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Cutaneous Lymphomas-Epidemiological and Clinicopathological Profile: A retrospective Study

Halima Megei[1@], Aisha Ben-Roween[2], Esseid Elzubi[1], Ali Elzurghany[1], Nadia El-houni[1] and Sumia Ezzdien[1]

[1] Department of Dermatology, Tripoli Central Hospital, Tripoli, Libya
[2]Department of Community, Faculty of Medicine, University of Tripoli, Libya

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ABSTRACT

Lymphomas are classified as either Hodgkin's or non-Hodgkin's. The two subtypes of non-Hodgkin's lymphoma that can present primarily in the skin are cutaneous T-cell lymphoma (CTCL) and cutaneous B-cell lymphoma (CBCL), both of which tend to be low-grade malignant neoplasms. Although primary cutaneous lymphomas (PCL) are the second most common group of extra-nodal non-Hodgkin lymphomas, few epidemiological data are available in the literature and till date. No data about the epidemiology of cutaneous lymphomas in Libya have been reported. Therefore this study was conducted to investigate the epidemiological and clinicopathological features of PCL diagnosed in the department of Dermatology -Tripoli Central Hospital.

Data were collected from the lymphoma clinic registry. A total of 54 cases of (CTCL) were diagnosed between the years 2008 and 2013 (including cases of parapsoriasis), No CBCL case has been diagnosed. There were 26 males and 28 females aged between 18 to 74 with a mean age of 40 ± 13. The most common skin type was type IV (79.6%). 59.3% of the patients were resident in Tripoli, classical mycosis fungoides was the most common disease diagnosed (83.2%), and the duration of disease prior to diagnosis varied between 2 months and 7 years. The most frequent presenting symptom was pruritus (61.1%).

The various clinical presentations recorded in these patients were infiltrated papules and plaques in 31 (57.4%), hypopigmented patches in 11(20.4%), lymphomatoid papulosis 4(7.4%), and 1(1.9%) case each of sezary syndrome, erythroderma and ichthyosiform presentation. In 24 (44.4%) patient the lesions were distributed all over the body. In 46 patients (85.2%) the diagnosis was confirmed histologicaly and most of the patients with mycosis fungoides (MF) were in stage Ib (71.1%).

Our study showed that from the PCL, MF variant of CTCL is the most common; CBCL was not recorded in our patients in the given period. More data collection from multi centers is needed to describe the epidemiologic characteristics in Libya.

Keywords - *Primary cutaneous lymphoma (PCL); Mycosis fungoides (MF).*

INTRODUCTION

The term cutaneous T-cell lymphoma (CTCL) describes a heterogeneous group of neoplasms of skin- homing T cells that show considerable variation in clinical presentation, histological appearance, immunophenotype and prognosis.[1] CTCL lymphomas includes multiple diseases: Mycosis fungoides (MF) with its varients, Lymphomatoid papulosis, CD30+ anaplastic large cell lymphoma, subcutaneous T-cell lymphoma, and natural killer cell lymphoma.[2] The most common type of which is classical Mycosis fungoides (MF) and the systemic stage of MF (Sézary syndrome). Other variants of MF are hypopigmented type, pagetoid reticulosis (Woringer-Kolopp disease), granulomatous slack skin syndrome and follicular mucinosis. Skin manifestations of the disease include patches, plaques, tumors, and erythroderma (inflammation and redness of the skin). The most common type of CTCL is the patch/plaque MF initially described by Alibert.[3] Indolent CTCL is often confined to the skin and can be treated effectively. Aggressive forms can extend beyond the skin to the lymph nodes, blood, and internal organs. The incidence of CTCL is increasing by 2.9 cases per million people per decade; the increase could be a result of changes in classification or improvements in diagnosis. CTCL incidence is about 50% greater in African Americans than Caucasians, and men are affected twice as often as women, CTCL incidence increases with age, with the greatest increase occurring at age of 70 or older.[4] Median age at diagnosis is 55 to 60 years, but MF may occur in children and adolescents as well.[5] CTCL should be ruled out if a clinical eruption that is initially thought to be banal is refractory to treatment. The clinician must attempt not only to make the diagnosis, but also to stage the extent of the disease once the diagnosis is made. Histological diagnosis with 4 to 6mm deep punch, incisional or excisional skin biopsies is the first step to confirm the diagnosis of lymphomas, immunophenotyping and T-cell receptor gene rearrangement analysis are also required for diagnosis and staging (Table 1). Early lesions of MF may pose a significant diagnostic challenge

@ Author to whom correspondence should be addressed Dr. Halima Megei, Tel:+218925249285; E-mail: Hamegei@gmail.com,

to clinicians and dermatopathologists. Many times, patients may need long-term follow-up and multiple skin biopsies to make a definitive diagnosis. In fact, the median duration from onset of symptoms to diagnosis is 4-6 years.[6] Treatment options for CTCL include: topical corticosteroids, oral and topical retinoids, phototherapy, topical and systemic chemotherapy and others.

