Tachycardia Related Cardiomyopathy: Response to Control of the Arrhythmia

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To evaluate the clinical response of five children with automatic atrial tachycardia (AAT) and associated cardiomyopathy to arrhythmia control, we compared pretreatment and posttreatment 24-hour ECG heart rates, cardiothoracic ratio by chest radiograph, and echocardiographic measures of ventricular function. Two children were treated with amiodarone, two with surgical excision and cryoablation of the ectopic focus, and one with digoxin alone. Significantly slower mean heart rates were achieved, along with a dominant sinus rhythm and improvement in symptoms. Control of the AAT resulted in improved mean cardiothoracic ratio (0.53 pre vs 0.49 post; P = 0.02), as well as improvement in a number of echocardiographic measurements: mean shortening fraction (20% pre vs 34% post; P = 0.006), mean ejection fraction (36% pre vs 50% post; P < 0.01), mean velocity of circumferential fiber shortening (0.62 pre vs 1.20 post; P = 0.003). Mean E-point septal separation corrected for end-diastolic dimension also showed a trend toward improvement (0.25 pre vs 0.16 post; P = 0.11). Right ventricular endocardial biopsies in four were nonspecific; an atrial biopsy from surgery showed a Purkinje fiber-like tissue in one patient, but was nonspecific in another. We conclude that cardiomyopathy can be causally linked to automatic atrial tachycardia and that aggressive medical and/or surgical management is warranted in those patients with signs and symptoms of impaired ventricular function. (J Interven Cardiol 1989:2:4)

Introduction

Supraventricular tachycardia (SVT) from an ectopic automatic atrial focus, herein called automatic atrial tachycardia (AAT), accounts for <10% of SVT in children[1,2] is usually slower than the more common reentrant forms of SVT, and may be virtually incessant. At one time considered benign[3–5] AAT, in the absence of structural heart disease, has recently been associated with cardiomyopathy (CM). Although AAT is often refractory to conventional medical therapy, several reports suggest that control of the arrhythmia improves cardiac performance.[6,7] In recent years, new pharmacologic agents[8–11] as well as surgical excision[12–19] and catheter electrical ablation[20–22] have led to successful control of intractable AAT. To further examine the proposition that control of persistent AAT favorably alters cardiac function in some patients with cardiomyopathy, we compared the clinical course and noninvasive measures of

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ventricular function before and after therapy in five children with AAT. In addition, the findings of two right atrial and three right ventricular biopsies obtained from these patients are summarized. Recommendations for treatment based on this experience are outlined.

Methods

Five patients referred to the Pediatric Arrhythmia Clinic at C.S. Mott Children's Hospital, University of Michigan, exhibited poorly controlled, virtually incessant SVT (Fig. 1) and had developed fatigue, exercise intolerance, increased heart size on chest radiograph, and echocardiographic findings of decreased ventricular function, suggestive of cardiomyopathy. Four patients underwent electrophysiologic study (EPS) using programmed extrastimulation (PES), overdrive pacing, and mapping of atrial activation during the tachycardia. Four patients had hemodynamic study and two right ventricular endomyocardial biopsy; one had a right ventricular biopsy and two atrial biopsies at surgery. The diagnosis of automatic atrial tachycardia (AAT) was based upon the criteria of Goldreyer[23] et al. and others[24,25] [initiation of the tachycardia by spontaneous atrial depolarizations identical to successive atrial depolarizations during the tachycardia, independence of the tachycardia cycle length on AV node conduction, successive shortening of the tachycardia cycle length after the initial several beats ("warm up"), atrial depolarization during the tachycardia that reset the atrial cycle, and failure of a single or a train of atrial premature depolarizations to initiate or interrupt the tachycardia]. In one patient the diagnosis was made by the surface ECG and Holter tracings alone (initiating P wave of the tachycardia as the same morphology of the subsequent beats, "warm-up" period, and atrioventricular dissociation during SVT). Persistent junctional reciprocating tachycardia was excluded by either the absence of 1:1 atrioventricular conduction during the tachycardia or the absence of ventriculoatrial conduction during ventricular pacing as well. The selection of medical or surgical treatment was based upon the duration of the patient's symptoms, their anticipated compliance with a medical regimen, and, in two patients, their decision against chronic antiarrhythmic medication.

