ORIGINAL RESEARCH

Fetal Atrial Flutter: Electrophysiology and Associations With Rhythms Involving an Accessory Pathway

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***Background*—**Atrial flutter (AFl) accounts for up to one third of all fetal tachyarrhythmias and can result in premature delivery, hydrops, and fetal death in 10% of cases; however, the electrophysiology of AFl in utero is virtually unstudied.

***Methods and Results*—**In this observational study, we reviewed 19 fetal magnetocardiography studies from 16 fetuses: 15 fetuses (21–38 weeks' gestation) referred with an echocardiographic diagnosis of AFl and 1 fetus (20 weeks' gestation) referred with a diagnosis of tachycardia that was shown by fetal magnetocardiography to have transient AFl in addition to atrioventricular reciprocating tachycardia. Thirteen fetuses showed AFl during the fetal magnetocardiography session, including 4 that presented prior to the third trimester. Five fetuses had incessant AFl; all but 1 of the others with AFl showed additional significant rhythms. Specifically, AFl showed a strong association with rhythms involving an accessory pathway: atrioventricular reciprocating tachycardia, blocked reentrant premature atrial contractions, and ventricular preexcitation. The observed initiations and terminations of AFl most often involved reentrant premature atrial contractions. Spontaneous termination of AFl showed AFl cycle length oscillations. Nine fetuses with 2:1 AFl also showed periods of 4:1 conduction or variable conduction that oscillated between 2:1 and 4:1; however, 3:1 AFl was relatively rare.

***Conclusions*—**Fetal AFl can occur as early as midgestation and is often accompanied by atrioventricular reciprocating tachycardia and other rhythms associated with an accessory pathway. The findings depict critical differences in the electrophysiology of AFl in the fetus versus the neonate. **(*J Am Heart Assoc*. 2016;5:e003673 doi: 10.1161/JAHA.116.003673)**

Key Words: atrial flutter • fetal • fetal heart • fetal magnetocardiography • magnetocardiography • supraventricular tachycardia

Fetal tachyarrhythmia is an uncommon condition that occurs in 0.4% to 0.6% of all pregnancies.[1] Atrial flutter (AFl) accounts for 26% to 29% of all fetal tachyarrhythmias[2,3] and is defined as a rapid regular atrial rate of 300 to 600/min, accompanied by variable atrioventricular conduction.[2] AFl can occur with structurally normal hearts or with congenital heart disease, including atrioventricular septal defect, Ebstein's malformation, hypoplastic left heart syndrome, and pulmonary atresia.[4–6] Although the incidence of hydrops fetalis is similar in sustained AFl and atrioventricular reciprocating tachycardia (AVRT),[2] the overall mortality of fetal AFl approaches 10% and is higher than that of AVRT, perhaps due to the higher incidence of congenital heart disease.[2]

Due to the difficulty of recording the fetal ECG, the electrophysiology of AFl in utero has not been investigated, except in small case studies. In this retrospective study, we utilized fetal magnetocardiography (fMCG), the magnetic analog of electrocardiography, to characterize the heart rate and rhythm patterns of fetuses presenting with AFl. We demonstrate a remarkably high incidence of AVRT and other rhythms associated with an accessory pathway.

Methods

The study cohort comprised pregnant women referred with a diagnosis of fetal AFl to the Biomagnetism Laboratories at the Department of Medical Physics, University of Wisconsin-Madison from 2002 to 2015. We also included 1 case in

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which the referral diagnosis was AVRT but AFI was also seen during the fMCG session. The study was approved by the University of Wisconsin Health Sciences Institutional Review Board. Informed consent was obtained from each participant.

The fMCG was recorded using a 37-channel (Magnes; 4D Neuroimaging, Inc., San Diego, CA) or a 21-channel (Model 624; Tristan Technologies, San Diego, CA) superconducting quantum interference device (SQUID) biomagnetometer, housed in a magnetically shielded room. The fMCG was recorded in 10-minute segments with a total recording time ranging from 20 to 100 minutes. Signal processing was used to remove maternal interference.

AFI was defined by a nearly constant atrial rate of >300/min, variable atrioventricular conduction with ratio >1:1, and abrupt onset and termination. AVRT was defined by heart rate >200/min with low baseline variability, 1:1 atrioventricular conduction, and abrupt onset and termination. We documented the cycle lengths and the percent time in AFI, AVRT, and the other observed rhythms.

We measured the PR, QRS, and QTc intervals in sinus rhythm, the PR, RP, and QRS intervals in AVRT, and the QRS interval during AFI. The QTc interval during tachycardia was difficult to measure due to overlap of the P and T waves. Cardiac time intervals were compared with those of normal fetuses from a reference database. Measurements exceeding the 95% prediction interval were considered to be prolonged.

Actocardiography was used to characterize the fetal heart rate patterns and to assess the effects of fetal movement on heart rate, rhythm, and conduction. Using autocorrelation to detect fetal QRS complexes, ventricular heart rate tracings were computed from the RR intervals, and actograms (tracings of fetal activity derived from movement-related changes in signal amplitude) were derived from the instantaneous QRS amplitudes.[7] Atrial heart rate tracings were also computed in subjects with large P-waves.

Results

Nineteen fMCGs were performed on 16 singleton fetuses at 20 to 38 (mean 28) weeks' gestation (Table). One fetus (#16) had Ebstein's anomaly; 1 had an HCN4 channelopathy (#12) with bradycardia; all others had structurally normal hearts. Nine fetuses were on medication at the time of fMCG (Table).

