Lactate Dehydrogenase Isoenzyme 1 in Testicular Germ Cell Tumors

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Introduction

In his thesis, Zondag (1964) described the lactate dehydrogenase (L-lactate: NAD⁺-oxidoreductase EC 1.1.1.27, LDH) isoenzyme patterns of human malignant diseases. Among other findings, he drew attention to the characteristic LDH isoenzyme pattern in germ cell tumors, which showed a predominance of LDH isoenzyme 1 (LDH-1), being deviant from those of other cancers. This LDH-1 pattern in tumor tissue has been confirmed in later investigations (Murakami and Said 1984; Takeuchi et al. 1979). Similarly, the serum activity is frequently raised in patients with tumors (von Eyben 1983). The increased LDH-1 level in testicular tumors could be due to polyploidization involving the gene locus encoding LDH-B, as LDH-1 is a homotetrameric combination of this subunit. The LDH-B gene is localized on the short arm of chromosome 12 (12p12.1–12p12.2), and multiple copies of isochromosome i(12p) are often present in human testicular germ cell tumors (Atkins and Baker 1982). The raised tissue LDH-1 could also be related to an increase in the rate of transcription of the LDH-B gene, an increased stability of the LDH-B mRNA, an increase in the translation of the LDH-B mRNA, or a combination of all these factors (Fig. 1).

As an approach to elucidate the background for the LDH-1 isoenzyme pattern in human testicular germ cell tumors, we measured the changes in the levels of human LDH-B mRNA in tumor tissue and in normal testicular tissue. In addition we determined the levels of transcripts from the proto-oncogene c-Ki-ras2, which like the LDH-B gene is localized on the short arm of chromosome 12 (12p12.1) (McKusick 1986). We compared the LDH-1 activity of tumor tissue with that in normal testicular tissue, and measured S-LDH-1 in blood from the testicular vein and a peripheral vein at orchectomy of the tumor patients. Finally, we compared the S-LDH-1 level in peripheral blood from tumor patients with that of controls.
Materials and Methods

Patients. Eighteen men were included in the study. All were admitted between August 1988 and July 1989 to the Dept. of Urology, Odense University, due to suspected testicular germ cell malignancy. Seven had a testicular germ cell tumor and underwent orchiectomy. Their median age was 45 years (range, 33–49 years). Six had a seminoma and one a nonseminomatous tumor (embryonal carcinoma, teratoma, and choriocarcinoma). Five had a stage 1 tumor, one a stage 2 tumor, and one a stage 3 tumor. Eleven had no tumor on surgical exploration. Their median age was 36 years (range, 20–52 years). Three had epididymitis, two periorchitis, two hydrocele, one Leydig’s cell hyperplasia, one testicular torsion, one an appendicular cyst, and one no abnormality of the testis.

Tissue Samples from Testicular Tumor and Nonmalignant Testis. We obtained tissue from the malignant part of the testis in all tumor patients as well as from the macroscopically normal part of the testis in four. However, microscopic examination of this part of the testis from two of the four patients revealed only tumor tissue. A testis with Leydig’s cell hyperplasia orchiectomized from one of the controls also served to estimate the LDH-1 level of nonmalignant testicular tissue.

RNA Isolation. Tissue was ground under liquid nitrogen and RNA was extracted by the hot phenol-guanidinium thiocyanate procedure (Maniatis et