

Possible False Positive Heart Fatty Acid Binding Protein in Patient Who Has a High Level of Creatinine Kinase

Kreatin Kinaz Düzeyi Yüksek Olan Hastalarda Heart Fatty Acid Binding Protein Hatalı Olarak Pozitif Olabilir

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Abstract

Serum heart fatty acid binding protein (H-FABP) is a novel sensitive marker for early diagnosis of acute myocardial infarction. However, H-FABP is less specific than troponins, because it is also found in skeletal muscle. Recently, we have observed 3 patients who had high CK levels due to destruction of skeletal muscle and they had false positive high H-FABP levels. (*JAEM 2012; 11: 241-2*)

Key words: Heart fatty acid binding protein, creatinine kinase, acute myocardial infarction

Özet

Heart fatty acite binding protein (H-FABP) erken dönemde akut miyokard enfarktüsünü gösteren yeni hassas bir belirteçtir. Troponin'den daha az özgüldür, çünkü ayrıca iskelet kasında da bulunur. Son zamanlarda iskelet kası yıkımına bağlı CK yüksekliği bulunan ve beraberinde hatalı pozitif H-FABP yüksekliği saptanan 3 hasta gözlemledik. (*JAEM 2012; 11: 241-2*)

Anahtar kelimeler: Heart fatty acid binding protein, kreatinin kinaz, akut miyokardiyal enfarktüs

Introduction

Heart fatty acid binding protein (H-FABP) is a new marker with a low molecular weight which indicates early myocardial tissue injury (1, 2). Various studies have shown that H-FABP becomes positive earlier than troponins and is more sensitive than myoglobin (3-5). Besides, the H-FABP found in skeletal muscle is approximately 10-20% of the concentration of H-FABP in heart muscle (6). Recently, we have observed 3 patients who had high creatinine kinase (CK) and H-FABP levels for various reasons.

Case Reports

Case 1

A 26-year-old male patient was admitted to the emergency room of our institution with atypical chest pain. The peak creatinine phosphokinase-MB isoenzyme (CKMB) was 34 IU/L, the troponin I concentration was <0.2 ng/mL and the H-FABP was 38 ng/mL. No risk factors associated with coronary artery disease (CAD) were reported in his personal history. His blood pressure (BP) was 130/80 mmHg and pulse rate was 92/min. The electrocardiography (ECG), chest X ray and echocardiography examinations were all within normal limits. In the second measurement of his cardiac enzymes performed on

the same day, the levels of H-FABP, CKMB and troponin I were found as 29 ng/mL, 90 IU/L and <0.2 ng/mL respectively. On follow-up, the serum CK value of the patient was found to be 3217 IU/L and troponin I was negative. His current high H-FABP and CK levels were estimated to be associated with his skeletal muscle destruction. The patient was discharged and directed to the rheumatology clinic.

Case 2

A 75 year-old male patient was admitted to the emergency room with a scorpion bite. After the initial intervention, the biochemical cardiac markers were measured as 27 ng/mL for H-FABP, 28 IU/L for CKMB and 0.26 ng/mL for troponin I levels. The patient was hospitalized with the diagnosis of acute coronary syndrome following scorpion sting poisoning. His BP was 140/90 mmHg and pulse rate was 82/min. The ECG and chest X ray examinations were within normal limits. Diastolic dysfunction was detected with echocardiography. In his second measurement of cardiac enzymes performed the next day, the levels of H-FABP, CK, CKMB and troponin I were measured as 47 ng/mL, 870 IU/L, 27 IU/L and <0.2 ng/mL respectively. However, in a test performed within 6 hours, the results of the analyses revealed H-FABP 38 ng/mL, CK 817 IU/L, CKMB 31 IU/L and troponin I <0.2 ng/mL. It was concluded that the high levels of H-FABP and CK in this patient occurred secondary to the muscle injury following the scorpion bite.