Response to therapy was evaluated by pre- and posttreatment 24-hour ambulatory electrocardiographic tracings (CardioData Corp., Northboro, MA, USA), chest radiographs, and two-dimensional and M-mode echocardiograms (Advanced Technology Laborotories, Seattle, WA, USA and/or Acuson Computer Sonography, Mountain View, CA, USA). All five patients were free of valvular, congenital, ischemic or other structural heart disease by two-dimensional echocardiogram, Doppler analysis, and cineangiography (four pa-

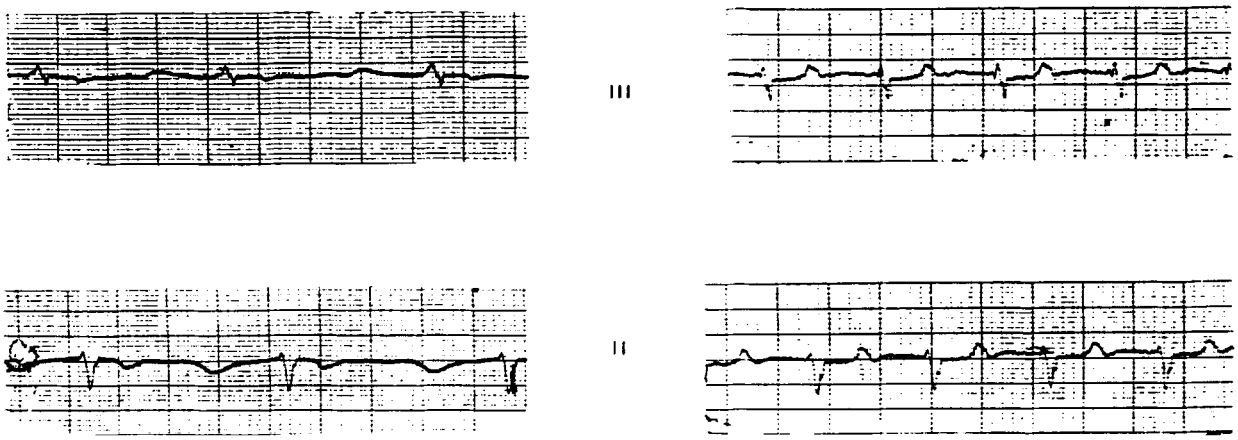

Figure 1. Representative ECG tracings from leads II and III from patient #4 before and after final treatment. Note the pre-treatment heart rate of 125 bpm and the inverted P waves in both leads (left hand tracings). Following treatment the rate is 75 bpm and the P waves are upright in both leads (right hand tracings).

tients). Cardiac rhythm and mean 24-hour heart rates were determined by computer generated analysis and confirmed by full disclosure tracings. The cardiothoracic ratio (CTR) was measured from the chest radiograph in the posterior-anterior projection during maximal inspiration. The left ventricular shortening fraction (SF), mean velocity of circumferential fiber shortening corrected for heart rate (VCF_c), E-point septal separation normalized for end-diastolic demension (EPSS/EDD) were measured from the M-mode echocardiogram; the left ventricular ejection fraction (EF) determined from the apical four-chamber view of the two-dimensional echocardiogram was calculated using the Simpson's rule algorithm. All pretreatment studies were obtained within 1 week prior to initiation of therapy. The mean interval between pre- and posttreatment examination was 1.5 years. Results are expressed as the mean ± one standard deviation and are compared using a paired *t*-test. Differences in the mean were considered significant when the P value was ≤ 0.05.

Results

Symptoms. The clinical data are summarized in Table I. All patients complained of easy fatigability, two noted dizziness, and one had exercise intolerance. Electrophysiological study in four patients localized the origin of the AAT at the coronary sinus os in two patients and the low septal right atrium in one. In the fourth patient, earliest atrial activation during SVT occurred both at the mouth of the coronary sinus and the atrioventricular node, suggesting that the abnormal impulse arose equidistant between these two points. Hemodynamic studies in the four patients undergoing electrophysiologic study demonstrated a mean left ventricular end-diastolic pressure (LVEDP) of 16 mmHg (range 10–26 mmHg), and a mean cardiac index of 2.8/min/m^2 (range 1.6–3.2 L/min/m^2).

