Serum Atrial Natriuretic Peptide Concentration is a Useful Predictor of Atrial Standstill in Patients With Heart Failure

Masahiko Suguta, MD; Kenichiro Hara, MD; Akihiko Nakano, MD; Akio Arano, MD; Akira Hasegawa, MD; Masahiko Kurabayashi, MD

Two cases of atrial standstill are presented, one with cardiac amyloidosis, the other with idiopathic dilated cardiomyopathy. The plasma atrial natriuretic peptide (ANP) concentration was normal to slightly elevated in both patients, despite a marked elevation of the plasma brain natriuretic peptide (BNP) concentration. In the patient with amyloidosis (ANP: 170 pg/ml, BNP: 1220 pg/ml), a dual chamber pacemaker was successfully implanted for the treatment of sinus arrest. However, loss of atrial capture occurred 1 month later. In the patient with dilated cardiomyopathy (ANP: 47 pg/ml, BNP: 422 pg/ml), an electrophysiologic study confirmed persistent atrial standstill and failure to pace from either the right atrium or the coronary sinus. The hypothesis is that the attenuated increase in plasma ANP concentration relative to the increase in the BNP concentration may be a sensitive and useful marker to confirm atrial standstill in the setting of congestive heart failure. (Jpn Circ J 2000; 64: 537–540)

Key Words: Atrial natriuretic peptide (ANP); Atrial standstill; Cardiac amyloidosis; Congestive heart failure

Atrial standstill is a rare disorder caused by injury to the atrium and a low plasma concentration of atrial natriuretic peptide (ANP) has been demonstrated in patients with this condition. However, ANP is also secreted from the ventricles of patients with heart failure? The dynamics of both ANP and brain natriuretic peptide (BNP) metabolism in patients with atrial standstill in the setting of congestive heart failure is unknown.

Case Reports

Patient 1

A 58-year-old man with no previous history of heart disease was admitted because of syncope. His ECG showed atrial fibrillation with low QRS voltage in the limb lead (Fig 1). Chest radiograph showed bilateral pleural effusion. Serial cardiac enzyme activities and renal function were normal, but a markedly elevated serum BNP concentration (1220 pg/ml, normal: <20) and a mildly elevated ANP concentration (170 pg/ml, normal: <43) were noted. Detailed echocardiography was performed (Fig 3) and revealed increased left and right ventricular wall thicknesses (18 mm in the interventricular septum and 14 mm in the left ventricular posterior wall), with a sparkling granular pattern to the myocardium. The left and right atrial myocardium and interatrial septum were also thickened. The left ventricular cavity size (51 mm left ventricular end-diastolic dimension, 32 mm left ventricular end-systolic dimension) and myocardial contractility (ejection fraction: 68%) were normal. Serum and urine protein electrophoresis revealed a monoclonal component of lambda chain derived from IgD. Bone marrow examination showed narrow plasmacytosis (>50%) with cells believed to represent multiple myeloma. These findings led to a diagnosis of cardiac amyloidosis complicated with multiple myeloma.

On the third hospital day, atrial fibrillation spontaneously terminated, resulting in cardiac arrest. After cardiopulmonary resuscitation with temporary ventricular pacing, a dual chamber permanent pacemaker was successfully implanted to treat the sick sinus syndrome caused by cardiac amyloidosis. Despite the inability to atrial sense, an adequate atrial pacing threshold could be obtained (1.0 V × 0.45 ms) (Fig 2). During dual chamber pacing, the mitral inflow Doppler velocities showed typical features of restrictive physiology: a diminished A wave, increased E wave, and a shortened deceleration time for the E wave (Fig 2). One month after pacemaker implantation, loss of atrial capture occurred. The ECG showed a regular junctional escape rhythm (Fig 1), and atrial capture could not be elicited with an electrical stimulus of 8.1 V, confirming a diagnosis of atrial standstill. The plasma concentration of ANP had decreased to 89.5 pg/ml, but the BNP concentration had not changed (1210 pg/ml).

Reprogramming the dual chamber pacemaker to ventricular demand mode was necessary to treat the atrial standstill. The patient died of congestive heart failure 4 months after admission. We obtained autopsy specimens of the heart. The heart weighed 660 g and there was diffuse thickening of both ventricles and atria. Histologic examination of the left ventricular septum and both atria revealed dense deposits of amyloid protein (Fig 3).

