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PITYRIASIS RUBRA PILAR: CASE REPORT AND LITERATURE REVIEW

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Abstract: Pityriasis Rubra Pilaris (PPR) is a rare dermatosis and its incidence, etiology and pathogenesis are uncertain. Classification systems for this dermatosis, consider its various clinical manifestations that subdivide it into 5 clinical types, based on characteristics, such as age of involvement, extension and prognosis. Soon, This article aims to present a case report of PRP type (I) that occurred in the municipality of Petrolina (Pernambuco - Brazil) in 2021, with excellent and fast response to the use of Methotrexate, as well as providing a descriptive overview of the pathology in question and its different forms of treatment through a brief review and discussion about this unusual comorbidity. To the preparation of this review, the PubMed, Medline and Lilacs in the period from March 2016 to August 2021. For collection of the articles, the descriptors, pityriasis rubra pilaris and treatment and considered only articles in the English language. 34 articles were considered for the extraction of data, which were analyzed independently in forms standardized. It was observed that promising results have been reported using of immunobiologicals. However, the therapeutic approach for cases of PRP remains challenging, there is a gap in guidelines and algorithms for treatment, as well as as efficient clinical studies to guide interventionist action, given the unsatisfactory outcome of some lines of treatment, the particularities of patients, as well as the high cost of biological therapies currently used.

Keywords: Pityriasis Rubra Pilar, Methotrexato, Adalimumabe

INTRODUCTION

Pityriasis rubra pilaris (PPR) is a rare dermatosis and its incidence is uncertain, ranging from 1 in 5,000 to 1 in 50,000 adult patients in different countries. In children, there is a report of a higher incidence, around 1 in 500 new cases.[1]

It is an inflammatory papulosquamous skin disease that presents with hyperkeratosis, follicular papules, scaly erythematous plaques, palmoplantar keratoderma and a tendency to progress to erythroderm. [2] It affects all races and has no sex predilection.[3]

In a histological study, the presence of acanthosis, diffuse orthokeratosis and horizontal and vertical parakeratotic spots is observed in the epidermis, in addition to superficial perifollicular dermal involvement and perivascular lymphohistiocytic inflammatory infiltrate. [4,5]

The etiology and pathogenesis of PRP is still uncertain.[6] The epidermis is in a hyperkinetic state and there is a hypothesis of deficient vitamin A functioning and low serum levels of retinol-binding protein, considering the clinical compatibility with known cutaneous conditions of phrynoderma. It is believed that viral and bacterial infections, autoimmune diseases and neoplasms may also be responsible for triggering this inflammatory dermatosis.[7,8] Complementary theories propose alterations in the retinoid signaling pathway due to immunological disorders, and abnormal keratin functioning, especially in cases with acantholytic dyskeratosis. [9]

In familial cases of PPR disease, activation of nuclear factor (NF)-jB related to heterozygous mutations in the recruitment of the caspase family domain (CARD14) have been identified as promoters of skin inflammation. CARD14 is a signaling activator and has been implicated in the pathology of inflammatory disorders. [10,11]

Classification systems for this dermatosis consider its various clinical manifestations, such as that of Griffiths, 1980, which subdivides it into 5 clinical types, based on characteristics such as age of involvement, extension and prognosis. 12.13

Type I (classic adult) corresponds to about

55% of cases, is more prevalent and has a good prognosis. It usually has an acute onset, initially affecting the upper half of the body, mainly the face and neck. Type II (atypical adult), in turn, has a more chronic course and does not follow cephalocaudal progression. Its clinical picture ranges from ichthyosiform dermatitis with a predilection for the extremities, to gross palmoplantar hyperkeratosis, hair thinning and alopecia. Type III (classic juvenile) occurs in childhood, in children aged 5 to 10 years, with a clinical disposition similar to subtype I, with a good prognosis, with most lesions showing spontaneous resolution within 1 year. Type IV (circumscribed juvenile) tends to affect children in prepubertal stages and develop demarcated areas of follicular hyperkeratosis and erythema on the elbows and knees. Its prognosis is less favorable than the classic juvenile. Type V (atypical juvenile) represents the majority of cases of familial PRP and is characterized by early onset and prolonged duration, with symptoms ranging from follicular hyperkeratosis and ichthyosiform features to sclerodermatosis changes in the hands and feet. A sixth subtype has been proposed in addition to the PRP classification scheme, which covers HIV-associated cases. 14 Individuals with this specific type of condition usually present with follicular occlusion, acne conglobata, hidradenitis suppurativa, and lichen-like lesions. In them, there may be inconsistent involvement of nails and palmoplantar regions. A feature of these cases are islands of erythroderma preservation. [1]

The main objective of this article is to present a case report that occurred in the municipality of Petrolina (Pernambuco - Brazil) in 2021, with an excellent and rapid response to the use of Methotrexate, as well as to provide a descriptive overview of the pathology in question and its different forms. of treatment through a brief review of the literature, in addition to promoting further discussions about this unusual comorbidity in the scientific academic environment in order to support and add up-to-date and useful knowledge capable of enabling improvements in care for the population affected by this dermatological condition.

