High Plasma Levels of the B-type Natriuretic Peptide in Patients Without Heart Failure: Is There Clinical Significance?

Long Hao Yu, MD1,2, Moo Hyun Kim, MD1,2, Jong Seong Park, MD1, Kwang Soo Cha, MD1, Tae Ho Park, MD1 and Young Dae Kim, MD1

1Department of Cardiology, College of Medicine, Dong-A University, Busan, 2Regional Clinical Trial Center, Dong-A University Hospital, Busan, Korea

ABSTRACT

We report a case of a 19-year-old female with an elevated plasma B-type natriuretic peptide (BNP) level, but without evidence of heart failure (HF). She presented with non-specific chest pain and a high level of the B-type natriuretic peptide, despite having unremarkable findings on physical examination, laboratory analysis, electrocardiogram, echocardiogram, chest X-ray, chest computed tomography, whole body scan, and coronary angiography. We attribute this finding to a genetic variation in the synthesis and cleavage of the natriuretic peptides. (Korean Circ J 2010;40:141-142)

KEY WORDS: Natriuretic peptide; Heart failure.

Introduction

The B-type natriuretic peptide (BNP) is synthesized predominantly by cardiac ventricular myocytes, the expression of which is regulated by changes in intracardiac pressure and/or stretch. Cardiac BNP gene expression and plasma levels generally increase in patients with heart failure (HF), myocardial infarction, hypertension, left ventricular (LV) hypertrophy, pulmonary hypertension, and renal failure. However, we have managed some patients with elevated concentrations of the BNP and no evidence of HF, hypertension, or renal dysfunction. Thus, we report an interesting case of a young female patient with an elevated plasma level of the BNP.

Case

A 19-year-old female patient presented for evaluation on 7 April 2008 of non-specific chest pain of 1 month duration. She had no history of hypertension, diabetes, or renal dysfunction. The physical examination was unremarkable. She had worked for 6 months in a cellular phone factory. There were no abnormal findings on the electrocardiogram, echocardiogram, and treadmill test. The cardiac markers were within the normal range. The results of the complete blood count, blood chemistry, and serum creatinine were all normal, except for a high plasma level of BNP (3,437.80 pg/mL). Pulmonary function testing showed that spirometry was within normal limits. She was discharged on diuretics and was symptom-free. During the follow-up, the BNP level was measured twice as an outpatient and was persistently elevated (2,904.1 pg/mL).
and 4,000 pg/mL) (Fig. 1).

Discussion

The BNP is synthesized and secreted primarily from LV cardiomyocytes in response to increasing wall stress, particularly during diastole. Cleavage of the precursor peptide (proBNP) produces BNP and the corresponding amino-terminal component (NT-proBNP), which are secreted in a 1:1 ratio and can be detected in the peripheral circulation. The plasma levels of these peptides correlate strongly with each other. The BNP is bioactive and has a shorter half-life as a result of clearance by neutral endopeptidase and natriuretic peptide C-type receptors. Thus, levels are lower than for the more stable NT-proBNP. The levels of both peptides increase with LV pressure or volume loading, and reflect the severity of LV dysfunction. In addition, the levels of both peptides correlate inversely with LV ejection fraction and positively with increasing LV mass and indices of LV filling pressure. There is wide inter-individual variation in BNP and NT-proBNP levels. Up to 80% of inter-individual variation in peptide levels is explained by LV and diastolic functions, right ventricular dysfunction, renal function, age, and mitral regurgitation. Although Baggish et al. previously reported the possible causes of NT-proBNP elevation unrelated to HF, such as heart muscle disease, valvular heart disease, atrial arrhythmias, anemia, critical illnesses, ischemic stroke, and pulmonary heart disease syndromes, the patient presented herein had none of these causes. Hereditary factors may be responsible for a significant proportion of residual variation in BNP levels. In this interesting case, the patient has no remarkable findings to account for the high levels of the BNP. We therefore suggest that hereditary factors may be responsible for a significant proportion of residual variation in BNP levels and further studies are required to describe the basis and need for treatment (if any) of elevated BNP levels in such patients.

REFERENCES

1) Horio T, Kawano Y. Bio-molecular markers for cardiovascular disease: significance of natriuretic peptides and adrenomedullin. Korean Circ J 2008;38:507-13.
2) Yasue H, Yoshimura M, Sumida H, et al. Localization and mechanism of secretion of B-type natriuretic peptide in comparison with those of A-type natriuretic peptide in normal subjects and patients with heart failure. Circulation 1994;90:195-203.
3) Hunt PJ, Yandle TG, Nicholls MG, Richards AM, Espiner EA. The amino-terminal portion of pro-brain natriuretic peptide (Pro-BNP) circulates in human plasma. Biochem Biophys Res Commun 1995;214:1175-83.
4) Lainchbury JG, Campbell E, Frampton CM, Yandle TG, Nicholls MG, Richards AM. Brain natriuretic peptide and N terminal brain natriuretic peptide in the diagnosis of heart failure in patients with acute shortness of breath. J Am Coll Cardiol 2003;42:728-35.
5) Nishikimi T, Yoshihara F, Morimoto A, et al. Relationship between left ventricular geometry and natriuretic peptide levels in essential hypertension. Hypertension 1996;28:22-30.
6) Troughton RW, Prior DL, Pereira JJ, et al. Plasma B-type natriuretic peptide levels in systolic heart failure: importance of left ventricular diastolic function and right ventricular systolic function. J Am Coll Cardiol 2004;43:416-22.
7) Baggish AL, van Kimmenade RR, Januzzi JL Jr. The differential diagnosis of an elevated amino-terminal pro-B-type natriuretic peptide level. Am J Cardiol 2008;101:43-8.
8) Wang TJ, Larson MG, Levy D, et al. Heritability and genetic linkage of plasma natriuretic peptide levels. Circulation 2003;108:13-6.