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CLINICAL CASE

Systemic erythroderma a rare entity to remember. Literature review

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Abstract

Erythroderma is an erythema in more than 90% of the body surface, being a dermatological emergency, which can have serious consequences. Erythrodermic psoriasis is a severe and rare variant of psoriasis vulgaris, the condition of which can be fatal. We present the case of a patient in the seventh decade of life, with no dermatological history, who started with erythrodermic psoriasis, developing a systemic inflammatory response, which was treated with systemic steroids and methotrexate, presenting an adequate response. A case of erythroderma is reported, corroborating the diagnosis through histopathology, being treated with immunosuppressants of lower cost and greater accessibility. The objective of presenting this case is to review the current treatment of this rare entity.

Keywords: *Psoriasis. Erythroderma. Methotrexate. Steroids. Low cost.*

Introduction

Psoriasis is an autoimmune inflammatory skin disease recognized by the WHO in 2014 as a serious non-communicable disease, highlighting the importance of diagnosis and timely treatment[1]. Psoriasis affects approximately 125 million people worldwide, having a variable distribution depending on the geographical region, affecting men and women equally, with a bimodal age distribution expressed between 18 and 39 years and between 50 and 69 years[2]. There are variants of psoriasis that include plaque psoriasis, guttate psoriasis, erythrodermic psoriasis, and pustular psoriasis. Depending on the variant of psoriasis the clinical features differ, most variants share three clinical features in common, which are erythema, thickening and scaling. Plaque psoriasis represents 80-90% and guttate, erythrodermic and pustular psoriasis only 2-3%[3]. Erythrodermic psoriasis in turn has an incidence of approximately 2%, being a severe variant that represents a dermatological emergency. Patients develop coalescent erythema, scaling, or exfoliation, affecting at least 75% of the body surface. The course of this dermatosis, as well as the prognosis, will depend on the severity, age group, added infections and adherence to treatment[4]. The objective of presenting this case is to review the current and timely treatment of this rare entity.

Clinical case

62-year-old man, peasant, resident of Veracruz. No history of previous illnesses, or drug use, with a smoking rate of 10 packs/year. He came with a condition of one month's evolution, characterized by unquantified fever, chest pain, dyspnea, and polyarthralgia. He received non-dermatological consultation and treatment with intramuscular steroids with no response. After a week, localized dermatosis was added to the

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trunk, which spread to the scalp and extremities. The examination revealed a generalized dermatosis that spared the mucosa, palms, and soles; characterized by diffuse erythema, desquamation with whitish scaling of small sheets easily detachable, in few areas with erythematous-scaly plaques of whitish scaling of medium sheets, in the rest of the skin and annexes, nails were found with the sign of mechanic's oil, in addition hands with increased volume in proximal interphalangeal joints and limited mobility (Figs. 1 and 2).

The patient had a fever of 38.5ºC with leukocytosis of 16,750 mm3, (Normal 5,000 mm3-12,000 mm^3), with a predominance of neutrophils (76%), the blood chemistry showed no alterations. Systemic inflammatory response syndrome and erythroderma were integrated.

The skin biopsy reported epidermis with psoriasiform hyperplasia, mild spongiosis, neutrophil infiltrate in the superficial layers, and parakeratosis; papillary dermis with dilated vessels and intense chronic inflammation (Fig. 3). To rule out psoriatic arthritis, X-rays of both hands were taken; with reports of degenerative changes of osteoarthritis.

The diagnosis of erythrodermic psoriasis was concluded and treatment was started with methotrexate 12.5 milligrams every week for 3 months, prednisone 40 milligrams daily, at a reduced dose for 3 months, together with folic acid 5mg once a week, emollients and soap substitute, with clinical improvement in the skin after a month with a decrease in joint edema. Liver function tests and blood counts were within normal parameters throughout his evolution.

The methotrexate dose was reduced to 7.5mg weekly for 2 months. Follow-up was given for 8 months with complete remission of the dermatosis and joint pain, continuing with topical treatment with emollients, 20% urea in thick skin areas. The patient is currently being monitored by the dermatology service (Fig. 4).

