Ovarian Carcinoma and Serum Lactic Dehydrogenase Levels

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Abstract: *Preoperative and postopertive levels of serum lactic dehydrogenase (LDH) were measured in 218 patients with various gynaecologic diseases. Among 119 patients with benign gynaecologic diseases, the LDH levels were in normal limit, except for two patients of endometriosis and benign cystic teratoma who showed silght elevated LDH values. The LDH levels were elevated in 36/51 patients (70.6 per cent) with ovarian carcinoma. All 8 patients with malignant germ cell tumors showed abnormal LDH levels, especially the average LDH value of dysgerminoma was about three times higher than the maximum normal value. The incidence of abnormal LDH in patients with advanced ovarian carcinoma was higher than in patients with stage I and II ovarian carcinoma (78.4 to 50.0 per cent). There were no elevations of LDH levels in patients with CIN, cervical and endometrial carcinoma. The results from this study suggest that in the presence of a pelvic mass together with an elevated LDH level, diagnosis of ovarian malignancy should be considered. (Thai J Obstet Gynaecol 1989 ; 1 : 57-62)*

Key words: ovarian carcinoma, serum lactic dehydrogenase

Several biochemical substances have been used as tumor markers in patients with gynaecologic cancers. The best known and most widely used markers were human chorionic gonadotropin , alpha-fetoprotein, and carcinoembryonic antigen[1]. Recently, radioimmunoassay using a monoclonal antibody to detect ovarian carcinoma has also been used[2,3].

Lactic dehydrogenase (LDH) is a glycolytic enzyme which is present in various normal tissues and nepolasms of the human body. There have been some reports of elevation of this enzyme in the patients with ovarian carcinoma[4-6].

The purposes of this paper are: 1) to compare the LDH levels in patients with benign and malignant gynaecologic diseases, 2) to study the LDH levels in

patients with various histologic types and stages of ovarian carcinoma.

Materials and Methods

Subjects for this study included 218 patients with various gynaecologic diseases who were admitted for operations in the gynaecologic ward, Siriraj Hospital between April 1987 and June 1988. All patients were free from myocardial infarction, breast disease, liver disease, leukemia, and lymphoma. Preoperative and postoperative serum lactic dehydrogenase determinations were performed in each patient. The LDH levels of 10 patients with normal intrauterine pregnancies were also studied for comparison. The LDH levels were determined by the method of Wroblewski and La Due with the normal value of 120-280 U/L. A histopathologic study was done postoperatively on the surgical specimen obtained from each patient. The Fisher exact probability test was used for statistical comparison.

Results

The ages of the patients, the diagnoses, and the levels of serum lactic dehydregenase before and after operation

Table 1. Serum LDH in 218 patients with various gynaecologic diseases and 10 normal pregnant women

Diagnosis	No. of patients	Age	LDH before operation (U/L)		LDH after operation (U/L)	
		mean ± SD	mean ± SD	abnormal cases (%)	mean ± SD	abnormal cases (%)
Ectopic pregnancy	5	29.4 ± 4.9	173.8 ± 55.0	0	194.8 ± 21.9	0
Pelvic infection	7	32.4 ± 5.9	180.7 ± 40.6	0	224.8 ± 31.4	0
Genital prolapse	21	54.7 ± 10.8	192.4 ± 42.9	0	191.1 ± 25.1	0
Myoma uteri	25	40.4 ± 6.3	204.2 ± 26.0	0	224.5 ± 36.5	0
Adenomyosis	9	41.3 ± 5.4	183.7 ± 25.6	0	206.8 ± 30.2	0
Endometriosis	17	32.6 ± 8.5	198.8 ± 48.5	1 (5.9)	212.2 ± 40.2	1 (5.9)
Benign ovarian tumor	35	34.3 ± 13.4	191.6 ± 37.9	1 (2.9)	221.7 ± 31.9	1 (2.9)
Ovarian carinoma	51	46.5 ± 15.4	439.2 ± 393.8	36(70.6)	419.4 ± 407.5	31 (60.8)
Cervical intra-epithelial neoplasia	23	37.2 ± 9.5	190.7 ± 30.7	0	183.2 ± 40.2	0
Cervical carcinoma	19	43.7 ± 11.0	184.9 ± 42.4	0	207.7 ± 35.8	0
Endometrial carcinoma	6	42.5 ± 17.1	197.0 ± 40.9	0	226.0 ± 31.9	0
Intrauterine pregnancy	10	25.9 ± 2.9	242.7 ± 29.2	0	-	-

