Cutaneous T-Cell Lymphomas in Oman

Venkataram Mysore, MD Dip RCPath(Lond)*,
Abdul Raouf Al-Suwaid, MD**,
Shivayogi Rudriah Bhusnurmath, MD***

**Junior Specialist; **Chief of Dermatology & Genito Urinary Medicine, Al Nahdha Hospital and Baushar Polyclinic; ***Associate Professor of Pathology, Sultan Qaboos University, Sultanate of Oman.*

SUMMARY

Seven cases of cutaneous T-cell lymphomas studied during the period 1990-1995 in Oman are described. There were four cases of mycosis fungoides, and three cases of nonmycosis T-cell lymphomas. The clinical presentations were varied, and often needed multiple biopsies and immunostudies. Recent diagnostic tools of cutaneous T-cell lymphomas are of great help. For proper management, proper clinical follow-up and clinicopathological correlation are necessary.

INTRODUCTION

Cutaneous lymphomas are uncommon disorders, with varied clinical manifestations. Diagnosis is often difficult, particularly in early cases, and may need histological and immunological studies. Recently, knowledge in this field has rapidly expanded, particularly in the fields of immunological markers and application of DNA analytical methods of diagnosis[1]. This has also lead to description of many new entities, and changing classifications. There is now a bewildering array of nomenclature, causing much confusion to the practicing clinician.

Cutaneous T-cell lymphomas are by far the common type of lymphomas of skin. We studied the cutaneous T-cell lymphomas diagnosed in the Sultanate of Oman in the years 1990-1995. The details of this study are presented with review of current literature.

Correspondence:
Dr. M.N. Venkataram
Baushar Polyclinic
Post Box 77, Postal Code 118, Al Harthy Complex
Muscat, Sultanate of Oman.
Fax: 968-594827

MATERIALS AND METHODS

Seven cases of Cutaneous T-cell lymphomas diagnosed during the years 1990-95 at Al Nahdha hospital and Baushar Polyclinic, Muscat were studied retrospectively. Detailed history and clinical findings, both cutaneous and systemic, were noted. All cases were studied with respect to the following features: Complete blood examination, bone marrow examination (whenever necessary), x-rays and ultrasound examination of abdomen and pelvis. Whole body CT scan (whenever necessary). Skin biopsy was performed, for routine H & E examination and immunomarker studies. The markers studied included Pan T and PanB cell markers. LCA, Mac 387, HLA-DR, and S-100. Lymph node biopsy was performed whenever necessary.

RESULTS

There were a total of seven patients with male to female ratio of 5:2. All patients were in the age group 4th-7th decade. All patients presented with asymptomatic skin lesions. One patient had weight loss and generalized pruritus. Duration of the lesions, varied from 2 months to 2 years.

Skin lesions consisted of hypopigmented patches with scaling (4 cases) plaque (5 cases) and nodules (3 cases). One case had ulcerated vegetative lesions, with oozing. The lesions were distributed mainly on the trunk (6 cases) and limb (3 cases). One patient had only a solitary plaque on left forearm. Axillae and groins were involved in one other case.

Systemic examination revealed lymphadenopathy and hepatomegaly in one case. All other cases had no systemic abnormality.

Of the seven cases, there were 4 cases of mycosis fungoides, 2 cases of non epidermotropic cutaneous T-cell lymphomas, and one case of Ki-1 positive anaplastic large cell lymphoma.

Mycosis fungoides:

Details of 4 cases of mycosis fungoides are shown in Table 1. Three cases presented with hypopigmented patches with fine superficial scaling (Fig. 1). For these patients, differential diagnosis of Hansen's disease, large plaque parapsoriasis, and postinflammatory hypopigmentation were considered. One patient had erythematous patches with scaling, and was through to be pityriasis rubra pilaris.

Table 1. Details of patients with Mycosis Fungoides.

