

Access this article online
Quick Response Code:

Website: www.ajts.org
DOI: 10.4103/ajts.AJTS_111_18

# Successful treatment of Sezary syndrome with extracorporeal photopheresis – The first attempt in India

Aseem K. Tiwari, Dinesh Arora, Pratibha Dhiman<sup>1</sup>, Sheilly Kapoor<sup>2</sup>, Geet Aggarwal, Ravi C. Dara<sup>3</sup>, Ashok Vaid<sup>4</sup>

## Abstract:

Sezary syndrome (SS) is more aggressive leukemic variant of cutaneous T-cell lymphoma in which a significant number of circulating malignant (Sezary) cells are observed in peripheral blood. Although single-agent or combination chemotherapy regimens have produced moderately high response rates in patients with advanced-stage SS, these responses are invariably not durable. Extracorporeal photopheresis (ECP) is recommended as an immunomodulator treatment, offering better life quality for patient. We would like to present the first SS case treated successfully with low-dose methotrexate and ECP in India. A 50-year-old male presented with rash and severe pruritus all over the body for 2 years. He had received various treatment regimens but without any symptomatic improvement. He underwent detailed examination and diagnosis of SS was established. Peripheral smear revealed total leukocyte count of 14900/ $\mu$ l with 55% cells reported as Sezary cells. Contrast-enhanced computerized tomography revealed few insignificant (<1.5 cm) bilateral nodes in the axillary and inguinal region. The patient's disease stage was determined IVA1, and grade was T4N0M0B2. He received six cycles of CHOP, which led to a short-term remission of <3 months, and he was started on single-agent methotrexate along with skin supportive treatment. He did not respond to low-dose methotrexate alone, and therefore, ECP was added to treatment regimen. This was possibly the first such treatment for SS patient in India. The patient had very good response after six cycles of ECP with pruritus and itching diminishing and scaly lesions down to <10% of body surface area. There was regrowth of hair all over affected area. Sezary cell counts also came down to 35%. The patient continues to do well post-ECP, with single-agent gemcitabine. ECP either as monotherapy or in combination with other immunotherapies offers a good treatment option to otherwise resistant cases of SS.

## Keywords:

Erythrodermic cutaneous T-cell lymphoma, extracorporeal photopheresis, mycoses fungoides

## Introduction

Sezary syndrome (SS) is an aggressive erythrodermic leukemic variant of cutaneous T-cell lymphoma in which a significant number of circulating malignant (Sezary) cells are observed in peripheral blood with clonally matching T-cells in

the skin.<sup>[1]</sup> The disease affects men more often than women and usually occurs in the fifth and sixth decade of life.<sup>[2,3]</sup> Patients with SS commonly present with erythroderma, diffuse skin involvement, alopecia, hypertrophic nails, and generalized lymphadenopathy.

There are several accepted treatment approaches for advanced-stage SS, and it includes systemic and skin-directed

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

**How to cite this article:** Tiwari AK, Arora D, Dhiman P, Kapoor S, Aggarwal G, Dara RC, *et al.* Successful treatment of Sezary syndrome with extracorporeal photopheresis – The first attempt in India. Asian J Transfus Sci 2019;13:66-9.

Departments of  
Transfusion Medicine,

<sup>1</sup>Heamto-oncology,

<sup>2</sup>Dermatology and

<sup>4</sup>Medical Oncology,  
Medanta-The Medicity,

Gurgaon, Haryana,

<sup>3</sup>Department of  
Transfusion Medicine,  
Manipal Hospital, Jaipur,  
Rajasthan, India

**Address for  
correspondence:**

Dr. Aseem K. Tiwari,  
Department of

Transfusion Medicine,

Medanta-The Medicity,

Gurgaon - 122 001,

Haryana, India.

E-mail: aseemtwr@yahoo.  
co.in

Submission: 10-09-2018

Accepted: 10-02-2019

therapy (SDT; topical corticosteroids, nitrogen mustard, total electron beam irradiation), biological response modifiers (interferon and retinoid), extracorporeal photopheresis (ECP), low-dose methotrexate, and histone deacetylase inhibitors, alone or in combination.<sup>[4,5]</sup> We would like to report a case of advanced SS treated successfully with a combination of low-dose methotrexate, SDT, and ECP.

## Case Report

### Medical history

A patient, 50-year-old male, had a history of rash and severe pruritus all over the body for the past 2 years. Initially, the disease presented as skin lesions and the patient was initially diagnosed as sebopsoriasis and treated with methotrexate 20 mg weekly for 8 weeks. However, the patient continued to have itching and spread of lesions with rising total leukocyte counts (TLCs) and no clinical or symptomatic improvement.

The patient consulted hematologist at our institute in light of persistent high TLC. The patient presented with scaly pruritic erythematous lesions involving more than 90% of body surface area. The patient also had hair loss and hypertrophic nails.

