An unusual cause of lone atrial fibrillation in a young female subject due to a rapid-cycling focal atrial trigger

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Introduction

Lone atrial fibrillation (AF) refers to the occurrence of AF in patients with structurally normal heart with normal function.[1] Lone AF is uncommon in children, with an estimated prevalence of 7.5/100,000 patients, though it appears to be more common with increasing age, in male subjects, and in obese children.[1–3] Electrophysiology (EP) studies have been performed in refractory AF in this population; however, there is conflicting information regarding the frequency and location of focal triggers for AF and outcome of ablation.[1,3–6] Here we report on a pediatric patient with refractory AF who had an excellent outcome after catheter ablation of a focal atrial trigger with a location and activation frequency that has never been reported before, and review the available literature on this topic.

Case report

The patient, a 13-year-old nonobese (body mass index: 20.05 kg/m^2) female subject with no significant prior medical history or family history of arrhythmias, was noted at a well child visit to have an irregular heart rhythm by her pediatrician. She was sent for evaluation at a cardiology clinic in an outside hospital, where she was found to be in AF (Figure 1A). She was admitted to the same hospital and she was cardioverted to sinus rhythm after documentation of the absence of intracardiac thrombus by echocardiogram. However, she had recurrence of AF on the same day during observation. At this point she was transferred to our institution, where we started flecainide, and cardioversion was repeated after several doses of this medication, with successful conversion to sinus rhythm. AF again recurred within 12 hours. This series of events was repeated with a trial of sotalol and then a trial of disopyramide, again with similar results: sinus rhythm for 10–12 hours after cardioversion. Her AF would recur in each case in the early morning hours while she was sleeping. Her ventricular rate at the time of recurrence of AF was typically in the 60–70 beats per minute range and the rhythm alternated from an organized atrial tachycardia to AF (Figure 1B and C). The atrial tachycardia, when organized, appeared to have a left atrial focus.

She next underwent an elective EP study and right-heart catheterization to evaluate for other causes of AF, including presence of an accessory pathway, atrioventricular (AV) reentrant tachycardia (AVRT), AV nodal reentrant tachycardia, or inducible atrial tachycardia. She was brought to the EP laboratory in AF and was cardioverted. She remained in sinus rhythm throughout the study, which demonstrated normal hemodynamics. The EP study demonstrated normal AV nodal physiology with no evidence of dual AV nodal physiology, accessory AV connection (manifest or concealed), or inducible tachycardia, including atrial tachycardia or AF, both at baseline and during isoproterenol infusion at 0.015 μG/kg/min. Following the procedure, she was discharged home in sinus rhythm on an amiodarone load. The next morning her parents recorded her heart rhythm using an AliveCor Kardia system (AliveCor Inc, Mountain View, CA), which demonstrated her to be in AF. Another attempt was made to cardiovert her after a load of amiodarone for 1 month, but her AF again occurred early the next morning. Cardiac magnetic resonance imaging was done at this point and did not demonstrate any evidence of atrial fibrosis or scar.

After this recurrence on the amiodarone load, the decision was made to have her undergo repeat EP testing with potential pulmonary vein isolation (or partial pulmonary vein isolation—left pulmonary veins) for AF at our partner adult institution. During this procedure, mapping of her atria while in AF demonstrated an area just proximal to the mouth of her left atrial appendage at the location of the ligament of Marshall with extremely rapid and irregular electrical far-field signals with a cycle length of 46–50 ms

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KEY TEACHING POINTS

- Lone atrial fibrillation is uncommon in children but can be recurrent and refractory to medical management.
- Electrophysiology study in these pediatric population reveal focal triggers or demonstrate atrial fibrillation associated with more common forms of supraventricular tachycardia such as atrioventricular reentrant tachycardia.
- Catheter ablation in this situation appears to be safe, with excellent immediate results.
- A rapidly cycling focal atrial trigger in the region of the ligament of Marshall can present with pediatric lone atrial fibrillation and respond well to catheter ablation.

