Short reports

Raised concentration of plasma creatine kinase BB isoenzyme in myelodysplasia

M Crook, A Williams, A Sankaralingam, P Tutt

Abstract

A 72 year old woman presented with a suspected myocardial infarction. An echocardiograph showed no acute changes but her plasma creatine kinase (CK) activity was increased at 343 U/l (<175 normal range). The apparent creatine kinase-MB activity by a CK-M subunit immunoinhibition assay was 350 U/l. In view of the discrepancy between the total creatine kinase and CK-MB activity plasma creatine kinase electrophoresis studies were performed which showed not only a band of creatine kinase-MM but also a band of creatine kinase-BB, 53% of the total creatine kinase activity. No band of CK-MB was seen. It later transpired that the woman had myelodysplasia. It is suggested that premalignant and malignant haematological conditions should be considered in patients with an unexplained increase in plasma CK-BB.

(*J Clin Pathol* 1994;47:552-553)

The enzyme creatine kinase [EC 2.7.3.2] is a dimeric molecule consisting of two separate subunits which may be either B or M. Three isoenzymes are usually found in plasma—namely, CK-BB, CK-MB, and CK-MM. Most of the plasma creatine kinase is the MM isoenzyme derived from skeletal muscle, while the CK-MB fraction, originating predominantly from cardiac muscle, is increased in myocardial infarction. However, normally there is little of the CK-BB isoenzyme present in serum.

Case report

A 72 year old woman was admitted to hospital with severe breathlessness due to pulmonary oedema secondary to cardiac failure. A myocardial infarction was suspected. An echocardiograph showed no acute changes but her plasma creatine kinase was increased at 343 U/l (normal range <175). The apparent CK-MB activity determined by a CK-M subunit immunoinhibition assay was 350 U/l. In view of the discrepancy between the total creatine kinase and CK-MB activity we performed plasma creatine kinase electro-

phoresis studies which showed not only a band of CK-MM but also a band of CK-BB, which was identified on the basis of its electrophoretic mobility and its resistance to CK-M antibodies. The CK-BB was quantified and found to be 53% of the total CK activity. No band of CK-MB was seen.

The patient was not receiving medication before admission and she had normal renal, liver, and thyroid biochemical function tests. Her pulmonary oedema was treated with diuretics and she made a quick recovery.

It later transpired that the patient had been diagnosed before with myelodysplasia. This diagnosis had been made following a full blood count which showed a haemoglobin concentration of 140 g/l, a white cell count of $22.6 \times 10^9/l$ (neutrophils $13.1 \times 10^9/l$ lymphocytes $2.03 \times 10^9/l$ monocytes $1.36 \times 10^9/l$, eosinophils $0.68 \times 10^9/l$ basophils $0.90 \times 10^9/l$ metamyelocytes $3.39 \times 10^9/l$ and myelocytes $1.13 \times 10^9/l$ and platelets $389 \times 10^9/l$. Furthermore, a bone marrow aspirate was hypercellular with an increase in myeloid cells but no excess of blast cells. A trephine biopsy specimen had confirmed hypercellularity, but there was no increase in reticulin. Cytogenetic studies showed no abnormality.

A few months later she was reviewed in the haematology outpatients department and a plasma total creatine kinase determination was 49 U/l but plasma creatine kinase electrophoretic studies again showed a high proportion of the CK-BB isoenzyme, this time being 56% of the total creatine kinase activity.

Methods

Plasma creatine kinase total activity and CK-MB (by immunoinhibition) were measured on a Kodak Ektachem analyser (Kodak, Welwyn, Herts, England). Blood counts were performed on a Sysmex E3000. Plasma creatine kinase electrophoresis was performed on agarose gels (Corning, Halstead, Essex, England) and the bands of creatine kinase activity visualised using total creatine kinase (NAC) and CK-MB (NAC) reagents from Merck (Poole, Dorset, England); the latter contained antibodies to the CK-M subunit. Quantitation of the fluorescent bands of enzyme activity was performed using a Corning (Halstead, Essex, England) densitometer.

Department of
Clinical Chemistry,
5th floor tower, Guy's
Hospital, London,
SE1 9RT
M Crook
A Sankaralingam
P Tutt

Department of
Haematology
A Williams

Correspondence to:
Dr M Crook

Accepted for publication
14 December 1993

Discussion

The CK-MB determination on the Ektachem uses an immunoinhibition method. Here an antibody to the CK-M subunit inhibits its activity in both CK-MM and CK-MB isoenzymes. Residual creatine kinase activity is then multiplied by 2 to give the CK-MB activity, the assumption being that there is negligible CK-BB activity present and that the M and B subunits have the same enzyme activity. The spuriously high "apparent" plasma CK-MB activity alerted us to the possibility of the presence of CK-BB in the sample.

We suggest that the explanation for this woman's increased plasma CK-BB is her myelodysplasia which is considered a pre-malignant haematological condition. In a review by Griffiths¹ CK-BB was reported to be increased in several malignant conditions. Another study by Rubery and co-workers² found that CK-BB was raised in about 34% of patients with malignant disease while Abbott and Lott³ found raised serum CK-BB in patients with acute myeloid leukaemia and

chronic lymphocytic leukaemia. Changes in cell differentiation seem to result in the increased production of CK-BB which could possibly be useful as a tumour marker.⁴

In conclusion, we report increased total plasma creatine kinase in a woman with myelodysplasia, which was mainly the CK-BB isoenzyme. Spuriously high apparent CK-MB activities, using an immunoinhibition method, should alert biochemistry staff to the possible presence of non-CK-M activity. Premalignant and malignant haematological conditions should be considered in patients with an unexplained increase in plasma CK-BB.

- 1 Griffiths JC. Creatine kinase isoenzyme. *Clin Lab Med* 1982;2:493-506.
- 2 Rubery ED, Doran JF, Thompson RJ. Brain type creatine kinase BB as a potential tumour marker. *Eur J Cancer Clin Oncol* 1982;18:951-6.
- 3 Abbott LB, Lott JA. Reactivation of serum creatine kinase isoenzyme BB in patients with malignancies. *Clin Chem* 1984;30:1861-3.
- 4 McGing PG, Teeling M, McCann A, Kyne F, Carney DN. Non-M CK, a practical measure of creatine kinase isoenzymes in cancer patients. *Clin Chim Acta* 1990; 187:309-15.