Case Report

False-Positive Elevation of CK-MB Levels with Chest Pain in Lung Adenocarcinoma

Takayo Ota^a Yoshikazu Hasegawa^a Eriko Murata^b Noriko Tanaka^c
Masahiro Fukuoka^a

^aDepartment of Medical Oncology, Izumi City General Hospital, Izumi, Japan;

^bDepartment of Cardiology, Izumi City General Hospital, Izumi, Japan; ^cDepartment of Radiology, Izumi City General Hospital, Izumi, Japan

Keywords

Chest pain · CK-MB · Lung adenocarcinoma

Abstract

The creatinine kinase (CK)-MB assay can be used for the early diagnosis of acute coronary syndrome. We describe the case of an 82-year-old male with lung adenocarcinoma who presented with chest pain. While laboratory findings showed elevated CK-MB levels, there was no cardiac injury. A chest computed tomography scan revealed pleural carcinomatosis. Later, electrophoretic analysis of CK showed a normal CK-MB range but increased CK-BB levels and the presence of macro CK type 2. We determined that the patient's chest pain originated from the visceral pleural invasion of lung cancer. Because of the methods used to measure the CK-MB isozyme, the CK-MB level appeared elevated.

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Introduction

Creatinine kinase (CK)-MB is a CK isozyme that exists mostly in the myocardium, but 5–7% of this isozyme exists in skeletal muscle [1]. CK-MB is a useful cardiac marker for acute myocardial infarction. However, with the introduction of troponin, which is more sensitive and accurate than CK-MB for detecting cardiac injury, the measurement of CK-MB is no longer required, and several guidelines state that CK-MB is not useful for the diagnosis of acute coronary syndrome [2, 3]. We report a case of chest pain in a patient with lung adenocarcinoma in which the CK-MB level was increased, but cardiac injury was not confirmed.

Dr. Takayo Ota
Department of Medical Oncology
Izumi City General Hospital
4-5-1, Wake, Izumi 594-0073 (Japan)
takayo.ota@gmail.com

Fig. 1. ECG showing a normal sinus rhythm with no ST-segment changes.

Fig. 2. Chest CT scan showing left pleural thickening (white arrowheads; **A**) and enlarged lymph nodes (white arrows; **B**).

Case Report

An 82-year-old male with stage IV lung adenocarcinoma presented with worsening chest pain while lying in bed. He was hospitalized 2 days earlier because of general fatigue and loss of appetite after vinorelbine treatment (25 mg/m^2), which had been administered as a second-line therapy 22 days before hospitalization.

He had been suffering from chest pain for 1 week without seeking any medical help. He had a similar episode of worsening chest pain in the sternum approximately 8 h earlier at night during his hospitalization stay. Measurement of his vital signs at that time showed a blood pressure of 128/77 mm Hg, a heart rate of 72 beats/min with a regular pulse, and a SpO_2 value of 96%. Because his vital signs were stable, his condition was monitored, and no further testing was performed.

Fig. 3. Electrophoresis of serum CK showing increased CK-BB and macro CK type 2 levels, migrating cathodal to CK-MM (arrow).

During the second episode of chest pain, measurement of his vital signs showed a blood pressure of 144/85 mm Hg, a heart rate of 68 beats/min with a regular pulse, and a SpO₂ value of 96% when breathing room air. An immediate ECG showed no ST-segment changes (Fig. 1). A nitroglycerine tablet did not reduce the pain. Blood tests revealed increased total CK (547 U/L) and CK-MB (200 U/L) levels but normal levels of troponin I. An ECG showed neither hypokinesia nor akinesia of either ventricle. A chest computed tomography scan showed left pleural thickening and enlarged mediastinal lymph nodes (Fig. 2).

On day four after the second chest pain episode, his laboratory findings still showed elevated CK (579 U/L) and CK-MB (379 U/L) levels. Electrophoretic analysis of serum harvested on day four revealed that 2% of the total CK content was CK-MB, which was in the normal range, and CK-BB and macro CK type 2 levels were increased (Fig. 3). These results indicate that our patient's chest pain did not originate from cardiac injury but rather from lung adenocarcinoma metastasis. Subsequently, his chest pain was controlled by hydromorphone administration, as requested by the patient.

Discussion

CK is an enzyme involved in energy metabolism that catalyzes the phosphorylation of creatinine and adenosine triphosphate [1]. Cytosolic CK exists as a dimeric molecule with two subunits, M and B. Three CK isozymes exist: CK-MM is expressed mainly in skeletal muscle, CK-MB is expressed primarily in the myocardium, and CK-BB is expressed mostly in the brain.

Moreover, CK is present as a higher-molecular-weight form, called macro CK [4], for which two types exist, type 1 and type 2. Macro CK type 1 comprises a complex of CK isozymes and an immunoglobulin, while macro CK type 2 constitutes a mitochondrial CK polymer. Electrophoretically, macro CK type 1 is depicted as an anodal CK, migrating between CK-MM and CK-MB, and macro CK type 2 is depicted as a cathodic CK, migrating cathodal to CK-MB [5]. The prevalence of type 1 is 0.43–1.2%, and that of type 2 is 0.5–3.7% [4, 5]. Macro CK type 1 is mostly found in patients with autoimmune diseases, and type 2 is found in severely ill patients, particularly in those with malignancies. While the presence of macro CK type 2 in

lung cancer has been reported in the English literature, it is not stated whether these cases include lung adenocarcinoma [6, 7].

Abnormal serum levels of CK-BB are also often associated with neoplastic diseases. In lung cancer, increased serum CK-BB levels have been reported in cases of adenocarcinoma, small cell carcinoma, and squamous cell carcinoma [8, 9]. The serum level of CK-BB is substantially increased in small cell carcinoma compared to that in other histological types of cancer [9]. The extent to which the serum CK-BB level increase is correlated with the number of metastatic sites, and a significant association exists between clinical response to therapies and serum CK-BB levels [10].

Increased levels of CK isozymes originate from tissues. Electrophoretic analyses of serum and lung cancer homogenate show the same patterns of CK-MB and CK-BB levels, indicating the tumor as the source of atypically increased CK isozyme levels [11].

In the present case, the laboratory findings showed increased serum CK and CK-MB levels. On the other hand, electrophoresis showed a standard range of CK-MB and elevated CK-BB and macro CK type 2 levels. CK-MB is measured by immuno-inhibition methods in which the M component is inactivated by an anti-M antibody, which leaves the B component active [12] (Cica Liquid CK-MB, Kanto Chemical Co., Inc.). By this method, after inactivating the M component, the remaining CK activity is doubled, which reflects a final CK-MB activity. CK-BB activity is thought to be initially inactive, and an anti-M antibody blocks CK-MM; the remaining CK activity is only from CK-MB. Since the M component is blocked, the CK-MB activity is halved. Hence, if some component is not able to be inactivated by anti-M antibodies, such as CK-BB or macro CK, the calculated CK-MB does not represent an accurate CK-MB activity.

In summary, we report the case of a patient with chest pain for whom the obtained results were confusing because of elevated CK-MB levels. The patient's chest pain did not originate from cardiac injury but rather from lung adenocarcinoma metastasis. When evaluating chest pain in malignancy, it is crucial to verify the origin, and not to rely on the CK-MB level only.

Statement of Ethics

The patient provided written informed consent for the publication of this case report and any accompanying images.

Disclosure Statement

We declare no conflicts of interest.

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Author Contributions

T.O. drafted the manuscript. All authors were involved in the patient management and critically reviewed the manuscript.

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