(Figures 2A–C and 3). Though there was always a rapid signal in this location, the local near-field and the distal atrial signal on the coronary sinus catheter alternated from this similar rapid signal to a more organized and regular atrial tachycardia (Figure 2A–C). Radiofrequency (RF) ablation at this site resulted in prolongation of the cycle length to 80 ms prior to sudden termination of the tachycardia and resumption of sinus rhythm (Figure 2D). This rapid tachycardia was no longer present throughout the rest of the study, including testing with high-dose isoproterenol. She did have a slower organized atrial tachycardia that was mapped to a similar location at the base of the left atrial appendage, which was successfully ablated with RF energy. At the end of the study she had no inducible tachycardia. The following morning, she had an episode of regular atrial tachycardia (same morphology seen in the EP study) that was treated with a single dose of amiodarone, which terminated her tachycardia (Figure 1D). She remained in sinus rhythm without recurrence in the early morning hours and was discharged home. She had a recurrence of this regular atrial tachycardia (cycle length of 320 ms), for which she was symptomatic at home later that day. She was admitted to our institution and started on flecainide, which terminated her tachycardia. She remained on flecainide for 6 months, at which point this medication was discontinued. She has had no recurrence of her tachycardia for the past 5 months. She has had no recorded atrial tachycardia or fibrillation and has recorded her heart rhythm several times with an AliveCor Kardia system (AliveCor Inc, Mountain View, CA).

Discussion

Lone AF is uncommon in children and can be recurrent, as in our patient (recurrence rate: 18%–31% at 3 months).[2,3] Although the underlying trigger for AF in this population is unclear, it has been considered to be multifactorial, with obesity as a recognized risk factor.[2] Familial aggregation of lone AF has also led to identification of an underlying genetic