Patient 2

A 50-year-old man was admitted to hospital with
Fig 1. Atrial fibrillation documented on admission electrocardiogram (Left). Note the flattened baseline and regular ventricular escape rhythm during atrial standstill (Right).

Fig 2. During dual-chamber pacing, there are atrial pacing spikes and P waves. Pulsed-wave Doppler recording on the mitral inflow velocity pattern during dual-chamber pacing reveals an increased E wave and no A wave.

dyspnea. A permanent VVI pacemaker had been implanted 7 years earlier for symptomatic bradycardia caused by sick sinus syndrome. Electrocardiogram showed a ventricular paced rhythm and flattened baseline in all leads (Fig 4). Echocardiography revealed a dilated left ventricle (62 mm left ventricular end-diastolic dimension) with diffusely reduced contractility (left ventricular ejection fraction: 35%) (Fig 4). Doppler study showed no A wave on the mitral inflow velocity pattern. On admission, the serum concentration of ANP was within normal limits (27 pg/ml), but the serum BNP concentration was increased (422 pg/ml). Coronary angiography revealed no stenoses, and endomyocardial biopsy specimens showed only evidence of fibrosis. Therefore, a diagnosis of idiopathic dilated cardiomyopathy was made.

An electrophysiologic study was performed. Detailed right atrial and coronary sinus mapping and failure to capture at any pacing site confirmed the presence of atrial standstill. The patient is currently being treated with diuretics and angiotensin converting enzyme inhibitor.

**Discussion**

Atrial standstill is a rare condition that is diagnosed on
Fig. 3. Parasternal long-axis view (Left, upper) and short-axis view (Left, lower) echocardiography showing a normal-sized left ventricle with a granular sparkling pattern, compatible with a diagnosis of cardiac amyloidosis. Pink eosinophilic deposits demonstrate amyloid in hematoxylin-eosin-stained myocardial tissue obtained from the right atrium (Right, x200).

Fig. 4. Electrocardiogram on admission. Note the flattened baseline with ventricular pacing (Left). Parasternal short-axis echocardiography showing typical findings of an idiopathic dilated cardiomyopathy (Right) with thinning of the left ventricular wall and dilation of the left ventricular cavity. Left ventricular contractility is also reduced.
the basis of characteristic electrophysiologic and hemodynamic findings, with the former showing failure of atrial excitation either spontaneously or by atrial electrical stimulation. Echocardiography reveals the absence of atrial contractions and A waves on the mitral inflow velocity pattern. There are reports that ANP secretion in patients with atrial standstill is abnormal but patients with heart failure or cardiac amyloidosis have not been studied.

The plasma concentration of ANP and BNP are elevated in proportion to the severity of congestive heart failure. Yasue et al recently showed that ANP is secreted mainly from the atria, whereas BNP is secreted mainly from the ventricles findings compatible with those of the present patient 2 (ie, the ANP concentration was within normal limits and the BNP was elevated in proportion to the degree of congestive heart failure). However, ANP is also secreted from the ventricles of patients with dilated cardiomyopathy and it is likely that ANP is also secreted from the ventricles, although the amount is very small compared with that secreted from the atria in patients with heart failure.

In contrast, Takemura et al reported that the plasma concentrations of both ANP (390.0±459.1 pg/ml) and BNP (1165.1±561.2 pg/ml) were elevated in patients with cardiac amyloidosis, and that the elevation of BNP was more extreme. Furthermore, the expression of ANP and BNP was increased at both the peptide and mRNA levels in ventricular myocytes from these patients, which is in agreement with the findings in the present patient 1 (the plasma concentration of ANP was 85.9–184 pg/ml during his hospitalization, despite the development of atrial standstill). In Takemura's report, the plasma BNP concentration was markedly elevated (640.5 pg/ml) in one patient, despite a slight elevation in the plasma ANP concentration (47.0 pg/ml).

Our findings have several clinical implications. In patients with atrial standstill complicated by cardiac amyloidosis, the plasma concentration of ANP may be normal, in contrast to a markedly elevated BNP concentration. In such patients, a VVI mode single chamber pacemaker may be more suitable. Furthermore, the mitral inflow velocity pattern may not be useful in detecting atrial standstill in patients with cardiac amyloidosis, because a diminished A wave may not be discernible with the restrictive physiology present.

We conclude that the attenuated increase in plasma ANP concentration relative to the increase in the BNP concentration may be a sensitive and useful marker to confirm atrial standstill in the setting of congestive heart failure.

References