The observed rhythms and their prevalence are compiled in Table. The rhythms included sinus rhythm, AFI, AVRT, and complex atrial ectopy. AFI showed conduction ratios of 2:1, 3:1, and 4:1, and variable conduction in which the ratio cycled between 2:1 and 4:1 in a regular pattern. Complex atrial ectopy showed 2 forms. The most common was premature atrial contractions (PACs) with fixed coupling interval, presumed to be reentrant PACs, which resulted in atrial bigeminy/trigeminy or couplets. The other was conducted PACs with a longer, variable coupling interval, presumed to arise from an automatic focus, which resulted in atrial bigeminy.

Two fetuses (#15 and #16) referred with a diagnosis of AFI showed only sinus rhythm during the fMCG study and another (#14) showed frequent ectopy but no tachycardia. The remaining 13 showed AFI. Two fetuses (#2 and #13) were studied in multiple sessions. An interesting and notable finding is that 4 of 14 fetuses (29%) presented with AFI during the second trimester, including 2 that had brief periods of AFI prior to 22 weeks gestation (#13 and #11).

Nine fetuses showed periods of 4:1 conduction (Figure 1B) and/or variable conduction that oscillated between 2:1 and 4:1 (Figures 1C and 3B). In all 7 fetuses with sustained 2:1 and 4:1 AFI, the mean RR interval in 4:1 AFI was less than twice the RR interval in 2:1 AFI, implying that the AFI rate was faster during 4:1 than 2:1 conduction.

AVRT was seen in 5 fetuses, comprising 38% (5 of 13) of those that also showed AFI during fMCG and 27% (4 of 15) of those with a dominant presentation of AFI at the time of referral. In 4 fetuses the RR interval was substantially shorter in AVRT (217–238 ms; mean 224.3 ms) than in 2:1 AFI (255–282 ms; mean 272.5 ms). In 1 fetus (#13) the RR intervals were nearly the same (232 ms versus 230 ms). This fetus was the youngest in the cohort (20 weeks) and had the highest flutter rate and lowest percent time in AFI of all fetuses that showed AFI. The rhythm patterns of AVRT observed here were compatible with those reported in previous fMCG studies.[8]

The most common form of atrial ectopy was blocked atrial trigeminy due to reentrant PACs. This was present in 6 of 16 (38%) fetuses, including 4 of 5 with AFI and AVRT, 1 of 8 with AFI alone, and 1 of 3 that did not show AFI during fMCG. One fetus with blocked atrial trigeminy (#10) also had blocked atrial bigeminy, which resulted in bradycardia. Three fetuses with blocked atrial trigeminy (#9, 10, and 14) showed blocked atrial couplets, which are relatively rare but have been seen previously in fetuses with blocked atrial bi/trigeminy.[9] One subject (#14) with blocked atrial trigeminy also showed atrial bigeminy due to conducted PACs with a relatively long, variable coupling interval.

Variable ventricular preexcitation was seen in 4 fetuses (Figures 1B, 1C, 1D, and 2E): 2 with AFI and AVRT; 2 with AFI alone.

Initiation and Termination of AFI

In several fetuses with intermittent AFI it was possible to observe the mechanisms of initiation and termination. The great majority of the initiation patterns involved reentrant

Table. Summary of fMCG Results

Fetus #	Gestational Age (wks)	Medication	Rhythm	Percent Time	RR (ms)	PR (ms)	QRS (ms)	QTc (ms)	Duration (s)
1	24	Digoxin, amiodarone	AFI 2:1	100	296	108	40	287	1200
2a	28	—	AFI 2:1	94	269	98	56	301	2400
			AFI Var	6	280/472				
2b	29	Digoxin, metoprolol	AFI 2:1	38	257	111	63	276	3000
			AFI Var	2	279/480				
			SR	60	407	94	61	395	
2c	32	Digoxin, metoprolol	SR	100	457	94	52	441	2400
3	26-6/7	—	AFI 2:1	74	269	73	60	366	3000
			AFI 4:1	6	530				
			AFI Var	20	273/502				
4	30	Digoxin	AFI 2:1	96	308	79	50	377	3000
			AFI 3:1	<1	432				
			AFI Var	3	293/488				
5	35-5/7	—	AFI 2:1	48	261	94	54	417	3600
			AFI 4:1	428	504				
			AFI Var	48	274/480				
6	32-5/7	Digoxin	AFI 2:1	47	282	39	36	369	2400
			AFI 4:1	<1	452				
			AFI Var	18	283/469				
			SR	34	440	99	40	501	
			AVRT	<1	221	94	36		
7	30-2/7	—	AFI 2:1	<1	301	81	44	414	4800
			SR	99	430	96	42	442	
8	35-3/7	Digoxin, Synthroid	AFI 2:1	82	288	63	48	382	3100
		(levothyroxine sodium)	AFI 4:1	<1	531				
			AFI Var	8	291/550				
			BAT	5	494/781				
			SR	4	401	109	61	346	
9	36-5/7	—	AFI 2:1	55	255	98	38	305	6000
			AFI 3:1	<1					
			AFI 4:1	4	478				
			AFI Var	15	279/504				
			BAT	3	469/761				
			AVRT	25	221	127	44	436	
10	24-3/7	Digoxin, sotalol, amiodarone	AFI 2:1	7	273	50	48	392	2400
			AFI 4:1	11	488				
			BAB,BAT	70	741 500/800				
			AVRT	14	238	111	46	275	
11	21-5/7	Digoxin	AFI 2:1	6	280	111	83	486	4900
			AFI 4:1	<1	513				
			BAT	22	458/769				
			SR	70	424	98	56	419	
			AVRT	<1	284	159	54	342	

