Porto Biomed. J. 2017;xxx(xx):xxx–xxx

PORTO BIOMEDICAL JOURNAL
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Porto Biomedical Journal

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Case Report

Monitoring the extracorporeal photopheresis by immunophenotyping in a Sézary syndrome patient

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ARTICLE INFO

Article history:
Received 1 March 2017
Accepted 26 April 2017
Available online xxx

Keywords:
T cell lymphoma
Sézary syndrome
Extracorporeal photopheresis
Immunophenotyping

ABSTRACT

The extracorporeal photopheresis is indicated as immunomodulatory treatment in primary cutaneous T-cell lymphoma. There are no guidelines about the most suitable immunophenotypic panel to monitor and correlate clinical evolution and laboratory parameters.

In this study we characterize a patient with Sézary syndrome stage III, who performed 98 sessions of photopheresis; in the last 30, the expression of T-cells in peripheral blood was evaluated.

The patient had exfoliative dermatitis (mainly in the lower limbs) and several analytical disorders: anemia, neutropenia and lymphocytosis; abnormal number of effector T-cells and a CD4/CD8 ratio higher than 10; atypical cells (CD7, CD26) with aberrant phenotype (characteristic of malignant T-cell clones); and regulatory T-cells indicating an immunotolerance state. The clinical evolution verified can be related with the therapeutic scheme adopted.

We propose a multiparameter flow cytometry approach to monitor patients with Sézary syndrome that realize photopheresis, including the aberrant cases.

Introduction

Sézary syndrome (SS) is the most aggressive form of Mycosis fungoides, a cutaneous T-cell lymphoma (CTCL), classified as non-Hodgkin lymphoma. This disease derives from skin-homing memory T-cells and is characterized by exfoliative erythroderma, generalized lymphadenopathy, Sézary cells with cerebriform nuclei circulating in peripheral blood (PB) ($\geq$1000/mm^3) and poor quality of life. The diagnosis represents a challenge due to the similarity with other dermatologic diseases and should be based on criteria defined by the International Society for Cutaneous Lymphomas (ISCL) and the European Organization of Research and Treatment of Cancer (EORTC).[1–3] After the diagnosis and the beginning of the treatment, it is important to monitorize the patient; however, there are no immunophenotyping standards to characterize the therapie's effectiveness. Extracorporeal photopheresis (ECP) is recommended as an immunomodulator treatment, offering better life quality for the patient. It is a personalized therapy, only available in specialized healthcare centers; normally performed as an adjuvant treatment, associated with protein inhibitors, steroids and chemotherapy. The ECP procedure is based on 8-methoxypsoralen effect (a photosensitizing agent), combined with UVA light, which is added to mononuclear cells collected by apheresis, and finally reinfused to the patient.[4,5]

We propose a multiparameter flow cytometry approach that can be used to monitorize Sézary syndrome patients performing ECP, including aberrant cases.

Clinical case

We describe a 56 years-old Caucasian male with SS stage III diagnosed in 2014 (according to TNMB classification of the ISCL/EORTC). The patient presented erythroderma, multiple palpable adenomegalies and lymphocytosis. He was initially treated with a combination of prednisolone, interferon-α (IFN-α) and ECP (bi-weekly); after, it was added systemic bexarotene. The pruritus was controlled with hydroxyzine and loratadine and the cutaneous lesions with local measures; a complex of iron, folic acid, vitamins D and B12 was also prescribed. Two years later (Fig. 1), we observe a positive clinical response with an improvement of the cutaneous exfoliation affecting mainly the back and the thorax without cracks

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◊ Financing Program: Research Grant (2016) by Liga Portuguesa Contra o Cancro – Núcleo Regional do Norte, Porto, Portugal.