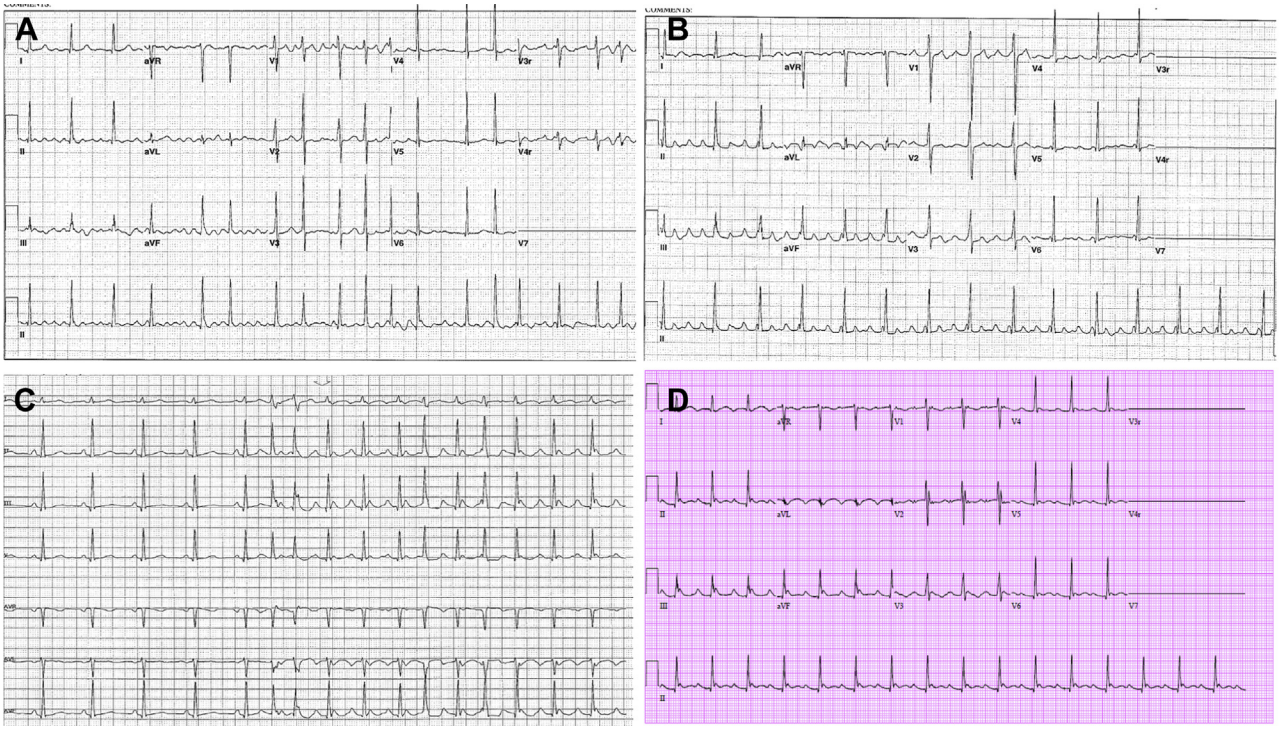

Figure 1 **A:** Electrocardiogram (ECG) on initial presentation, demonstrating disorganized atrial rhythm with variable A-V conduction consistent with atrial fibrillation. **B:** ECG demonstrating organized atrial activity with 2:1 A-V conduction consistent with atrial flutter. **C:** ECG demonstrating initiation of tachycardia with organized atrial rhythm. **D:** ECG demonstrating slower atrial tachycardia with 2:1 A-V conduction after focal radiofrequency ablation.

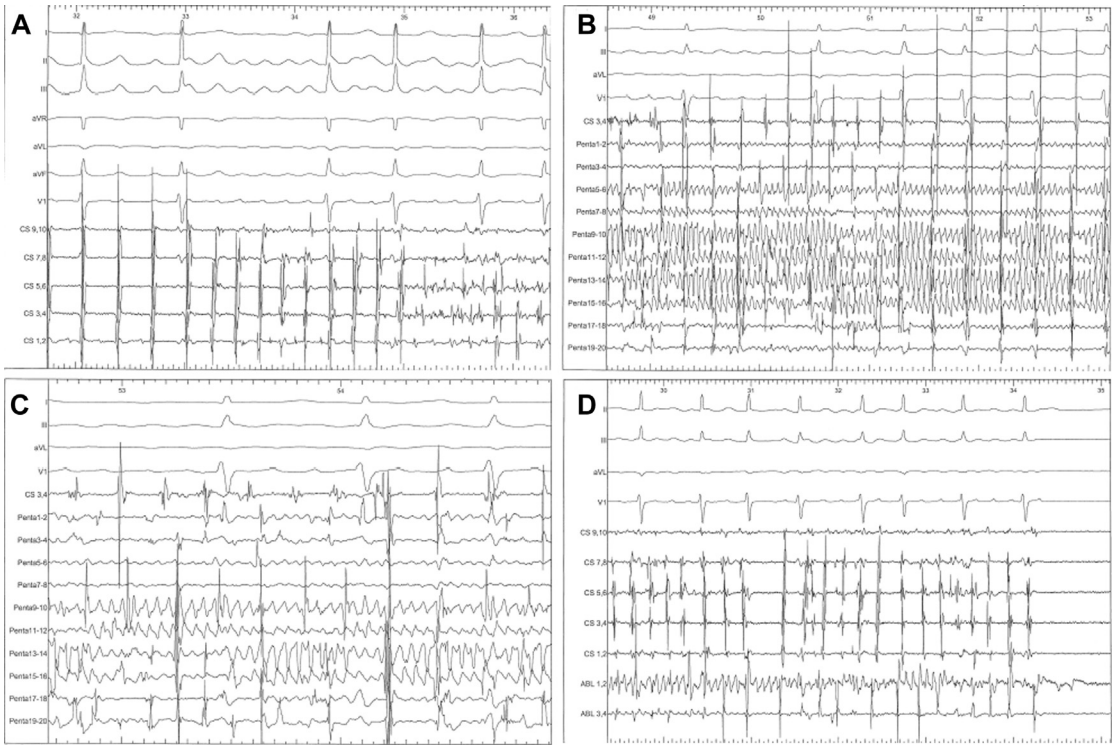

Figure 2 **A:** Intracardiac electrograms demonstrating a regular atrial tachycardia recorded in the coronary sinus (CS) catheter that transitions to atrial fibrillation during the electrophysiology study. **B:** Atrial fibrillation recorded from the CS catheter, which organized to atrial tachycardia, with high-frequency atrial electrograms noted in the PentaRay catheter at the base of the left atrial appendage throughout the recording. **C:** Atrial fibrillation in the CS catheter with continued high-frequency fractionated atrial electrograms noted in the PentaRay catheter at the base of the left atrial appendage. **D:** Termination of high-frequency irregular atrial electrograms with radiofrequency ablation at the base of the left atrial appendage.