Continued

Table. Continued

Fetus #	Gestational Age (wks)	Medication	Rhythm	Percent Time	RR (ms)	PR (ms)	QRS (ms)	QTc (ms)	Duration (s)
12	36-2/7	—	AFI 2:1	2	296	78	38	349	3000
			SR	98	569	116	48	533	
13a	20	Digoxin	AFI 2:1	1	230	86	46	444	6000
			BAT	7	449/772				
			SR	74	520	106	61	416	
			AVRT	18	232	119	52	430	
13b	20-4/7	Digoxin	SR	29	440	108	65	425	6000
			AVRT	71	253	150	58	443	
14	31-4/7	—	BAT	2	453/786				2400
			CAB	11	269/448				
			SR	87	422	108	48	417	
15	29-1/7	Digoxin, magnesium	SR	100	444	100	54	473	4800
16			SR	100	505	182	94	449	5720

Fetal magnetocardiography (fMCG) results of 16 fetuses studied in 19 sessions, listing for each session the observed rhythms with the percent time present, cycle lengths (RR), and waveform interval measurements. The total duration of the fMCG recordings is shown in the last column. The fetuses are ordered by total percent time in AFI during the first session. Serial sessions for fetuses #2 and #13 are listed consecutively in chronological order with the different session indicated by a suffix (a, b, c). Fetus #16 had Ebstein's anomaly. AFI Var indicates atrial flutter with variable AV conduction with RR interval oscillating between the values shown in column 6; AVRT, atrioventricular reciprocating tachycardia; BAB, blocked atrial bigeminy due to reentrant premature atrial contractions (PACs); BAT, blocked atrial trigeminy due to reentrant PACs with oscillating RR interval (column 6); CAB, conducted atrial bigeminy due to conducted PACs from an automatic focus with oscillating RR interval (column 6); SR, sinus rhythm.

PACs, including the examples of transient AFI shown in Figure 1A and 1E. Sustained AFI was observed to initiate with reentrant PACs from sinus rhythm (Figure 2A), blocked atrial trigeminy, and immediately after a pause following termination of AVRT (Figure 2B). AFI was also seen to initiate with a rapid, irregular atrial rhythm, resembling fibrillation (Figure 2C). AFI was observed to terminate to AVRT and sinus rhythm. Unlike the transitions from AVRT to AFI, the transitions from AFI to AVRT typically showed no break in tachycardia (Figures 2D and 4). Spontaneous termination of AFI to sinus rhythm showed AFI cycle length oscillations (Figure 2E).

Cardiac Time Intervals and Waveform Morphology

The cardiac time intervals in sinus rhythm were normal, except for 1 fetus (#11) with shortened PR and prolonged QRS during intermittent ventricular preexcitation, 2 fetuses that showed modest QTc prolongation (#12 and #6), 1 fetus with Ebstein's anomaly (#16) that showed marked PR (180 ms) and QRS (85 ms) prolongation, and the HCN4 subject (#12) with sinus bradycardia. Three fetuses showed very large P-waves compatible with atrial hypertrophy. Two fetuses (#5 and #2) showed fractionated flutter waves (Figure 1C).

The 5 subjects with AVRT showed RP/RR ratios in the range 0.27 to 0.56 (mean 0.46). Two showed QRS prolongation with bundle branch block during AVRT. One showed ST depression with QRS/T discordance (Figure 1E).

Fetal Actocardiograms

Five fetuses had incessant AFI. Of these, 1 (#1) showed only 2:1 conduction with nearly constant heart rate (Figure 3A). This was perhaps the sickest patient, with moderate ventricular dysfunction, short inflow Doppler, and moderate to severe AV valve regurgitation. The others showed at least some degree of variable conduction (Figure 3B). Fetal movement had little effect on the AFI rate, but could enhance AV conduction.

The most complex actocardiograms were seen in fetuses with diverse intermittent rhythms (Figure 4). The data in Figure 4A encompasses a period when a number of rhythms were present intermittently: AVRT, AFI with 2:1, 4:1, and variable conduction, and a trigeminal rhythm due to blocked atrial couplets. The different rhythms usually had distinct heart rates and/or heart rate patterns that allowed them to be distinguished. Occasionally, however, the heart rate patterns showed deviations that caused them to resemble those of other rhythms (Figure 4). The data in Figure 4B are notable for the pronounced beat-to-beat fetal heart rate variability in AFI and AVRT. The atrial rate in AFI was relatively constant, implying that the heart rate variability in AFI was due to marked changes in AV conduction. Previously, we have attributed similar heart rate oscillations in fetal tachycardia to the existence of dual AV pathways.[8]