No.	Age/Sex	Clinical Diagnosis	Histological diagnosis		
			Biopsy 1	Biopsy 2	Biopsy 3
1	44 / M	Parapsoriasis	Non-sp 1991	Large Plaque Parapsoriasis 1992	Mycosis Fungoides 1994
2	52 / F	Pityriasis Rubra Pilaris	Non-specific 1992	Large Plaque Parapsoriasis 1993	Mycosis Fungoides 1994
3	50 / M	Parapsoriasis Hansen's Dis	Large Plaque Parapsoriasis 1990	Mycosis Fungoides 1994	-
4	44 / M	Parapsoriasis Hansen's Dis Postinflamm. Hypopig.	Non-specific 1990	Large Plaque Parapsoriasis 1993	Mycosis Fungoides 1994

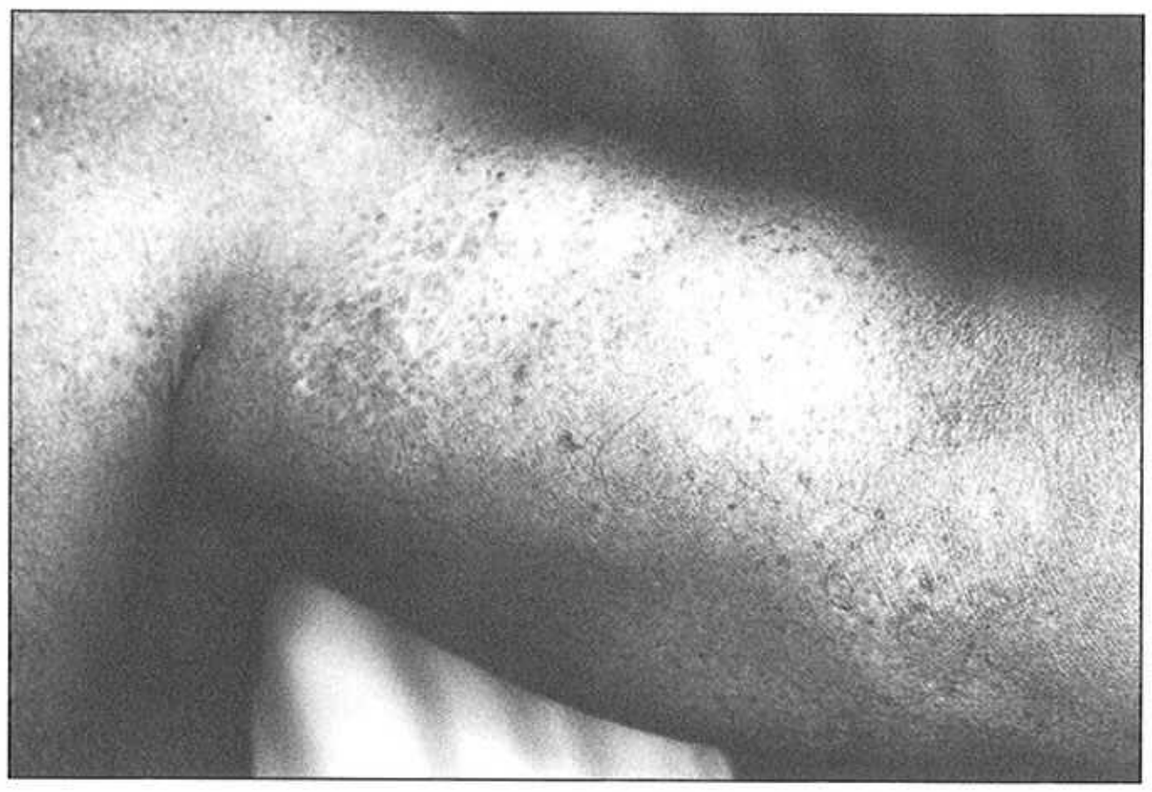


FIG. 1: Hypopigmented patches of mycosis fungoides over left arm.

Two cases developed plaques during a follow-up period of 3 years, and one case developed poikilodermatous changes after 2 years.

In all these cases, the initial histological picture showed a nonspecific superficial dermal lymphocytic infiltrate with only a slight epidermotropism, and no atypical cells, and hence, was not specific for mycosis fungoides. Further repeat biopsies over the next 1-2 years, showed thinning of epidermis, marked epidermotropism, atypical lymphocytes and Pautrier's microabscesses, thus confirming the diagnosis mycosis fungoides (Fig. 2).

