Cardiac Enzymes and Hypothyroidism

To the Editor:

We recently described the case (1) of a 74-year-old man admitted to hospital with hypothyroidism and in myxedema coma. His plasma cardiac enzyme activities, as measured at admission and on serial measurement thereafter, raised the possibility of acute myocardial infarction. Total creatine kinase (CK) activity was above normal, as were both the activity and proportion of the relatively myocardial-specific CK-MB isoenzyme. The CK activity declined in a manner consistent with myocardial infarction. However, aspartate aminotransferase (AST) and lactate dehydrogenase (LD) activities declined more slowly than seen in myocardial infarction. Because other investigations of his cardiac status were negative, we concluded that he had not suffered a myocardial infarction, but rather that the increased activity and proportion of CK-MB represented ectopic synthesis in skeletal muscle. Although we favored a hypothyroid myopathy as the cause of his enzyme changes, we could not completely exclude hypothermia as the cause of the observed changes. One month after the commencement of thyroid-replacement therapy, enzyme activity and thyroid function were all within normal limits.

Six months after therapy commenced, this patient was seen in the Outpatient Clinic. He admitted that he had recently ceased taking his thyroid medications. He was not hypothermic and investigations performed at this time revealed (normal values in parentheses):

- CK (25–200 U/L) 241 U/L
- CK-MB (by immunoinhibition, U/L) 19 U/L
- CK-MB (electrophoresis, <5%)
- LD (110–200 U/L) 196 U/L
- LD1:LD2 (<0.75) 0.82
- Thyroxin (70–140) 48 nmol/L
- Thyrotropin (<5 milli-int. units/L) 46 milli-int. units/L

Results of an electrocardiogram made at this time were normal.

Three weeks after recommencing thyroxin, his CK had decreased to 104 U/L and his CK-MB to 6 U/L. His thyroxin concentration in plasma was 77 nmol/L and the thyrotropin concentration was still slightly above normal, 10 milli-int. units/L.

Thus in the presence of normal body temperature we have evidence of increased synthesis of CK-MB in skeletal muscle. We conclude that the high activity and proportion of CK-MB observed on this occasion were due solely to the hypothyroid myopathy. These findings suggest that the abnormal enzyme patterns seen at the time of his admission in myxedema coma were caused predominantly by the hypothyroid myopathy rather than the associated hypothyromatia.

Reference


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Increased Diagnostic Potential of a Monoclonal Assay of Carcinoembryonic Antigen

To the Editor:

In a recent comparison (1) of two new commercial kits for measuring carcinoembryonic antigen (CEA), the authors indicate that use of a monoclonal method may make CEA analysis more sensitive in the diagnosis and monitoring of colorectal carcinoma compared with polyclonal methods. We would like to present some data supporting this hypothesis.

We compared the Abbott CEA RIA, a monoclonal-antibody-based assay, with an in-house radioimmunoassay, using samples from 53 patients (mean age 66 y, range 37 to 88 y) with clinically and histologically confirmed colorectal carcinoma and 12 patients (mean age 55 y, range 29 to 73 y) with other forms of cancer (nine gastric, two breast, and one ovarian). The in-house method was a double-antibody technique based upon a previously described method (2). We used only patients' sera with increased in-house CEA values >30 μg/L (in-house reference interval: <15 μg/L). The CEA values determined by the in-house method are different from usually quoted figures, because these figures were assigned before an international reference standard became available.

Increased CEA values can also be seen in smokers, and in patients with liver diseases, ulcerative colitis, and several other disorders. However, CEA values exceeding five times the upper limit of normal are usually only seen in cancers of the gastrointestinal tract. For the in-house assay this would be >75 μg/L, and for the Abbott assay (reference interval: <3 μg/L), >15 μg/L.

The aims of this comparison were (a) to establish whether more or fewer patients would be in the "grey area" of diagnosis and (b) to monitor and estimate any difference in the percentage increases in CEA, depending on the method used.

On comparing the two methods, we found that the in-house method produced "grey area" results in 31 patients with colorectal cancer, compared with only 19 patients with the Abbott assay (Figure 1a). Therefore, we found a greater number of patients with unequivocally increased values if we used the Abbott assay instead of the in-house assay—which may indicate that the monoclonal kit could be a more sensitive indicator of disease. In other forms of cancer, we found no difference in the number of unequivocally in-
increased CEA results. CEA was not determined on any samples with in-house CEA values <30 μg/L; therefore, the Abbott assay could be even more sensitive than was initially thought.

Generally, values measured with the Abbott assay were relatively higher than those with the in-house assay in patients with malignancies (Figure 1b), possibly because of a lower background nonspecificity with the monoclonal kit. This may mean that more dramatic changes in CEA will be seen when cases are followed up.

Possibly the broader specificity of a polyclonal assay could give rise to a greater number of increased values in cancer patients. Indeed, two patients with colonic tumors and five patients with other tumors had normal CEA values when measured by the Abbott assay but increased values by the in-house method. However, in all seven patients CEA values were only slightly increased, i.e., were "grey area" results. Thus, any diagnostic potential of using a polyclonal assay would be offset by the uncertainty in interpreting slightly increased CEA values. We are currently collecting further data that support this idea, evaluating more than 800 patients in whom we have measured CEA by a polyclonal method and the Hybritech monoclonal assay. Only one patient has shown significantly increased CEA values (i.e., more than fivefold the upper reference limit) by the polyclonal assay and a normal value by the monoclonal assay.

References


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