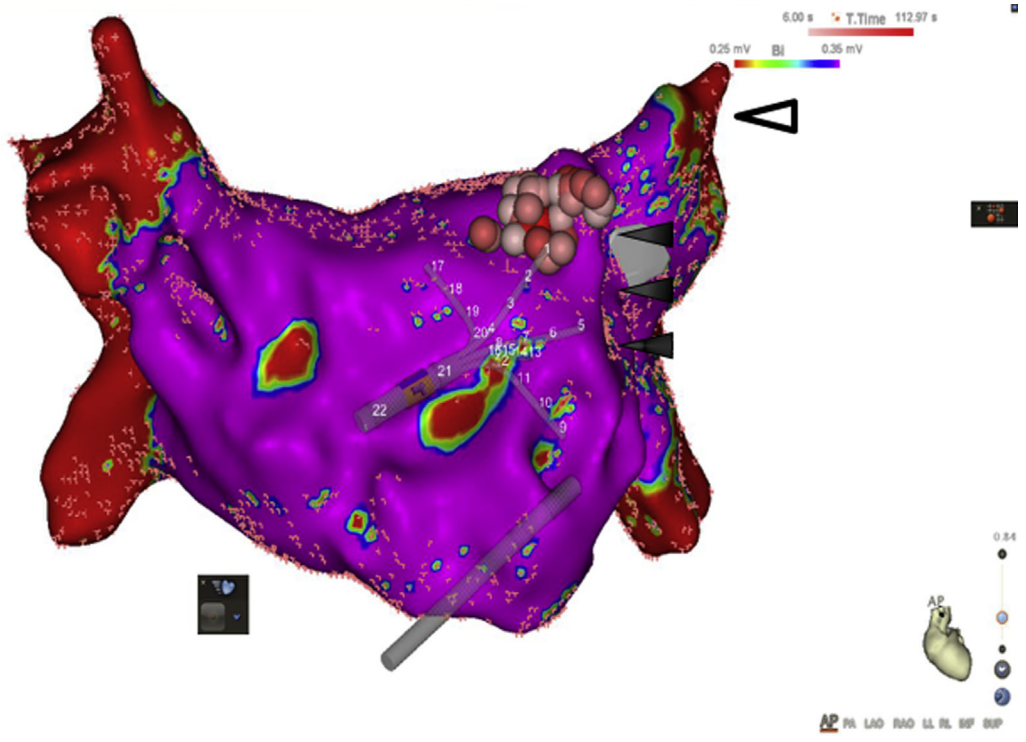

Figure 3 Anteroposterior projection of the left atrium on Carto-3D voltage map using the PentaRay catheter denoting the location of the site of radiofrequency ablation of the atrial focal trigger and the area of the slower atrial tachycardia that occurred after ablation. Closed arrowheads denote the location of the lateral ridge where one would expect the ligament of Marshall and the open arrowhead denotes the left upper pulmonary vein.

Table 1 Summary of clinical characteristics of prior case series and present report of patients with lone atrial fibrillation

	No. of patients	Mean age (years)	Focal trigger	Coexisting SVT	Therapeutic procedure	Acute procedure success	Relapse after ablation	Complications of EPS/ablation
Ceresnak et al (multicenter): 2013[1]	18	17.9 ± 2.2	0 (0%)	7 (39%) (5 typical AVNRT, 2 AVRT – concealed AP)	AP (2), AVNRT (5)	100%	0%	0%
Nanthakumar et al: 2004[4]	9	15.9 ± 3.3	9 (100%) (LA: 2, CT: 2, PV:4, CT/PV: 1)	0%	RLPV (1), RUPV (1), RLPV/LLPV (1), RUPV/LUPV (1) RLPV/CT (1), CT (2), LA (1)	89% (1 patient underwent Maze owing to multiple LA foci)	22% (1 CT, 1 RUPV/LUPV)	0%
Mills et al (multicenter): 2013[3]	12		2 (17%) (PV: 2)	4 (33%) (1 AP, 1 AVNRT, 2 A.Flut)	AP (1), AVNRT (1), A.Flut (2), PV (2)	N/A	2 (17%) (2 A.Flut)	N/A
Balaji et al: 2016[5]	4	16 ± 0.8	2 (50%) (PV: 2)	0%	All pulmonary vein isolation (3), LLPV (1), LLPV/ LUPV/RUPV (1)	75%	25% (1 all pulmonary vein isolation)	0%
Strieper et al: 2010[6]	4	16.5 ± 0.5	1 (25%) (PV: 1)	3 (75%) (1 AP, 2 A.Flut)	AP (1), Adj.RUPV (1), A.Flut (2)	100%	1 (25%) (1 A.Flut)	0%
Present report	1	13	1 (LA: 1)	0%	LA (1)	100%	No recurrence (5 months)	0%
Total	48		15	14	31			

