Adenosine Triphosphate-sensitive Micro-reentrant Atrial Tachycardia Originating from the Crista Terminalis in a Patient with Chronic Renal Failure due to Thrombotic Thrombocytopenic Purpura

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A 57-year-old woman with chronic renal failure due to the thrombotic thrombocytopenic purpura complained of palpitation. A 12-lead ECG showed supraventricular tachycardia with a cycle length of 375 ms. During the electrophysiological study, a tachycardia with a cycle length of 375 ms was reproducibly induced and terminated by atrial extrastimulation. The tachycardia exhibited an inverse relationship between the coupling interval of extrastimulus initiating the tachycardia, and the first postpacing return cycle, as well as an increasing pattern of resetting the tachycardia with an atrial extrastimulus. Ventricular burst pacing during tachycardia produced AV dissociation. Intravenous injections of a low dose (4 mg) of adenosine triphosphate (ATP) terminated the tachycardia without a preceding atrio-His bundle block. The tachycardia was diagnosed as an ATP-sensitive micro-reentrant atrial tachycardia. Real-time endocardial activation mapping using an electroanatomical mapping system revealed that the earliest activation site of the tachycardia was located at the mid-lateral portion of the crista terminalis. The tachycardia was abolished by focal ablation targeting the earliest activation site during tachycardia. This is the first reported case of an ATP-sensitive micro-reentrant atrial tachycardia associated with thrombotic thrombocytopenic purpura.

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Introduction

Thrombotic thrombocytopenic purpura (TTP) is a disorder characterized by the abrupt development of platelet-rich thrombi in the arterioles and capillaries, and a dramatic response to plasma infusion or plasma exchange. TTP is defined by the classic pentad of clinical features: thrombocytopenia, microangiopathic hemolytic anemia, neurological symptoms, renal function abnormalities, and fever. Although cardiac involvement in patients with TTP has been recently reviewed, cardiac arrhythmias
have only been described in case reports, and their frequency cannot be estimated. Here we describe a case in which the mechanistic cause and origin of atrial tachycardia was clarified using electroanatomical mapping in a hemodialysis patient with TTP.

Case Report
A 57-year-old female with a 20-year history of rheumatoid arthritis was referred to our hospital because of fever, thrombocytopenia (platelets of $36 \times 10^3/\mu l$), hemolytic anemia (hemoglobin of 7.9 g/dl and reticulocyte of 7.3%), renal insufficiency (BUN of 47 mg/dl and creatinine of 5.84 mg/dl), general malaise, and confusion, and was diagnosed with TTP. She underwent plasma exchange therapy, but could not recover renal function and became dependent on dialysis. Three months later since the inception of the hemodialysis, she intermittently complained of palpitation. A 12-lead ECG showed supraventricular tachycardia with a cycle length of 375 ms, a positive P wave morphology in leads V1 through V4, and a biphasic morphology in leads II, III, and aVF (Figure 1). The tachycardia was terminated by an intravenous infusion of 2 mg of verapamil. Chest X-ray was normal, and transthoracic echocardiography revealed no structural heart disease, no atrial or ventricular dilatation, no myocardial hypertrophy, and no hyperechoic texture of the myocardium (granular sparkling texture). Serum atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) levels were 32.5 pg/mL and 39.1 pg/mL, respectively.

An electrophysiological study was performed after obtaining written informed consent from the patient. After internal jugular and femoral vein punctures were performed, a heparin bolus (100 U/kg) was administered followed by continuous infusion of heparin. Surface ECG and bipolar endocardial electrograms were continuously monitored and stored on a computer-based digital amplifier/recorder system for offline analysis (Bard Electrophysiology). Intracardiac electrograms were filtered from 30 to 500 Hz and measured at a sweep speed of 100 mm/s. The electrograms from the high right atrium, the His bundle, the right ventricular

![Figure 1](image.png)

