



# **A Clinically Asymptomatic Patient with a Flowcytometry Profile of Mycosis Fungoides/Sezary Syndrome**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. Author CCK designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors BLTB and SACDR managed the analyses of the study, performed the statistical analysis and managed the literature searches. All authors read and approved the final manuscript.*

## **Article Information**

### Editor(s):

(1) Dr. Juan Carlos Troiano, University of Buenos Aires, Argentina.

### Reviewers:

(1) Azza Mahmoud Kamel, Cairo University, Egypt.

(2) Raghunadharao Digumarti, Homi Bhabha Cancer Hospital & Research Centre, India.

(3) Arthur Chuemer, University of Port Harcourt, Nigeria.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/55579>

**Case Report**

**Received 12 January 2020**

**Accepted 20 March 2020**

**Published 27 March 2020**

## **ABSTRACT**

**Introduction:** Mycosis fungoides (MF) is the most common type of cutaneous T –cell lymphoma accounting for 50% of all cutaneous lymphomas. Sezary Syndrome (SS) and MF are closely related T –cell neoplasms. They are considered separately on the basis of clinical features and cell of origin. Flowcytometry plays an important role in the diagnosis of MF/SS with a characteristic immunophenotypic expression of a lack of CD 7 as a common feature in all stages of the disease. Our case is a clinically asymptomatic patient with a flowcytometric pattern of Mycosis fungoides/Sezary syndrome. There is no documentation of such a case in the literature.

**Case:** A 55 - year – old male presented with persistent lymphocytosis. Investigations revealed a Hb of 15.5 g/dl, ESR 03 mm/1st hour, platelet count of 178,000/cu mm, total WBC count of 10,700/cu mm and an absolute lymphocyte count of 7000/cu mm (62%). The serum protein electrophoresis was normal. LDH was 149 IU/L (150-250) IU/L. A chest X-ray showed no pathology.

The patient was followed up for a period of five months with full blood counts (FBC), monospot test,

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ultrasound scan of abdomen, full body CT scan, LDH level and viral studies. During this period, the lymphocytosis persisted. Serial absolute lymphocyte counts were 6332/cu mm, 4918/cu mm, 5749/cu mm, 6890/cu mm and 7820/cu mm. Viral studies revealed CMV IgG antibody positivity and Hepatitis A (HAV) IgG positivity. Studies for HIV were negative. Monospot test for infectious mononucleosis was negative. Ultrasound scan of abdomen and full body CT scan were normal. Blood picture revealed small to medium sized lymphocytes with scanty cytoplasm. Bone marrow examination revealed a reactive marrow with a normal lymphocyte count of 15-20%. Flowcytometry was performed using peripheral blood and bone marrow samples 5 months apart.

**Results:** Flowcytometry of peripheral blood and bone marrow revealed that T-lymphocytes percentage was 92.0% and 82.0%, respectively. The immunophenotypic results for both blood and bone marrow revealed almost identical findings on LST (Lymphoid Screening Tube) and TCLPD (T Cell Lymphoproliferative Disorder) panels showing bright positivity of smCD3, CD4, CD2, TCR $\alpha\beta$ , CD5 and dim positive CD8. Negative results were CD7, TCR $\gamma\delta$ , CD25, CD26 and CD4+/ CD8+ ratio was 3.0/2.3 respectively.

**Conclusion:** The criteria of International Society of Cutaneous Lymphomas (ISCL) and the European Organization for Research and Treatment of Cancer (EORTC) to stage Mycosis fungoides and Sezary Syndrome were not present in our patient who was asymptomatic but showed a typical immunophenotypic pattern of MF/SS.

**Keywords:** Mycosis fungoides; Sezary Syndrome; flowcytometry; skin lesions; ICSL and EORTC staging.

## 1. INTRODUCTION

Mycosis fungoides (MF) is the most common type of cutaneous T – cell lymphomas and accounts for 50% of all cutaneous lymphomas [1]. They manifest heterogeneous clinical, histologic, immunophenotypic, and cytogenetic features. MF is associated with several professions which have high risk of exposing petrochemical, textile and metal industry, painting, woodworking, and carpentry [1].

Sezary syndrome (SS) and MF are closely related T-cell neoplasms, but they are considered separately on the basis of differences in the clinical features and cell of origin. Erythroderma, generalized lymphadenopathy, the presence of clonal neoplastic T cells with cerebriform nuclei (Sezary cells) in peripheral blood, skin and lymph nodes are the main features of the Sezary syndrome. Mycosis fungoides has an indolent course with slow progression over years characterized by patches, plaques and eventually tumours. Both SS and MF patients are adult/elderly and have male predominance [1].

