Successful Surgical Excision of Focal Paroxysmal Atrial Tachycardia

Observations In Vivo and In Vitro

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SUMMARY A 41-year-old man had chronic, recurrent, drug-resistant paroxysmal right atrial tachycardia. Electrophysiologic studies revealed features suggesting atrial reentrance, including induction and termination of tachycardia with rapid atrial pacing and atrial extrastimuli. Endocardial catheter mapping localized the origin of tachycardia to the right atrial appendage. Intraoperative epicardial mapping refined the localization to the posterolateral rim of the appendage. The appendage was excised and the tachycardia was permanently cured. Microelectrode studies on the excised tissue revealed an inducible rhythm localized to a small area of the atrial endocardium, characterized by rapid pacing induction, rhythmicity generated from a suprathreshold afterdepolarization, low maximum diastolic potential, low overshoot potential and a smooth transition from phase 4 to phase 0, suggesting triggered automaticity. This is the first observation in man of probable triggerable atrial automaticity, which may be a direct counterpart of the clinical arrhythmia. The successful surgical outcome indicates that a focal atrial tachycardia can be excised in selected patients.

MOST PAROXYSMAL supraventricular tachycardias (PSVT) appear to reflect reentrance within the atrioventricular (AV) node, reentrance via an anomalous AV pathway, or reentrance within the atria. In patients with intractable PSVT, drug therapy, based upon chronic electrophysiologic study, is usually successful in predicting effective antiarrhythmic therapy. In patients totally resistant to drugs, palliation is possible with the use of a radiofrequency or other pacing device for self-initiated termination of PSVT. A surgical cure may also be attempted by transection of one of the limbs of a reentrant circuit or by production of AV block distal to an ectopic focus or site of reentrance.

Surgical cure of focal paroxysmal atrial tachycardia has been reported only once. In the present study, we report in vivo and in vitro electrophysiologic observations in a patient with recurrent drug-resistant PSVT due to a right atrial “focus,” in whom surgical excision was curative and in whom the in vitro studies suggested the presence of “triggerable automaticity” as the mechanism of PSVT.

Case Report

A 41-year-old male was referred to the University of Illinois Hospital in July 1978 for management of chronic recurrent PSVT. Myxedema had been diagnosed in 1972 and had been controlled with thyroxine, 100 μg/day.

Attacks of PSVT began in 1975, lasting from 1 hour to 2 weeks, occurring at least once per month, requiring monthly visits to emergency rooms, and five hospitalizations for cardioversion in 4 years. During PSVT, he experienced dizziness, dyspnea and sweating. He had been previously treated unsuccessfully with digoxin, propranolol and quinidine, alone and in combination. In the 6 months before this admission, arrhythrias had been totally incapacitating. At admission, he was clinically and chemically euthyroid. Cardiovascular examination was within normal limits. Chest x-ray revealed slight cardiomegaly. Complete diagnostic cardiac catheterization revealed a mild restrictive cardiomyopathy.

Electrocardiograms

ECGs in sinus rhythm revealed a P-wave axis of 15° and an S1Q3 pattern but no other abnormality. ECGs during PSVT (fig. 1) showed a P-wave axis of 60°, with morphology slightly different from sinus P waves (fig. 2A), an atrial rate of approximately 140 beats/min, periods of 1:1 AV conduction (fig. 1, top) and also periods of variable AV block (fig. 1, bottom) with resultant ventricular rates of 70–145 beats/min, and normal QRS complexes.
Initial Electrophysiologic Study

Electrophysiologic study was performed in July 1978 after discontinuation of chronic antiarrhythmic agents for 48 hours. Standard multipolar electrode catheter techniques were used to record from multiple right atrial sites, left atrial sites via the coronary sinus, main pulmonary artery, and the His bundle. After initial study, "chronic" electrophysiologic study was performed with an indwelling quadripolar right atrial catheter, as recently described.

Paroxysmal high right atrial tachycardia could be reliably induced by atrial pacing or with single atrial stimuli (fig. 2). Induction of PSVT was independent of the presence or absence of AV nodal conduction. The atrial tachycardia cycle length was 460–520 msec, with variable AV nodal block. Tachycardia was reset by single stimuli applied to the high right atrium at coupling intervals of 350–280 msec, and could be reproducibly terminated by short bursts of atrial pacing at cycle lengths of 320–250 msec or by double extrastimuli. P-wave morphology during tachycardia resembled that of the spontaneous arrhythmia. The tachycardia could be initiated and sustained despite administration of propranolol, ouabain, procainamide and quinidine. A subsequent outpatient trial of procainamide and propranolol also failed to prevent PSVT.

