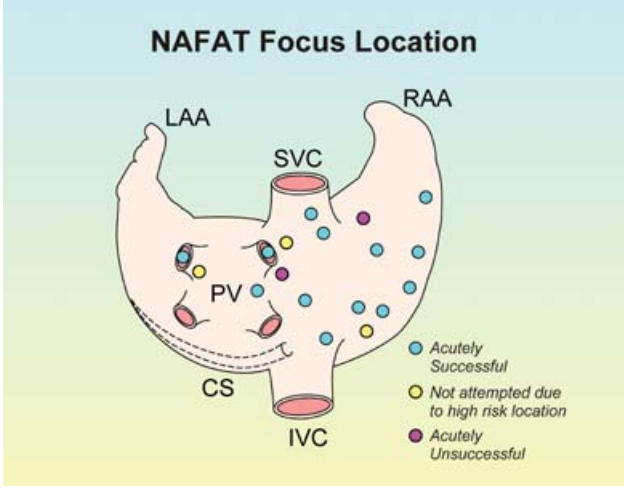

Figure 5. *Mapped locations of the 18 NAFAT foci. A posterior two-dimensional view of the atria is shown. Green dots indicate those foci successfully ablated. High-risk locations in which RF was deferred are shown in yellow. Red dots indicate sites of unsuccessful ablation attempts.*

TABLE 3
Comparison of NAFAT and IART Mapping and Ablation Characteristics

Measured Parameter	NAFAT Mean (±SD)	IART Mean (±SD)
Time to 1st ablation (min)	106 (50)	219 (72)
No. of RF applications until success	5 (6)	7 (10)
RF time to success (sec)	245 (343)	352 (451)
RF total time (sec)	454 (399)	763 (527)
Total time to success (min)	69 (72)	106 (71)

RF = radiofrequency ablation.

sensitive cardiac structures (e.g., bundle of His, phrenic nerve), the location of the NAFAT focus did not impact on acute ablative success.

In no case were we able to identify the presence of a NAFAT focus from clinical or noninvasive EP data. In a number of patients, NAFAT mimicked the ECG appearance and occurred in a clinical setting typical of atrial flutter (i.e., in adults with complex congenital heart disease). Focal atrial tachycardia mimicking atrial flutter on surface ECG has been reported by others as well.[5] In these cases the distinction between macroreentrant atrial tachycardia and a NAFAT focus requires careful analysis of the CARTO® propagation map. As shown in Figure 4, NAFAT foci demonstrate radial spread of activation from an atrial point source, in contrast to the circuit of activation characteristic of macroreentrant atrial tachycardia. Though not routinely utilized in this series, others have reported that adenosine might prove valuable in distinguishing between these mechanisms as well, with the majority of NAFAT foci being adenosine sensitive and the majority of macroreentrant atrial flutter circuits being adenosine resistant.[3,8] Other patients in this group had presumptive diagnoses of EAT, AVNRT, or unspecified SVT. These patients tended to be younger and more often had structurally normal hearts. In Figure 2 there is an example of an ECG during NAFAT that resembles EAT, with discreet P waves, a long R-P interval, and interspersed isoelectric time. It is not clear whether the different surface ECG appearances of NAFAT have mechanistic implications or whether they are simply varying manifestations of the same disorder in patients with different electroanatomic substrates.

The mechanism underlying NAFAT is unknown. Both triggered and microreentrant mechanisms have been suggested.[1,4,8,11] Distinguishing between these during standard clinical EP study has proved difficult because they have similar electrophysiologic manifestations despite the fundamental mechanistic differences between them.[1,4,8,11] Both mechanisms have been observed in experimental, as well as clinical settings.[1,12,13] Both triggered and microreentrant mechanisms can be pace-induced and terminated.[1] Similarly, responsiveness to adenosine does not distinguish between these mechanisms. Adenosine might terminate triggered rhythms due to drug-mediated antiadrenergic effects and lowering cellular cAMP levels. Microreentrant rhythms, in contrast, may be terminated by adenosine's effect on potassium channels (I_{KAdo}), resulting in membrane hyperpolarization and shortening of refractory periods.[3,8] Entrainment appears to be one of the few distinguishing electrophysiologic properties and seems to be specific to reentrant mechanisms,[1,14] though even with this, the distinction can be difficult.[11] In our series, entrainment mapping was not routinely employed, though in the one case when utilized, the NAFAT proved entrainable.

In our comparative analysis between NAFAT and IART with respect to time to first ablation (mapping time), ablation time until success, total ablation time, and total time to success, it was our subjective impression that mapping and ablating NAFAT targets were "easier" than macroreentrant targets. Indeed, there was a trend toward shorter ablation times and shorter time to success in the NAFAT group. This would appear to be due, in part, to more detailed mapping necessary to characterize IART circuits as well as more extensive ablation to create a line of block rather than eliminating a discrete focus.

Our study is limited by its retrospective design and the relative rarity of this condition in a predominantly pediatric setting. Characterization of the NAFAT foci, apart from localization and acute response to ablative efforts, was incomplete, both in terms of drug testing (such as response to adenosine), electrophysiologic features such as entrainability, and evaluation of long-term ablative success. As such, we are unable to shed light on hypothesized mechanisms underlying NAFAT or the late outcome of patients having undergone acutely successful RF ablation of a NAFAT focus.

Conclusions

NAFAT is an infrequently encountered form of atrial tachycardia in a pediatric tertiary cardiac care facility, principally found in this setting in adults with congenital heart disease. Clinical and electrocardiographic features of this arrhythmia are indistinguishable from other forms of atrial tachycardia (IART or EAT) without a formal intracardiac EP study. NAFAT foci are predominantly found in the RA and are acutely amenable to catheter ablation therapy. More study is needed to better characterize the precise mechanism of this arrhythmia as well as the long-term results of ablative therapy in this patient population.

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