Journal of Clinical & Experimental Dermatology Research

Saif., J Clin Exp Dermatol Res 2016, 7:2
DOI: 10.4172/2155-9554.1000342

Research Article Open Access

Prognostic Significance of Serum Lactate Dehydrogenase in Saudi Patients with Mycosis Fungoides: A Retrospective Study of 47 Patients

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Received date: February 23, 2016; **Accepted date:** March 30, 2016; **Published date:** April 04, 2016

Abstract

Background: Mycosis fungoides (MF) is the most common cutaneous T-cell lymphoma and its advanced-stage (MF; stage IIB to IV)) has aggressive behavior. Lactate dehydrogenase (LDH) has been demonstrated to correlate with progression of malignancy specially lymphoma and leukemia. The LDH level is expected to be useful clinical tool for evaluating the progression of MF.

Objective: This study aimed to evaluate the pretreatment LDH as a prognostic factor in Saudi patients with Mycosis fungoides.

Methods: We designed a retrospective study using biopsy-based data collected from 1997 to 2015 at King Khalid University Hospital. The correlation of LDH levels with clinical stages of Mycosis fungoides was studied.

Results: Of the 47 MF patients, there were 25 male and 22 female patients for a male: female ratio of 1.4:1. The mean patient age was 39 years; 87.2% (n=31) had limited stage of MF and 12.8 (n=6) had an advanced stage >IIA. There were 13 patients with a raised LDH at the time of diagnosis. All stage IA patients had normal LDH levels while stage IB, IIA and advanced stage had 20%, 50% and 100% elevated LDH, respectively.

Conclusions: Our results suggest that high LDH level may be used as an independent prognostic factor to measure the progression of Mycosis fungoides.

Keywords: Cutaneous T-cell lymphoma; LDH; mycosis fungoides; Saudi

Introduction

Mycosis fungoides (MF) is a common type of cutaneous T-cell lymphoma with an indolent clinical course and a low risk of mortality in early disease. The Tumor-Nodes-Metastasis-Blood (TNMB) staging of mycosis fungoides (Table 1) is an important prognostic factor in MF and patients with Stage IA, IIB and IIA disease have "limited-stage" disease. The overall survival in these patients is good. In contrast, patients with stage 11B and higher usually have "advanced-stage" disease with aggressive behavior and worse prognosis [1].Other risk factors for survival in MF are male sex and older age, elevated lactate dehydrogenase (LDH), and histologic features of folliculotropism (FT) and large-cell transformation [1,2].

Lactate dehydrogenase (LDH) is a cytoplasmic enzyme that is widely expressed in tissues. LDH is an enzyme that catalyzes the conversion of lactate to pyruvate the last step of glycolysis. The pyruvate transformation to lactate is increased in malignancies which lead to tumor microenvironment acidification by which tumors control their own blood supply via vascular morphogenesis and finally promote tumor progression and metastasis [3]. High serum lactate dehydrogenase has been documented as a poor prognostic indicator in malignant lymphoma, pancreatic carcinoma, colorectal cancer and consider one important factor in staging and progression of melanoma [4-9]. In MF, routine blood analyses are of limited value. LDH is a non-specific marker of tumor burden but associated with poor prognosis in MF [10]. There is less data available on the serum level of LDH as a marker of disease activity and progression in Saudi patients with MF. The aim of this retrospective study was to investigate the serum LDH in different stages of Mycosis fungoides.

Methods

The patient record system at the Department of Dermatology in King Khalid University hospital was used to identify all patients who had been diagnosed with MF based on clinical and histopathology data from January 1997 to December 2015. Data collection was approved by IRB (number: E-16-1777). The exclusion criteria were any patient with disease that can increase LHD including malignancy (leukemia and systemic lymphoma), liver disease, IHD, renal impairments and any muscle injury. We only included patients who had serum LDH before starting treatment. The normal value range of LDH was 120–227 U/L for male patients and120–227 U/L for female patients. MF staging was made according to the European Organization of Research and Treatment of Cancer (EORTC).

Results

There were 133 patients registered as having MF; 86 patients were excluded due to chronic diseases or lack of baseline LDH measurements. There were 47 patients with clinically and histologically

verified MF included in the study (Table 2). Of these, 25 were males (57.5%) and 22 (42.5%) were females. Male: female ratio was 1.4:1.

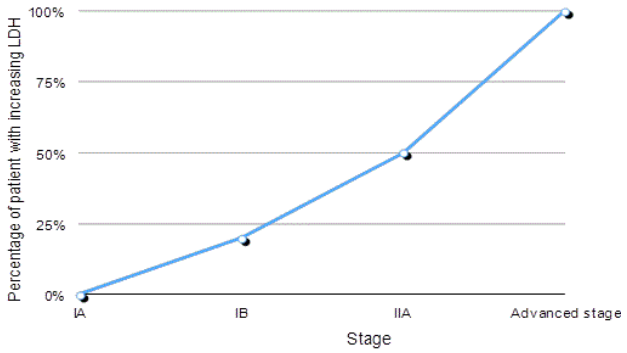

Figure 1: Curve of increment of LDH according to stages of MF.

