Case Report: Changes in Creatine Kinase Isoenzymes after Myocardial Infarction in a Patient with Prostatic Carcinoma

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The detection of serum proteins that can serve as tumor markers has been reported with increased frequency in patients with various localized or metastatic cancers. Many of these reports have concerned patients with prostatic carcinoma, who had normal or increased concentrations of creatine kinase (EC 2.7.3.2) in serum. In many instances the creatine kinase BB isoenzyme was increased in these patients. I describe the case of a patient with carcinoma of the prostate (stage D), who had a myocardial infarction three to four days after admission. The serum activity of the MM, MB, and BB isoenzymes changed markedly after the infarction. These changes and the possible tissue source(s) of this isoenzyme are discussed in relationship to the clinical symptoms of the patient.

Since the development of relatively rapid and sensitive electrophoretic and column-chromatographic techniques for the separation of creatine kinase (CK; EC 2.7.3.2) isoenzymes, several reports have appeared relating the presence of the BB isoenzyme in serum to a variety of disease processes. Increased serum concentrations of this isoenzyme have been found in malignant hyperthermia (1), chronic renal failure (2, 3), brain damage (4), cardiac surgery (5), critical-care patients (6), and pregnant and post-partum patients (3, 7). Recently, increased amounts of BB in serum have been reported in patients with cancer, including gastric carcinoma (8, 9), metastatic carcinomas of the breast and colon (10), oat-cell carcinoma of the lung (9, 11), and prostatic carcinoma with and without metastases (9–16).

This report concerns a patient who was admitted with stage D metastatic carcinoma of the prostate and suffered a myocardial infarction shortly after entering the hospital.

Case Report

The patient was a 69-year-old black man diagnosed three years earlier, after a transurethral resection, as having carcinoma of the prostate with distant metastases (stage D disease). Roentgenograms revealed metastases to the ribs, and estrogen (5 mg of diethylstilbestrol per day) and radiation therapy were instituted. Thirty-two months later the patient was admitted to the hospital in a weakened condition, complaining of nausea, vomiting, and increased bone pain. Roentgenograms showed metastases to the ribs, clavicles, and pelvis. An electrocardiogram showed occasional premature atrial and ventricular contractions compatible with anterior ischemia. Hematologic values were characteristic of a chronic anemia with a hemoglobin of 59 g/L. The chemistry profile taken at admission showed calcium, 70 mg/L; total protein, 52 g/L; albumin, 23 g/L; alkaline phosphatase (EC 3.1.3.1), 1265 U/L (normal, 90–200 U/L); aspartate aminotransferase (EC 2.6.1.1), 63 U/L (normal, 10–50 U/L); and lactate dehydrogenase (EC 1.1.1.27), 340 U/L (normal, 90–200 U/L). The serum iron value was normal, with a decreased total iron-binding capacity and folic acid concentration. Serum ferritin was markedly increased to 1400 μg/L (normal, 20–200 μg/L).

The patient was given meperidine hydrochloride for pain and oral potassium chloride for a mild hypokalemia. Two units of packed cells were transfused on the first and third days after admission without evidence of a reaction. The fourth day after admission the patient developed a rapid pulse, hypotension, and clinical symptoms suggestive of congestive heart failure. An electrocardiogram on the afternoon of the fourth day revealed signs of a recent antero-septal myocardial infarct. Analysis of blood drawn at this time showed a total CK activity of 243 U/L (normal, <112 U/L) with increased MM, MB, and BB isoenzymes. Lactate dehydrogenase and aspartate aminotransferase were increased to 1310 U/L and 128 U/L, respectively. On the fifth day after admission, the patient showed signs of mild renal failure secondary to congestive heart failure. The condition of the patient deteriorated for the next 15 days with periods of mental confusion and loss of consciousness. On the twentieth day after admission, the patient died. An autopsy was not performed.

Materials and Methods

CK and lactate dehydrogenase isoenzymes were separated on cellulose acetate with the Helena electrophoresis system (Helena Labs., Beaumont, TX 77704). The isoenzyme bands were made visible with ultraviolet light; the relative percentages of each fraction were determined by using a scanning densitometer ("Quick Quant II", Helena). A CK–lactate dehydrogenase isoenzyme control was obtained from Helena Labs. Total creatine kinase was measured with an ABA-100 analyzer (Abbott Labs., South Pasadena, CA 91030) and the Abbott A-gent reagent. Chemistry admission profile values were measured with the SMA 12/60 analyzer (Technicon Corp., Tarrytown, NY 10591). Serum iron and total iron-binding capacity were determined with the Hyland Ferro-Chek II kit (Hyland, Div. Traveln Laba., Costa Mesa, CA 92626). Folic acid and ferritin were measured by radioimmunoassay.

Results

Figure 1 shows increases in all three CK isoenzymes in serum obtained on the afternoon of the fourth day after admission, compared with patterns obtained from a control and from an apparently normal individual. The BB isoenzyme accounted for about 47% and the MB 7% of the total CK activity (243 U/L), as shown in Figure 2. MB isoenzyme values that exceed 5% of the total CK activity are considered abnormal in this laboratory. No MB and BB isoenzymes are
detected by this method in serum obtained from normal individuals. On the seventh day after admission or about three days after the myocardial infarction, total CK activity was essentially unchanged (228 U/L); however, the MB activity had decreased to 3% and the BB to 9.3% (Figure 2). The total lactate dehydrogenase activity increased to 1310 U/L on the fourth day and decreased to 725 U/L on the seventh day after admission. Quantitation of the lactate dehydrogenase isoenzymes in serum obtained on the seventh day showed increased relative percentages of fractions four and five.