Flowcytometry plays an important role in diagnosis of MF / SS as it has characteristic immunophenotypic pattern. Flowcytometry analysis of peripheral blood lymphocytes of MF shows CD2+, smCD3+, CD4+, TCR $\alpha\beta$ +, CD5+,

TCR $\gamma\delta$ - expression. A lack of CD7 is common in all stages of the disease [2].

The neoplastic T cells of SS have an immunophenotypic pattern of CD3+, CD4+, CD8. Characteristically lack of CD7 and CD26 is common in SS [1].

Our study is a case of a clinically asymptomatic patient presenting with a flowcytometric pattern of Mycosis fungoides/Sezary syndrome. There was no documentation of such a case in the literature survey.

## 2. CASE PRESENTATION

A 55 - year – old male presented to a tertiary care hospital on account of persistent lymphocytosis.

There was no history of lymphadenopathy, organomegaly or significant skin lesions. He gave a history of an itchy rash that was previously diagnosed and treated as dermatitis. He did not give a history of radiation exposure but had a childhood history of close contact with *batik dyes*. Investigations revealed a Hb of 15.5 g/dl, ESR 03 mm/1st hour, platelet count – 178,000/cu mm, WBC of 10,700/cu mm and absolute count of lymphocyte of 7000/cu mm (62%). Serum Protein electrophoresis was normal. LDH level was 149 IU/L (150-250) IU/L. And the Chest X-ray showed no acute pathology.

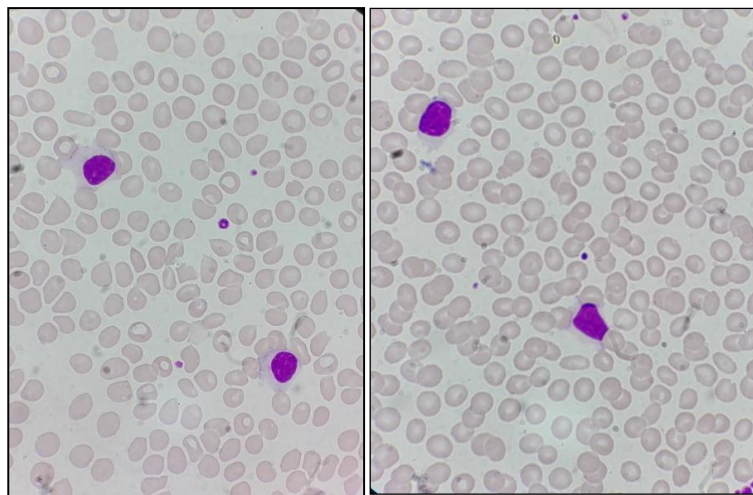
The patient was clinically observed for a period of five months. Investigations carried out in the Haematology clinic included full blood counts (FBC), monospot test, ultrasound scan of abdomen, full body CT scan, LDH level and viral studies. During this period, lymphocytosis persisted with eosinophilia. The counts were as follows, 6332/cu mm, 4918/cu mm, 5749/cu mm, 6890/cu mm and 7820/cu mm. Viral studies revealed CMV IgG antibody positivity and Hepatitis A (HAV) IgG positivity. Studies for HIV were negative. Monospot test was negative. Ultrasound scan of abdomen and full body CT scan were normal. Blood picture revealed small to medium sized lymphocytes with scanty cytoplasm. Bone marrow aspiration biopsy showed reactive marrow with high, normal lymphocyte count. Lymphocyte count was approximately 15 -20% of the nucleated marrow cells. Plasma cells not increased and the blast

percentage was less than 3%. The findings of Bone marrow trephine biopsy were consistent with the bone marrow aspiration findings.

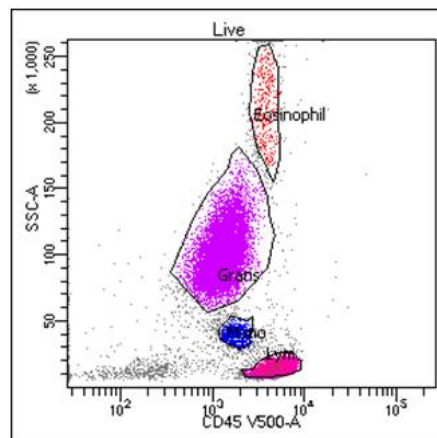
To confirm/ exclude chronic lymphoproliferative disorder, flowcytometry was performed using peripheral blood and bone marrow samples.