Objectives

- To describe the patients regarding: age of the patients, sex, residency and skin type.
- To find out the most common clinical presentations of cutaneous lymphomas in our patients.
- To find out the median duration from time of onset of symptoms to diagnosis.
- To find out treatment types received by our patients.

MATERIALS AND METHODS

Study design: Case series study.

Study place: Lymphoma clinic in dermatology department, Tripoli central hospital.

Study period: April 2008 to April 2013.

Study population: All medical records of patients attending the clinic for diagnosis, treatment and follow up.

Data management and analysis: The data which was drowning from medical records include: Age of the patients, sex, their residency (inside or outside Tripoli), also the clinical data as: skin phototype, clinical presentation, duration and distribution of the disease, staging, treatment type, and the follow up regularity. Haematoxylin and eosin-stained slides from the patient's skin biopsies were eviewed for hitological diagnosis.

Data was packaged and analyzed by SPSS software program. Mean, standard deviation and percentage were used for descriptive statistics.

RESULTS

Total number of 54 patients were registered in our clinic from April 2008 to April 2013 were evaluated. 51.9% were females and 48.1% were males with the minimum age of 18 years, maximum age of 74 years and mean age of 40 ±13. Skin phototype IV was the most common skin type (79.6%). 59.3% were resident in Tripoli and 40.7% were from the surrounding areas.

Table 2 shows in more details the sociodermographic characters of the patients treated in our clinic. All our patients were cases of CTCL; mainly of classical MF (83.5%) with its different variants (Table 3), one case of pagetoid reticulosis (1.9%), one case of nasal type natural killer/T-cell lymphoma (NK/ T-cell lymphoma) (1.9%) and 3 cases with parapsoriasis (5.6%). We did not diagnose any case of CBCL. The most frequent presenting symptom was pruritus (61.1%), 11.1% of the patients came because of cosmetic disturbance, (7.4%) because of dryness but (18.5) were asymptomatic. At the time of presenting to us 31 (57%) of the patients had their skin lesion for more than 5 years, the rest of the patients' duration varied from 2 months to 7 years. Regarding distribution of the lesions; (44.4%) had lesions all over the body, in (29.6%) the face was spared, extremities (one or more) were involved in (13.0%) of the cases, while trunk only was involved in (5.6%) and face alone was involved only once (1.9%). The histological examination of the skin lesions was confirmative in (85.2%) of the cases while it was highly suspicious in (14.8%) of the cases. The staging of MF patients showed: (69.6%) were stage Ib, (17.4%) stage Ia, (8.7%) stage IIb, (2.2%) stage III and (2.2%) stage IVa. Phototherapy was the treatment of choice in (87%) of our patients.

DISCUSSION

From the previous records, the epidemiology of cutaneous lymphomas in general revealed that the incidence of lymphomas differed depending on various factors including geographical area, race, sex and others and the relative frequency of different PCL subtypes differ according to geographical location.[7] A total of 54 patients were registered in our lymphoma clinic in a period of five years including three parapsoriasis patients for whom regular long term follow up is important and although parapsoriasis is considered a separate entity, and there is still debate about this issue, but many authors think that large plaque parapsoriasis is in fact MF.[8,9] The diagnosis was made by clinical as well as hitopathological examination, for staging some hematological as well as radiological investigations were required. The most common age group affected was the fourth decade of life (40.7%) (Table 2), nearly the same result of recent large population-based study in Asian (any age group may be involved, but there is a higher incidence in the fourth to sixth decades)[10], male: female ratio was nearly equal [1:1.1] a result which is different from most of the previous results reported (cutaneous T-cell lymphoma has a sex predilection, being more common in men than women by a ratio of approximately 2:1).[11]

Most of the patients presented to us because of pruritus (61.1%) while others presented only because of asymptomatic rash (18.5%), 11.1% complained of cosmetic disturbance; mainly of hypopigmented patches (Figure 1). At the time of presentation (38.9%) of them had their complaint for more than 6 years (Figure 2), the same result as mentioned by Van Doorn R *et al.*, the median duration from onset of symptoms to diagnosis is 4-6 years].[5] According to the World Health Organization-European Organization for Research and Treatment of Cancer (WHO-EORTC) classification for primary cutaneous lymphomas.[12] We have made the diagnosis of 46 cases of Mycosis fungoides, one case NK/T-cell lymphoma and four lymphomatoid papulosis (Table 3). We did not diagnose any case of B-cell lymphoma, most of the studies from Asia and Far East, concluded higher incidence of CTCL than CBCL (Compared with Western countries, Korea had higher rates of NK/T cell lymphoma and subcutaneous panniculitis-like T-cell lymphoma and a much lower rate of B-cell lymphoma).[13] Another study