Discussion

Several recent reports have shown that the BB isoenzyme is increased in the serum of patients with metastatic cancer of tissues of endodermal origin (8–16). Increased serum BB isoenzyme has been reported in patients with all stages of carcinoma of the prostate (9–16). Patients with benign prostatic hypertrophy have also been found to have increased concentrations of BB isoenzyme (16). In an investigation of 19 patients with stage D prostatic carcinoma, nine had increased BB isoenzyme activity ranging from 10 to 81% of the total serum CK activity (12); only three of these nine patients had increased total CK activity, and none had an increase in the MB isoenzyme. A more recent study of 109 patients with prostatic cancer showed increased concentrations of immunoreactive BB isoenzyme in four of 25 patients with stage B disease, two of 35 patients with stage C disease, and 12 of 46 patients with stage D disease; three patients with stage A disease had normal BB isoenzyme concentrations, and all had normal total CK activities (15).

The patient I have described had marked changes in all three CK isoenzymes within one week after admission. His increased total CK activity and unusually large increase in the BB isoenzyme are similar to values reported in three patients with stage D disease (12). Quite possibly, MM and BB isoenzymes were increased in this patient for some time before the myocardial infarction; myocardial damage could have contributed to these increases. Evidence that myocardium contains BB isoenzyme has been conflicting. Two studies have shown that myocardium contains BB isoenzyme activity up to 14% of the total CK activity present in this tissue (17, 18). Others have found minimal or no BB isoenzyme activity in myocardium (19, 20). Serum BB isoenzyme concentrations have been reported to be increased in myocardial infarction, congestive heart failure, cardiomyopathy, and prolonged atrial fibrillation (5, 6). Increased BB isoenzyme has been found postoperatively in the sera of patients undergoing cardiac surgery (5, 6, 13, 18, 20, 21); however, these concentrations are relatively low and in one study were reported to average 10% of the total CK activity (18).

The marked decrease in the BB and increase in the MM isoenzyme activities observed in this patient after a myocardial infarction have not been reported previously in other patients. However, similar changes in the BB isoenzyme activity have been noted in patients undergoing cardiac surgery. In many of these patients the serum BB isoenzyme activity was increased immediately after surgery, with a rapid decrease to normal activity by the fourth postoperative day (5). Although significant increases in serum BB isoenzyme have been reported in patients with myocardial infarction (4, 5, 18), none of these studies have measured the rate of disappearance of the isoenzyme in serum after the infarction. These findings suggest that the myocardium may contain BB isoenzyme that is released into body fluids after insult or tissue damage, which could explain the changes observed in BB isoenzyme activity in this patient three to four days after the infarction. The fourfold increase and decrease in serum lactate dehydrogenase activity after the infarction probably reflect a release of this enzyme from myocardium, although other tissues may be involved. The increased relative percentages of lactate dehydrogenase isoenzymes 4 and 5 in serum obtained on the seventh day after admission are characteristic of, but not specific for, metastatic carcinoma of the prostate (22).

BB isoenzyme has been isolated from brain, lung, kidney, thyroid, bladder, stomach, and prostate (23, 24). This isoenzyme has been found in tissue homogenates of cancerous prostate tissue (9, 14) and in bone marrow serum (11). Prostatic tissue must be capable of producing relatively large amounts of the BB isoenzyme, because a recent study (16) has shown that prostatic fluid obtained from two benign prostate glands contained 50 mg of immunoreactive BB isoenzyme per liter, a 10,000-fold increase above concentrations found in normal serum. In this same study BB isoenzyme was identified in the cytoplasm of both benign and malignant prostate epithelium by means of an immunoperoxidase-staining proce-
dure. Also, 18 patients with metastatic prostatic carcinoma, who were being given chemotherapy and were in remission, did not have increased concentrations of immunoreactive BB isoenzyme in their serum (16). This and other evidence supports the belief that malignant prostatic tissue is an important source of the BB isoenzyme in body fluids. The contribution that distant metastases in other tissues might make is not known.

Cancer of the prostate is the second or third leading cause of death due to cancer in men in the United States (25). Unfortunately, most diagnoses of prostatic carcinoma are made in the later stages of the disease. Laboratory tests are not available that are sensitive and specific enough to establish a diagnosis in all patients with early prostatic carcinoma. Recent tests such as the radioimmunoassay of both prostatic acid phosphatase (26) and a newly discovered protein secreted by the prostate (27) may improve diagnostic capability in the laboratory. The detection of increased serum concentrations of BB isoenzyme is not specific for prostatic carcinoma and lacks sensitivity. However, the increasing number of reports concerning the localization of the BB isoenzyme in cancerous tissue and the presence of this isoenzyme in the serum of many cancer patients justifies further study of this protein as a possible tumor marker.

References