CASE REPORT

The patient, male, 43 years old, white, from the city of Lagoa Grande-Pernambuco, came to the dermatology outpatient clinic, referring that 2 months ago, he developed redness, associated with intense itching on the face, scalp, palm region. -plant with generalization in a few days. He attributed the clinical condition to contact with dust from old wood, since the dermatological condition started 2 days after this event. Physical examination showed erythematous plaques, mostly erythematous-scaly to psoriasiform in some areas, and orange-red in others, in addition to erythematous and erythematous-keratotic follicular papules, interspersed with areas of apparently healthy skin, affecting the face, upper limbs and lower. (Fig 1). He also had palmoplantar hyperkeratosis. The suspected diagnosis was Pityriasis rubra pilaris. Complementary tests and skin biopsy were requested. For symptomatic relief, oral dexchlorpheniramine maleate + betamethasone and topical betamethasone dipropionate + salicylic acid ointment were prescribed. The histopathological study showed compact hyperkeratosis with parakeratosis, accompanied by psoriasiform acanthosis of the epidermis, follicular hyperkeratosis and lymphocytic inflammatory infiltrate around the superficial vessels in the dermis (figure 2). Corroborating the initial diagnostic clinical suspicion. Along with the clinical picture, he was diagnosed as PRP type (I). Results of complementary exams: Blood glucose - 131 mg/dL; Total Cholesterol - 297