Endocardial Mapping

Endocardial mapping was performed in October 1978 with a #7F, 100-cm Zucker catheter advanced from a femoral vein and directionally oriented with the aid of biplane fluoroscopy and a Cook directional guide system. Bipolar electrograms, filtered at 120–2000 Hz were recorded from 25 right atrial sites during induced PSVT (fig. 3). The cycle length of PSVT was 400–540 msec. The earliest recorded atrial endocardial site was in the posterolateral region of the right atrial appendage synchronous with the onset of the P wave on surface ECG leads. The remaining atrial sites were activated in a more-or-less centrifugal fashion from this site. Activity was recorded as late as 240 msec after the onset of the P wave in the region of the high anterior tricuspid valve. All left atrial sites (data retrieved from previous study and not shown in figure 3) were recorded 75–100 msec after the onset of the P wave of the tachycardia.

Epicardial Mapping and Surgery

Median sternotomy was performed on October 19, 1978. The right atrium was dilated and showed patchy fibrosis. Rather dense fibrosis involved the anterior rim adjacent to the right AV groove.

Epicardial mapping was performed during sinus rhythm (fig. 4) and during pacing-induced PSVT (fig. 5) using techniques similar to those described previously. Recordings were made on an oscilloscopic recorder (Electronics for Medicine, Model VR-12) using multiple surface ECG leads, isolated and filtered at 0.1–50 Hz, a bipolar right atrial reference electrode and bipolar electrograms from an exploring hand-held probe, isolated and filtered at 100–2500 Hz. The onset of the P wave in multiple leads was used as the reference point for measurement of local activation times in milliseconds. The atrial epicardial sequence during sinus rhythm is shown in figure 4. The sinus cycle length was 710 msec. Activation began 20 msec before the onset of the P wave just
below and lateral to the junction of the superior vena cava and the right atrium and rapidly spread inferiorly and leftward to activate the left margin of the left atrium by 95 msec after the onset of P. No activity could be recorded from the band of fibrotic right atrial wall abutting the AV groove.

The atrial activation sequence during pacing-induced PSVT is shown in figure 5. The cycle length of PSVT was 450 msec. Activation began 13 msec before the onset of the P wave at a site approximately 6 cm from the site of initial activation in sinus rhythm. This site was in the posterolateral rim of the right atrial appendage. Activation was again more rapid in an inferior and leftward direction than it was anteriorly. The latest identified activity was adjacent to the right AV groove, 377 msec after the onset of the P wave, during apparent electrical diastole on the surface ECG. Despite this marked delay, the sequence of atrial activation appeared to be a more or less centrifugal process originating from the site of earliest ac-

**FIGURE 2.** Induction of paroxysmal right atrial tachycardia by programmed stimulation. (A) Sinus rhythm. (B) Induction of tachycardia by rapid atrial pacing. Note slight change in P-wave morphology and presence of variable atrioventricular block. (C) Induction of tachycardia by a single atrial extrastimulus (S₂) delivered at a coupling interval of 270 msec during regular atrial pacing (S₁) at a cycle length (CL) of 750 msec. HRA = high right atrial electrogram; HBE = His bundle electrogram; S = pacing stimulus; P = P waves; A = atrial electrogram; H = His deflection.
atrial paroxysmal tachycardia, showing the right atrium with the anterolateral wall disconnected through the tricuspid valve and laid open posteriorly. Local bipolar activation times are shown in milliseconds after the onset of the P wave. Isochrones are drawn in 5-msec intervals from 10–40 msec, and thereafter at 10-msec intervals. The earliest onset of endocardial activity was in the posterosuperior region of the right atrial appendage (0 msec). SVC = superior vena cava; RAA = right atrial appendage; SEP RV = septal right ventricle; ANT RV = anterior right ventricle; TV = tricuspid valve; IVC = inferior vena cava; F = fossa ovalis; C = coronary sinus os; N = AV node.