Adj. = adjacent; A.Flut = atrial flutter; AP = accessory pathway; AVNRT = atrioventricular nodal reentrant tachycardia; AVRT = atrioventricular reentrant tachycardia; CT = crista terminalis; EPS = electrophysiology study; LA = left atrium; LLPV = left lower pulmonary vein; LUPV = left upper pulmonary vein; N/A = not applicable; PV = pulmonary vein; RLPV = right lower pulmonary vein; RUPV = right upper pulmonary vein; SVT = supraventricular tachycardia.

etiology in a minority of these patients.[7,8] There have been 5 case series (total of 47 patients) in which pediatric patients with lone AF underwent EP study and catheter ablation (Table 1).[1,3–6] None of the pediatric studies have reported findings similar to our patient in regard to the rapidly cycling focal atrial tachycardia that acted as trigger for the AF. In most of these studies, the EP study was performed secondary to refractory or recurrent AF. The broad etiologic classifications for lone AF in the pediatric population include (1) focal triggers (abnormal automatic/reentrant foci in pulmonary veins or atrium) and (2) AF associated with other more common supraventricular tachycardias (SVTs) (atrial flutter, AVRT, or AV nodal reentrant tachycardia) seen in this population.

Focal triggers or drivers are in line with classical paroxysmal AF mechanisms described in adults, such as ectopic focus and single-circuit reentry or more novel mechanistic concepts such as stable rotors.[9] A focal trigger or a reentrant mechanism was also found in the majority (29/48; 60%) of the previously reported pediatric patients who underwent EP study. A single focal trigger in the left atrium, as in our patient, was reported in only 1 other patient who had a single left atrium focus. There was resolution of AF on RF ablation of this area; the authors, however, did not comment on the characteristics of the focal electrograms.[4] The patient in the present report had an extremely rapidly cycling focal atrial tachycardia and irregular cycle length with variable conduction to the atrium. The unambiguous far-field nature of the electrograms and the RF time needed for termination suggest that the arrhythmia could have been localized in the ligament of Marshall. Although AF secondary to focal trigger from the ligament of Marshall has been well studied in the adult population, to the best of our knowledge, no such case has been reported before in a pediatric patient.[10] The cycle length of this atrial focus is, to our knowledge, the fastest that has been reported in any pediatric patient. Of note, cardiac magnetic resonance imaging did not show any fibrosis in this area.

Association of SVT with AF has also been well documented in pediatrics. Ceresnak and colleagues[1] demonstrated that 39% of pediatric patients with lone AF have inducible SVT during an EP study. This association has also been noted in adults; however, the mechanisms underlying this have been elusive.[11] The short cycle length during SVT that results in reduced atrial refractory period has been hypothesized to result in increased vulnerability for AF.[12] Among the 4 patients with AVRT due to a concealed accessory pathway, 3 had left-sided accessory pathway and accessory pathway location was not reported in 1 other patient.

Conclusion

Although lone AF is rare in the pediatric population, it can be refractory and differs significantly from AF in the adult population. Among patients with refractory AF, EP study commonly reveals reentrant or focal triggers for AF. Catheter ablation in these situations seem to be safe, with excellent immediate result. However, recurrence does occur in a minority of the patients, especially among those with atrial flutter. In the present report, the underlying mechanism was an extremely rapidly cycling focal left atrial trigger that localized to the ligament of Marshall, which has not been previously reported in pediatric patients. Performing an EP study during tachycardia may identify a treatable cause that may not otherwise be inducible or seen in sinus rhythm. Future studies need to evaluate the frequency of occurrence of such rapid cycle length in pediatric patients with lone AF.

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