Treatment. An average of 2.3 drug trials were used in three patients before satisfactory control of the AAT was achieved (Table I). Digoxin alone provided adequate control in only one patient. Beta blockade was ineffective in the two patients in whom it was tried. Two patients, ages 9 and 11 years, received amiodarone therapy for control of the SVT. After initial success with amiodarone, atrioventricular block occurred in one of these patients. Amiodarone was withdrawn and flecainide initiated with a return of control of the tachycardia. The remaining two patients, ages 15 and 20 years, who had received digoxin and propranolol

Table I. Clinical, Therapeutic, Biopsy, and Follow-up Data

Patient	Current Age	Duration of SVT	SVT Heart Rate (*bpm*)	Symptoms	Early Treatment	Duration of Conventional Therapy	Subsequent Treatment	Myocardial Biopsy	Outcome	Duration of Subsequent Treatment
1	9.3 years	3.5 years	140	fatigue, dizziness	digoxin verapamil flecainide	2 years	amiodarone	Not available	NSR	1.5 years
2	9.8 years	0.6 years	135	fatigue	digoxin flecainide	0.5 year	amiodarone flecainide	R Vent: Normal	90% NSR 10% SVT	1.0 year 0.5 year
3	11.3 years	0.1 year	175	fatigue, dyspnea	digoxin	—	digoxin	R Vent: Normal	NSR	1.0 year
4	14.1 years	13.8 years	130	fatigue, dizziness	digoxin	13 years	cryoablation/ digoxin	R Atrium: Normal	60% NSR 40% SVT	3 years
5	19.5 years	13.5 years	135	fatigue, exercise intolerance	digoxin nadolol quinidine propranolol	8 years	cryoablation/ excision	R Atrium: Purkinje-like Fibers RAA: Purkinje-like Fibers R Vent: Normal	NSR RARE APB	3 years

APB = atrial premature beat; bpm = beats per minute; NSR = normal sinus rhythm; R = right; RAA = right atrial appendage; SVT = supraventricular tachycardia; Vent = ventricle.

either alone or together for greater than 13 years, elected surgery. The five patients have been followed for an average of 1.5 years.

Heart Rate and Cardiothoracic Ratio. There was a significant ($P \leq 0.002$) reduction in the mean heart rate (128 ± 24 vs 91 ± 10 bpm) as determined by 24-hour ambulatory electrocardiograms. The dominant mechanism of the post-treatment cardiac rhythm was sinus (Fig. 1) in all five patients. Patients 1–3 were treated medically, and each required adjustments of the medication, including other antiarrhythmia trials, for satisfactory control (a few isolated atrial premature beats). Patient 4 had marked reduction in the incidence and persistence of SVT but still had runs of tachycardia. Patient 5 is virtually free of arrhythmia with only a few isolated atrial premature beats and a normal heart rate response to treadmill exercise (i.e., no ectopic tachycardia during exercise). Along with the above noted return to a slower sinus rhythm, there was a significant reduction in the CTR by chest x-ray (53% precontrol vs 49% postcontrol, $P = 0.02$).

Echocardiographic Measures of Ventricular Function. Figure 2 summarizes the improvement in cardiac function. Both the systolic and diastolic dimensions significantly decreased yielding an improved shortening fraction (mean 21% to mean 34%, $P \leq 0.05$). The two-dimensional echocardiographic ejection fraction, reflecting a more global measurement, also increased from a mean 36% to mean 50% following control of the tachycardia ($P \leq 0.01$). The mean heart rate corrected VCF increased from a mean of 0.62 to a mean of 1.20 circs/sec ($P = 0.003$). The EPSS/EDD, a measure independent of preload, was abnormal (i.e., greater than 0.2—the 95th percentile) in three of the five patients prior to treatment. Although one of these three remained >95th percentile following arrhythmia control, all three were improved.