Electrophysiologic Studies In Vitro

The surgically removed specimen of atrial tissue was immersed immediately in cooled, oxygenated Tyrode's solution and transported to the University of Chicago. The composition of the Tyrode's solution in mM concentrations was NaCl, 137; NaHCO₃, 22; NaH₂PO₄, 2.7; MgCl₂, 2.2; CaCl₂, 1.8; KCl, 4.0; and dextrose 11.0. The Tyrode's solution was equilibrated with 95% O₂ and 5% CO₂ and the pH was 7.3. The temperature of the Tyrode's solution in the tissue bath was maintained at 36 ± 0.5°C. The preparation was stimulated extracellularly with a pair of silver wire electrodes, insulated to the tip, placed on the surface of the preparation (fig. 6, site S). Transmembrane voltages were detected using glass microelectrodes filled with 3 M KCl that had a DC resistance of 10–20 MΩ and tip potentials of less than 5 mV. The tissue bath was kept at virtual ground using a Tektronix Type 0 operational amplifier. The transmembrane voltage was amplified by a high-impedance, variable-capacity neutralization amplifier, displayed on a dual-beam oscilloscope and photographed.

The tissue was allowed to equilibrate for 45 minutes. Observation through a Zeiss dissecting microscope showed the preparation to be quiescent. One or more extracellular stimuli, however, could initiate sustained contractions in an area of atrial endocardium near the cut edge that measured approximately 0.5 × 0.5 mm (fig. 6, site R). This area was 10 mm from the stimulating electrodes and will be referred to as the "focus." The application of one or more stimuli repeatedly terminated the induced contraction of the focus.

The focus and surrounding endocardium were probed with microelectrodes. The initiation and termination of rhythmic activity by extracellulary delivered stimuli applied at a site remote from the focus during the recording of the transmembrane
depolarization (phase 0) of the first action potential was followed by an early afterdepolarization, which appears as a shoulder on the plateau. After completion of the repolarization phase (phase 3) of the first action potential, \( V_m \) became more negative than it had been before phase 0 at \( V_r \). This deflection is termed a delayed afterhyperpolarization. The delayed afterhyperpolarization was followed by a delayed afterdepolarization of sufficient amplitude to attain threshold and produce an action potential. Each subsequent action potential was followed by a delayed afterhyperpolarization and suprathreshold afterdepolarization, resulting in sustained tachycardia. These action potentials showed a smooth transition of slow diastolic depolarization (phase 4) into the upstroke (phase 0), highly suggestive of a cell within or very near an automatic center. The rhythm accelerated to a cycle length of 750 msec (80 beats/min). Once membrane activity stabilized, the maximum diastolic transmembrane voltage \( (V_{md}) \) was \(-57\) mV and the peak overshoot was \(15\) mV. The cycle length increased to 800 msec (75 beats/min) before the termination of the rhythm by the first of three extracellularly applied stimuli (fig. 7C). After termination, some subthreshold oscillatory membrane activity was noted. Shortly thereafter, the oscillatory activity subsided, and \( V_r \) returned to \(-52\) mV (fig. 7D). Five minutes later, extracellular stimuli again were applied to the quiescent preparation (fig. 7E). The second stimulus triggered a sequence of events essentially identical to those previously observed (fig. 7B). These events meet the criteria for triggered sustained rhythmic activity, and the morphology of the action potential suggests triggered automaticity. \(^8-10\)

Mapping of many sites on the endocardial surface of the free atrial wall and of the trabeculae near the focus failed to locate a spontaneous or inducible pacemaker in the surrounding tissue. Similarly, no evidence was found for slow conduction encompassing the cycle time of the induced tachycardia to suggest reentrance outside the \(0.5 \times 0.5\) mm focus. Activation proceeded centrifugally from the focus in all directions.

After an hour, the preparation became difficult to capture with the extracellular stimuli, and \( V_r \) in the focus had become lower \((-28\) mV\). For this reason, epinephrine \((2 \times 10^{-8}\text{M})\) was added to the perfusate. Epinephrine not only facilitated extracellular stimulation, but induced a spontaneous pacemaker at a site remote from the focus. Action potentials from the focus driven by this pacemaker had a cycle length of 1870 msec (32 beats/min), a \( V_{md} \) of \(-32\) mV, and overshoot of \(6\) mV, and showed a more abrupt transition between phase 4 and phase 0 (fig. 8A). This configuration, as well as endocardial mapping, demonstrated that the spontaneous pacemaker was remote from the focus of interest, but the pacemaker region itself was not identified.

The triggering of sustained rhythmic activity within the focus was again possible. The induced rhythmic activity had a cycle length of 980 msec (61 beats/min), and both the \( V_{md} \) and the overshoot were slightly more

**Figure 5.** Epicardial map during atrial tachycardia. Conventions as in figure 4. The cycle length of tachycardia is 450 msec. The onset of epicardial activity is 13 msec before onset of the tachycardia P wave at a site superior and anterior to that initiating activity in figure 4, in the posterolateral lip of the right atrial appendage. Again, marked delay was encountered in the anterior portion of the appendage and along the right atrioventricular groove.