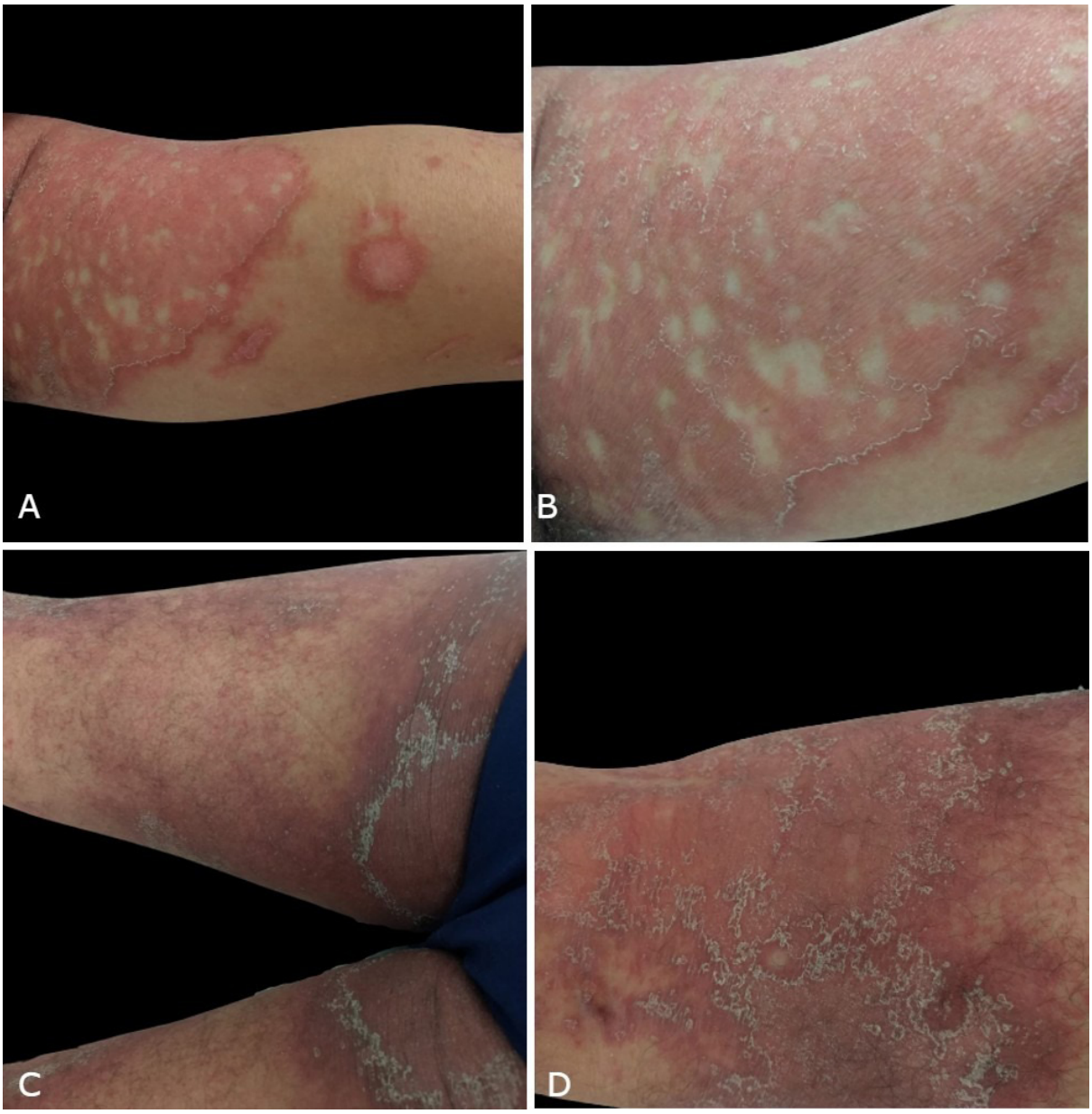

Figure 1. Erythematous-scaly to psoriasiform plaques, as well as red-orange in color, in addition to erythematous and erythematous-keratotic follicular papules, interspersed with areas of apparently healthy skin, affecting upper (A,B) and lower limbs (C,D).

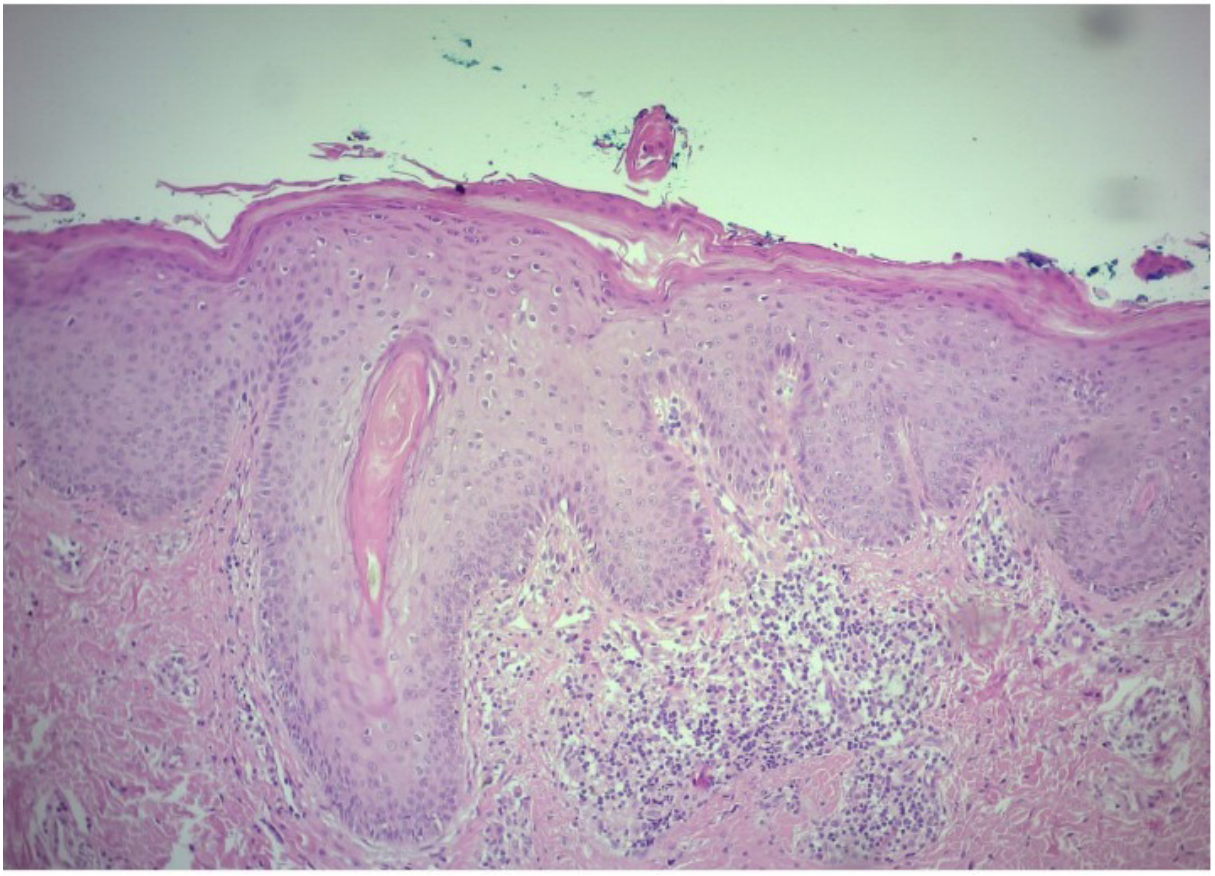

Figure 2. Microscopy characterized by compact hyperkeratosis with parakeratosis. Accompanies psoriasiform acanthosis of the epidermis. There is also follicular hyperkeratosis. The dermis exhibits lymphocytic inflammatory infiltrate around the superficial vessels. 100X magnification