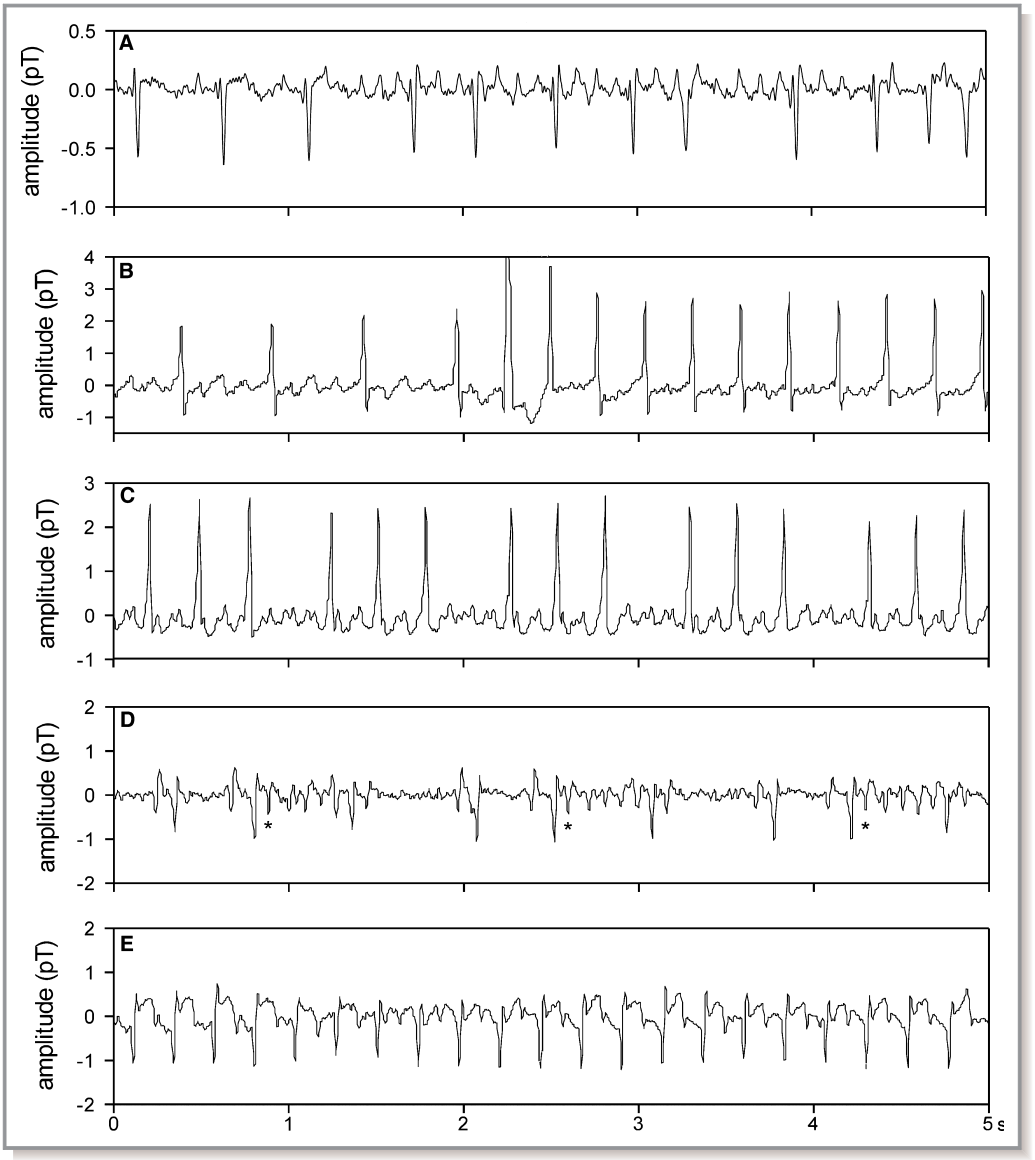

Figure 1. Notable rhythm patterns. A, Short burst of AFI with variable conduction in fetus #13, the youngest fetus in the cohort, studied at 20 weeks. The last several beats show reentrant PACs. B, Transition from 4:1 AFI to 2:1 AFI with variable preexcitation in fetus #11 at 21-5/7 weeks. The first beat of 2:1 AFI is aberrantly conducted. The flutter waves are obscure after the transition; however, they are visible at the termination of AFI, shown in Figure 2E, which occurs ≈60 seconds later. C, AFI with variable conduction ratio in fetus #5, showing Wenckebach-like phenomenon and fractionation of the flutter wave. The RR intervals are slightly longer than twice the PP intervals, and the PR intervals progressively increase prior to the nonconducted beat, which results in an effective conduction ratio of 8:3. Variable preexcitation is present. D, Trigeminal rhythm involving paroxysms of AFI-like rhythm initiated and terminated by nonconducted reentrant PACs in fetus #9. The coupling time from the initiating PAC (asterisks) to the first AFI wave is longer than the flutter cycle length. E, AVRT showing ST depression (inverted projection) and QRS/T discordance in fetus #10 at 24-3/7 weeks. The T-wave showed cyclical amplitude and morphology variations of uncertain origin with a period of ≈3 seconds. The termination of this episode of AVRT is shown in Figure 2B. AFI indicates atrial flutter; AVRT, atrioventricular reciprocating tachycardia; PACs, premature atrial contractions.

Discussion

Our study is the first to comprehensively characterize the associations between AFI and rhythms involving an accessory pathway prior to birth. Intermittent AVRT was seen in 5 of 13 (38%) fetuses that showed AFI during the fMCG session. In addition to AVRT, our fetuses showed ventricular preexcitation