Flowcytometry of peripheral blood revealed that T-lymphocyte percentage was 92.0%. Accordingly, B- lymphocytes and NON-T/B- cells were 6.0% and 2.0%.

The immunophenotypic results of LST (Lymphoid Screening Tube) and TCLPD (T Cell Lymphoproliferative Disorder) panels showed bright positivity of smCD3, CD4, CD2, TCR $\alpha\beta$ , CD5 and dim positive CD8. Negative results were CD7, TCR $\gamma\delta$ , CD25, CD26 and CD4+/CD8+ ratio was 3.0.



**Fig. 1. Morphology of peripheral blood**



**Fig. 2. Live cells gated by CD45**

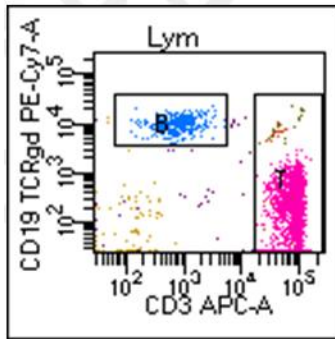


Fig. 3. lymphocytes gated by CD3 and CD19

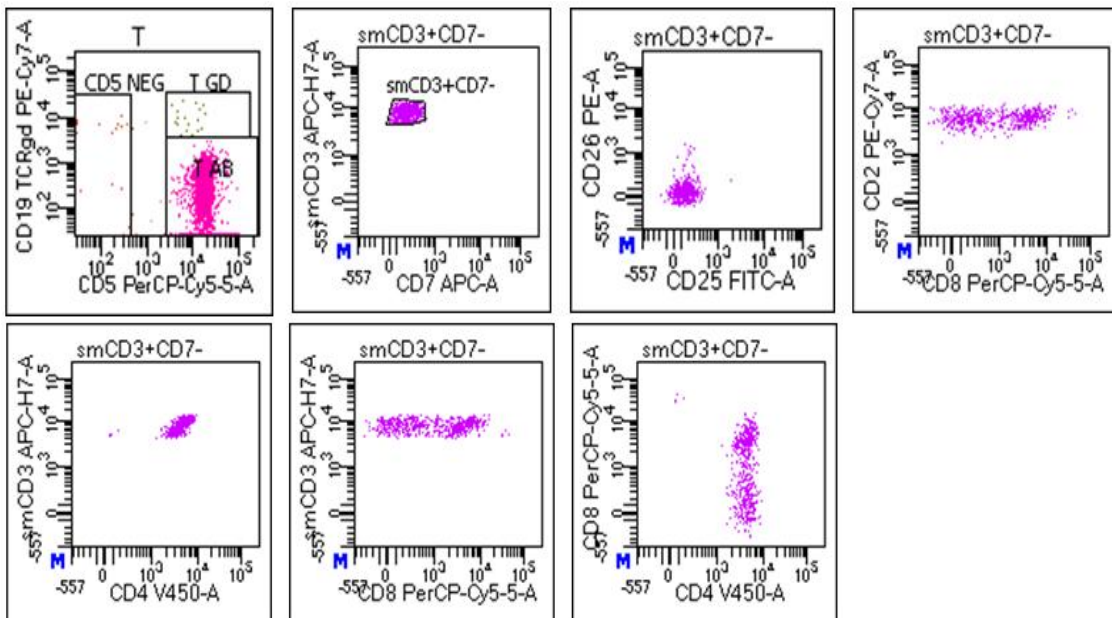


Fig. 4. Flow charts of smCD3 positive, CD7 negative lymphocytes

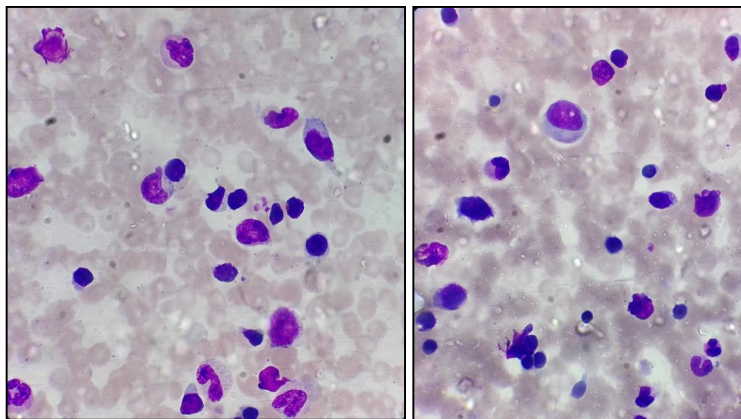


Fig. 5. Morphology of bone marrow

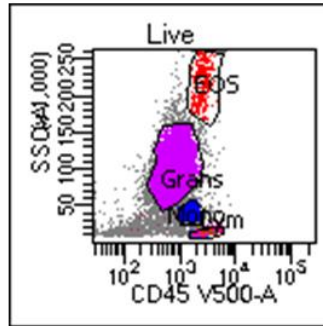


Fig. 6. Live cells gated by CD45

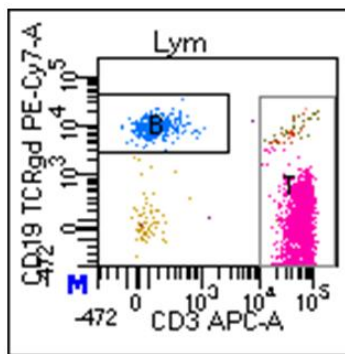


Fig. 7. lymphocytes gated by CD3 and CD19

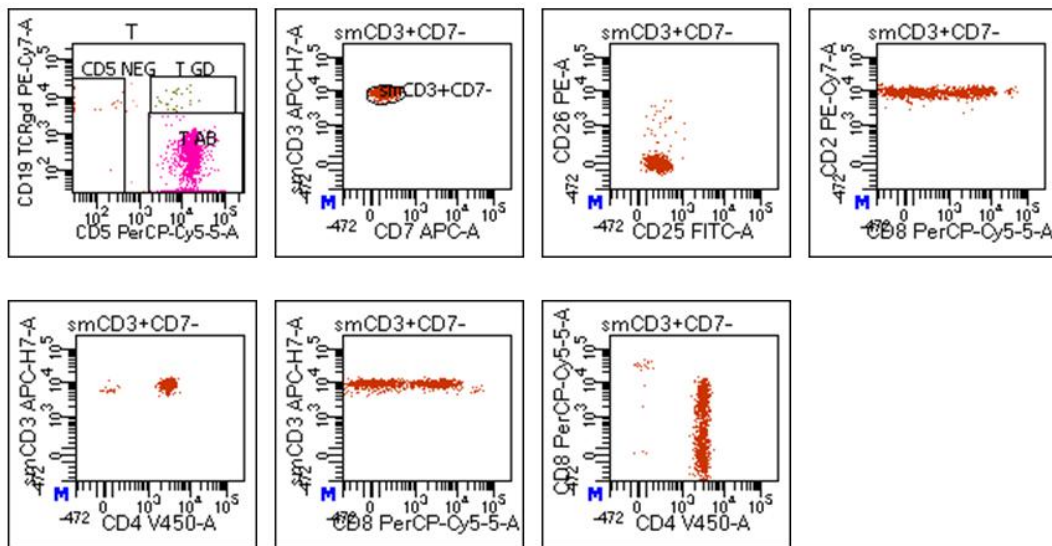


Fig. 8. Flow charts of smCD3 positive and CD7 negative lymphocytes

Flowcytometry of bone marrow revealed that T-lymphocytes percentage was 82.0%. Accordingly, B- lymphocytes and NON-T/B -cells were 16.0% and 2.0%.

The immunophenotypic results of LST and TCLPD panels showed bright positivity of smCD3, CD4, CD2, TCRαβ, CD5 and dim positive CD8. Negative results were CD7,

TCR $\gamma\delta$ , CD25, CD26 and CD4+/ CD8+ ratio was 2.3.

#### 4. DISCUSSION

According to staging of MF/SS by International Society of Cutaneous Lymphomas (ISCL) and the European Organization for Research and Treatment of Cancer (EORTC) criteria, to describe a patient under the stage I(A) (T1,N0,M0,B0-1), he should have at least limited patches, papules and/or plaques covering <10% of the skin [3]. A patch means a skin lesion of any size without significant elevation or induration [3]. Our patient showed no skin lesions, no abnormal lymph nodes or visceral organ involvement and absence of significant morphological changes of the lymphoid cells in the blood.

Premycotic, mycotic, and tumor stage are the three traditional stages of the MF [4]. The blood picture findings of the premycotic stage of the disease are not diagnostic and it is represented by chronic nonspecific dermatitis [5]. As the symptoms and skin biopsy findings are similar to those of other skin conditions it is difficult to diagnose MF in its early stages [6].