### Clinical examination and laboratory findings

After detailed clinical examination, psoriasis, atopic dermatitis, contact dermatitis, and scabies were ruled out and a provisional diagnosis of SS was made. Peripheral smear revealed TLC was 14900/ $\mu$ l with 55% cells being reported as Sezary cells. It was confirmed by flow cytometry and skin biopsy that was CD3+CD4+ CD7-CD8- on immunohistochemistry [Figures 1 and 2]. Absolute CD8+ cell count (586/cu mm) and CD4+/CD8+ ratio (2.09) were within normal range. Serum lactate dehydrogenase was raised at 726 U/L. Contrast-enhanced computerized tomography revealed few insignificant bilateral nodes (<1.5 cm) in axillary and inguinal region. No visceral involvement was detected. Other routine investigations including liver function tests and kidney function tests were within normal range.

### Clinical stage and grade of disease

On the basis of clinical examination and laboratory findings, the disease was graded as T4N0M0B2 (T4 [>80% skin involvement], N0 [no nodal involvement], M0 [no visceral organ involvement], B2 [>1000 Sezary cells/ $\mu$ l in peripheral blood]). In accordance with joint revision by the International Society for Cutaneous Lymphoma and the Cutaneous Lymphoma Task Force of the European Organization for Research and Treatment of Cancer, 2007, the disease stage was determined to be IVA1.<sup>[6]</sup>

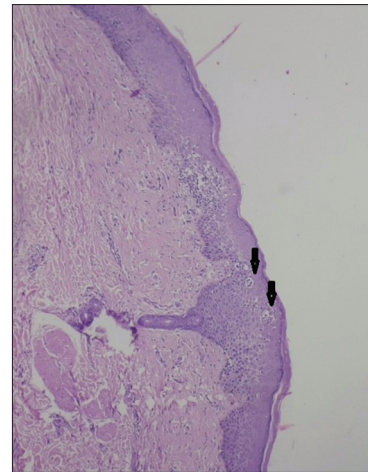


Figure 1: Atypical lymphoid cells infiltrating dermoepidermal junction as well as epidermis (H and E)

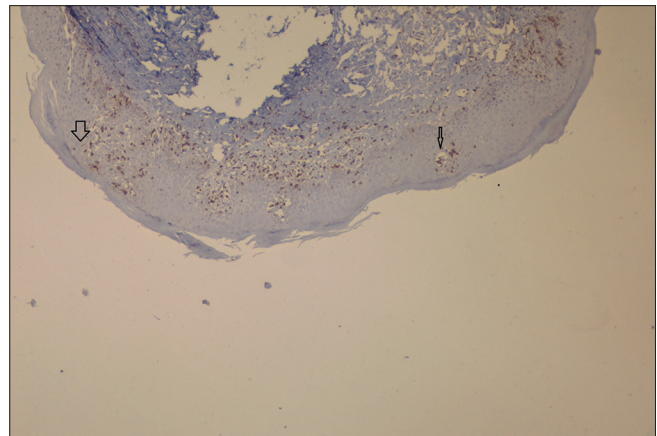


Figure 2: Immunohistochemistry staining showing CD4 positivity



Figure 3: Picture of the scalp at the time of initial presentation

### Treatment approach

He received six cycles of CHOP with partial response for not more than 3 months and then started on low-dose methotrexate. With no clinical response to previous treatment (methotrexate; 20 mg/week),

and after discussions with the patient, a decision was taken to change methotrexate treatment to low dose (methotrexate; 10 mg/kg) and ECP with adjuvant SDT (calamine lotion and steroid for local application). Empirically, valacyclovir and fluconazole for viral and fungal infection prevention, respectively, were initiated.

### Treatment with extracorporeal photopheresis

A long-term indwelling intravenous catheter (Permacath) was secured for prospective multiple leukocyte harvests. The harvest was performed on COM.TEC (Fresenius Kabi, Germany) with P1YA kit using auto-MNC protocol. About 120–150 ml product volume was targeted in each harvest cycle. For irradiation of collected product, UVA-PIT system with single-use disposable kit (Med Tech Solutions GmbH, Germany) was used. As per the UVA-PIT system operator’s manual, hematocrit was adjusted to 3%–6% by addition on normal saline, and thereafter, 0.017 ml of 8-methoxypsoralen (8-MOP; methoxsalen; S.A.L.F. S.p.A. Laboratorio Farmacologico, Italy) was added for each ml of diluted product. This system exposes the product to ultraviolet-A (UV-A) irradiation at 2 joules/cm<sup>2</sup>.<sup>[7]</sup> Once irradiated, the product was infused back into the patient, immediately, using a standard blood transfusion set. The patient did not have any adverse effects to product transfusion. The patient was instructed to avoid direct sunlight exposure to the skin and eyes. No concurrent blood component transfusion was given to the patient.