are shown in Table 1. Among 119 patients with benign gynaecologic diseases, there were only 2 patients with elevated LDH; one of endometriosis and the other of benign cystic teratoma. However, both patients had levels below 300 U/L (284 U/L and 294 U/L respectively). Of 51 patients with ovarian carcinoma, the levels before operation elevated in 36 patients (70.6 per cent) with a maximum value of 2,721 U/L. After their operations, the levels decreased to normal in only 5 patients. There were no elevated LDH levels in patients with cervical intraepithelial neoplasia, cervical and endometrial carcinoma, nor in normal pregnant women.

Table 2 shows the levels of LDH before and after operation relating to the histopathologic diagnoses of ovarian carcinoma. Of 9 patients with mucinous cystadenocarcinoma, the mean value of LDH was in the normal range, with abnormal levels in 4 patients (44.4 per cent) before operation and 1 patient (11.1 per cent) after operation. All 8 patients with malignant germ cell tumors showed abnormal levels, which is quite significant when compared to the abnormal levels of 26/39 patients (66.7 per cent)

Table 2. Serum LDH in 51 patients with ovarian carcinoma

Tumor cell types	No. of patients	Age	LDH before operation (U/L)		LDH after operation (U/L)	
		mean ± SD	mean ± SD	abnormal cases (%)	mean ± SD	abnormal cases (%)
Serous cystadeno-carcinoma	19	49.5 ± 12.4	481.2 ± 550.9	14 (73.7)	453.1 ± 479.3	12 (63.2)
Mucinous cys-tadeno carcinoma	9	55.4 ± 8.5	260.1 ± 69.4	4 (44.4)	246.6 ± 37.9	1 (11.12)
Adenocarcinoma	3	47.3 ± 10.8	439.3 ± 108.9	3 (100)	366.7 ± 91.7	3 (100)
Clear cell carcinoma	3	38.7 ± 8.9	558.0 ± 280.6	3 (100)	292.0 ± 62.6	2 (66.7)
Endometrioid carcinoma	5	41.6 ± 14.8	367.2 ± 226.7	2 (40)	578.8 ± 682.4	2 (40)
Immature teratoma	1	44	306	1 (100)	397	1 (100)
Endodermal sinus tumor	3	19 ± 2.2	482.0 ± 246.8	3 (100)	659.3 ± 513.2	3 (100)
Dysgerminoma	3	36.0 ± 17.0	887.3 ± 288.4	3 (100)	516.7 ± 263.6	3 (100)
Malignant mixed germ cell tumor	1	16	367	1 (100)	316	1 (100)
Granulosa cell tumor	1	74	365	1 (100)	408	1 (100)
Metastatic tumor	3	55.0 ± 7.8	314.7 ± 149.2	1 (33.3)	346.0 ± 94.0	1 (33.3)

with malignant epithelial tumors ($p = 0.057$). The 3 patients with dysgerminoma showed markedly elevated LDH, with an average value about three times higher than the maximum normal value. For metastatic ovarian carcinoma, only 1 patient (33.3 per cent) showed abnormal level.

The stages of the ovarian carcinoma according to the International Federation of Gynecology and Obstetrics (FIGO), and the levels of LDH before and after operation are shown in Table 3. Before operation, the abnormal levels were found in 7/14 (50 per cent) of the patients with stage I and II diseases. It was significantly less than those found in 29/37 (78.4 per cent) of the patients with stage III and IV diseases ($p < 0.05$).