Wojdylo MS, et al. [7] showed that flowcytometry analysis of peripheral blood revealed an increased proportion of CD4/CD8 ratio of 8:1 and elevated LDH level (626 U/L). But in our study it was 3/2.3 respectively in blood and bone marrow and LDH was normal.

The neoplastic cells in MF have a pattern of CD3+, CD4+, CD45+ T-cell phenotype with usual expression of TCR $\alpha\beta$ +. Among the pan-T antigens (CD2, CD3, CD5, CD7), CD7 is the most frequently lost antigen. In rare cases of MF, a CD4 – /CD8 + mature T-cell phenotype may be seen [8,9].

In the blood, some of CD4+ T-cells express CD26, whereas neoplastic T-cells in SS display dim CD26 and often aberrant expression of CD7 [10,11].

The clonality of Sezary Syndrome can be proved at the molecular level. The most frequent genetic lesions include monosomy 10, losses of 10q and 17p, gains of 8q24 and 17q, and diverse structural alterations involve in these regions [12].

In Mycosis fungoides, most common imbalances are gain of chromosome regions 1p36,7, 9q34,

17q24-qter, 19, and loss of 2q36-qter, 9p21 and 17p [13].

#### 5. CONCLUSION

The criteria of International Society of Cutaneous Lymphomas (ISCL) and the European Organization for Research and Treatment of Cancer (EORTC) to stage Mycosis fungoides and Sezary Syndrome were not present in our patient who was asymptomatic but showed a typical immunophenotypic pattern of MF/SS.

#### CONSENT

Written informed consent was obtained from the patient for publication of this case report.

#### ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

#### REFERENCES

1. Swerdlow SH, Campo E, Harris NL, et al. WHO classification of tumours of haematopoietic and lymphoid tissues. 4 Ed. 2017;385-391.
2. Gorczyca W. Flowcytometry in neoplastic hematology morphologic-immunophenotypic correlation. 2<sup>nd</sup> Ed. 2010;230-234.
3. Olsen E, Vonderheid E, Pimpinelli N, et al. Revisions to the staging and classification of mycosis fungoides and Sezary syndrome: A proposal of the International Society for Cutaneous Lymphoma (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer (EORTC). *Blood*. 2007;110(6):1713-1722.
4. Murphy GF, Schwarting R. Cutaneous lymphomas and leukemias. In *Lever's histopathology of the skin*. Lippincot Williams and Wilkins. 9<sup>th</sup> Ed. 2005;927–978.
5. Khunger JM, Khunger N, Azad K, Srivastava S. Mycosis fungoides: A case

- report. Indian Journal of Hematology and Blood Transfusion. 2008;26(1):12–14.
6. Akinbami AA, Osikomaiya BI, John-Olabode SO. Mycosis fungoides: Case report and literature review. Clinical Medicine Insights: Case Reports. 2014;7:95–98.
  7. Wojdyło MS, Rybak WB, Cegielska A. Atopic dermatitis-like Pre-Sézary Syndrome: Role of immunosuppression. Acta Dermato-Venereologica. 2011;91: 574–577.
  8. Berti E, Tomasini D, Vermeer MH, et al. Primary cutaneous CD8-positive epidermotropic cytotoxic T cell lymphomas. A distinct clinicopathological entity with an aggressive clinical behavior. American Journal of Pathology. 1999;155:483–92.
  9. Whittam LR, Calonje E, Orchard G, et al. CD8-positive juvenile onset mycosis fungoides: An immunohistochemical and genotypic analysis of six cases. Br J Dermatol. 2000;143:1199–204.
  10. Foucar K. Mature T-cell leukemias including T-prolymphocytic leukemia, adult T-cell leukemia/lymphoma, and Sezary syndrome. American Journal of Pathology. 2007;127:496–510.
  11. Jones D, Dang NH, Duvic M, et al. Absence of CD26 expression is a useful marker for diagnosis of T-cell lymphoma in peripheral blood. American Journal of Clinical Pathology. 2001;115:885–92.
  12. Izykowska K, Przybylski GK. Genetic alterations in Sezary Syndrome. Journal Leukaemia and Lymphoma. 2011;52(5): 745-753.
  13. Prochazkova M, Chevret E, Mainhaguet G, et al. Common chromosomal abnormalities in mycosis fungoides transformation. Genes, Chromosomes and Cancers. 2007;46(9):828-838.

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