PROGNOSTIC SIGNIFICANCE OF SERUM LACTIC ACID DEHYDROGENASE IN EWING'S TUMOR OF BONE

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Lactic acid dehydrogenase (LDH) is a glycolytic enzyme whose serum levels can become elevated in a large number of diseases. Serum LDH levels have been recently found to be useful as prognostic markers even in several neoplastic diseases, particularly in non-Hodgkin's lymphoma. In Ewing's tumor, on the contrary, the prognostic significance of serum LDH levels is still uncertain.

The purpose of this paper is to evaluate serum LDH levels as prognostic indicators in 82 consecutive cases of Ewing's tumor of bone observed during last years at the Centro Tumori Ossei of the Istituto Ortopedico Rizzoli, Bologna, Italy.

MATERIALS AND METHODS

Selection of patients

Eighty-two previously untreated patients with typical histologic features of Ewing's tumor of bone were admitted to the Centro Tumori Ossei of the Istituto Ortopedico Rizzoli between January 1979 and December 1982. All patients underwent physical examination, plain X-rays and computerized tomographic scan of the primary lesion, chest radiography, complete lung tomography, total body scan and iliac crest biopsy. In patients under 14 years of age, urinary catecholamines were measured. Lymphangiography was performed in 15 cases only. Out of the 82 patients, 59 presented with localized disease and 23 had metastatic disease.

Key-words: Enzymes; Ewing's tumor; Lactic acid dehydrogenase; Neoplastic diseases.

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**Enzyme assay**

All patients had pretreatment complete blood counts, urine analysis, creatinine clearance, serum bilirubin, liver enzymes and alkaline phosphatase determinations.

Serum activity of total LDH was estimated employing an 'optimized standard method' according to recommendations of the German Society for Clinical Chemistry. Nicotinamide adenine dinucleotide (0.18 mM/l) phosphate buffer, pH 7.5 (50 mM/l) and pyruvate substrate (0.6 mM/l) were employed as reagents. The reaction was carried out at 25 °C, continuously recording its rate at 340 nM.

Patients with localized disease had serum analyses (including LDH) every three weeks during 18 months of chemotherapy (see below) and subsequently every three months. LDH levels were recorded without attempting to relate them to the size of tumor mass. Serum LDH levels lower than 240 IU/l were considered normal, as this value corresponds to the extreme range that can be found in a normal population using the above described method; levels higher than 240 IU/l were considered pathological.

**Treatment**

After diagnosis, the 23 patients with metastatic disease were referred to other hospitals for treatment; we did not examine the type of treatment nor the survival time of these patients. The 59 patients with localized disease were treated at our institution. The treatment of the initial lesion was individually determined as a function of tumor site, its extension and the patient's age. Thirty-one cases were locally treated by radiation therapy (5,000-6,000 rads), 9 had surgery only (amputation in 6 and wide resection in 3 patients) and 19 patients had surgery (marginal or intra-lesion resection) plus radiation therapy (4,000-5,000 rads).

All these 59 patients also received adjuvant chemotherapy (represented by a combination of Adriamycin, cyclophosphamide, vincristine and daunomycin) for 18 months, according to a previously reported therapeutic protocol. Chemotherapy was started in association with radiotherapy or 10-15 days after surgery. Only in 10 patients with pelvic lesions radiotherapy and/or surgery was preceded by a 2-month induction chemotherapy.

**RESULTS**

**Correlation between serum LDH levels and stage of the disease**

Elevated levels of serum LDH were observed at admission in 46 out of 82 (56%) patients (fig. 1). The percentage of patients with elevated serum LDH levels was higher in the group with metastatic disease (20 out of 23, 87%) than in the group with localized disease (26 out of 59, 44%); this difference is statistically significant (p = 0.001).

Among the 23 patients with metastatic disease, 11 (48%) had serum LDH levels higher than 500 IU/l. In the 59 patients with localized disease (fig. 2) a serum LDH level higher than 500 IU/l was observed in 4 cases only (7%); the difference in these results is statistically significant (p = 0.01).