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CASE REPORT

A Case of Pseudo-Elevation of CK-MB without Myocardial Infarction

Gangfeng Li, Tao Lu, Ningping Shan

Department of Clinical Laboratory Center, Shaoxing People's Hospital, Shaoxing, P.R. China

SUMMARY

Background: **CK-MB is a subtype of creatine kinase isoenzyme, mainly present in myocardial tissue. When myocardial tissue damage is severe, CK-MB is released into the blood, and the serum level significantly increases, which is an important indicator for diagnosing acute myocardial infarction.**
Methods: **We reported a case of pseudo-elevation of CK-MB without acute myocardial infarction.**
Results: **The immunosuppressive assay showed that the activity of CK-MB isoenzyme was 903.0 U/L, which was significantly increased. The patient underwent examinations such as cardiac ultrasound and coronary artery imaging, and no obvious abnormalities were found. Suspected interference, CK-MB was measured using mass immunoassay, and the result was 1.96 ng/mL, which is within the normal range.**
Conclusions: **When the CK-MB level (immunosuppressive assay) abnormally increases but clinical examination does not support the diagnosis of acute myocardial infarction, laboratory personnel should be aware of the shortcomings of this method and use mass immunoassay to detect CK-MB to eliminate interference, and avoid unnecessary examinations and treatments for patients due to inaccurate results.**
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Correspondence:
Ningping Shan
Department of Clinical Laboratory Center
Shaoxing People's Hospital
Shaoxing 312000
P.R. China
Phone: +86 13957558155
Email: 553897163@qq.com

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KEYWORDS

CK-MB, polyethylene glycol, mass immunoassay

INTRODUCTION

Creatine kinase (CK) is a dimeric molecule composed of two independent M and B subunits, producing three isoenzymes: CK-BB, CK-MB, and CK-MM [1-2]. When myocardial infarction occurs, the serum CK-MB rapidly increases and is an important marker of myocardial injury [3]. We found a case of false elevation of serum CK-MB without evidence of myocardial injury. The specific situation is as follows:

CASE PRESENTATION

The patient is a 28-year-old male. On June 2, 2024, due to "back pain for 10 days" at Binhai Hospital, the cardiac machine biomarker indicators were CK 800 U/L and CK-MB 1,085.0 U/L. On June 5, 2024, the patient came to our hospital for a follow-up examination of myocardial markers: CK 853.8 U/L and CK-MB 1,053.6 U/L.

The patient was admitted due to back pain for 10 days and elevated myocardial markers. During hospitalization, multiple tests for CK and CK-MB were conducted, and the results were far beyond the normal reference range (Table 1). Simultaneously conducting electrocardiogram examination, CT chest plain scan (chest) examination, cardiac B-ultrasound examination, thyroid and neck lymph node B-ultrasound examination showed no obvious abnormalities. Coronary artery imaging examination suggests that there is no stenosis in the coronary lumen and no evidence of myocardial infarction. After admission, relevant examinations were completed. There were no abnormalities in troponin, blood routine, coagulation function, and anti nuclear antibodies.

The patient's lung CT showed no interstitial changes and the anti nuclear antibody spectrum was negative. The patient has no recent muscle pain or joint swelling or pain in the proximal limbs. Serum tumor markers of the patient are normal. After ruling out myocardial infarction, autoimmune myopathy, tumors, and exercise injuries, the clinical doctor was puzzled by the sustained elevation of myocardial markers in the patient and contacted laboratory staff.

After receiving this situation, the laboratory staff first checked the condition of the specimen on June 9th and ruled out the increase in results caused by hemolysis. Simultaneously evaluating the internal quality control of the biochemical analyzer during the testing period, it was found that there were no quality issues during the hospitalization of the patient. Therefore, false increases caused by instrument, reagent and human operation issues were excluded. We analyzed the report and found that CK-MB > CK. In theory, this possibility should not exist because CK includes three subtypes: CK-MB, CK-MM, and CK-BB. According to literature review reports, macro CK may cause a false increase in the results of CK-MB isoenzyme enzyme activity assay, leading to CK-MB > CK. So we sent the specimens to the testing platform of Shaoxing Traditional Chinese Medicine Hospital, who used CK-MB mass immunoassay to eliminate interference. After retesting, the result of CK-MB was 1.96 ng/mL (reference value: 0 - 5 ng/mL), which is within the normal range. Simultaneously, the patient's serum samples were pretreated with polyethylene glycol (PEG) to precipitate macro CK. After precipitation, CK and CK-MB significantly decreased, and CK even returned to the normal range (Table 1). Therefore, we speculate that the elevated CK-MB in the patient is a pseudo-elevation caused by macro CK.

