Brain Natriuretic Peptide and Cardiac Rupture after Acute Myocardial Infarction

Naoshi Arakawa, Motoyuki Nakamura, Hiroshi Endo, Shoma Sugawara, Tomomi Suzuki and Katsuhiko Hiramori

Abstract

Cardiac rupture is a fatal complication in the acute stage of myocardial infarction (MI). However, no measures have yet been established to predict it. Herein we describe three MI patients with cardiac rupture in whom plasma brain natriuretic peptide (BNP) and atrial natriuretic peptide (ANP) concentrations had been serially monitored from the onset of MI to cardiac rupture. In these cases, plasma BNP levels increased without symptomatic and hemodynamic changes and reached their highest level immediately before cardiac rupture, while plasma ANP levels remained unchanged. These cases suggest that the increased plasma BNP concentrations without symptomatic and hemodynamic changes may be a useful marker for predicting cardiac rupture after acute MI.

We have already reported that the increase in plasma BNP is correlated with infarct size (5), and we and others have found that plasma BNP concentrations may be a useful marker for predicting survival after MI (6, 7).

We report here 3 cases in whom cardiac rupture occurred 36 to 72 hours after onset of MI with measurement of plasma BNP and atrial natriuretic peptide (ANP) concentrations from onset of MI to immediately prior to cardiac rupture or death. The study protocol was approved by the ethics committee of our university hospital, and informed consent was obtained from patients or their family.

Case Report

Case 1

An 80-year-old woman with a 5-year history of treatment for hypertension but no history of angina pectoris was admitted to our hospital with chest pain. Electrocardiography (ECG) showed ST elevation in leads I, aVL, and V2-5, and ST depression in leads II, III, and aVF. A chest X-ray showed heart enlargement (cardio-thoracic ratio: 56%) but no pulmonary congestion. Echocardiography revealed extensive akinesis of the left anterior ventricular wall. Based on the diagnosis of acute MI, emergency coronary angiography was performed. Because a complete occlusive lesion was observed on the left anterior descending branch, 64x10^4 units of tissue-type plasminogen activator (t-PA) was infused for thrombolysis into the left coronary artery. However, recanalization was not achieved. Left ventriculography showed extensive akinesis of the left anterior ventricular wall. Left ventricular ejection fraction (LVEF) was 46%. Mean pulmonary capillary wedge pressure (PCWP) obtained via a Swan-Ganz catheter was 23 mmHg and cardiac index (CI) was 1.67 l/min/m^2. Because of low cardiac output, intra-aortic balloon pumping (IABP) was used and catecholamine was administered. At 48 hours after onset, the patient’s blood pressure dropped suddenly and she became apneic. An ECG showed electro-mechanical dissociation and the patient finally died. Immediately prior to death, PCWP was 24 mmHg, CI was 1.75 l/min/m^2 and chest X-ray showed no pulmonary congestion.
Because echocardiography revealed an echo-free space in the pericardial lesion, there was strong suspicion of pericardial effusion (tamponade) due to cardiac rupture. Autopsy showed a fresh transmural infarction associated with bleeding extending from the anterior wall of the left ventricle to the septum and an approximately 0.5 cm linear rupture in the left ventricular wall at the apex, permitting a definitive diagnosis of myocardial rupture to be made. There was 95% stenosis of the left anterior descending artery and a 150 ml blood clot was found in the pericardial sac.

Figure 1 shows the time course of changes in plasma BNP and ANP concentrations and creatine kinase (CK) values for the period from onset until immediately before death. Blood specimens were drawn from a forearm vein and plasma levels of BNP and ANP were determined using commercially available radioimmunoassay kits (Shionoria, Shionogi, Osaka, Japan). The peak CK value (4,754 IU/l) occurred 24 hours after onset. Plasma BNP levels peaked transiently 24 hours after onset, but increased again, reaching their highest point (323.0 pg/ml) immediately prior to cardiac rupture. In contrast, plasma ANP levels did not change. There were no other particular changes in hemodynamics during the experimental period.

Case 2
A 76-year-old woman was admitted to our hospital with cardiogenic shock. A chest X-ray showed pulmonary congestion. ECG showed ST elevation in leads II, III, aVF and V^4. Echocardiography revealed akinesis of the left ventricular infero-lateral wall. LVEF was 37%. Based on the diagnosis of MI, emergency coronary angiography was performed. A complete occlusive lesion was observed on both the left anterior descending (with intra-coronary collateral flow) and the circumflex branch. Thrombolysis was attempted by infusing 64x10^4 units of tissue plasminogen activator into the left coronary artery, but recanalization was not achieved. The patient was intubated and treated with IABP and catecholamine. PCWP was 18 mmHg and CI was 2.51 l/min/m² under these conditions. Liver dysfunction and renal failure were also evident (ALT: alanine amino transferase 546 IU/l, creatinine 4.8 mg/dl). At 48 hours after onset, systemic blood pressure began to decline and pericardial effusion appeared on echocardiography. Immediately prior to shock, hemodynamic parameters had not changed significantly compared to those at admission (PCWP, 17 mmHg; CI, 2.01 l/min/m²). Although pericardial effusion drainage was performed, the patient finally died 4 days after onset of MI. Autopsy revealed a hemorrhagic infarct of the lateral and posterior walls of the left ventricle and pericarditis with bloody effusion, suggesting oozing rupture. Maximum serum CK level was 8,200 IU/l 18 hours after onset, followed by a gradual decrease, while plasma BNP started to rise again 36 hours after onset and reached a maximum level (1,700 pg/ml) 48 hours after onset (Fig. 2).