from Taiwan in 2010 by Liao JB *et al.*[14], showed also higher incidence of CTCL than CBCL and Riou-Gotta MO *et al.*[15], from France published in 2008 [Data were collected from the Doubs cancer registry from 1980 to 2003. Seventy-one patients with PCL were investigated. 82% were cutaneous T-cell lymphoma (CTCL) and 18% were cutaneous B-cell lymphoma (CBCL)]. 34 cases were of classical Mycosis fungoides (MF) going with the fact that MF is the most common type of CTCL in almost all of the previous literature[15,16], one of them with systemic stage of MF(Sézary syndrome), 11 cases were of hypopigmented type and one Pagetoid reticulosis, from the classical MF 14 patients were in patch stage while 11were with patchs and plaques, while it was recorded before that the patch/plaque stage is the most common presentation of MF[3], five patients had only plaques, one case was in tumor stage, one was erythrodermic and one presented with ichthyosiform eruption (Figure 3). Regarding distribution of the lesions; (44.4%) had lesions all over the body with predilection to classical sites (Figure 4). Diagnosis was confirmed histologically in (85.2%) of patients and in (14.8%) of them histological examination was only suggestive of CTCL were we depended mainly on the clinical picture and behavior of the disease.[7] The clinical picture may be more suggestive than the histopathologic features. This implies that criteria for distinguishing between benign and malignant lymphoid infiltrates in the skin are not available or at least are not reliable in the early stage of MF).[7]

87% of our patients were in TNM stage Ib followed by Ia, (Figure 5) which has made phototherapy our treatment of choice (Table 3).

CONCLUSION

The current study showed that from the PCL, MF variant of CTCL is the most common; CBCL was not recorded in our patients in the given period. Comparing our study with previous studies, we concluded that the relative frequency of lymphomas differs widely with geography and ethnicity, and the relative frequency of different PCL subtypes differ according to geographical location.

RECOMMENDATIONS

There is a need to collect more data to describe the epidemiologic characteristics in Libya.

There is a need for a multi center large population prospective study with long-term follow-up to determine the exact epidemiological trends and disease outcome in Libya and immunophenotyping should be done for further classifying lymphomas whenever possible for prognostic implications.

Limitations: This study was retrospective depending on medical records, with small sample size and based on a single-center experience.

Table 1: Tumor-node-metastasis staging of Mycosis fungoides.

TNM stage	Clinical findings
IA	< 10% BSA patch or plaque (T1)
IB	> 10% BSA patch or plaque (T2)
IIA	Patch or plaque (T1-2) and clinical lymphadenopathy (biopsy negative)
IIB	Cutaneous tumors (T3)
III	Erythroderma (T4)
IVA	Nodal involvement and T1-4 and nodal involvement (biopsy positive)
IVB	Visceral involvement and T1-4

TNM: Tumor-node-metastasis; BSA: Body surface area

Table 2: Sociodermographic characters of lymphoma patients.

Character	Frequency	Percentage
Age group:		
< 20 yrs	1	1.9%
21- 30 yrs	11	20.4%
31-40 yrs	22	40.7%
41-50 yrs	6	11.1%
51 60- yrs	7	13.0%
> 60 yrs	7	13.0%
Sex:		
Male	26	48.1%
Female	28	51.9%
Residency:		
Inside Tripoli	32	59.3%
Outside Tripoli	22	40.7%

Table 3: Clinical profile of our lymphoma patients.

Character	Frequency	Percentage
Skin phototype:		
Skin type III	8	14.8%
Skin type IV	43	79.6%
Skin type VI	3	5.6%
Clinical diagnosis:		
Mycosis fungoides	46	85.1%
NK / T-cell lymphoma	1	1.9%
Lymphomatoid papulosis	4	7.4%
Parapsoriasis	3	5.6%
Histological diagnosis:		
Confirmative	46	85.2%
Suggestive	8	14.8%
Treatment type:		
Phototherapy	47	87.0%
Local steroids	10	18.5%
Systemic retinoid	6	11.1%
Methotrexate	2	3.7%
Systemic chemotherapy	4	7.4%
Electon beam radiation	2	3.7%
Follow up:		
Regular	25	46.3%
Irregular	6	11.1%
Therapy failure	2	3.7%
Drop out	21	38%

