A RARE CASE OF MIXED ERYTHRODERMA (MYCOSIS FUNGOIDES AND PSORIASIS) IN A PATIENT WITHOUT SYSTEMIC ANTI-TNF THERAPY

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Abstract: *Mycosis fungoides and erythrodermic psoriasis are two clinical entities whose association is rarely cited in literature. We report a 22-year-old patient with a 5-year history of psoriasis vulgaris, who in the last 2 years had two episodes of erythroderma which required association of systemic retinoids to topical treatment. Lymphadenopathies, weight loss, fatigue, low grade fever and erythroderma occurred six months prior to report. Repeated skin biopsy reconfirmed the psoriasis, but by expanded investigations (lymph node biopsy, serological and immunological investigations) the mycosis fungoides was diagnosed. After the first chemotherapy cycle erythrodermic appearance has improved, lymph node masses were halved, weight curve went up (3 kg gain), but the patient refused further treatments. In conclusion, the literature description of mixed erythroderma (psoriasis and mycosis fungoides) in a patient without systemic anti-TNF therapy or other immunosuppressant's is rare, like in our case.*

INTRODUCTION

Psoriasis vulgaris is a chronic inflammatory disorder with predominant cutaneous manifestations, with possible joint damage and dysmetabolic diseases. Psoriatic erythroderma is a dermatological emergency which may endanger the patient's life by electrolyte and acid-base imbalances.

Erythroderma can generally be triggered by several dermatological disorders (psoriasis, eczema, lichen etc.), by certain medications and neoplasms, particularly hematological ones (T-cell lymphomas, such as Sezary syndrome).(1) Psoriasis is the most common cause of erythroderma in adults.(2)

Psoriatic erythroderma can occur during the evolution of psoriasis as a result of disease neglect, inadequate therapies or extremely aggressive triggering factors, i.e. neuropsychological, medication (systemic steroid therapy, sudden interruption of systemic therapies, lithium concentrates, antimalarials, interleukin II), infectious, allergic, natural or artificial phototherapy, alcohol abuse, hypocalcemia.(3) Approximately 3% of psoriatic patients may experience one or more episodes of erythroderma in their lifetime.(4)

Mycosis fungoides is the most common form of cutaneous T-cell lymphoma (about 50%) (5), that may be clinically manifest as erythroderma. There have been reported cases of association between anti-TNF therapies used in psoriasis treatment and cutaneous lymphomas, a relationship that has not been fully established yet.(6) The risk of T-cell lymphomas developing during the anti-TNFα therapy is worth pointing out.(7)

In practice, it is essential to differentiate between benign and malignant erythrodermas. In certain cases, when the aetiology of erythroderma is not obvious, repeated complex investigations are needed.

CASE REPORT

Patient, 22 years old, diagnosed 5 years ago with a histologically confirmed psoriasis vulgaris, who has suffered from 2 episodes of erythroderma/year in the last 2 years, comes to our clinic with a new episode of erythroderma. Initially, psoriasis responded well to treatment with methotrexate, to topical anthralin, keratolytics and dermatocorticoids. The more and more pronounced and persistent infiltrative cutaneous aspect and repeated relapses of erythroderma prompted us to perform two other skin biopsies in the last 2 years, which reconfirmed the diagnosis of psoriasis vulgaris.

Due to the severity of the eruption, it was necessary to associate systemic retinoids (Acitretin 30mg/day, the dose slowly decreasing over periods of 3 months) to topical keratolytics and dermatocorticoids.

One year from the last hospitalization the patient returned with a new episode of erythroderma (figure no. 1), with erythematous, infiltrated plaques, which gave the patient's cephalic extremity a leonine appearance, bleeding flexural lesions, palmoplantar keratoderma, partial eyebrow and scalp alopecia, dystrophic nails, weight loss (20 kg/last year), asthenia, low-grade fever (37.2 to 37.6°C). The clinical examination indicated painless bilateral inguinal, axillary and lateral cervical lymphadenopathy blocks, raising suspicion of lymphoma.

The skin biopsy indicated acanthosis, the marked elongation of the epidermal ridges, hyperkeratosis with focal parakeratosis, Munro's abscesses, absent granular layer, dermis with chronic inflammatory infiltrate and capillary congestion.