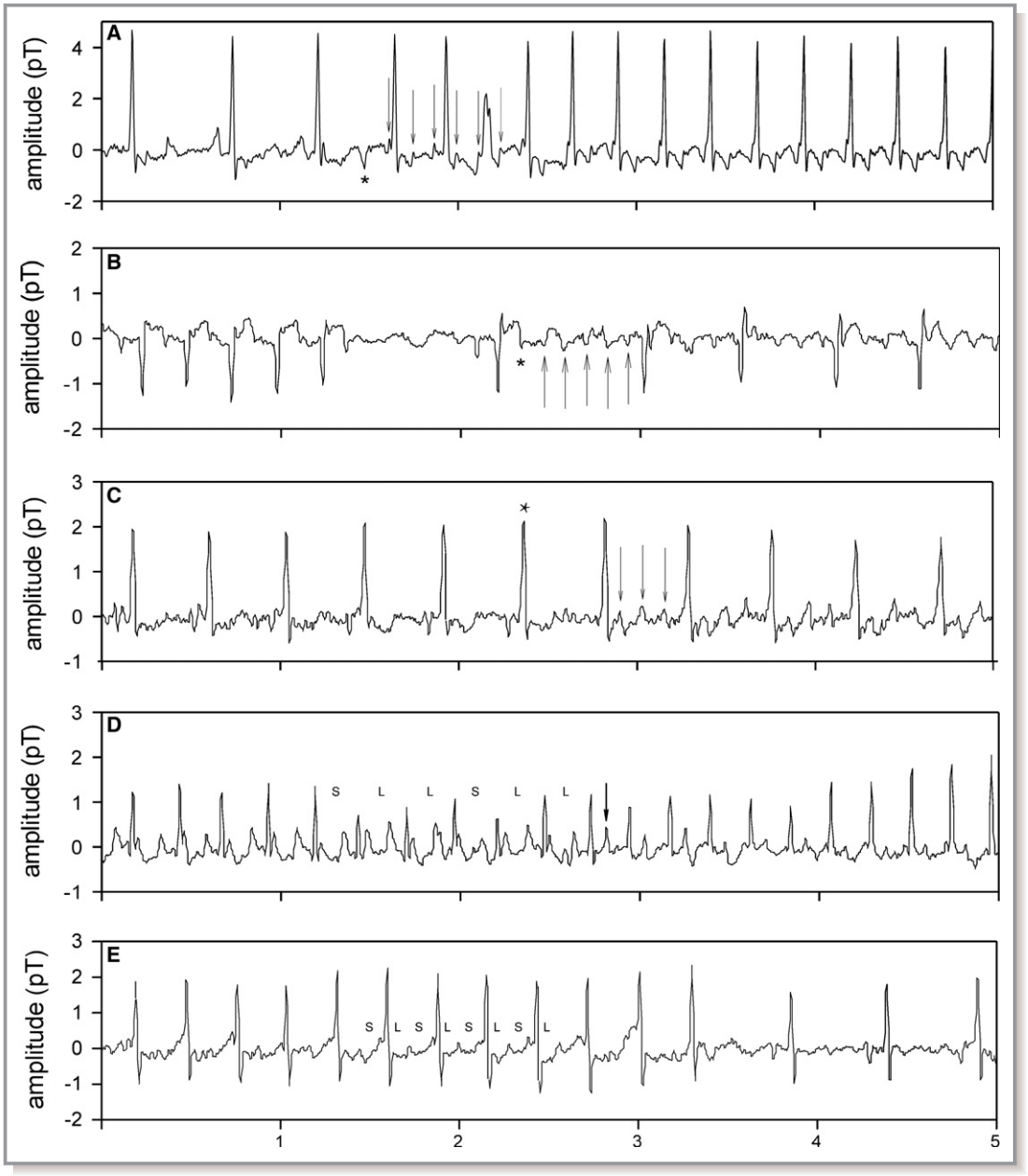

Figure 2. Initiation and termination of fetal AFI. A, Initiation of 2:1 atrial flutter by a conducted PAC (asterisk), probably reentrant due to negative polarity, with PR prolongation in fetus #11. The first few flutter waves (arrows) are visible due to the variable RR interval at onset, but thereafter the QRS complex substantially overlaps every other flutter wave. The sixth beat has the shortest RR and is aberrantly conducted; however, aberrancy was less common and less pronounced in AFI than in AVRT. B, Initiation of AFI with the beat immediately following AVRT in fetus #10. A reentrant PAC (asterisk) initiates AFI (arrows). Given the pause following the termination of AVRT, the slow AV conduction is somewhat surprising. The pause and slow AV conduction could be due to autonomic activity. C, Initiation of 4:1 atrial flutter during sinus rhythm in fetus #11. During the time between the last sinus P-wave (asterisk) and the first regular flutter waves (arrows), the atrial rhythm is rapid and irregular with no P-wave, suggesting that AFI is initiated by a fibrillation-like rhythm. Notice that the RR intervals are relatively uniform throughout the transition. D, Termination of atrial flutter by AVRT in fetus #9. A modest, but abrupt, cycle length shortening occurs at the onset of AVRT (arrow) with no break in tachycardia between the rhythms. Although the AFI rhythm is regular, the RR interval at termination shows a short-long-long (S-L-L) oscillation pattern, presumably due to changes in AV conduction. E, Termination of AFI with AFI short-long (S-L) cycle length oscillations in fetus #11. Variable degrees of preexcitation are seen during AFI. AFI indicates atrial flutter; AVRT, atrioventricular reciprocating tachycardia; PACs, premature atrial contractions.