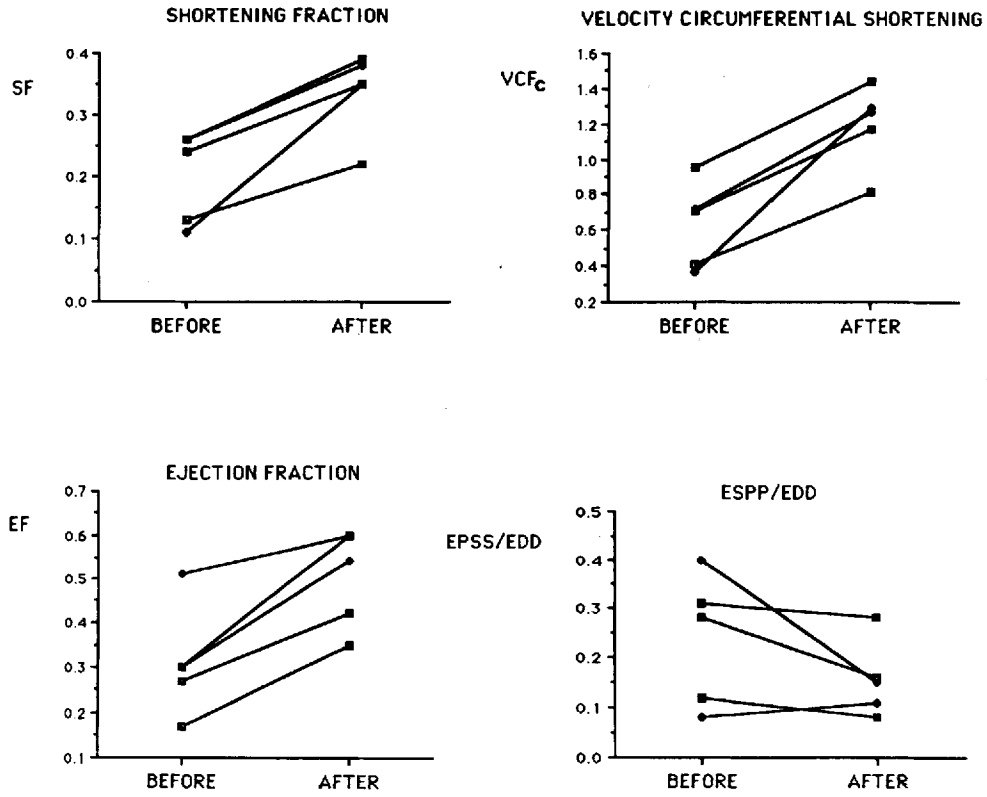

Figure 2. Echocardiographic measures of left ventricular function before and after final treatment in the five patients. SF = shortening fraction; VCF_c = velocity of circumferential fiber shortening corrected for heart rate; EF = ejection fraction; EPSS/EDD = E-point septal separation/end-diastolic dimension.

Patient 2 is of particular interest (Fig. 3). Amiodarone successfully restored sinus rhythm but was discontinued because of hyperactivity possibly related to hyperthyroxinemia. Although flecainide replaced the amiodarone, the AAT resumed. After thyroid function was determined to be normal, amiodarone was restarted with return to sinus rhythm. Thus, during two separate treatment periods over a 6-month period, a direct relationship between the control of the tachycardia and normal echocardiographic measured cardiac function was observed.

Myocardial Biopsies. Light microscopic examination of the biopsies from the right ventricle showed no evidence for myocarditis or storage disease in any patient. Nonspecific myofibril hypertrophy and focal fibrosis that were within the range of normal were present in two patients (Table I). The atrial biopsy from patient 4 disclosed normal atrial tissue. In contrast, the atrial