Non epidermotropic cutaneous T cell lymphoma:

Case-1: A 44-year-old female patient, presented with an asymptomatic erythematous plaque on left forearm which had been slowly growing, to the present size of 5 cm x 6 cm. (Fig. 3). There were no systemic abnormalities. Clinically the diagnoses considered were cutaneous lymphoma, pseudolymphoma, and granulomatous conditions such as tuberculosis, leprosy, and leishmaniasis. Biopsy (Fig. 4) revealed a dense, diffuse, monomorphic infiltrate throughout the dermis extending around blood vessels, appendages and in to subcutis. Immuno staining revealed a predominant T cell infiltrate, confirming the diagnosis of T-cell lymphoma.

Case 2: A 70-year-old male presented with asymptomatic skin nodules and plaques over trunk of 4 months duration. Patient also had axillary and inguinal lymphadenopathy, and hepatomegaly. He had hypercalcemia. Bone marrow examination was normal. A clinical diagnosis of tumor stage of mycosis fungoides was made. Biopsy from multiple sites revealed a superficial nodular infiltrate of lymphocytes, many of which had large atypical nu-

Table 2. New classification for CTCL: Combined clinical, histological, and immunophenotypic approach.[18]

Low grade:	1. MF 2. MF variants	
Step-1		a) Follicular Mucinosis b) Pagetoid Reticulosis c) Granulomatous Slack skin Syndrome.
	3. Sezary syndrome	
Step-2	4. CD30 +ve disorders	a) CD +ve LCL b) Lymphomatoid Papulosis c) Regressing Atypical Histiocytosis d) Borderline cases
High grade		
Step-3	CD30 +ve lymphomas	a) pleomorphic Large Cell b) Immunoblastic
Undetermined CTCL		a) CD8 +ve CTCL b) Pleomorphic c) Angiocentric L d) Others

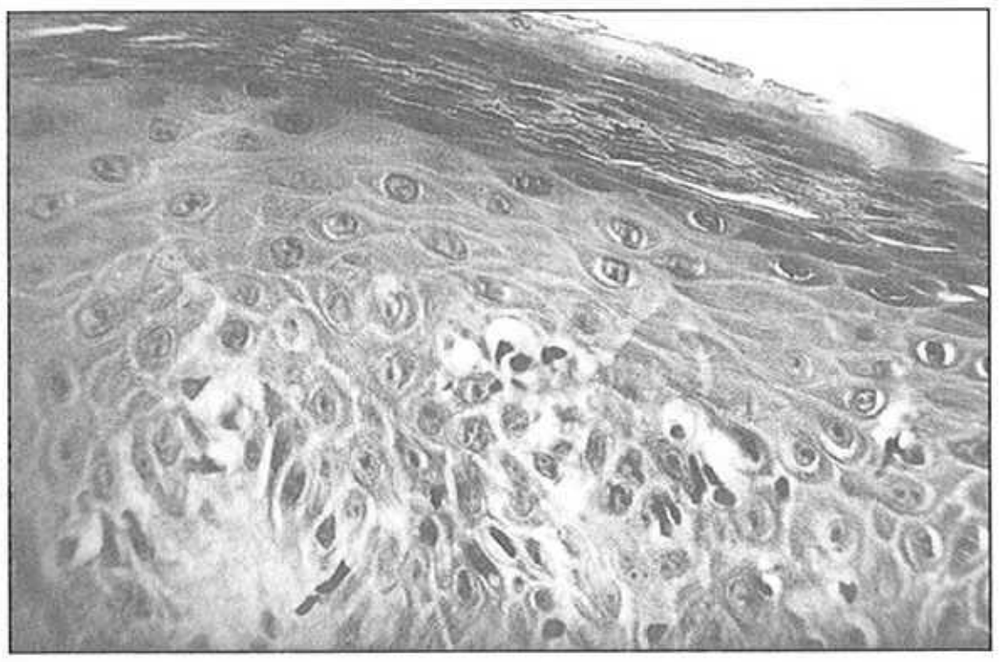


Fig. 2. H & E section (X40) showing epidermotropism and Pautrier microabscess.

clei. There was no significant epidermotropism or Sezary cells on multiple sections, even in biopsies from plaque lesions. Cells were found to be predominantly T cells. A diagnosis of cutaneous T cell lymphoma (Non-epidermotropic) was made. The patient developed severe pneumonitis and died after two months.