One session constitutes leukocyte harvest, adjustment of hematocrit, addition of 8-MOP, exposure to UV-A, and reinfusion back into the patient. Two back-to-back sessions on consecutive days comprised one cycle. Six such cycles were performed fortnightly. After six cycles of ECP, the patient had shown marked clinical improvement (partial remission). Scaly lesions reduced to <10% BSA; pruritus

diminished and affected areas showed hair regrowth remarkably on scalp [Figures 3 and 4]. The Sezary cell counts reduced from 55% to 35% on peripheral smear [Figure 5].

### Follow-up

Ideally, ECP treatment should be continued for 6 months according to the published guidelines before tapering to one cycle every 6–12 months.<sup>[8-10]</sup> However, due to financial constraints, the patient was unable to continue beyond six cycles. To maintain the attained response, he was counseled and continued on steroids (for local application) with addition of oral gemcitabine (1000 mg/m<sup>2</sup>) on day 1, 8, and 15 in a 28-day cycle. The patient completed six such cycles of gemcitabine. The patient continues to be in partial remission at last follow-up 6 months after discharge.

### Case Discussion

Clinicians differ in their preferred treatment approach as there is no standard initial therapy and paucity of controlled clinical trial data to direct the selection of treatment modality. There are several accepted treatment approaches for advanced-stage SS. This was possibly the first SS patient, in India, treated with ECP in conjunction with low-dose methotrexate and SDT. Authors approach to therapy was consistent with consensus recommendations regarding the treatment of SS that has been proposed by almost all professional bodies including the United States Cutaneous Lymphoma Consortium and the National Comprehensive Cancer Network.<sup>[4,8]</sup> ECP either as monotherapy or in combination with other therapies offers good treatment alternative and the possibility of prolonged survival. Further studies focusing on ECP treatment in combination with other therapies in SS patients are needed.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the



Figure 4: Picture of the scalp after six cycles of extracorporeal photopheresis

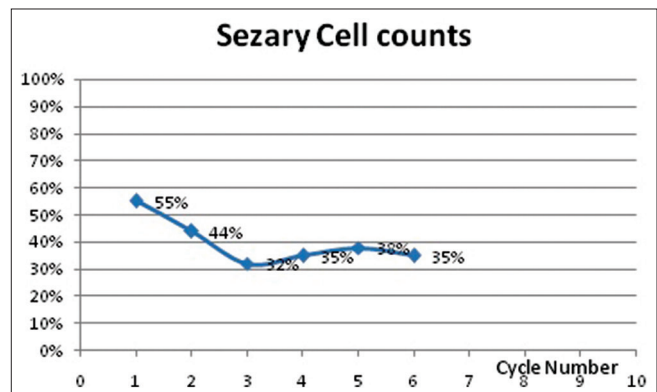


Figure 5: Percentage of Sezary cells in response to treatment cycles

patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

### References

1. Miyagaki T, Sugaya M. Erythrodermic cutaneous T-cell lymphoma: How to differentiate this rare disease from atopic dermatitis. *J Dermatol Sci* 2011;64:1-6.
2. Sant M, Allemani C, Tereanu C, De Angelis R, Capocaccia R, Visser O, *et al.* Incidence of hematologic malignancies in Europe by morphologic subtype: Results of the HAEMACARE project. *Blood* 2010;116:3724-34.
3. Bradford PT, Devesa SS, Anderson WF, Toro JR. Cutaneous lymphoma incidence patterns in the United States: A population-based study of 3884 cases. *Blood* 2009;113:5064-73.
4. NCCN Clinical Practice Guidelines in Oncology: Non-Hodgkin's Lymphomas (Mycosis Fungoides/Sezary Syndrome), version 4; 2014.
5. Zic JA. Extracorporeal photopheresis in the treatment of mycosis fungoides and Sézary syndrome. *Dermatol Clin* 2015;33:765-76.
6. Olsen E, Vonderheid E, Pimpinelli N, Willemze R, Kim Y, Knobler R, *et al.* Revisions to the staging and classification of mycosis fungoides and Sezary syndrome: A proposal of the international society for cutaneous lymphomas (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer (EORTC). *Blood* 2007;110:1713-22.
7. User's Manual for UVA PIT System, Med Tech Solutions GmbH. Am Farrnbach Cadolzburg, Germany; 2015.
8. Olsen EA, Rook AH, Zic J, Kim Y, Porcu P, Querfeld C, *et al.* Sézary syndrome: Immunopathogenesis, literature review of therapeutic options, and recommendations for therapy by the united states cutaneous lymphoma consortium (USCLC). *J Am Acad Dermatol* 2011;64:352-404.
9. McGirt LY, Thoburn C, Hess A, Vonderheid EC. Predictors of response to extracorporeal photopheresis in advanced mycosis fungoides and sézary syndrome. *Photodermatol Photoimmunol Photomed* 2010;26:182-91.
10. Scarisbrick JJ, Taylor P, Holtick U, Makar Y, Douglas K, Berlin G, *et al.* U.K. Consensus statement on the use of extracorporeal photopheresis for treatment of cutaneous T-cell lymphoma and chronic graft-versus-host disease. *Br J Dermatol* 2008;158:659-78.