Discussion

Serum lactic dehydrogenase levels have been reported to be elevated in patients with lymphoma, granulocytic leukemia, carcinoma of the pancreas and gall bladder, metastatic carcinoma of the breast and metastatic carcinoma of the liver. Such findings have also been noted in cases of myocardial infarction, infectious mononucleosis, thrombocytopenia, obstructive jaundice, and acute hepatitis[7-9].

LDH is major enzyme in glycolysis and reversible catalyzes pyruvate to lactic acid. Malignant tissue has high glycolytic activity as Cori and Cori[10] and Warburg[11] reported many years ago. Thus, one would expect that patients with increased glycolytic activity will consequently have an elevation of LDH level. The ovary is a multipotential and totipotential organ. During malignant change, it may show high glycolytic activity resulting in an increased LDH level which can be measured in the circulating plasma. So the LDH test may be useful in the diagnosis of ovarian carcinoma.

Previous reports have shown that LDH was elevated in the presence of

Table 3. Serum LDH in patients with various stages of ovarian carcinoma

Stages	No. of patients	Age	LDH before operation (U/L)		LDH after operation (U/L)	
		mean ± SD	mean ± SD	abnormal cases (%)	mean ± SD	abnormal cases (%)
I	10	30.6 ± 11.3	354.7 ± 317.6	5 (50)	319.7 ± 200.4	4 (40)
II	4	55.0 ± 9.2	465.3 ± 310.5	2 (50)	248.3 ± 55.5	1 (25)
III	30	49.9 ± 13.8	466.8 ± 452.1	23(76.7)	452.6 ± 469.7	22(73.3)
IV	7	49.4 ± 14.5	427.0 ± 202.8	6(85.7)	517.1 ± 400.2	4(57.1)

ovarian carcinoma but not in benign tumors of the ovary, leiomyoma of the uterus, carcinoma of the endometrium, carcinoma of the cervix, or carcinoma of the sigmoid colon[4,5]. In this study, LDH levels were elevated in about two-thirds (70.6 per cent) of the patients with ovarian carcinoma. In other benign gynaecologic diseases, cervical and endometrial carcinoma, and pregnancy, the LDH levels were still within normal limits. There were abnormal levels in each case of endometriosis and benign cystic teratoma, but the values were only slightly elevated to 284 and 294 U/L respectively.

LDH levels were found to be elevated in all cases of malignant germ cell tumors, with striking elevation in patients with dysgerminoma. The marked elevation of LDH in dysgerminoma was also reported by several authors[5,6,12,13]. In patients with ovarian carcinoma of common epithelial cell types, LDH levels were found to be elevated in two-third of the cases. It should be noted that the mucinous type of ovarian carcinoma showed an average levels approaching the upper limit of normal value. Burrows[14] reportd serum LDH levels of 61 patients with ovarian malignancies which were approaching the upper limit of normal value, and there was considerable overlap with the normal range.

The present study shows that there are higher incidence of abnormal LDH levels in advanced ovarian carcinoma (FIGO stage III and IV). It is assumed that more tumor cell volumes will have more glycolytic activity, resulting in enzyme LDH elevation.

Awais[4,5,13] reported that after effective treatment of carcinoma of ovaries, LDH levels decreased to normal range and remained normal as long as the carcinoma was under control. In this study, the LDH levels, after treatment, did not decrease satisfactorily to normal range. Therefore, they can not be used as a monitoring parameter for an assessment of the effectiveness of therapy.

Although the results of the present study show that serum lactic dehydrogenase seem to be helpful in the diagnosis of carcinoma of ovary, no decisive or unequivocal claim is made. Any woman with a pelvic mass together with an elevated serum lactic dehydrogenase level could be considered having carcinoma of ovary, and diagnosis of ovarian carcinoma should be included until proved otherwise.

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