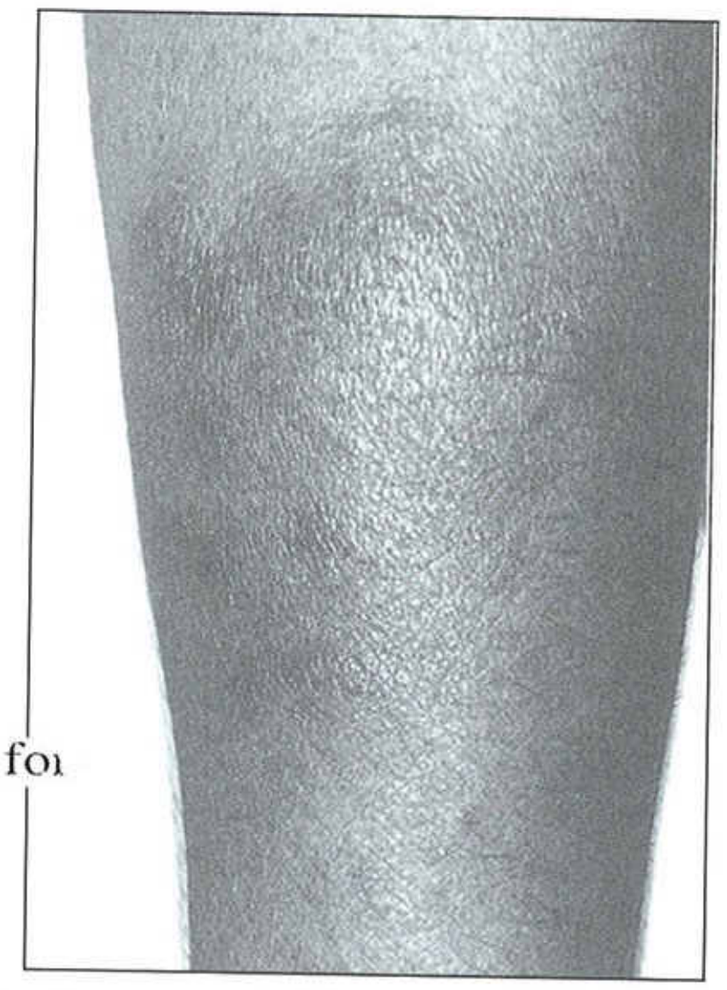
Ki-1 positive Anaplastic Large Cell Lymphoma (Ki-1 ALCL):

A 65-year-old female patient presented with ulcerated, vegetative lesions over axilla, inframammary region, and plaques over left supra-clavicular area. The patient did not have any lymphadenopathy or hepatosplenomegaly. It was initially diagnosed as pemphigus vegetans in view of the distribution and the vegetative nature of the lesions. X rays, ultrasound, CT scans, and marrow examination were within normal limits. Biopsy revealed dense dermal, pleomorphic infiltrate of large cells with atypical nuclei, and many atypical mitotic figures, with an admixture of plasma cells, macrophages and small lymphocytes.

Immuno staining showed the cells to be negative for both, T and B cell markers. Some cells were positive for Mac 387 and for LCA. A Preliminary diagnosis of histiocytic lymphoma was made. Further processing revealed staining of majority of cases to KI-1 antigen and a diagnosis of Ki-1 ALCL was made. By this time patient had received intralesional steroid, as the initial clinical diagnosis was pemphigus vegetans. Surprisingly all lesions had completely resolved, and did not recur during the follow-up period of 4 months.

DISCUSSION

Though the number of cases in the present series is small, it shows much variety in the clinical pre-



were trea..
twice daily fo
cal treatm

Fig. 3. Erythematous, infiltrated plaque over left forearm in the patient with non-epidermotropic CTCL.