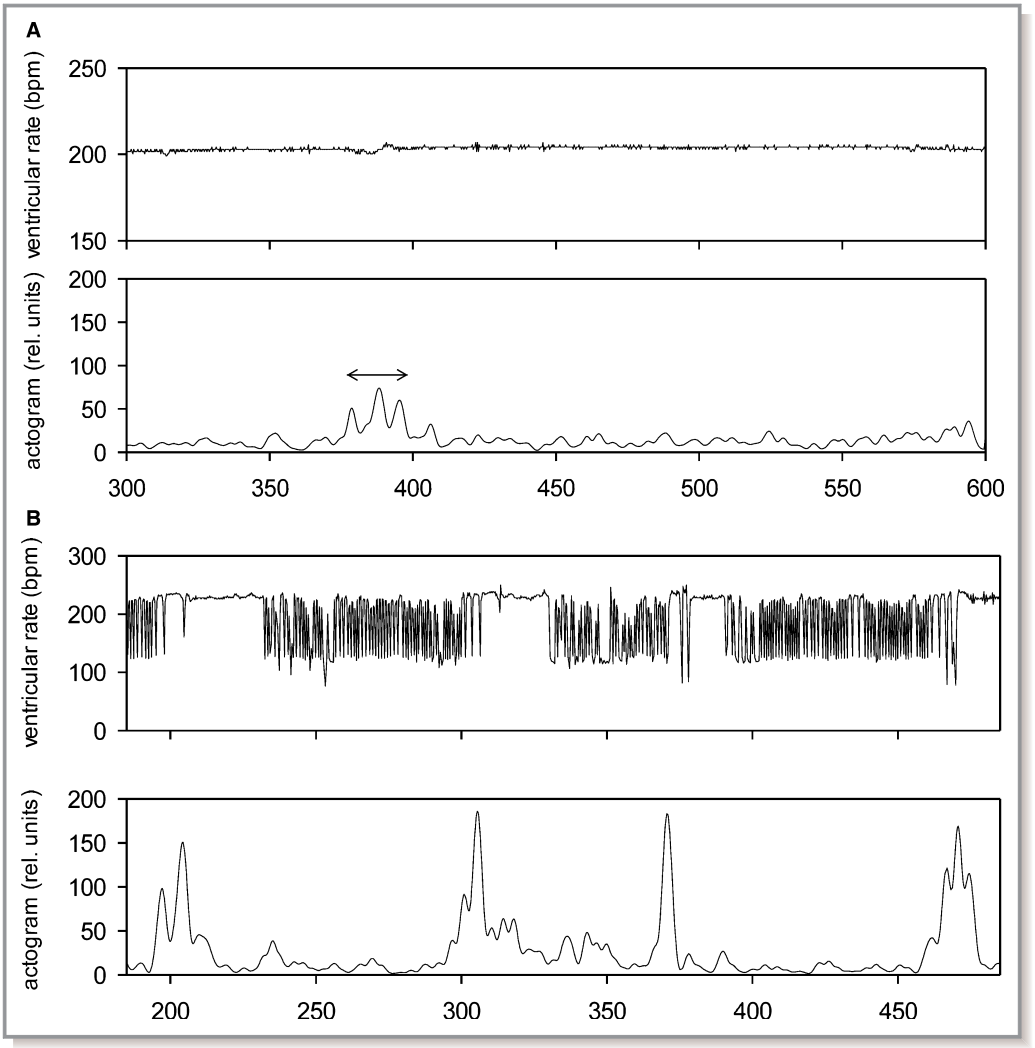

Figure 3. Actocardiograms in incessant fetal AFI. A, Fetus #1 had incessant 2:1 AFI. The heart rate, plotted below on an expanded scale, was nearly constant throughout, showing little variation with fetal movement (double-headed arrow). B, Fetus #5 showed highly variable atrioventricular conduction. The occasional periods of 2:1 AFI were strongly associated with fetal movement. AFI indicates atrial flutter.

and complex atrial ectopy due to reentrant PACs. Alternation of these rhythms with AFI resulted in complicated heart rate and rhythm patterns, underscoring the importance of the accessory pathway for providing a comprehensive explanation. Blocked atrial bi/trigeminy, including blocked atrial couplets, were seen in 6 of 16 (38%) fetuses, including 4 of 5 (75%) with AFI and AVRT. Thus, if AFI is noted to occur in conjunction with periods of complex atrial ectopy, the medical team should assess for the presence AVRT, given that its presence may influence therapy.

Most prior studies of fetal tachycardia have not reported on the co-occurrence of AFI and AVRT or imply that the rate is low. For example, the large fetal tachycardia studies of Krapp and coworkers[2] and Jaeggi and coworkers[3] made no mention of co-occurrence. van Engelen and coworkers[6] reported that only 1 of 30 fetuses with AFI also showed episodes of AVRT. An early study of fetal tachycardia by Maxwell and coworkers[10] involved 12 cases of AVRT, 8 of AFI, and 3 cases in which the rhythm varied between AVRT and AFI. The characteristics of the rhythms were not reported; however, the proportion of fetuses with AFI that showed AVRT alternating with AFI (27%) was similar to that in our study. Other reports of co-occurrence have been largely confined to case studies.[11]

The association between AFI and accessory pathways was first highlighted by Till and Wren.[12] In a cohort of 9 subjects with AFI in utero or at birth, 3 showed AVRT following dc cardioversion. In a postnatal transesophageal electrophysiologic study of 30 subjects with supraventricular tachycardia, Naheed and coworkers[13] found that 22 had AVRT and 8 had AFI. Of the 8 with AFI, 5 (62.5%) had inducible AVRT. None, however, were noted to have spontaneous AVRT, and postnatal AVRT is generally uncommon in patients with