**Figure 6.** Excised specimen showing the endocardial aspect of the right atrial appendage. \( S \) = site of extracellular stimulation; \( R \) = "focus" of interest, site of intracellular recordings shown in figures 7 and 8.
negative and positive, respectively, than before triggering (−34 mV and 8 mV, respectively). Morphologically, the induced action potentials were characterized by delayed afterhyperpolarizations leading into suprathreshold afterdepolarizations and by a smooth transition from phase 4 into phase 0 (fig. 8B). This sustained activity was terminated by a single extrastimulus, and the slower, more distant pacemaker activity resumed. After termination, a subthreshold delayed afterdepolarization occurred at a cycle length of 980 msec, suggesting that after the last action potential produced by the rapid, triggered site within the focus, the cells within the focus continued to have oscillatory activity sufficient only to generate a subthreshold response (fig. 8C). The pacemaker induced by epinephrine had been somewhat suppressed by the more rapid triggered rhythm, but soon accelerated and returned to a cycle length of 1520 msec.

Thereafter, the preparation gradually lost the ability to generate activity in response to chemical or electrical stimuli. The response to such agents as verapamil or manganese, therefore, could not be tested.

Histologic Examination

A separate small portion of the excised atrium was completely serially sectioned. The myocardium was markedly infiltrated with mononuclear cells and showed considerable increase in connective tissue. The epicardium was also infiltrated with mononuclear cells. There was no evidence of amyloid deposition.

Follow-up After Surgery

Postoperative recovery was uneventful. Repeat electrophysiologic study using the radiofrequency atrial pacemaker (paced cycle length of as short as 200 msec) revealed inability to induce PSVT. Subsequent close follow-up for 18 months, including outpatient follow-up, telephonic ECG monitoring and ambulatory ECG monitoring, demonstrated total cure of PSVT.

Discussion

Most examples of PSVT appear to reflect reentrant mechanisms. The ability to initiate and terminate tachycardia by appropriately timed single stimuli or rapid pacing is a generally accepted criterion for electrophysiologic diagnosis of reentrance. At the moment of initiation of tachycardia it is usually possible, in AV reentrant tachycardia and in some forms of ventricular tachycardia, to show that initiation is dependent upon achieving a critical amount of delay in conduction through some portion of the reentrant circuit. Similarly, at the moment of termination of tachycardia, block of an impulse is usually demonstrable in some portion of the reentrant loop. In the present patient, rapid pacing and single stimulus...
induction and termination were possible during electrophysiologic study. Marked intraatrial delay was also observed, but this did not appear to be critical to initiation of tachycardia.

On the other hand, recent studies in vitro on canine coronary sinus and atrial muscle,\textsuperscript{a} sheep Purkinje fibers,\textsuperscript{b} rabbit right atrial muscle\textsuperscript{c} and in primate\textsuperscript{a} and human\textsuperscript{d} mitral valve preparations have shown that sustained rhythmic activity of a single cell or small group of cells can be triggered by rapid pacing or a single stimulus in the presence or absence of epinephrine. These observations of triggered automaticity question the reliability of clinical pacing criteria for the diagnosis of reentrance.

Our electrophysiologic studies in vivo and in vitro strongly suggest the presence of triggerable automaticity in a cell or small group of cells within the excised fragment of right atrium. First, while mapping in vivo probably cannot exclude microscopic reentrance, it failed to show a large reentrant circuit. Second, the electrophysiologic studies in vitro found that extracellular stimulation distant from the focus could induce sustained rhythmic activity within the focus. The recordings of the transmembrane voltage within the focus showed triggered afterpotentials, including both early afterdepolarizations and delayed afterhyperpolarizations leading to suprathreshold afterdepolarizations, a low maximum diastolic and peak overshoot potential, an acceleration in the rate of the triggered rhythm after initiation, and the brief persistence of afterpotentials after termination of the activity by extracellularly applied stimuli. The morphology of the triggered activity, moreover, suggested the membrane activity to be automatic in that there was a smooth transition from phase 4 into the upstroke of phase 0. The transition was much more abrupt when the preparation was controlled either by remote extracellular stimulation or by the remote pacemaker induced by epinephrine. Finally, endocardial mapping with microelectrodes failed to define a reentrant loop. We could not exclude microentry involving a circuit that plunged into the depths of the atrial preparation or within the 0.5 × 0.5 mm focus itself. Despite the limitations of the experimental methods and the difficulty in extrapolating the observations in an isolated preparation to the clinical situation, the case for triggered sustained automaticity is quite strong.