Fig. 4. H & E section (X 10) showing nodular infiltrates of lymphoid cells in the mid and lower dermis.

sentations and diagnoses, and some conclusions can be drawn. Firstly, the condition is not rare. Secondly, the initial manifestations are often atypical and a high degree of clinical suspicion is necessary for early detection.

Mycosis Fungoides was the commonest type of CTCL, as is to be expected. However, the majority of cases in this study had hypopigmented patches as the initial presentation, causing diagnostic confusion with large plaque parapsoriasis, Hansen's disease and post inflammatory hypopigmentation. Various atypical manifestations of mycosis fungoides have been reported, including hyperpigmented form, bullous, hyperkeratotic lesions, pokilodermatous, ulcerative, follicular and pustular forms. Hypopigmented patches have been reported to be uncommon[2,3]. Hence, this fact should be kept in mind, particularly for patendemic areas, in view of diagnostic confusion with Hansen's disease.

Initial histological diagnosis of mycosis fungoides is often difficult. In our study, a period of 3-4 years elapsed before the diagnosis could be confirmed. Most patients have a pre MF stage of 6-7 years[1]. Diagnosis of early mycosis fungoides is based on classical histological presentations of a skin biopsy, such as atypical lymphocytes with hyperconvoluted cerebriform nuclei, epidermal exocytosis, and appearance of Pautrier microabscesses [2,4]. However, these criteria have limitations, as emphasized by the fact that a mean of 3.8 years elapsed between onset of skin lesions, and development of diagnostic histological features.4 There was 40% false negative rate and 44% false positive rate, when only histopathological features were used for diagnosis[4]. Attempts at standardization of histological criteria have failed. Also, distinction from large plaque parapsoriasis can be quite difficult, as many authorities feel that these are the same entities, and any distinction is perhaps largely artificial[5].

It has been emphasized that the overall pattern of lymphocytic infiltrate may be important for the diagnosis of early lesions of mycosis fungoides and the following criteria have been described as a significant pattern for diagnosis of early Mycosis Fungoides[5]:

1- Presence of lymphocytes linearly along the basal layer of the epidermis.

2- Presence of lymphocytes, larger in the epidermis than in dermis.

3- Presence of wiry bundles of collagen in upper dermis.

Recently, T-cell receptor gene analysis by polymerase chain reaction for detection of clonality has been applied for the diagnosis of early Mycosis Fungoides[6,7]. However, till these newer techniques become available for practical use, routine histology by serial biopsies with H & E, and proper clinicopathological correlation, remain the gold standard for the diagnosis of early mycosis fungoides[5].

It is important to note that non-mycotic T cell

lymphoma of skin is not uncommon and many new entities have been described.8-10 One such entity is the Ki-1 or CD30 positive large cell anaplastic lymphoma. This is usually of T cell, but rarely of B cell or null cell origin, and can occur in children elderly adults, or in patients with preexisting dermatoses such as mycosis fungoides, eczemas, icthyosis etc[11]. The clinical presentation is usually with nodules, plaques or ulcers, and the course can often be benign and even self limiting. It has recently been proposed that CD30 positively indicates good prognosis[12]. In or case, the condition underwent remission with steroid therapy[13].

Non epidermotropic CTCL can occur either per se or, as in our case, as the result of progression from previous Mycosis Fungoides[14]. It has been recommended that in al such cases, biopsies from patch or plaque lesions will reveal epidermotropism, and hence differentiate the two variants[14]. Loss of epidermotropism indicates poor prognosis, as in our patient who expired in 2 months. This category has been elucidated as part of a spectrum with MF at one end of the spectrum. Any histological type as in Kiel classification can occut[15].

Cutaneous T cell infiltrate is usually a superficial infiltrate, while B cell infiltrate extends into lower dermis and subcutis, and this is regarded as a major distinguishing feature between the types[16]. However, this description is not true in all cases, as was the case in patient No. 3 in this study who had a B cell pattern of T cell infiltrate. Such lymphomas can cause great diagnosis confusion with pseudolymphomas. Proper clinicopathological correlation and follow-up are necessary for proper diagnosis in all such cases[17].

