Increased Activities of Creatine Kinase and Lactate Dehydrogenase Isoenzymes in a Patient with Metastatic Ovarian Tumor

Ronald H. Ng, Sukumar Ethirajan, Mary O'Neill, and Bernard E. Statland

A 50-year-old woman with metastatic rhabdomyosarcoma of the ovary had increased activities of creatine kinase (CK; EC 2.7.3.2), CK-MB isoenzyme, lactate dehydrogenase (LD; EC 1.1.1.27), and LD-2 isoenzyme in her serum. The isoenzyme activities did not show a pattern of increasing, then decreasing. Clinical findings, including electrocardiograms, did not support the diagnosis of myocardial infarction. We suggest that high activities of CK-MB and LD-2 in serum may serve as a marker of rhabdomyosarcoma.

Additional Keyphrases: myocardial infarction · rhabdomyosarcoma · electrophoresis · agarose · cancer

Increased activities of creatine kinase (CK; EC 2.7.3.2) MB and lactate dehydrogenase (LD; EC 1.1.1.27) 1 isoenzymes are regarded as highly diagnostic for acute myocardial infarction (1). However, recent studies indicate that CK-MB may be increased in patients without cardiac disorders (2–5), in healthy subjects after prolonged and strenuous exercise (6, 7), and in patients with cancer (8–11). Here we report a case of high CK-MB activity in serum, associated with metastatic rhabdomyosarcoma of the ovary and without clinical evidence of myocardial infarction. Interestingly, the LD-2 activity in serum was also increased in this patient.

Case Report

A 50-year-old woman was admitted to the hospital because of abdominal pain and abdominal distention that had lasted for three weeks, and a tender right-lower-quadrant mass. Computed tomographic (CT) scans of the abdomen revealed a large, poorly marginated mass filling the pelvis and extending to the umbilicus. The mass was not clearly separable from the anterior abdominal wall. An exploratory laparotomy revealed a ruptured ovarian mass—pale-white to pink, smooth, and slightly lobulated, with areas of congestion. The tumor and the ovary were surgically removed. Light microscopy of the removed tissue revealed a mixed mesodermal tumor with undifferentiated papillary adenocarcinoma and a rhabdomyosarcomatous component.

After surgery, the patient was treated intraperitoneally with cisplatinum, but showed signs of acute renal failure after the chemotherapy and required renal dialysis. One month later, surgery was performed again, to remove the uterus and metastasized, disseminated tumor in the abdomen. Histological studies again showed a mixed mesodermal tumor, the predominant component being a rhabdomyosarcoma, as was confirmed by electron microscopic analysis. The patient was in poor clinical condition during the entire hospital course. Two weeks after the second surgery, she experienced a sudden onset of dyspnea, chest pressure, and sinus tachycardia. Multiple determinations of CK- and LD-isoenzyme activities (Table 1) were requested. Electrocardiograms showed ST changes that were not specific for a diagnosis of acute myocardial infarction. Pulmonary angiograms revealed a pulmonary embolus, which probably caused the patient’s symptoms.

After three weeks of worsening clinical conditions, including sepsis and hematologic and pulmonary problems, the patient died from respiratory failure. No autopsy was performed.

Materials and Methods

CK and LD activities in serum were assayed at 37 °C with the RA-1000 "random-access" analyzer (Technicon Instruments Corp., Tarrytown, NY 10691). The RA-1000 method for CK is based on that reported by Rosalki (12), but modified by the addition of N-acetylcycteine and P1-P5-diadenosine-5’-pentaphosphate. The RA-1000 LD method is based on that reported by Amador et al. (13), but modified by use of Tris buffer. CK- and LD-isoenzymes were measured by electrophoresis on agarose plates (Ciba-Corning Diagnostics Corp., Medfield, MA 02052).