The triggerable activity in vitro may have been the counterpart of the arrhythmia in vivo. However, it has been shown that diseased human atria may contain cells with low resting membrane potentials in the absence of clinical tachyarrhythmias. The examples of triggerable automaticity shown in primate\textsuperscript{a} and human\textsuperscript{d} mitral valve tissue were also in the absence of significant arrhythmia in vivo. Thus, these studies suggest caution in attributing the clinical arrhythmia in the present case directly to the phenomena in our microelectrode studies.

Because it has been postulated that cells capable of triggered automaticity might involve activity of the slow, calcium-mediated membrane channel, it would have been of great interest to observe the abolition of the induced tachycardia by verapamil, either in vivo or in vitro. Unfortunately, because of limitations of experimental protocol in our clinical studies and to the short life of the excised specimen in the studies in vitro, the effects of verapamil were not examined.

**Figure 8.** Transmembrane voltage recordings of triggered membrane activity in the presence of a competing pacemaker induced by epinephrine. The site of extracellular stimulation was remote from the "focus" on which the recording microelectrode was located. 

- **(A)** Spontaneous automatic rhythm induced by epinephrine. Maximum diastolic potential (\(V_{md}\)) was -32 mV and the cycle length was 1870 msec. Note the relatively abrupt transition of phase 4 to phase 0.

- **(B)** Extracellularly applied stimuli (not shown) initiated this more rapid rhythm. \(V_{md}\) was -32 mV and the cycle length was 980 msec. Note the smooth transition from phase 4 to phase 0.

- **(C)** Termination of the triggered rhythm by a single stimulus (filled circle) followed by a delayed afterdepolarization that was less than threshold (\(dad < th\)) and resumption of the slower, epinephrine-induced pacemaker. Note the overdrive suppression. Subsequently, the epinephrine-dependent pacemaker accelerated to its original cycle length.

**Approach to Management**

Failure to find an agent that prevents sustained tachycardia indicates the need for more invasive therapy, as in the present case. This patient’s tachycardia could be initiated and sustained despite the administration of digitalis, propranolol, procainamide and quinidine. This correlated with occurrence of spontaneous episodes with all the above drugs.
addition, sufficient AV nodal block to render the patient asymptomatic could not be produced by the combination of digoxin and propranolol. The electrophysiologic study showed that rapid atrial pacing termination was reliable and predicted that the radiofrequency pacing system would successfully allow termination of clinical arrhythmia, should it recur despite surgery.

A good correlation was obtained between catheter endocardial mapping and the intraoperative epicardial map during PSVT. These techniques localized the earliest activity to the posterolateral rim of the right atrial appendage. This was confirmed by subsequent abolition of tachycardia during application of the atrial clamp, and the inability to reinduce tachycardia after excision of the appendage. We believe that the subsequent demonstration of inducible rhythmicity in the excised tissue may have been the cellular counterpart of the clinical arrhythmia.

Surgical therapy for PSVT has previously included incision, diathermy or cryothermy of the accessory pathway or the His bundle in patients with AV macroreentrant PSVT via accessory pathways as one limb of the circuit. A, B, D, I, Pritchett et al. described cure of PSVT after surgical trauma to the AV node (unsuccessful attempt at producing surgical AV block in a patient with AV nodal reentrant PSVT). Coumel et al. described cure of PSVT after an encircling incision made around an identified focal left atrial tachycardia adjacent to a pulmonary vein. There is no previous report of direct excision of a focus responsible for chronic paroxysmal atrial tachycardia.

Clinical Implications
The present case illustrates the feasibility of direct surgical excision of an atrial focus producing tachycardia. The present patient had a number of features making this approach to management both desirable and feasible: (1) frequent and severe tachycardia necessitating a vigorous attempt at cure; (2) a sustained paroxysmal tachycardia that was easily induced and terminated with cardiac stimulatory techniques, facilitating extensive preoperative and intraoperative electrophysiologic studies; (3) failure of chronic electrophysiologic study to find an agent that prevented induction of sustained tachycardia, coupled with the occurrence of spontaneous tachycardias despite vigorous empiric antiarrhythmic therapy; (4) an accessible site of origin of tachycardia, facilitating endocardial and epicardial mapping, as well as surgical cure.

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