The median age was 39 years (range was 10-86 years). At the time of diagnosis, 87.2% (n=31) had limited stage of MF, 31.9 % were stage IA, 42.5% had stage IB and 12.8 had stage IIA. There were 12.8% (n=6) with advanced stage (>IIA), and 13 patients had elevated LDH at the time of diagnosis. All stage IA patients had normal LDH level while stage IB, IIA and advanced stage had 20%, 50% and 100% raised of LDH, respectively (Figures 1 and 2).

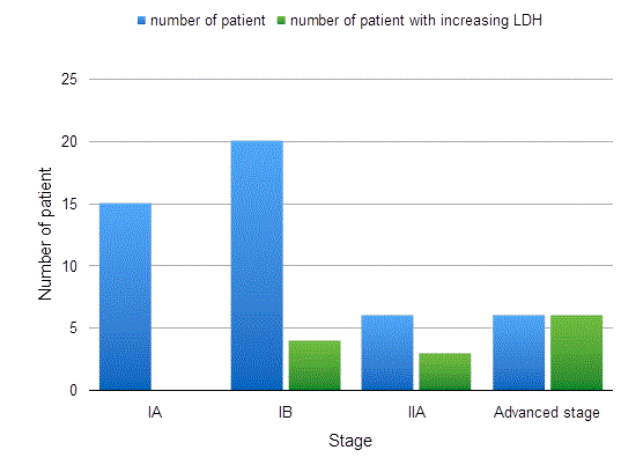

Figure 2: LDH frequency in different stages of MF.

Discussion

Mycosis fungoides is the most common subtype of cutaneous T cell lymphoma characterized by low malignancy, chronic nature and slow progress [1]. The peak age at presentation is around 55 to 60 years with a 2:1 male:female ratio [1,11,12]. The median age at initial diagnosis in our study was 39 years, which is lower than in those reported internationally but nearly equal to the median age of Saudi and Iranian patients [13,14]. On the other hand, we should consider the effects of excluding MF patients with chronic diseases that usually occurred in old age in explanation of early age of onset. The M:F ratio was 1.4:1, which is lower than previously reported for Saudi patients [13].

stage	T	N	M	B
IA	1	0	0	0,1
IB	2	0	0	0,1
II	1,2	1,2	0	0,1
IIB	3	0-2	0	0,1
III	4	0-2	0	0,1
IIIA	4	0-2	0	0
IIIB	4	0-2	0	1
IVA1	01-Apr	0-2	0	2
IVA2	01-Apr	3	0	0-2
IVB	01-Apr	0-3	1	0-2

Table 1: ISCL/EORTC revision to the staging of mycosis fungoides Source: ISLC/EORTC (2007) [14].

Olsen et al. published the staging of MF and Sézary syndrome (SS) as a result of the International Society for Cutaneous Lymphomas (ISCL) - European Organization of Research and Treatment of Cancer (EORTC) discussions considering cellular and molecular biology and diagnostic methods [15,16]. In our study, the stage at diagnosis showed that 87.2% (n=31) had limited stage of MF-31.9 % were in stage IA, 42.5% were stage IB, 12.8 were stage IIA, and 12.8 (n=6) were advanced stage >IIA. These results are compatible with results reported in the literatures [17]. Staging is still the most important prognostic factor and guides management of this complex disease.

No.	Sex	Age	LDH level	Stage of the disease
1	male	26	124	IA
2	male	32	126	IA
3	female	50	128.2	IB
4	female	28	131	IB
5	male	37	132	IB
6	male	36	144	IB
7	male	60	145	IB
8	female	21	146	IA
9	male	30	147	IA
10	male	50	147	IB
11	male	45	149	IA
12	female	49	154	IA
13	female	28	154	IB
14	male	64	156	IA
15	female	36	158	IB

16	female	36	165	IIA
17	male	50	167	IA
18	male	24	170	IA
19	male	69	169	IB
20	male	35	176	IA
21	female	30	179	IA
22	male	47	180	IB
23	female	60	180	IA
24	female	45	182	IB
25	male	44	188	IB
26	male	29	189	IA
27	male	58	189	IA
28	female	70	198*	IB
29	male	86	203	IB
30	female	15	204	IB
31	female	15	209	IB
32	female	31	209	IA
33	female	52	216*	IB
34	female	25	216	IIA
35	male	14	224	IIA
36	female	35	226	IB
37	male	13	231	IB
38	male	20	252	IIA
39	male	17	259	III
40	male	43	277	IIA
41	female	10	283	IB
42	male	57	296	III
43	male	49	318	IIA
44	female	24	420	III
45	female	34	460	III
46	male	34	547	III
47	male	71	1445	IV

Table 2: Demographic profile and basic data of 47patients with mycosis fungoides arranged according to LDH value.

Elevated LDH is significantly associated with a worse survival [18]. It has been widely acknowledged that elevated LDH is associated with unfavorable prognosis for different types of lymphoma [19-21]. In our study, there was a significant correlation between high LDH and advanced stages of MF (Figure 1). We found that 100% of patients with advanced stage had high LDH. An elevated serum LDH level at the time of diagnosis may supplement clinical judgment in detecting the high-risk group.

Limitations of the study

A key limitation of this study was the small number of patients, which led to relatively low statistical power. Further prospective studies with much larger patient populations are needed to clarify this association.

In conclusion, higher LDH level at the time of diagnosis was implicated in aggressive MF. This simple, inexpensive, and routinely measured marker may be an independent prognostic factor.

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