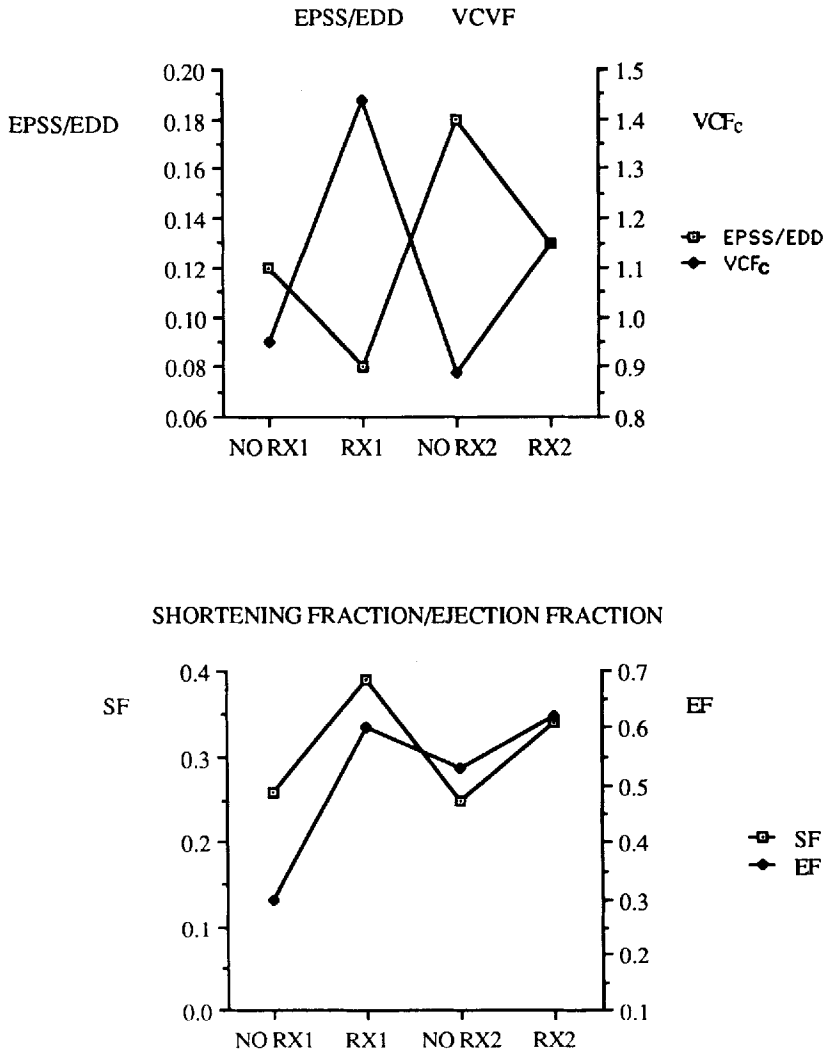

Figure 3. Echocardiographic measures of left ventricular function in patient #1 during two trials of amiodarone. The interval between NORX1 and RX1 is 7 months; between RX1 and NORX2, 14 months; and between NORX2 and RX2, 4 months. EPSS/EDD = E-point septal separation/end-diastolic dimension; VCF_c = velocity of circumferencial fiber shortening corrected for heart rate; SF = shortening fraction; EF = ejection fraction.

tissue excised from patient 5 during surgery demonstrated Purkinje fiber-like tissue in specimens from the coronary sinus, the mapped origin of his tachycardia, as well as from the right atrial appendage (Table I).

Complications. No significant complications were encountered. Patient 2 required evaluation of his thyroid function because of the suspicion that he might be thyrotoxic. However, further thyroid studies excluded this possibility and amiodarone was resumed. Patient 4 experienced 2:1 heart block postoperatively, but permanent normal 1:1 conduction resumed within 5 days.

Follow-up. All patients except patient 4 are asymptomatic and virtually free of their tachyarrhythmia at mean 1.5 years following treatment. Following control of the tachycardia, three patients resumed full activity, and the other two have had a marked but not complete return to previous activity level. Patient 4 was recently hospitalized following a suicide attempt. Non-invasive evaluation at that time disclosed normal left ventricular function by echocardiogram, normal cardiac size on chest radiograph, normal exercise treadmill test, normal sinus rhythm during 12 of the 24 hours on Holter electrocardiography, and much less tachycardia that during the pretreatment period. Because of a complex social situation, further cardiac and arrhythmia evaluation was deferred.