Case 3
A 75-year-old man was admitted to our hospital with a diagnosis of MI. ECG showed ST elevation in leads V, and QS pattern in V. Echocardiography revealed akinesis of the left ventricular antero-septal wall. LVEF was 43%. X-ray showed no heart enlargement (cardio-thoracic ratio: 51%) and no pulmonary congestion. PCWP was 11 mmHg and CI

![Figure 1](image-url)
was 3.00 l/min/m² on admission. Emergency coronary angiography was performed 6 hours after onset. Because an incomplete occlusive lesion was observed on the left anterior descending branch, thrombolysis was not initiated. Two days after onset, systemic blood pressure dropped suddenly and the patient lost consciousness. Massive pericardial effusion was found on echocardiography. Immediately prior to shock, PCWP was 16 mmHg, CI was 2.52 l/min/m² and chest X-ray showed no pul-

Case 2

Figure 2. Time course of plasma levels of brain natriuretic peptide (BNP), atrial natriuretic peptide (ANP) and creatine kinase (CK) in case 2 after onset of acute myocardial infarction. ICT indicates intracoronary thrombolysis.

Case 3

Figure 3. Time course of plasma levels of brain natriuretic peptide (BNP), atrial natriuretic peptide (ANP) and creatine kinase (CK) in case 3 after onset of acute myocardial infarction.
monary congestion. The patient died 1 day later after failing to respond to mechanical circulatory support. In this case, plasma BNP levels continued to increase until 48 hours after onset, immediately prior to cardiac rupture, while plasma ANP levels remained unchanged (Fig. 3).

**Discussion**

Prior to the advent of thrombolytic therapy for acute MI, cardiac rupture occurred as a complication within 2 weeks of the onset of symptoms, with the peak incidence on day 5 (8). However, after the introduction of thrombolysis in the acute phase of MI, cardiac rupture was found to occur earlier, 24 to 48 hours after onset (8–10). The overall percentage of in-hospital deaths from MI has declined as a result of thrombolytic therapy. However, the risk of cardiac rupture in the acute phase (24–48 hours after onset) may have increased (10). Consequently, it is very important that a marker be found which will allow prompt detection of imminent cardiac rupture.

Plasma BNP concentrations have been reported to gradually increase soon after the onset of symptoms of MI and to peak 16–24 hours after onset and then decrease (4, 5). In Fig. 4, we present, as a control, the changes in plasma levels of BNP in 24 patients with acute myocardial infarction who did not have cardiac rupture (5). A second peak 4–5 days after onset has also been reported to be associated with ventricular remodeling in patients with large infarcts and decreased cardiac function (4). In case 1, plasma BNP levels increased gradually for the first 24 hours after onset, as described in other reports (4, 5). However, these levels increased abruptly again without symptomatic or hemodynamic changes, with values reaching their highest point 48 hours after onset. Similarly, in the other 2 patients described above, plasma BNP reached its highest levels immediately before cardiac rupture. In case 2, although plasma BNP on admission was relatively higher (1,400 pg/ml) than that of the other 2 patients, reflecting the severity of disease, a second peak was observed 40 to 48 hours before cardiac rupture as seen in case 1. In case 3, plasma BNP levels increased continuously to the time point immediately before rupture (48 hours after onset). The time course of changes in plasma BNP levels in these 3 cases demonstrates a pattern that differs clearly from cases without cardiac rupture (see Fig. 4).

Increases in ventricular wall stress/tension due to ischemia and infarction appear to be an important factor in the synthesis and secretion of BNP by cardiomyocytes. It has been postulated that this mechanism underlies the increase in plasma BNP concentrations seen in MI (4–6). It may therefore be possible to interpret the present findings as meaning that an excessive increase in wall stress/tension at the border of the infarction area may stimulate BNP secretion from ventricular cardiomyocytes, and particularly in cases complicated with cardiac rupture. The time course of changes in plasma BNP concentrations in these patients complicated by cardiac rupture was characterised by certain features that differed from cases of uncomplicated MI in our previous experience. In addition, the phenomenon of a second increase observed in cases 1 and 2 and the continuous increase observed in case 3 before cardiac rupture (36 to 48 hours after onset) may be highly indicative. While only so much can be inferred on the basis of case reports, it appears at the present time, in the absence of any other predictors of cardiac rupture, that a sudden increase in plasma BNP levels should be considered a predictor of cardiac rupture in the acute stage of MI, and that this should be further investigated in a larger number of MI cases complicated by cardiac rupture.

**References**

8) Becker RC, Charlesworth A, Wilcox RG, et al. Cardiac rupture associ-
Arakawa et al