mg/dL; Triglycerides 497 mg/dL; GT 102 range up to 54 U/L; Hemoglobin - 14.6 g/dL; Leukogram - 9,400/mm3; Platelets - 167,000/mm3. It was decided to start treatment with acitretin, 25 mg/day. However, the patient's condition worsened and, 3 weeks later, he was replaced by Methotrexate (MTX), at a dose of 15 mg/week - 10 mg on one day and 5 mg on the following day, followed by folic acid, 5 mg. in the two days after the use of MTX, in addition to topical emollients with a very satisfactory evolution in 15 weeks after the beginning of the treatment (Fig 3).

METHOD

For the preparation of this review, the PubMed, Medline and Lilacs databases were consulted in the period from March 2016 to August 2021. For the collection of articles, the descriptors, pityriasis rubra pilaris and treatment were used and only articles in the language were considered. English. For inclusion in this study, the title and abstract of the publications were evaluated, resulting in 43 articles. Subsequently, 34 articles were considered for data extraction, which were independently analyzed using standardized forms (Table 1).

DISCUSSION

Pityriasis Rubra Pilaris is an inflammatory dermatosis of uncertain pathophysiology.

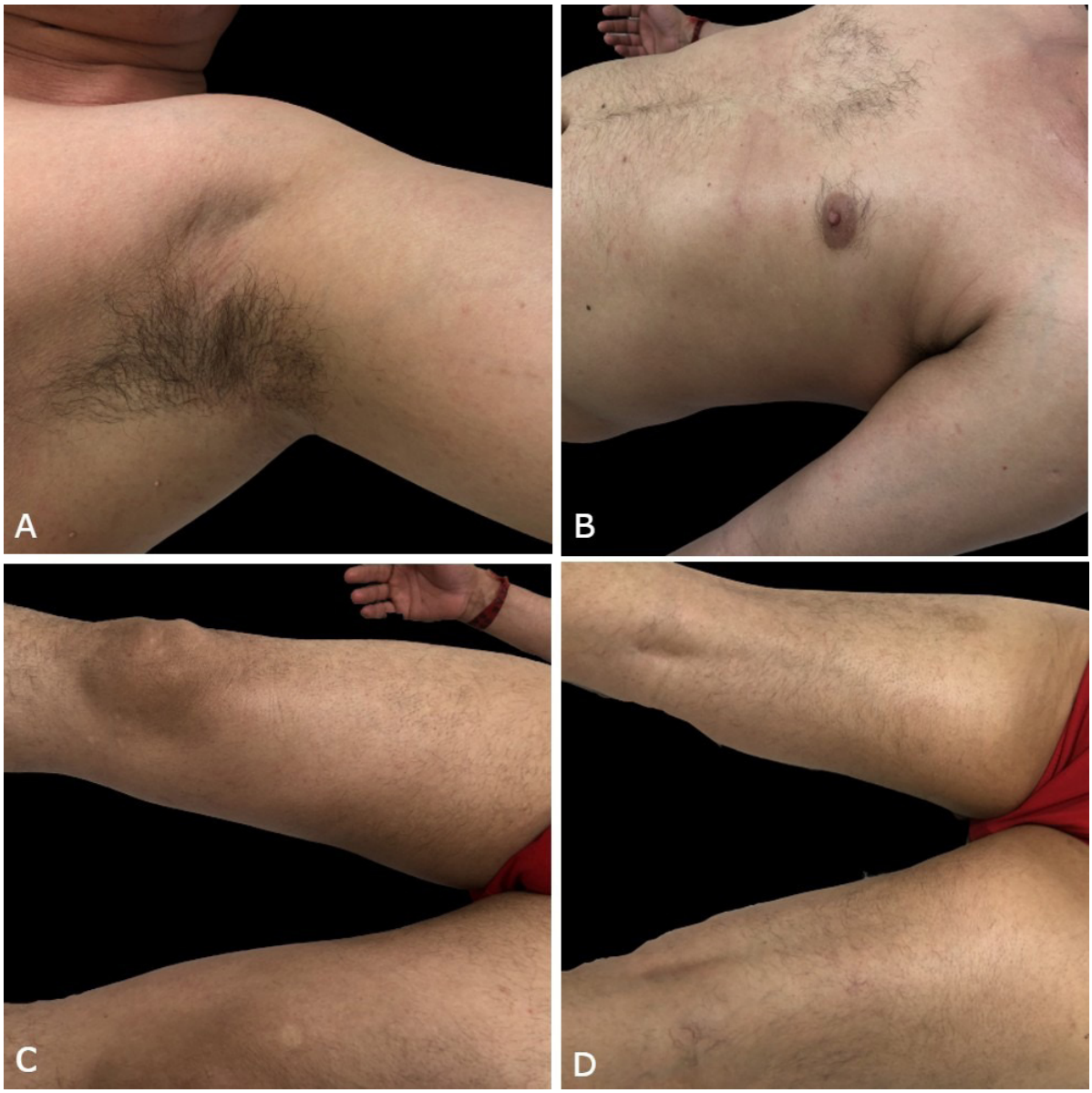

Figure 3. Satisfactory evolution in 15 weeks after starting treatment

Study/Yeat	Age/Gender	Treatment	Treatment result
Gauci et al. (2016)	33/F	Secukinumab in combination with cyclosporine and prednisone (10 mg/day). The patient received 5 weekly subcutaneous injections of 300 mg followed by monthly injections.	Secukinumab: clinical efficacy and quality of life at 4 weeks. No recurrence in a period of 6 months. It was well tolerated, except for the appearance of oral and esophageal candidiasis.
Yun et al. (2016)	15/M	Topical and oral corticosteroid, acitretin (10 mg/day) and UVB-NB phototherapy. Hyperkeratotic plaques spread peripherally after 4 weeks of treatment. When, then, they were replaced by oral alitretinoin (30 mg/day, 0.5 mg/kg/day) for 7 months.	Seven months after treatment with alitretinoin, the pruritus and skin lesions improved, with discrete erythematous-scaly lesions remaining. No recurrence in 9 months.
Schuster et al. (2016)	67/M	Treatment was started with acitretin, 35 mg/d, (0.5 mg/kg/d). for 5 weeks, followed by monthly injections.	After 3 weeks of treatment with secukinumab, scaling and itching improved and disappeared after 8 weeks. Palmoplantar keratoderma disappeared after 6 months of treatment.
Stacey et al. (2016)	03/M	Oral isotretinoin 15 mg/day (1 mg/kg/d). Topical steroids twice daily, including triamcinolone 0.1% ointment for trunk and extremities, clobetasol 0.05% scalp foam and desonide 0.05% face ointment. He received hydroxyzine and various emollients to control symptoms. The duration of isotretinoin therapy was 6 months.	The patient began to develop easy peeling of the skin with mild trauma, but overall his symptoms were well controlled. At the end of the treatment period, all signs and symptoms had resolved, leaving only areas of post-inflammatory hyperpigmentation.