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Case 3

A 64 year-old female patient applied to the emergency room with complaints of atypical chest pain and extensive body pain. The values measured for the levels of H-FABP, CKMB and troponin I were 32 ng/mL, 36 IU/L and I <0.2 ng/mL respectively. The patient was diagnosed with acute coronary syndrome and admitted to the coronary care unit. She was reported to have had a coronary bypass surgery in her history. She had been treated with atorvastatin for hyperlipidemia for the last 3 months. Her BP was 130/80 mmHg and pulse rate was 80/min. No pathological features were observed in her physical examination. The results of her ECG were within normal limits; her chest x-ray films revealed an increased heart shadow; and no localized wall motion abnormalities were observed with echocardiography. In her second measurement of cardiac enzymes performed on the same day, her CK was found as 1342 IU/L and troponin I as <0.2 ng/mL. It was concluded that with extensive body pain, the patient had high CK levels due to atorvastatin and this drug was withdrawn. Her current high H-FABP and CK levels were estimated to be associated with atorvastatin myopathy constructive effect. The patient was discharged and called for a follow-up visit after 2 weeks when it was observed that her high CK was back to normal and her H-FABP levels were negative. These results confirmed the idea that CK increased due to atorvastatin use, which, in turn, led to an increase in H-FABP levels.

Laboratory: CK and CKMB activity in serum was measured by the Olympus Chemistry Analyzer AU640. The dynamic range of this multiple-point rate test was calculated as 8.1% at 43 U/L. Point of Care Testing (POCT) systems were used for Troponin I assessments. Serum CK-MB ≥ 25 IU / L and Troponin I ≥ 0.2 ng/mL were considered as positive. The principle of the newly developed whole-blood rapid H-FABP test was based on a dual monoclonal antibody sandwich method using 2 distinct monoclonal antibodies and a gold label method. The rapid H-FABP test was calibrated to detect a serum H-FABP concentration of >6.2 ng/mL as a positive line, because other clinical investigations of this quantitative assay using the same monoclonal antibodies showed a cut-off level for diagnosing acute myocardial infarction (AMI) of 6.2 ng/mL (2, 5, 7-9).

Discussion

Cardiac troponins are highly sensitive and specific markers of myocardial damage (10, 11). They are mainly found as structural proteins but they become detectable in the serum by 4 to 6 hours after myocardial injury (12). In particular, early diagnosis is known to be extremely important in AMI. Thus, H-FABP has started to be used recently as a new cardiac marker which may increase at an earlier stage in AMI (1, 2).

H-FABP is a new cardiac marker with a low molecular weight (15 kDa) that sensitively reveals myocardial injury (1-5, 13). Its concentration in blood starts to increase in 1.5 hours and remains positive for nearly 24 hours. As a cytoplasmic protein, H-FABP plays a significant role in the intracellular transport of fatty acids for oxidation in mitochondria (14). Being tissue-specific, it is named after the tissue of origin (Liver; L-FABP, Heart; H-FABP, Intestinal; I-FABP). It is most commonly found in the heart and liver. It is also known that the concentration of H-FABP in skeletal muscle is approximately 10-20% of its concentration in heart muscle (6).

As a new marker, known to be more sensitive than troponins and myoglobin in diagnosing AMI in the first 2 hours, it has been recently started to be used. However, except for cardiac injury, what leads to high levels of H-FABP and what decreases its specificity are not clear. In our clinic, we detected high levels of H-FABP along with high levels

of CK due to muscle destruction in the 3 cases reported above. The troponin I levels did not show any increase in these patients. We suggest that this protein, known to be present in muscle tissue, might increase as a result of muscle injury.

Conclusion

Consequently, physicians should be well aware that in patients who apply to emergency room with complaints of chest pain and had a diagnosis of high level of CK due to skeletal muscle destruction, as was the case with our patients, the H-FABP level might lead to false positive results and therefore, the level of troponin I should also be taken into consideration.

Conflict of Interest

No conflict of interest was declared by the authors.