Results and Discussion

Table 1 shows CK, LD, and the corresponding isoenzymes in serum samples collected at the onset of the patient’s dyspnea, chest pressure, and sinus tachycardia. Total CK activity was slightly increased in most of the specimens; the proportion of CK-MB was greatly and consistently increased in all specimens tested, but without the pattern of an increase and decrease that is characteristic for myocardial infarction. Total LD activity was highly increased; the proportion of LD-2 was increased, but LD-4 and LD-5 were approximately at the lower limit of the reference range. The LD-1/LD-2 ratio was consistently 0.6.

No clinical evidence of myocardial infarction was seen in this patient to account for the increase in CK-MB. Persistent increases of CK-MB in serum have been reported in several patients with metastatic tumors, i.e., poorly differentiated adenocarcinoma of the colon (8), lung carcinoma (9), prostatic cancer (10), and rhabdomyosarcoma (11). Current reports indicated that 20% to 40% of the myocardial CK is of the MB form. Serum CK-MB is <40% of total CK, even in most pathological conditions; in malignancies, however, it may exceed 50% (8, 10, 11). Thus, a highly increased proportion of CK-MB, 43% to 62% in our patient’s case, suggests ectopic production by a tumor. Although we did not measure the CK-MB of our patient’s specimens by a specific immunological CK-MB assay, it is unlikely that the serum CK-MB, >50% of the total CK when measured by electrophoresis—and from a patient with rhabdomyosarcoma—was attributable to a variant CK isoenzyme.

Malignant diseases are usually associated with increased LD activity in serum. Occasionally, the isoenzyme pattern of the increase in LD may reflect the organ affected by the malignancy, but most often it shows only a nonspecific
increase in the slow-moving forms (LD-4 and LD-5), suggesting that the tissue has regressed into producing the more embryonic, anaerobic types of LD \(8, 14\). An unusual exception to this is the substantial increase in LD-1 in germ-cell tumors. Furthermore, in a report on exudative effusions, the LD-2 activity in fluids obtained near or adjacent to malignancies was high in about 33% of cases, in half of whom LD-2 exceeded 35% of the total LD activity \(14\).

To our knowledge, there is only one other report \(11\) of increased CK-MB activity (29% to 64% of total CK) in a patient with rhabdomyosarcoma; the LD-isoenzyme pattern was not mentioned. Our findings suggest that increases in CK-MB and LD-2 to >40% of the total activity of their respective enzymes may serve as a marker of rhabdomyosarcoma.

## Table 1. Serum CK and LD Activities in Our Patient

<table>
<thead>
<tr>
<th>Date of assay (1986)</th>
<th>CK, U/L</th>
<th>CK-MB, %</th>
<th>LD, U/L</th>
<th>LD-1</th>
<th>LD-2</th>
<th>LD-3</th>
<th>LD-4</th>
<th>LD-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/14</td>
<td>228</td>
<td>36.0</td>
<td>1434</td>
<td>25.2</td>
<td>41.7</td>
<td>20.0</td>
<td>6.6</td>
<td>6.5</td>
</tr>
<tr>
<td>8/15</td>
<td>229</td>
<td>38.3</td>
<td>1370</td>
<td>26.3</td>
<td>43.5</td>
<td>19.4</td>
<td>5.6</td>
<td>5.2</td>
</tr>
<tr>
<td>8/16</td>
<td>190</td>
<td>44.5</td>
<td>1330</td>
<td>26.4</td>
<td>43.5</td>
<td>19.4</td>
<td>5.8</td>
<td>5.0</td>
</tr>
<tr>
<td>8/17</td>
<td>178</td>
<td>49.2</td>
<td>1152</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8/19</td>
<td>173</td>
<td>54.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8/26</td>
<td>292</td>
<td>62.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8/28</td>
<td>276</td>
<td>43.1</td>
<td>1488</td>
<td>17-27</td>
<td>28-36</td>
<td>19-27</td>
<td>5-16</td>
<td>5-16</td>
</tr>
<tr>
<td>Normal</td>
<td>10-180</td>
<td>0-3</td>
<td>60-220</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CK-BB was <3% in all cases.

References