Alazemi, et al. (2017)	03/F	Oral methotrexate 5 mg/week. There was an increase in dosage 3 weeks later to 7.5 mg Urea emollients were used for topical treatment.	Marked improvement in 1 month after initiation of therapy and complete remission 3 months. No recurrence in 06 months.
Boyd et al. (2017)	08/M	Oral methotrexate 12.5 mg/day (0.5 mg/kg) for 3 months.	Marked improvement after 6 weeks and near resolution at 3 months, with a sustained response after 9 months.
Davenport et al. (2017)	58/M	Topical betamethasone dipropionate 0.05% ointment and acitretin 25 mg/day. Due to lack of response, after 6 months, methotrexate 10 mg/week was added, but it was discontinued after 3 weeks due to a considerable increase in TGP (from 24 to 169 U/L (normal range 5–40 U/L). response after 6 weeks of UVB-NB (3 times/week) or infliximab 5 mg/kg (weeks 0, 2, 6 and 14) Fifteen months after presentation, secukinumab 300 mg/month was started, remaining on acitretin 25– 50 mg/day for the entire period.	Gradual improvement was observed in the severity and extent of erythema and scaling, and in the thickness of keratoderma, even after discontinuation of secukinumab after 9 months of use. As the PRP lesions disappeared, asymptomatic EGR-like lesions (Erythema gyratus repens) (concentric annular rings of erythema and scale), asymptomatic, were observed on the trunk and proximal limbs. Unlike true EGR, which is itchy and often associated with malignancies. Five months later, the EGR reappears. There was an option to continue with acitretin at a reduced dose of 10 mg per day.
Lora et al. (2017)	13/M	Subcutaneous etanercept in 50 mg injections (once a week). After 8 weeks, administration every 10 days for another 1 month.	Complete clinical remission was observed after 8 weeks of treatment.
Napolitano et al. (2017)	N=5 52/M;43/M;58/M;28/F;62/F	Three subcutaneous doses of 45 mg ustekinumab at weeks 0, 4 and 16. Clinical response was assessed monthly during treatment and up to 15 months follow-up period. Only one case had a partial response and was treated concomitantly with 0.2 mg/kg per day of acitretin for 6 weeks from week 16.	Significant improvement of skin lesions was observed in all patients, with a decrease in erythema, follicular hyperkeratosis and desquamation, and a slight improvement in palmoplantar keratoderma. Four of the five patients showed complete resolution of the condition. Only one case had a partial response and was treated concomitantly with acitretin, showing moderate improvement of palmoplantar lesions.

