Hypothermic Myxedema Coma错误诊断为心肌梗死因为CREAST Kinase MB

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As is well recognized, activities of creatine kinase (CK, EC 2.7.3.2) and lactate dehydrogenase (EC 1.1.1.27) in plasma may be substantially increased in hypothyroidism. We emphasize here that an increase and decrease in CK-MB isoenzyme, characteristic of acute myocardial infarction, can occur in hypothyroid myxedema coma without myocardial infarction.

Additional Keyphrases: thyroid status - isoenzymes

Accurate diagnosis of acute myocardial infarction may be confounded by the absence of a classical history and the lack of specificity of electrocardiographic changes (1). The finding of increased activity of creatine kinase (CK, EC 2.7.3.2) MB isoenzyme (CK-MB) is important in confirming the diagnosis and assessing infarct size and prognosis.

We report a case of hypothermic myxedema coma in which extensive myocardial infarction was erroneously diagnosed on the basis of a characteristic pattern of this isoenzyme.

Case Report

A 70-year-old woman was admitted, having been found unconscious at home. No history was available from the patient, but a relative described a general deterioration in the patient over the previous few weeks without noticeable specific problems. Past medical history was not relevant; specifically, there was no history of cardiac or thyroid disease and no recent surgery. She had not been taking any medication and did not drink alcohol.

The outside temperature on the day of admission ranged from −0.8 to −5.5 °C. On examination the patient was found to be hypothermic (rectal temperature 28.2 °C). She was shivering, conscious but drowsy, and her speech was unintelligible. Her pulse rate was 40/min and regular. Arterial blood pressure was 24/16 kPa (180/120 mmHg), heart sounds were normal, jugular venous pressure was not increased but bilateral ankle edema was present. Some fine respiratory crepitations were audible over the lung bases. The abdomen was soft, and bowel sounds were present. There were no focal neurological signs. Plantar responses were flexor. The primary diagnosis was accidental hypothermia and passive rewarming was begun. Results of routine hematological and electrolyte evaluations at admission were within normal limits, as was a chest roentgenogram.

The initial electrocardiograph showed a sinus bradycardia with shivering artifact. Low-voltage complexes were present throughout and there was T-wave inversion in leads II, III, AVF, and V1–V6. There were no J waves. Blood was taken for estimation of CK activity and thyroxin and thyrotropin concentrations.

During the next few hours the patient’s temperature gradually increased, and she became more alert. Further details of her recent history became available from relatives who described episodes of bizarre behavior, compatible with a diagnosis of "myxedema madness." Primary hypothyroidism was confirmed by the serum thyroxin concentration, 16 nmol/L (reference interval 60–135) and a thyrotropin concentration of 72 int. units/L (0.5–5.5). Oral treatment with 25 μg of thyroxin per day was commenced on the day after admission.

CK activities estimated 2 and 24 h after admission were 7698 and 3246 U/L for total CK and 831 and 471 U/L for CK-MB (10% and 16% of total CK, respectively). Total CK activity was measured in a centrifugal analyzer at 37 °C (CK-NAC optimized; Boehringer Corp. Ltd.); CK-MB activity was measured with the same reagents after immunoinhibition and immunoprecipitation (Isomune CK; Roche Diagnostics Ltd.) to remove interference from CK-BB or atypical forms of CK.

The increased activities of CK, combined with the initial electrocardiograph changes, suggested a diagnosis of acute myocardial infarction. Subsequent electrocardiographs, however, showed a generalized flattening of the ST segments, upright T waves, and no Q waves. Despite the extremely high activities of CK, heart failure did not occur. The patient made a full recovery and was discharged home. At follow-up she remains well, and an echo-cardiogram and resting cardiac scan with thallium show no evidence of myocardial infarction.

Discussion

The demonstration of a rise and fall in CK-MB isoenzyme within 48 h is considered a sensitive and specific indicator of acute myocardial infarction (2, 3), a cardiac origin being assumed when the MB fraction exceeds 5% of total CK activity.

There are many causes of above-normal activities of total CK and CK-MB (5–8) in serum: exercise, trauma, surgery, fits, hyperpyrexia, pneumonia, stroke, carcinomas of the bronchus and colon, and poisoning by aspirin-like drugs, theophylline, alcohol, or carbon monoxide. In all cases, the enzyme in the serum is believed to come from skeletal muscle. Normally, the MB fraction constitutes less than 5% of the total CK activity in serum.

Total CK was first shown to be significantly increased in hypothyroidism in 1963 (9). Activities up to 16 000 U/L have been reported in myxedema (10). The predominant isoenzyme is CK-MM; enhanced permeability of the muscle cell
membrane is believed to cause loss of cytosolic enzymes into the plasma (11). A small increase in immunoreactive CK-B subunit concentration has been observed in primary hypothyroidism, which is attributed to efflux of CK-MB from cardiac muscle fibers or diminished clearance from the circulation (12). However, CK-MB is present in skeletal muscle in variable amounts, depending on the fiber type (13), and skeletal muscle CK-MB can increase the CK-B concentration or CK-MB activity in plasma to above normal when total CK exceeds the upper limit of the reference range by more than three- to five-fold (14).

Myocardial damage is known to complicate accidental hypothermia, leading to high total-CK concentrations in plasma (15). Experimental hypothermia in anesthetized dogs led to a myocardial loss of the enzyme during rewarming (16), and high activities of CK-MB (up to 32% of total CK) have been reported in six patients with hypothermia who had no clinical or postmortem evidence of myocardial infarction (16). It is thought that the myocardium is involved in a diffuse ischemic process in hypothermia and that cytosolic enzymes leak across myocardial as well as skeletal muscle cell membranes. The efflux of enzymes from myocardial cells does not occur after hypothermic cardioplegic cardiac arrest procedures, probably because continued cardiac work during hypothermia is necessary for myocardial injury to occur (17).

This case demonstrates that the presence of electrocardiographic abnormalities and increased activities of CK-MB isoenzyme in patients with myxedema and hypothyroidism do not necessarily indicate acute myocardial infarction.

References