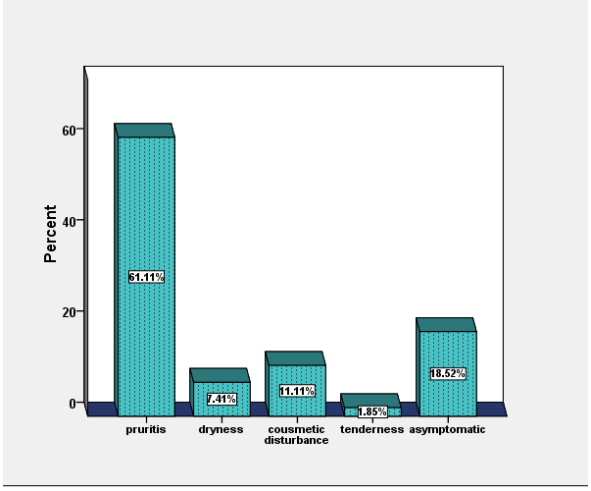

Figure 1: Associated symptoms.

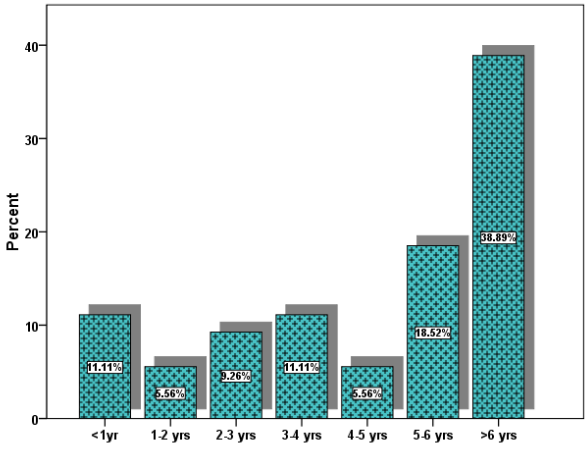

Figure 2: Duration of the disease.

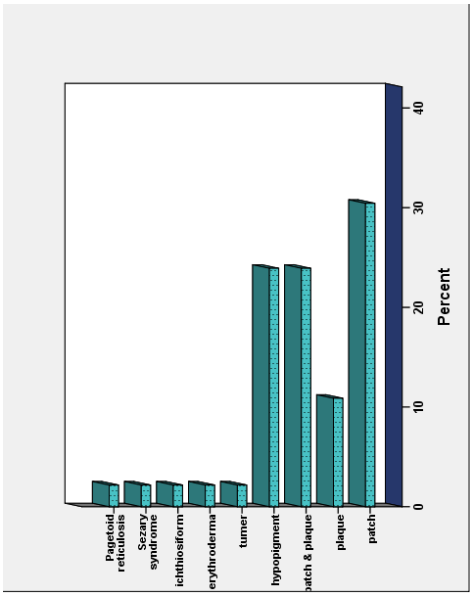

Figure 3: MF varients.

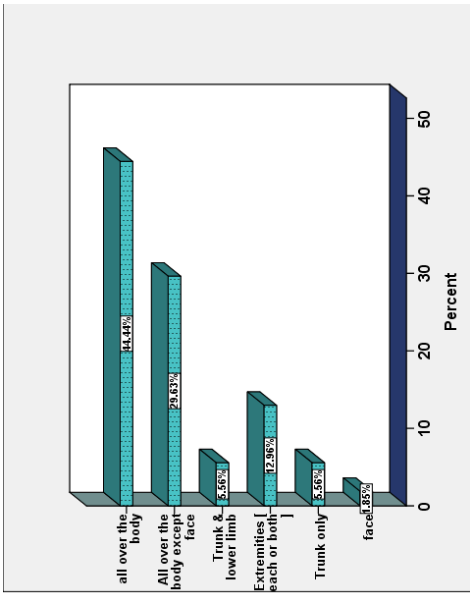

Figure 4: Duration of the skin lesions.

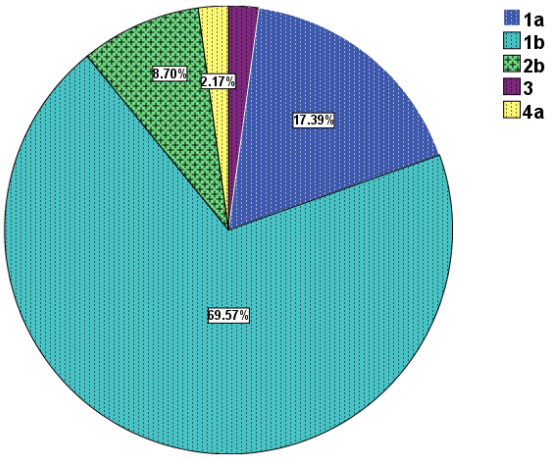

Figure 5: TNM staging of the patients.

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