Atzori et al. (2018)	51/M	Acitretin 0.7 mg/kg/day (50 mg/day). Dosage was reduced to 25 mg for 2 months, and to 10 mg for another 3 months.	There was complete and gradual improvement with acitretin from the first week of use, with lesions disappearing within 30 days. No recurrence in 1 year.
Bonomo et al. (2018)	07/F	Cyclosporine 100 mg / 3 times a week combined with biweekly phototherapy and tacrolimus 0.1% ointment, triamcinolone 0.1% ointment for the body and hydrocortisone butyrate ointment for the face. The patient showed great worsening in the fifth month of treatment, and 45 mg of ustekinumab SC was added at weeks 0 and 4 and then every 12 weeks. For the second injection of ustekinumab, cyclosporine was reduced to 100 mg twice weekly.	Four weeks after the second injection, the patient showed continued clinical improvement; then cyclosporine was reduced to once weekly at this time and subsequently discontinued at week 12. After 6 doses of ustekinumab, and 1 year of treatment the patient became asymptomatic and had no relapse during follow-up.
Cho et. al (2018)	60/F	Apremilast at 30 mg/day for 6 months.	The skin lesions improved after 2 months of use, except for the palmoplantar regions, No recurrence in 6 months of treatment. As an adverse effect, the patient had only mild headache, which was controllable with oral analgesia.
Hanfstingl et al. (2018)	68/M	Acitretin 25 mg/day with no satisfactory remission. The palmoplantar skin observed worsening, with the formation of rhagades. Therefore, we opted for an off-label use of ixekizumab.	Gradual improvement and remission of lesions within 4 weeks after introduction of ixekizumab.
Heibel et al. (2018)	63/M	Acitretin 50 mg/day, with initial improvement, followed by gradual exacerbation. MTX was added at a dose of 10 mg/wk. Without clinical improvement, etanercept (50 mg twice a week) was added to both drugs. Patient discontinued etanercept after 1 month of therapy for perceived exacerbation. Ixekizumab was subsequently started (initial dose 160 mg, 80 mg every 2 weeks for 3 months, 80 mg monthly thereafter) with continued acitretin and methotrexate.	There was significant clinical improvement at week 4 and 8 weeks after starting ixekizumab, at which point acitretin was discontinued. Long-term remission continued over 12 months of therapy with ixekizumab as the only therapeutic agent without adverse events.
Ismail et al. (2018)	74/F	MTX 17,5 mg/week/3 months, replaced by acitretin 25 mg/day due to lack of response, and discontinued after 3 months due to adverse effects and lack of efficacy. Ustekinumab was initiated and administered at 45 mg at weeks 0, 4, and 12.	Ustekinumab, proved effective after 6 weeks of use, with almost complete dose remission at week 12.