DISCUSSION

There are three isoenzymes of CK in the cytoplasm: CK-MM, CK-MB, and CK-BB. CK-MM mainly comes from skeletal muscle, CK-BB mainly comes from the brain, and CK-MB mainly comes from the myocardium. CK-MB is one of the sensitive indicators of myocardial injury. When myocardial injury occurs, CK-MB is released from myocardial cells into the bloodstream, leading to an increase in serum CK-MB levels. In the process of myocardial injury, the increase of CK is mainly caused by the increase of CK-MB, manifested as a simultaneous increase of both.

In theory, CK-MB cannot be greater than CK, but in practical work, CK-MB may be greater than CK due to the measurement method. At present, the immunosuppressive assay is the most commonly used method for measuring CK-MB. The principle is that the CK isoenzymes in normal human blood are CK-MM, CK-MB, and a very small amount of CK-BB. Due to the negligible content of CK-BB, this method assumes that only CK-MM and CK-MB are present in the serum. During measurement, the addition of M subunit antibodies binds to the M subunit in the serum, causing it to lose activity. The remaining activity is mainly generated by the B subunit, and multiplying the result by 2 gives the activity of CK-MB. Therefore, when using this method to measure CK-MB, there may be two possible reasons for CK-MB being greater than CK: First, the abnormal increase in CK-BB was ignored, and the measured activity of the B subunit was the sum of the B subunits in CK-MB and the B subunits in CK-BB, multiplied by 2, resulting in a false increase in CK-MB and possibly greater than the total CK. Second, there is the presence of macro CK in the serum, which is usually a complex of CK-BB and IgG, cross-linked into a large complex containing a large number of B subunits and can resist the inhibition of M subunit antibodies. The activity of B subunits is multiplied by 2, leading to a false increase in CK-MB results [4].

Considering the shortcomings of this methodology, we sent the patient samples to a testing platform using mass immunoassay for testing, and the results were within the normal range, consistent with the patient's clinical manifestations. CK-MB mass immunoassay is a laboratory technique used to detect serum CK-MB mass concentration. It uses monoclonal antibodies targeting CK-MB, which have high specificity and can distinguish CK-MB from other isoenzymes. This method avoids the problem of false increase in CK-MB activity caused by the presence of CK-BB or macro CK in CK-MB activity determination [5]. Research has shown that the use of polyethylene glycol precipitation method can eliminate the interference of macro CK [6,7]. We also performed PEG preprocessing on the samples, and the CK and CK-MB results were significantly reduced, with CK dropping to the normal reference range. We speculate that this patient has a false increase in CK-MB due to the presence of giant CK1 in the serum.

In summary, this case emphasizes that laboratory staff should fully understand the limitations of the immunosuppressive assay for detecting CK-MB. When CK-MB abnormally increases and clinical diagnosis does not support acute myocardial infarction, it is necessary to be vigilant for the presence of macro CK or CK-BB and use the mass immunoassay or PEG precipitation method to eliminate interference and avoid misdiagnosis and

Table 1. The serum CK and CK-MB levels of patients during hospitalization (U/L).

	CK	CK-MB
June 5th, 2024	**853.8**	**1,053.6**
June 7th, 2024	**660.4**	**946.3**
June 9th, 2024	**586**	**903.7**
June 9th, 2024 (PEG treatment)	**109.9**	**145.3**
Reference range	**38 - 174**	**0 - 25**

unnecessary treatment.

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Declaration of Interest:
All authors declare that they have no competing interests.

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