In conclusion, much confusion now exists regarding the exact nosology of many entities and the acceptable classification. Recently, Slater[9] et
a concept to explain pseudo
prelymphomatous states, low gr
as MF, and high grade lymphomas
based on the fact that CD30 positive
prognosis, was proposed by Willemze et al.
2). Recent availability of lymphocyte histochemical markers, T cell receptor gene analysis by PCR, electron microscopic analysis of nuclei, DNA flowcytometric analysis of aneuploidy, have helped to clarify this concept to a great extent. However, more clarity needs to be achieved before becoming practically relevant, and applicable. Till then, clinico pathological correlation, and proper follow-up remain most important tools for diagnosis.

REFERENCES

1. Herrman JJ, Kinzel TM, Rosle S, et al. Proceedings of second study symposium on CTCL. J Am Acad Dermatol 1994; 31:819-22.

2. Kuzel TM, Roenigk HH, Rosen ST. Mycosis Fungoides and the Sezary syndrome. A review of pathogenesis, diagnosis and therapy. J Clin Oncol 1991; 9:1298-1353. ,

3. Epstein EH Jr, Leur DL, Croft JN Jr et al. Mycosis fungoides-survival, prognostic features, response to therapy and autopsy findings. Medicines 1972; 15: 61-72.

4. Olerud JE, Kulu PA, Chew DE et al. Cutaneous T cell lymphomas-Evaluation of pretreatment skin biopsy specimens by a panel of pathologists Arch Dermatol 1992; 128: 501-507.

5. Nickoloff P. Patch/plaque stage of Mycosis fungoides.Am J dermatopathol 1986; 10:6; 472-476.

6. Weinberg JM, Rook AH. Molecular diagosis of lymphocytic infiltrates of skin. Arch Dermatol 1993; 129: 1491-1500.

7. Hunt. S, Charles M, Jegasothy V. CTCL - Utility of antibodies to the variable regions of human T-cell antigen receptor.J Am Acad Dermatol 1992; 26: 552-558.

8. Kaplan EH, Leslie W.T. Cutaneous T cell Lymphoma-Current Opinion in oncology. 1993; 5: 812-868.

9. Slater DN. Cutaneous lymphoproliferative disorders.Br J Dermatol 1991; 124: 309-323.

10. Slater DN. Diagnostic difficulties in nonmycotic cutaneous lymphomas. Histopathol 1992; 21: 203-213.

11. Bannerjee SS, Heals J, Harris P. Twelve cases of Ki-1 +ve Anaplastic Large Cell Lymphoma of the skin. J Clin Pathol 1991; 44: 119-125.

12. Berjaard RC, Deijer CJLA, Schetter E. et al. Prognostic significance of CD30 (Ki-1/Ber H2) expression of primary cutaneous large cell lymphoma of T cell origin. A clinico pathological and immunological study of 30 patients.Am J Pathol 1989; 135; 1169-1178.

13. Venkataram MN, Al Suwaid AR, Bhusnurmath SR, Banodkar DD.Ki-1 anaplastic large cell lymphoma- A case report. International Journal of Dermatology (in press).

14. Edelson RL. Cutaneous T cell Lymphoma: Mycosis fungoides, Sezary syndrome and other variants. J Am Acad Dermatol 1980; 2: 89-106.

15. Stansfleed AL, Diebole J, Kapansi M. Updated Kiel classification for lymphomas. Lancet 1988; 1: 292-293.

16. Kerl H, Ackerman B. Cutaneous pseudolymphomas. In: Fitzpatrick TB, Eisen AZ, Wolff K, et al eds. Dermatology in General Medicine. New York: McGraw-Hill, 1987: 1166-78.

17. Rijlaarsdam JV, Scheffer E, Meijer CJLM et al. Cutaneous T cell Pseudolymphomas. Cancer. 1992; 3: 717-724.

18. Willemze. R., Beljaard RC, Meijer CJLM. Classification of Primary Cutaneous T cell lymphomas. Histopathol 1994; 24: 405-415.