References

1. Tanaka T, Hirota Y, Sohmiya K, Nishimura S, Kawamura K. Serum and urinary human heart fatty acid-binding protein in acute myocardial infarction. *Clin Biochem* 1991; 24: 195-201. [CrossRef]
2. Glatz JF, van der Vusse GJ, Simoons ML, Kragten JA, van Dieijen-Visser MP, Hermens WT. Fatty acid-binding protein and the early detection of acute myocardial infarction. *Clin Chim Acta* 1998; 272: 87-92. [CrossRef]
3. Okamoto F, Sohmiya K, Ohkaru Y, Kawamura K, Asayama K, Kimura H, et al. Human heart-type cytoplasmic fatty acid-binding protein (H-FABP) for the diagnosis of acute myocardial infarction: clinical evaluation of H-FABP in comparison with myoglobin and creatine kinase isoenzyme MB. *Clin Chem Lab Med* 2000; 38: 231-8. [CrossRef]
4. Ishii J, Wang JH, Naruse H, Taga S, Kinoshita M, Kurokawa H, et al. Serum concentrations of myoglobin vs human heart-type cytoplasmic fatty acid-binding protein in early detection of acute myocardial infarction. *Clin Chem* 1997; 43: 1372-8. [CrossRef]
5. Seino Y, Ogata K, Takano T, Ishii J, Hishida H, Morita H, et al. Use of a whole blood rapid panel test for heart-type fatty acid-binding protein in patients with acute chest pain: comparison with rapid troponin T and myoglobin tests. *Am J Med* 2003; 115: 185-90. [CrossRef]
6. Van Nieuwenhoven FA, Kleine AH, Wodzig WH, Hermens WT, Kragten HA, Maessen JG, et al. Discrimination between myocardial and skeletal muscle injury by assessment of the plasma ratio of myoglobin over fatty acid-binding protein. *Circulation* 1995; 92: 2848-54.
7. Watanabe T, Ohkubo Y, Matsuoka H, Kimura H, Sakai Y, Ohkaru Y, et al. Development of a simple whole blood panel test for detection of human heart-type fatty acid-binding protein. *Clin Biochem* 2001; 34: 257-63. [CrossRef]
8. Tsuji R, Tanaka T, Sohmiya K, Hirota Y, Yoshimoto K, Kinoshita K, et al. Human heart-type cytoplasmic fatty acid-binding protein in serum and urine during hyperacute myocardial infarction. *Int J Cardiol* 1993; 41: 209-17. [CrossRef]
9. Ohkaru Y, Asayama K, Ishii H, Nishimura S, Sunahara N, Tanaka T, et al. Development of a sandwich enzyme-linked immunosorbent assay for the determination of human heart-type fatty acid-binding protein in plasma and urine by using two different monoclonal antibodies specific for human heart-type fatty acid-binding protein. *J Immunol Methods* 1995; 178: 99-111. [CrossRef]
10. Katus HA, Remppis A, Neumann FJ, Scheffold T, Diederich KW, Vinar G, et al. Diagnostic efficiency of troponin T measurements in acute myocardial infarction. *Circulation* 1991; 83: 902-12.
11. Jaffe AS, Ravkilde J, Roberts R, Naslund U, Apple FS, Galvani M, et al. It's time for a change to a troponin standard. *Circulation* 2000; 102: 1216-20.
12. Katus HA, Remppis A, Scheffold T, Diederich KW, Kuebler W. Intracellular compartmentation of cardiac troponin T and its release kinetics in patients with reperfused and nonreperfused myocardial infarction. *Am J Cardiol* 1991; 67: 1360-7. [CrossRef]
13. O'Donoghue M, de Lemos JA, Morrow DA, Murphy SA, Buross JL, Cannon CP, et al. Prognostic utility of heart-type fatty acid binding protein in patients with acute coronary syndromes. *Circulation* 2006; 114: 550-7. [CrossRef]
14. Schaap FG, van der Vusse GJ, Glatz JF. Fatty acid-binding proteins in the heart. *Mol Cell Biochem* 1998; 180: 43-51. [CrossRef]