Discussion

Our data are in accord with the observations of others that indicate that sustained automatic atrial tachycardia at only moderately elevated rates above normal (120–170 bpm) may produce significant impairment of cardiac function. Furthermore, our experience demonstrates that this impairment is associated with the appearance of symptoms. Finally, our experience confirms not only improved control of the tachycardia following pharmacological and/or surgical intervention, but also, as a result, significant recovery of cardiac function.[6,7,13,14,26]

The exact causal relationship between chronic atrial tachycardia and the development of a cardiomyopathic state has not been fully established. Recent studies[27–29] have demonstrated that ventricular pacing of the canine heart at accelerated rates produces congestive heart failure in 2–3 weeks. Although no direct evidence for a similar effect of chronic atrial pacing has been reported, the association of sustained supraventricular tachycardia and congestive heart failure in infants[30,31] as well as in older individuals[4] has been recognized for several decades. The progression to a myopathy is less clear. Nonetheless, a number of reports[6,7,13,16–18,26] that indicate resolution of a dilated heart after control of supraventricular tachycardia, along with our experience, support these experimental data. Patient 3 represents a fortuitous clinical experiment supporting those observations. This patient demonstrated over a 6-month period a direct relationship between control of the tachycardia and improvement in ventricular function. Further, the observation from our two operated patients that the return of cardiac function was not instantaneous suggests that the observed change in the echocardiographic measures of ventricular function are not simply a function of heart rate but reflect genuine improvement in ventricular performance.

Previous reports[14,32,33] have suggested Purkinje-like or mesenchymal type tumors causing automatic tachycardia as well as other complex arrhythmias; on the other hand atrial biopsies in 10 other patients with sustained AAT[6,12,15,17,19] were nonspecific. Patient 5 had Purkinje-like fibers excised from the area of tachycardia focus. Interestingly, similar cells were found in his incidentally discarded right atrial appendage taken for cannulation. These abnormal mesenchymal cells/Purkinje fibers argue against a cardiac muscle abnormality as the cause of the AAT and lead to the possibility of multiple subclinical abnormal cells in patients with automatic atrial tachycardia, giving rise to the possibility of late recurrence. In contrast, the atrial tissue excised from Patient 4 failed to disclose unusual cells, perhaps suggesting an incomplete ablation of her ectopic focus and, thus, explaining, in part, her less successful result. The nonspecific right ventricular biopsy material from our three patients, along with the five reported by others,[6] underscores the absence of a primary ventricular abnormality as the proximate cause of the observed impairment in cardiac function.

Conventional therapy is rarely effective. Digoxin alone failed to control the SVT in four of our

five patients; the addition of beta blockade in two patients was also unsuccessful. Both patients who received amiodarone converted to sinus rhythm. Thus, similar to other reports,[34,35] our experience suggests that no single therapeutic regimen emerges as the clear treatment of choice. Because of the infrequency of this disorder, its variable natural history, including documented spontaneous remission of the tachycardia[34,35] and the nonrandom use of the different forms of therapy, a single optimal treatment for all patients will probably not be forthcoming. Thus, a step-wise approach may be prudent. In the absence of symptoms and with no evidence of impaired ventricular function, therapy may not be necessary. Because control of the tachycardia will restore ventricular function, with increasing improvement over time, noninvasive evidence for decreased ventricular function warrants treatment. New antiarrhythmic medications, including flecainide, encainide, ethmozine, and amiodarone,[8-11] along with the development of electrophysiological-cryosurgical techniques[12-18] offer several avenues for management. However the recent experience with flecainide and encainide[36] underscores the need for a careful weighing of the risks of treatment (as well as no treatment) along with the benefits expected before initiating unexplored pharmacological therapy.

Conclusions

We conclude that AAT may be causally linked to the development of cardiomyopathy. Poorly controlled AAT may present clinically as congestive heart failure, or more subtly, with impairment of ventricular function prior to the onset of overt failure. In the experience reported herein, as well as those of others, aggressive management results in resolution of the SVT, symptomatic improvement, and normalization of ventricular function. Because AAT is a treatable arrhythmia, any child presenting with symptoms, signs, and echocardiographic evidence of cardiomyopathy should be carefully evaluated by ECG, 24-hour ambulatory ECG, and, if necessary, electrophysiologic studies. Treatment should be instituted if either symptoms or the noninvasive findings of decreased ventricular function are present.

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