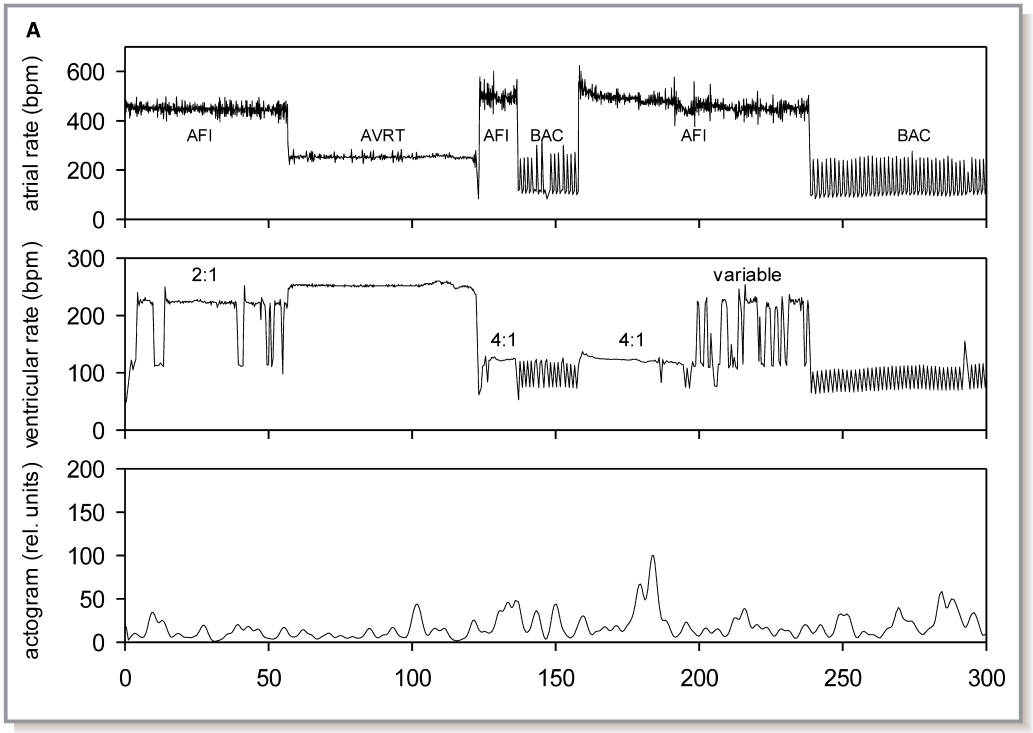

Figure 4. Diversity and intermittency of the fetal rhythms depicted by actocardiograms. In (A and B) the three panel shows the atrial heart rate (top), ventricular heart rate (middle), and actogram (bottom). A, Fetus #10 showed complex heart rate patterns due to alternation between intermittent AVRT, AFI with 2:1, 4:1, and variable conduction, and a trigeminal rhythm involving blocked atrial couplets (BAC). AFI was easily identified by the high atrial rate (>400/min). The conduction ratio varied between 2:1 and 4:1, as indicated in the ventricular heart rate tracing. AVRT showed the same tachycardic heart rate in both the atrial and ventricular tracings. BAT gave rise to prominent heart rate oscillations. Notice that during the last episode of AFI the flutter rate was not constant. It started out high and gradually declined, which is more typical of AVRT than AFI. The conduction ratio was initially 4:1 and improved with decreasing flutter rate. This fetus was relatively inactive, and the rhythm transitions were not strongly associated with fetal movement. B, Fetus #9 showed pronounced beat-to-beat heart rate variability during both AFI and AVRT. The first 40 seconds of the tracings showed predominantly 2:1 AFI with occasional isolated slow beats corresponding to 4:1 conduction. Notice that the slow beats were relatively uniform in cycle length, compared to the slow beats during AVRT in the second half of the tracing. The high heart rate variability in AFI was due to an irregular short-long-long oscillation pattern. The flutter rate was constant, implying that the variability was due to changes in AV conduction. The high heart rate variability was consistently attenuated by fetal movement (asterisks). The heart rate variability in AVRT is due to a regular short-long pattern in which the RP (VA) interval is constant but PR (AV) oscillates, again implying that the variability is due to changes in AV conduction. Usually, the periods of AVRT and 2:1 AFI could be discriminated based on the higher heart rate during AVRT; however, the episode of AFI preceding the transition from AFI to AVRT at 515 seconds (arrow) has relatively high heart rate and variability that makes it appear to be a resumption of the prior episode of AVRT. The onset of AVRT was associated with fetal movement, as has been described previously.[8] AFI indicates atrial flutter; AVRT, atrioventricular reciprocating tachycardia; BAT, blocked atrial trigeminy.

prenatal AFI. Our study not only corroborates an association between AFI and accessory pathways in the fetus, but also demonstrates that accessory pathways in the fetus exhibit a greater propensity for spontaneous, natural conduction, compared to the neonate. This finding suggests that accessory pathways often become nonfunctional at late stages of fetal development.

The reason for the association between AFI and AVRT is unknown. Till and Wren[12] noted that AVRT impairs cardiac function and may cause atrial dilatation, which may facilitate initiation and maintenance of AFI. Naheed and coworkers[13] similarly speculated that simultaneous ventriculoatrial contraction, atrial distension, and functional atrioventricular valve incompetence from annular enlargement occur during AVRT, and may predispose the fetal or neonatal atrium to the development of intraatrial reentrant tachycardia. The fetuses in our study showed atrial rhythms with large P-wave amplitude, fractionated flutter waves, and frequent atrial