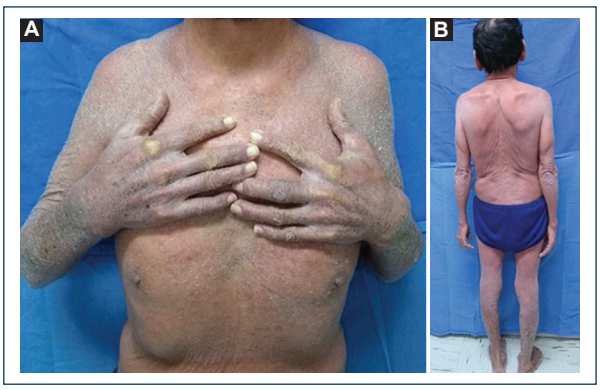

Figure 1. A and **B:** generalized dermatosis characterized by diffuse erythema, desquamation with whitish scaling of small, easily detachable sheets.

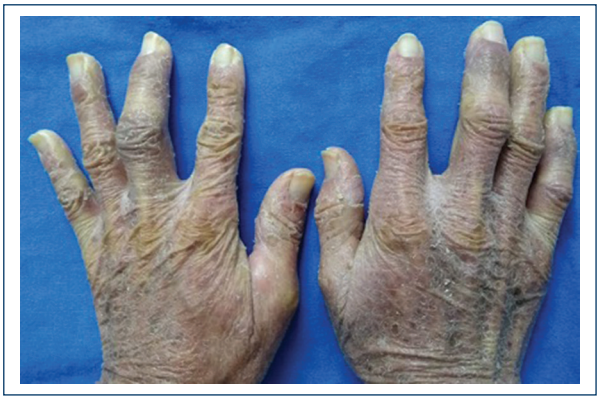

Figure 2. Mechanic's oil sign.

Discussion

Erythrodermic psoriasis is a rare and severe variant that affects 1-2.25% of patients with psoriasis, being the most common cause of erythroderma, responsible for approximately 25% of cases[5].

Risk factors for the development of the disease include genetic factors, multiple alleles such as HLA-Cw6, HLA-DQ*02:01, CCHCR1, CYP1A1 and loci PSORS1-9, PERSOSASI. Among the environmental factors most involved are smoking, obesity, alcohol consumption, the intake of some drugs such as beta blockers, lithium, antimalarials, streptococcal infection, HIV, and behavioral factors that are closely associated with the stress load[6,7]. In the case here described, smoking was found to be the triggering factor.

An important trigger for erythrodermic psoriasis is treatment with systemic glucocorticoids or abrupt discontinuation of systemic antipsoriatic drugs such as methotrexate or cyclophosphamide. In a retrospective study Gregorie et al evaluated the exacerbation of psoriasis after exposure to systemic glucocorticoids, the authors demonstrated that the rates of psoriasis episodes were very low in patients taking systemic corticosteroids and that these episodes were mild[8].

The understanding of the risk factors has helped us to explain the predisposition that our patient had.

The pathogenesis of psoriasis is triggered by activated dendritic cells that produce IL-23 and TNF a, stimulating the activation of CD4 Th 17 lymphocytes and cytotoxic CD8 lymphocytes that recognize epidermal autoantigens that are keratin 7, antimicrobial

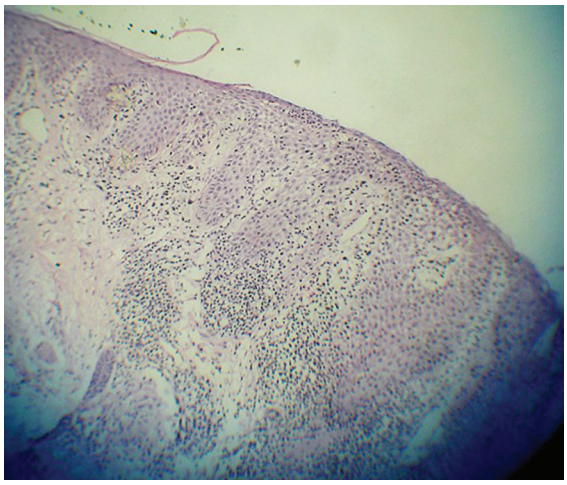

Figure 3. H&E 10X: Epidermis with parakeratosis, hypogranulosis, irregular acanthosis at the expense of interpapillary processes, with areas of spongiosis, inflammatory infiltrate made up mainly of polymorphonuclear cells (neutrophils), with formation of Munro-Sabouraud microabscesses, papillary dermis with dilated vessels and intense chronic inflammation.