Koch et al. (2018)	N=3 55/M; 50/M; 83/M	Case 01: Initial treatment of MTX 20 mg SC/ week, followed by 5 mg of oral folic acid on the following days. MTX was increased to 25 mg once a week. The treatment lasted 13 months.	Case 01: In 1 month, there was considerable improvement in the erythema on the trunk, with persistence of scaling and erythema on the arms and palmoplantar keratoderma. Trunk erythroderma continued to improve in the fourth month of follow-up, however, palmoplantar keratoderma only slightly improved, only disappearing in the ninth month of treatment, which later completely disappeared after 9 months. MTX was then consecutively reduced each month to 7.5 mg/week and discontinued after 4 months of clinical improvement. The total dosage of Methotrexate used was 817.5 mg, with no adverse reactions.
		Case 02: Treatment with MTX 10 mg/SC/ week, followed by 5 mg of oral folic acid every following day. MTX dose was increased by 2.5 mg/week to 20 mg weekly with normal regular laboratory controls.	Case 02: At the 6-week follow-up, the skin worsened showing erythroderma and MTX increased to 25 mg/week. Three weeks later, the erythema slowly and progressively reduced, with marked improvement 4 months after initiation of therapy. At the last follow-up, the patient received a total methotrexate dose of 1237.5 mg with stable disease.
		Case 03: Acitretin, 30 mg/day, was started and increased to 50 mg/day in 2 months with worsening erythroderma. When then it was replaced by MTX (10 mg/SC/week), followed by 5 mg oral folic acid on the following days.	Case 03: Clinical improvement in 2 months. MTX was increased to 12.5 mg/week. At the 3-month follow-up, only single plates remained in the trunk and both arms. Therapy was continued. At follow-up a total dose of 392.5 mg.
MacGillivray et al. (2018)	08/M	Acitretin 25 mg orally daily and topical corticosteroids, with minimal response within 1 month. MTX. 10 mg v.o weekly was added and in 3 months there was a marked improvement.	This combination resulted in a marked improvement in the skin, with total improvement after 3 months of use.
Aragon-Miguel et al. (2018)	30/M	Acitretin 50 mg/day with PUVA 3 times a week for 8 weeks. Thereafter, ustekinumab was started at 45 mg at weeks 0 and 4 and then every 12 weeks.	Previous treatment with acitretin and PUVA was ineffective. Ustekinumab demonstrated efficacy after 4 weeks, with reduction of erythema, scaling and pruritus and global improvement after 9 months of treatment.
Pellonnet et al. (2018)	47/M	Initial unspecified topical treatment, followed by acitretin 25 mg/day, progressively increasing to 40 mg, associated with UVB for 7 months. Then, oral apremilast 10 mg/day was started with an increase to a dose of 30 mg, twice a day, after 5 days.	Treatment with ointments, followed by acitretin, associated with UVB, without effectiveness, apremilast was added, with significant improvement of erythema and palmoplantar keratoderma after 1 month of use. Complete cure was achieved after 2 months of treatment. Seven months later, still using apremilast 30 mg twice a day, remission was maintained. The treatment had no side effects on the patient.
Chastagner et al. (2019)	48/F	Initially, MTX (20 mg orally/week for 1 month) combined with clobetasol was unsuccessful. Then Acitretin (up to 50 mg/ day) and infliximab (5 mg/kg), which was discontinued. Subsequently, adalimumab (80 mg at week 0 and 40 mg every two weeks) was administered with acitretin, with no results. Finally, ixekizumab at 80 mg every 2 weeks was added to acitretin.	MTX was discontinued after 1 month due to ineffectiveness and adverse effects. Infliximab was discontinued after 3 infusions for anaphylactic shock. The combination of adalimumab and acitretin did not result in improvement after 3 months. Finally, ixekizumab plus acitretin demonstrated marked efficacy after 5 months of treatment with only 5% of the body surface involved. No relapses occurred after 1 year of follow-up.

Cole et al. (2019)	61/F	The patient had been unsuccessfully treated with etanercept (mild improvement), alefacept (mild improvement), MTX (elevated liver function tests), acitretin for a further 2 years (mild improvement, but ongoing pruritus and skin lesions), UVB-NB for more than 10 years (possible burn), and apremilast for more than 1 year (improvement of pruritus, but frequent attacks). Given the refractory nature of her disease, the patient was started on secukinumab for 7 weeks.	The use of secukinumab was efficient from the first injection (week 0) with resolution of pruritus and lesions after the second injection (week 1), with resolution of the lesions after seven weeks of use, leaving post-inflammatory hyperpigmentation and mild hyperkeratosis of the palms. The patient maintained secukinumab and in the last follow-up, months after its initiation, the present continued without crises or adverse effects.
Klosowicz et al. (2019)	07/F	Oral acitretin 10mg/day, moisturizing creams, and topical with 10% urea (hands and feet) and topical salicylic acid 5% ointment (scalp). The duration of therapy was 3 months.	Within 2 months the patient improved remarkably, the papules and plaques resolved completely with hyperpigmentation and no adverse effects except cutaneous xerosis.
Pilz et al. (2019)	N=2 65/M; 75/M	Guselkumab 100mg SC week 0 and 4 followed by injections every 8 weeks.	A decrease in affected body surface area was observed from 95% to 5% in patient 1 and 98% to 15% in patient 2.
Rosa et al. (2019)	60/M	Cyclosporine 4mg/kg/day combined with topical corticosteroids. After no improvement and presentation of severe pain and pruritus, the use of cyclosporine was discontinued and treatment with brodalumab 210 mg SC was started.	Complete clinical response was obtained after 8 weeks of use of brodalumab and was maintained with a 6-month follow-up.
Amat-Samaranch et al. 2020)	36/M	Treatment with UVB-NB, topical corticosteroids and cyclosporine 4 mg/kg/day. Then, ustekinumab 45 mg and acitretin 25 mg/day were started. Subsequently, treatment with brodalumab was initiated.	Treatment with UVB, topical corticosteroids and cyclosporine had no effect and the lesions progressed to generalized erythroderma within 10 weeks. Ustekinumab showed only a partial response after 5 months of use Brodalumab caused a partial response and almost complete relief of itching 4 weeks after use and a complete response with residual post-inflammatory hyperpigmentation after 10 weeks of treatment.
Camela et al. (2020)	N=2 65/M; 66/F	Case 1: acitretin 35 mg/day and UVB-NB therapy twice weekly.	Case 1: A slow but increasing improvement was observed reaching a complete remission after 5 months of treatment.
		Case 2: the patient's comorbidities (SAH, dyslipidemia and osteoporosis) contraindicated acitretin or MTX; in addition, the patient refused phototherapy. Ustekinumab SC was administered at a dose of 45 mg/month for 8 weeks, then quarterly.	Case 2: There was a significant improvement with treatment as early as 8 weeks, with complete clinical remission at week 12 and no relapse observed within 36 weeks.
Felice et al. (2020)	52/F	Etanercept SC 50 mg/2 times a week. Then ustekinumab 45 mg (SC). Thereafter, brodalumab 210 mg (SC) was administered every 2 weeks after 3 loading doses at weeks 0, 1 and 2.	Etanercept was discontinued after 3 months due to ineffectiveness. Ustekinumab had its use discontinued after 15 months because it provided initial improvement, followed by progressive worsening of the disease. Brodalumab was introduced with significant skin improvement after 1 month and total improvement after 2 months of treatment, including resolution of palmoplantar keratoderma. The treatment was continued and in the 5th month the patient was free of lesions and without side effects to the drug.
Leite et al. (2020)	60/F	Oral MTX, 15 mg/week for 9 months.	MTX showed improvement in erythrodermia after three months, when its reduction was initiated The skin surface normalized nine months after the onset of the disease.