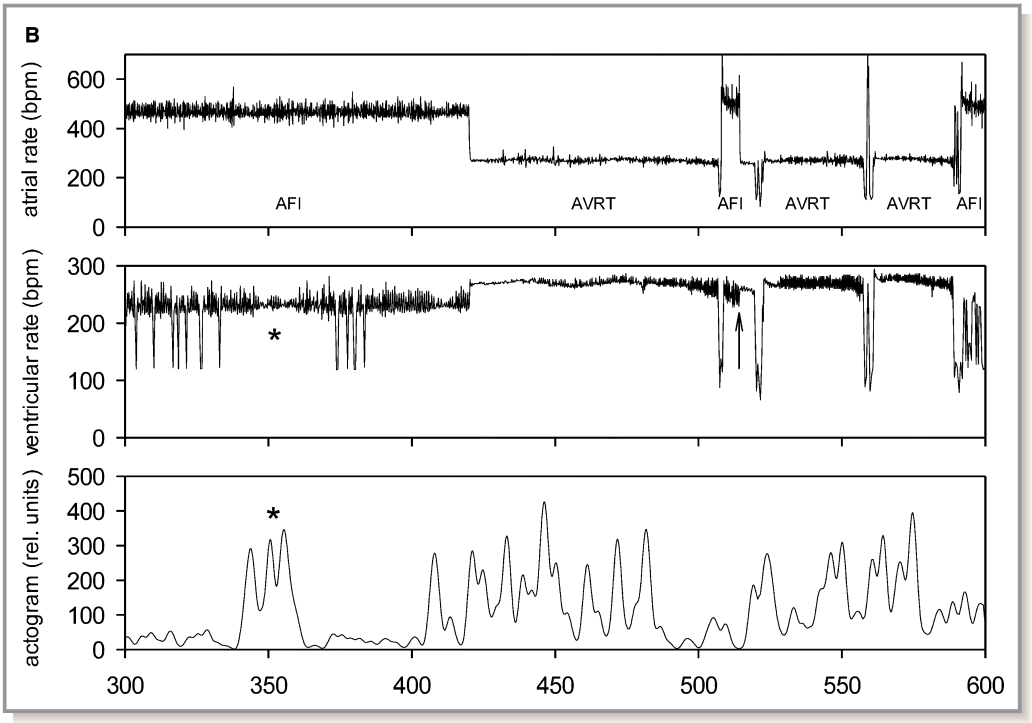

Figure 4. continued.

ectopy, which are suggestive of atrial dilatation and conduction impairment.

Nine fetuses with AFI (69%) showed periods of 4:1 AFI or AFI with variable conduction that oscillated between 2:1 and 4:1 AFI, whereas 3:1 AFI was relatively rare. A possible explanation for the rareness of 3:1 AFI is that the AV node may have 2 distinct levels of block, with the lower level having a lower conduction rate. In this circumstance, the overall conduction ratio will be a multiple of the conduction ratio of the upper level. If the conduction ratio of the upper level is 2:1, then the overall conduction ratio can be 2:1 or 4:1. A 3:1 conduction ratio is possible if the conduction ratio of the upper level is 1:1 or 3:2, but these are much less likely. This explanation is compatible with the observation that the heart rate in 4:1 AFI was slightly greater than half the rate in 2:1 AFI.

Little is known about the spontaneous initiation and termination patterns of AFI. Even postnatal data are scarce due to the rarity of AFI and its often incessant nature. In this study, AFI was observed to initiate with atrial ectopy, or due to AV reentry or a rapid, irregular rhythm, resembling fibrillation. The ability of reentrant PACs to initiate and terminate AFI was remarkable, and further supports the association between AFI and accessory pathways.[12] A termination pattern characterized by AFI cycle length oscillations was also seen. This pattern was observed by Ortiz and coworkers in a canine model and was attributed to changes in conduction in an area of slow conduction.[14] The intermittency of the rhythms and the abruptness of the transitions between them, often with little change in cycle length, undoubtedly contribute to the difficulty of detecting them using echocardiography.

Another notable observation was that 4 of 14 fetuses (29%) presented with AFI during the second trimester, including 2 that presented prior to 22 weeks. Others have reported that the initial presentation of AFI occurs mainly during the third trimester.[3,15] They speculated that the paucity of presentation at <30 weeks' gestation is due to the inability of the small, immature atrium to maintain a continuous atrial macroreentrant circuit. The relatively early detection of AFI among subjects in this study suggests that it is important for the medical team to consider AFI as a potential mechanism in the fetus that presents with tachycardia at any gestational age.

This finding, however, cannot be attributed to our use of fMCG. All of the subjects were referred with a diagnosis of AFI, except for 1 subject at 20 weeks that was referred with a diagnosis of fetal tachycardia and showed AVRT with only a few brief periods of AFI.

Prolonged, continuous monitoring by fMCG can provide a more accurate evaluation of complex, intermittent rhythms, including the percent time spent in each rhythm. Also, assessment of waveform morphology by fMCG can ascertain the degree to which conduction occurs through the accessory pathway versus the AV node. In this study, variable preexcitation during AFI was seen in 4 fetuses; however, none showed a sustained wide-QRS rhythm. Krapp and colleagues reported that digoxin was used as first-line therapy in 67.6% of cases. Conversion to sinus rhythm was achieved in 32 of

71 cases (45.1%) with digoxin treatment alone.[2,4,5,16] Recently, sotalol has been recommended as first-line therapy, as in several published series it has been most effective in restoring sinus rhythm, even in the hydropic fetus.[1,3,17,18] Our finding that an accessory pathway may be present in some fetuses with AFI suggests that if AFI occurs in conjunction with supraventricular tachycardia, implying the possibility of preexcitation, sotalol might be a better choice over digoxin for treatment. For more refractory AFI with hydrops, intramuscular digoxin and/or amiodarone can successfully restore sinus rhythm or slow the ventricular rate to improve hemodynamics.[19,20] Amiodarone has been shown to slow the fetal heart rate in AFI; however, the conversion rate is low. Treatment strategies for fetal arrhythmias are described in the American Heart Association's recent scientific statement on fetal cardiac disease.[21]

Study Limitations

The study was observational. Patients came from multiple centers across the United States, which made it difficult to obtain follow-up information. Therapy and the timing of the studies with respect to therapy were not controlled, which limited our ability to assess the effects of therapy on rhythm. The referral pattern was not preselected, and it is possible that cases referred represented more complex rhythm patterns, where fMCG could potentially be complementary to echo diagnosis. The referral of patients was limited to those who were stable and could travel to the Biomagnetism Laboratory. This likely reduced the number of subjects close to term, when atrial flutter is often noted, as well as the sickest patients with prolonged inpatient stays. The lower signal-to-noise ratio of fetal MCG, compared to that of postnatal ECG, limited the resolution of the P and T waves in the raw tracings, especially at early gestational ages.

Conclusions

Fetal AFI can occur as early as midgestation and is often accompanied by AVRT and other rhythms associated with an accessory pathway. The study validates the concept that the electrophysiology of the fetus and neonate show important differences, and further demonstrates the efficacy of fMCG for precise assessment of fetal rhythm.

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Disclosures

None.

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