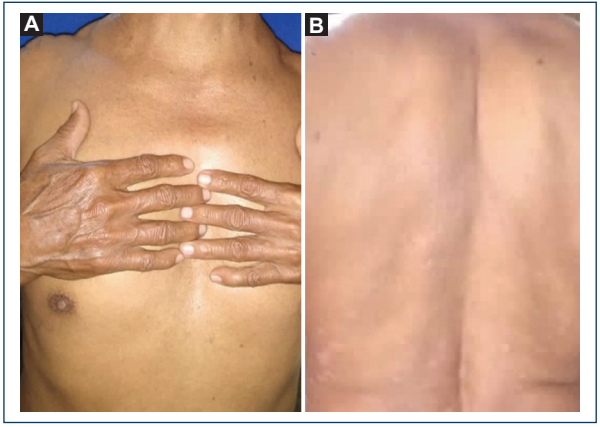

Figure 4. A: anterior thorax with healthy skin. **B:** posterior thorax, presence of residual hypochromic spots.

peptide LL37 in keratinocytes and melanocyte antigen. ADAMTSL5, These lymphocytes secrete IL 17 and IL 22 that sustain the inflammatory process and generate the epidermal hyperproliferation characteristic of the disease[9].

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The severity of the symptoms depends on the multiple inflammatory pathways activated. The main clinical manifestation of erythrodermic psoriasis is the appearance of a generalized confluent erythema that affects between 75-90% of the total body surface. It has a rapid onset over several days or a gradual onset over several weeks, followed by exfoliation and desquamation of the skin that develops several days after the appearance of the erythema. The desquamation is usually accompanied by pain, itching, finding an Auspitz sign (bleeding points where the scales are removed) and photosensitivity in the areas with the greatest exfoliation activity; the Koebner phenomenon (appearance of lesions in areas of skin affected by trauma) is also present[10]. Most patients present nail disorders such as the formation of dimples in the nail plate (pits), Beau's lines, onychomadesis, trachyonychia, nail dystrophy, even affecting onycholysis[11]. The extra-cutaneous manifestations are fever, chills, malaise, tachycardia, arthralgia, and lymphadenopathy[12,13].

It is proposed to evaluate the severity of erythrodermic psoriasis, considering moderate-severe erythrodermic psoriasis with at least two clinical characteristics, while mild erythrodermic psoriasis with less than two of the following characteristics: body temperature above 37.3°C on admission, swelling and exudation of more than half of the skin lesion or edema of the lower extremities and superficial lymphadenopathy[14]. This to guide us to a timely diagnosis that leads to a good outcome of the disease.

The diagnosis should be made by investigating the personal or family history of psoriasis, history of possible triggers for the disease and coexistence of clinical characteristics, emphasizing a physical explanation of the skin. No serological test confirms the diagnosis of erythrodermic psoriasis, so it is essential to perform a skin biopsy[15]. The results of the histopathological study may be nonspecific, reporting hyperkeratosis, parakeratosis, acanthosis, and chronic inflammatory infiltrate with or without eosinophils. Rothet highlighted the importance of clinical and histological correlation for the diagnosis of erythrodermic psoriasis[16]. The histological characteristics that most support the diagnosis of erythrodermic psoriasis were acanthosis, diffuse parakeratosis, diffuse hypogranulosis, and the presence of neutrophils in the epidermis and hypodermis[17]. The

histological characteristics in the biopsy were compatible, which confirmed the diagnosis in our case.