The investigations conducted revealed leukocytosis (17720/mm3) with neutrophilia (72%), hyperuricemia (8mg/dl), hypoproteinemia (5.1 g/dl). HIV, hepatitis, syphilis serology and HTLV were negative. IDR was also negative. The osteomedullary biopsy indicated granular megakaryocytic hyperplasia.

The lymph node biopsy revealed a partially retained follicular architecture, with areas of hyperplastic follicles with normal or smaller germinal centres and nodular areas delineated by thin fibrous septa presenting atypical small lymphocytes, reactive lymphocytes, plasma cells, grouped macrophages containing hemosiderin, phagocytosis; mild hyperplasia on the postcapillary veins; without traces of Hodgkin/Reed Sternberg cells (figure no. 2).

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Figure no. 1. Clinical aspect of erythroderma, at hospitalization

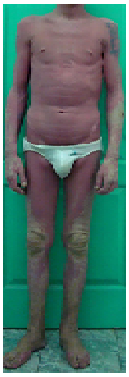
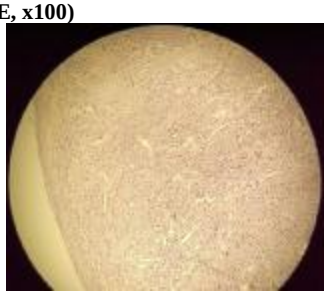


Figure no. 2. The histopathological aspect of mycosis fungoides (HE, x100)



The immunohistochemistry aspect was suggestive for lymphadenopathy with small T-cells infiltration (CD3, CD5-positive in the lymphoid population, focal CD10-positive in the germinal centres, CD20-positive in the reactive T-cells, CD30-positive in the activated immunoblasts from the germinal centres, Ki67 – 35% of the germinal centres and 10-15% of the remaining lymph node).

In compliance with the clinical ISCL/EORCT staging, mycosis fungoides was included into stage III and a Cyclophosphamide – Idarubicin - Vincristine cure was administered, which was well tolerated. Chemotherapy improved the clinical aspect of mycosis fungoides, the lymph node masses were reduced by 50% and the patient presented an upward weight curve (3 kg gain). The dermatocorticoids and emollients improved the psoriasis appearance. However, the patient refused further treatments. Due to the treatment noncompliance we are unable to control or monitor the disease evolution.

DISCUSSIONS

In the pathogenesis of psoriasis, the increased activity of T-lymphocytes, antigen-presenting cells and Th1 cytokines is well-known. Recent studies has highlighted an upward trend in the association of psoriasis with other Th1-mediated diseases (non-Hodgkin's lymphoma, rheumatoid arthritis), especially in the elderly. The risk factors determining increased incidence of mycosis fungoides in psoriatic patients, identified by Gelfand et al, are the severe forms of the disease and immunosuppressive and biologic therapies, particularly anti-TNF ones.(8)

In erythroderma, the pathogenic mechanisms are different depending on the aetiological factors. A central pathogenic role in erythroderma is played by the interaction between the leukocyte and the endothelium, with the increase in the expression of adhesion molecules VCAM-1, ICAM1 and E-selectin.(9) In psoriatic erythroderma, they stimulate the release of pro-inflammatory cytokines (IL 1, 2, 8, TNF), with a pro-inflammatory and promitotic effect.(10)

About ¼ of erythoderma cases are induced by lymphoma, leukemia and psoriasis. In literature, the association between psoriasis without biological therapies and mycosis fungoides is extremely rare (we found one reported case). In mycosis fungoides, Th2 cytokines (IL-4, 5, 6 and 10) are prevalent, whereas psoriasis is a Th1-mediated disease.(9)

Even if the identification of erythroderma aetiology can sometimes be difficult, determining its benign or malignant nature is essential, influencing disease treatment, evolution and prognosis. Prognostic assessment in psoriasis is easy, mainly based on clinical and laboratory criteria, whereas, in mycosis fungoides, it is sometimes necessary to perform gene rearrangement molecular tests for the clonal T-cell receptor, which are more accurate in appraising the clonality of histologically negative T-cells in the lymph nodes. In our case, erythroderma aetiology was mixed (psoriasis and mycosis fungoides), without a clear boundary between psoriatic and mycosis fungoides erythroderma. The appearance of mycosis fungoides was not favoured by immunosuppressive treatment or biological agents.

CONCLUSIONS

The appearance of mycosis fungoides, against a background of psoriatic erythroderma, with no immunosuppressants or biological therapies, in a young patient with no another associated pathology, is a rare case.

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