(Left panel): Twelve-lead ECG during the atrial tachycardia. The atrial cycle length was 375 ms with 1:1 atrioventricular conduction. P wave morphology positive in leads V1 through V4 and biphasic in leads II, III, aVF. (Right panel): Twelve-lead ECG during sinus rhythm.
apex, and the coronary sinus were recorded. Baseline electrophysiological properties (atrial-His interval, His-ventricular interval, and sinus and atrioventricular nodal function) were within normal limits. Tachycardia with a cycle length of 375 ms was induced reproducibly by high right atrial extrastimulation. The tachycardia exhibited an inverse relationship between the coupling interval of extrastimulus initiating the tachycardia and the first postpacing return cycle, as well as an increasing pattern of resetting the tachycardia with an atrial extrastimulus (Figure 2). Ventricular burst pacing during tachycardia produced AV dissociation without affecting the atrial cycle length (Figure 3). Intravenous injections of ATP at a low dose (4 mg) terminated the tachycardia with slight prolongation of the tachycardia cycle length without preceding atrio-His bundle block (Figure 3). The tachycardia was diagnosed as an ATP-sensitive reentrant atrial tachycardia. Real-time endocardial activation mapping using an electroanatomical mapping system revealed that the earliest activation site of the tachycardia was located at the mid-lateral portion of the crista terminalis (Figure 2). The local electrogram of the earliest activation site during the tachycardia exhibited a fractionated potential, entrainment with concealed fusion (same P wave and activation sequence), and a postspacing interval equal to the tachycardia cycle length (Figure 3). Entrainment pacing performed from the upper part or lower part of the crista terminalis during tachycardia showed a longer postspacing interval with respect to the tachycardia cycle length (Figure 3), indicating the critical circuit of the tachycardia was very small. Radiofrequency ablation targeted to the earliest activation site for 60 seconds (maximum tip temperature set at 60°C, maximum output 30 watts) terminated the tachycardia (Figure 4). The tachycardia could no longer be induced either by atrial extrastimulation or by rapid atrial pacing (up to 300 min-1). The patient remained free of arrhythmias over a 12-month follow up period.

**Discussion**

Here we describe the case of an ATP-sensitive
micro-reentrant atrial tachycardia originating from the crista terminalis in a hemodialysis patient with TTP. The tachycardia showed a focal activation pattern on the electroanatomical mapping, which was successfully abolished by radiofrequency ablation.

Hawkins et al. have recently reviewed the clinical cardiac involvement in TTP.3) They analyzed 111 eligible patients from 30 articles, and analyzed several cardiac events, including infarction (26 patients), congestive failure (17 patients), arrhythmias (10 patients), cardiogenic shock (6 patients), and sudden cardiac death (8 patients). Arrhythmias described as complete heart block or electromechanical dissociation were the most commonly reported arrhythmias, described in six patients. Two patients had supraventricular tachycardias, one patient had atrial-ventricular junctional tachycardia, and one patient had ventricular arrhythmia. Clinical evidence for cardiac involvement in TTP is surprisingly limited. Our case included an atrial tachycardia, the origin and mechanism of which was clarified by the use of an electroanatomical mapping and entrainment pacing method.

Seferović et al. have reviewed cardiac arrhythmias and conduction disturbances in autoimmune rheumatic diseases.7) They reported that coronary artery disease was a major contributor to the increased risk of sudden cardiac death in rheumatoid arthritis, leading to acute coronary syndrome and ventricular arrhythmias, and that the primary infiltration of the atrio-ventricular node or other conducting tissue by mononuclear cells or rheumatoid granulomas is possible in patients with conduction disorders. Cardiac arrhythmias are also frequent in hemodialysis patients. Ansari et al. have reported that the risk factors for symptomatic atrial arrhythmias in hemodialysis patients may include hyperparathyroidism, chamber enlargement, valvular lesions, or ventricular dysfunction.8) In our case, echocardiography revealed no structural heart disease, normal chamber
sizes, normal ejection fraction, and no evidence of hyperechoic texture of the myocardium (granular sparkling texture). The electrophysiological study showed normal sinus and AV node function, and BNP levels were below 100 pg/mL. It is difficult to determine the relationship of rheumatoid arthritis or hemodialysis to atrial tachycardia in our patient. Moreover, the influence of drugs on the occurrence of atrial tachycardia seems very small because the patient was on the same medications at the same doses after the ablation procedure.

Repetitive focal atrial tachycardia appears to be more frequent in patients with organic heart disease, particularly cardiomyopathy, cardiac amyloidosis, and cardiac sarcoidosis. In addition to chronic heart disease, atrial tachycardia can also be associated with acute events such as a myocardial infarction, pulmonary decompensation, infection, alcohol excess, hypokalemia, hypoxia, stimulants, cocaine, and theophylline. However, atrial tachycardia can occur in the absence of heart disease and in such instances, it has a benign prognosis.\textsuperscript{9-13} The crista terminalis is an area of marked anisotropy due to poor transverse cell-to-cell coupling. In addition, the normal sinus pacemaker complex is distributed along the long axis of the crista terminalis.\textsuperscript{14} Such anisotropy and cells with nodal-type action potentials, by creating a region of slow conduction, favors the development of microreentry.\textsuperscript{9,10} No information is available about atrial tachycardias in patients with TTP. This case provides clinically important information on a potential relationship between TTP and arrhythmia.

References