The differential diagnosis should be made on atopic dermatitis, seborrheic dermatitis, which are the most frequent associated skin diseases. Drug reactions account for 20% of erythroderma and the rarest causes are pityriasis rubra pilaris, cutaneous T-cell lymphoma, paraneoplastic syndrome, and graft-versus-host disease in patients with a history of transplantation[18].

Among the complications of erythrodermic psoriasis, hemodynamic alterations such as peripheral edema, high-output heart failure, shock, or acute renal failure have been described. The thermoregulatory alterations generated by the inability to regulate body temperature generate loss of water and electrolyte abnormalities. Infections due to loss of the skin barrier are frequent and staphylococcal septicemia stands out in particular. On rare occasions, an acute respiratory distress syndrome can be generated as a result of the sum of the aforementioned alterations[19,20]. Being a systemic inflammatory disease, it is associated with several comorbidities, including psoriatic arthritis, uveitis, cardiovascular disease, metabolic and non-alcoholic syndrome, fatty liver disease, depression, and Crohn's disease[21]. Due to acute complications, timely management is important, such as that implemented in the patient.

There is no consensus on the management of erythrodermic psoriasis. The most useful support recommendations are hemodynamic and body temperature monitoring, fluid and electrolyte replacement, nutritional support, treatment of associated infections, skin care with moist dressings, hydration oatmeal baths and topical corticosteroids to reduce pain and itching[22].

Systemic psoriasis therapy should be started immediately and should be chosen with respect to severity, patient comorbidities, and drug availability[23]. The recommended first-line therapies are: cyclosporine (with an initial dose of 3 to 5mg/kg/day), which produces significant improvement in the first month and complete remission after one year. The most frequent adverse effect is nephrotoxicity, which limits the duration of treatment that should not exceed one year of treatment and should be discontinued after 4 months without response to treatment.

It also presents arterial hypertension, risk of infections and neoplasias[24]; Infliximab (with an initial dose of 5mg/kg at week zero, two, six, followed by 5mg/kg every 8 weeks). In this case, if no significant improvement is observed at 4 to 6 weeks, the benefit of continuing it is insignificant. With this treatment, an improvement of 50% of the lesions is seen at 4 weeks. The most reported adverse effects are reactions to the infusion, infections, exacerbation of heart failure, demyelinating disease, and neoplasms[25-27].

Alternative therapies for the treatment of erythrodermic psoriasis that are used when cyclosporine or infliximab are contraindicated are: Methotrexate (with a weekly dose of 7.5mg to 25mg per day with folic acid supplementation 1mg/day), observing improvement after the first weeks of starting treatment, if no signs of improvement are observed after four weeks, we must discontinue the treatment. In countries with little access to drugs such as cyclosporine, infliximab or new biologic therapies, either due to high cost or adverse effects, methotrexate and oral corticosteroids have been chosen as second line. As it is an immunosuppressive drug that inhibits the dihydrofolate reductase enzyme, side effects such as gastrointestinal discomfort, hepatotoxicity, myelosuppression, and pulmonary toxicity have been described, and it is contraindicated in patients with active infectious disease, neoplasia, bone marrow suppression, or pre-existing liver or kidney disease[28].

Other emerging therapies only in clinical trials with new biological drugs are etanercept, adalimimab, ustekinumab, ixekinumab, secukinumab [29-31].

Stress, depression, and other feelings of stigmatization have been shown to decrease quality of life. However, stress is pointed out as one of the triggering factors in the exacerbation of psoriasis. For this reason, cognitive behavioral therapy, stress control and abandonment of other factors such as alcoholism and smoking have shown improvement with respect to controlling the disease. Other therapies such as acupuncture and meditation have also been described[32]. In our case, the patient gave up smoking. The case described here represents an unusual form of presentation of Psoriasis, as the dermatosis initially manifests on more than 90% of the body surface, reaching an erythrodermic phase, an unusual presentation given the multiple treatments currently available.

Conclusion

In erythrodermic psoriasis, histopathology is essential to confirm the presumptive diagnosis. Treatment with oral corticosteroids and methotrexate showed an excellent benefit; being this one of lower cost and greater accessibility.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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