http://dx.doi.org/10.1016/j.pbj.2017.04.008

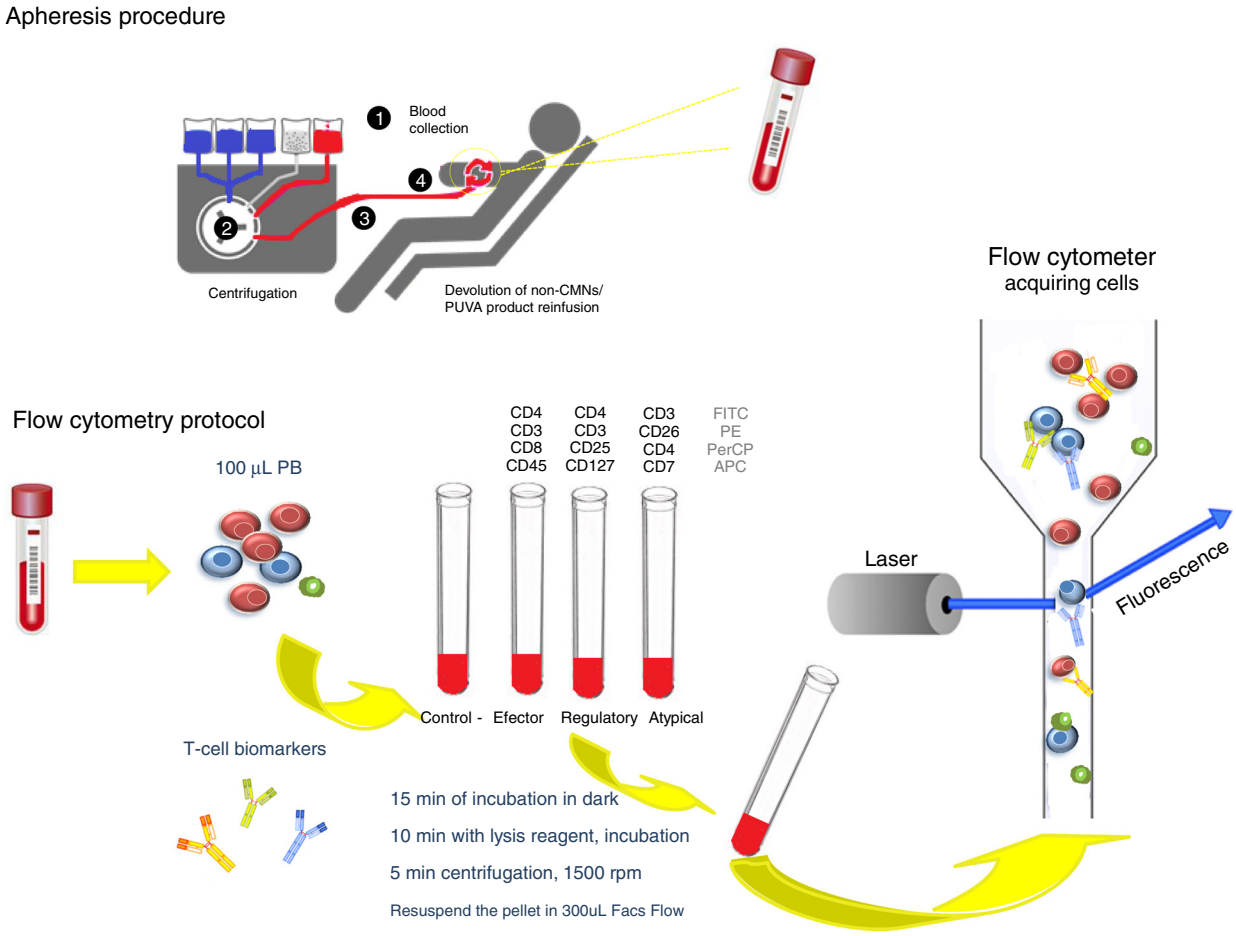

Fig. 1. Schematic representation of the flow cytometry protocol.

or maceration; the dark-red color of skin also shows some decrease. However, he maintains itching specially in the face and lower limbs.

The PB was analyzed before and after each ECP by an automated hematology analyzers and through flow cytometry (FACSCanto II) using a biomarkers panel to characterize effector, regulatory and atypical T-cell populations. The protocol is schematically represented in Fig. 2. We also evaluated results obtained from a healthy control.

Results and discussion

ECP has a recognized long-term immunomodulatory effect. In that way we observe, 2 years after, some improvement in patient's skin and a gradual decrease of lymphocytosis; however, the low value of hemoglobin has no change was well as the neutropenia (mostly post-session) (Table 1).

The circulating T-cells express an aberrant and stable immunophenotype over the ECP treatment, as represented in Fig. 3.

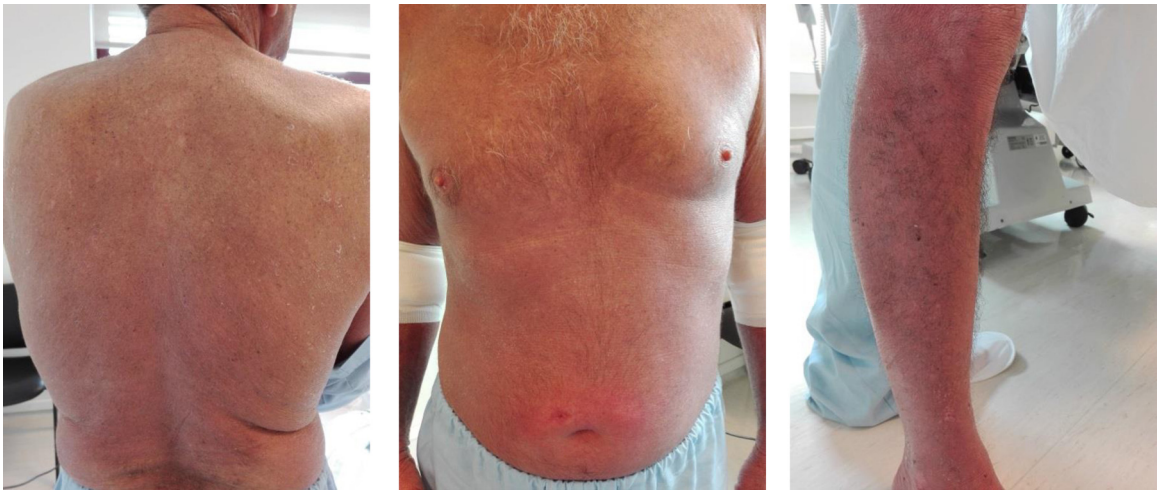

Fig. 2. The skin of a Sézary syndrome patient with exfoliative erythroderma in back, trunk and lower limbs.

Please cite this article in press as: Rodrigues T, et al. Monitoring the extracorporeal photopheresis by immunophenotyping in a Sézary syndrome patient. Porto Biomed. J. 2017. http://dx.doi.org/10.1016/j.pbj.2017.04.008