Liang et al. (2020)	07/M	Oral isotretinoin (20 mg/day for 3 months) and oral cyclosporine (75 mg/day for 2 months). After ruling out infection, secukinumab 150mg/sc once weekly for 5 weeks.	Progressive improvement. After the last dose of the drug, there was almost complete remission of the skin lesions.
Nagai, et al. (2020)	47/F	Etretinate 30 mg/day (orally). Oral therapy with apremilast and phototherapy (PUVA bath) combined with topical steroid. Guselkumab 100 mg (subcutaneous injection). After 04 weeks, the administration of Guselkumab 100 mg was repeated and its use continued at 8-week intervals.	Etretinate 30 mg/day (orally) was ineffective and discontinued. Oral therapy with apremilast and PUVA phototherapy) combined with topical steroids also had no therapeutic effects. After 4 weeks of Guselkumab use, the severity and extent of the erythema decreased slightly. At 24 weeks after the first injection, the patient's BSA went to 2% and sPGA to 1. After 38 weeks after the initial injection, erythema and pruritus had become completely absent and there was no relapse 36 weeks after the last injection. injection.
Ricar J, Cetkovska P. (2020)	51/F	Risankizumab 150 mg given at weeks 0 and 4 and every 12 weeks thereafter. Patient continued to use topical corticosteroids intermittently during risankizumab treatment.	At week 12, her BSA was 3% and her DLQI was 2. At week 32, her BSA was 01% and her DLQI was 0 (zero). In the 52nd, the findings remained unchanged and the medication still provided excellent control of disease symptoms with no adverse effects.
Penalba-Torres et al. (2020)	83/F	Acitretin 25 mg/day associated with topical bemethasone once/day. Isoniazid 300 md/day (latent tuberculosis infection). Rifampicin 600 mg/day for 4 months. Subsequently, ixekizumab was started. Patient used this medication for 9 months.	Acitretin and betamethasone are not effective after 1 month of use. Isoniazid 300 md/day triggered hypertransaminasemia. After normalization of the liver profile, rifampicin was started. Treatment with ixekizumab after 6 weeks showed improvement of skin lesions, with reduction of pruritus. At week 9, the patient had a BSA of 28% and a DLQI of zero and no itching. The patient had BSA 0 from the 16th week onwards. The patient remained in remission during the 32-week follow-up period.
Kohn T, Wetzig D (2020)	88/F	Prednisolone 0.5 mg/kg per day. acitretin 20 mg/day. After improvement, prednisolone was gradually tapered. 02 injections of guselkumab 100 mg every 4 weeks. Methotrexate 15 mg s.c/week alternate. Ixekizumab 160 mg initial dose, then 80 mg every 2 weeks until week 12. End of therapy after 16 weeks.	After 2 weeks with ixekizumab, there was significant improvement in the patient's skin. The erythema disappeared and the hyperkeratoses decreased. After 8 weeks of therapy, the skin was almost completely normal, with some minimal plaques and subtle circumscribed palmar hyperkeratosis.
Zhong et al. (2020)	07/F	The patient was successfully treated with a combination of weekly intravenous dose of methotrexate at 7.5 mg weekly and subcutaneously injected with etanercept 12.5 mg twice weekly.	After 3 weeks, the erythematous lesions had completely subsided, leaving hyperpigmented macules. Palmoplantar hyperkeratosis was also relieved, and the skin smoothed. No recurrent lesions were observed during the 0.5-year follow-up period.

Table 1- Literature review Pityriasis rubra pilaris

Elevated levels of Th17 and Th1 cytokines have already been observed in the lesional skin of affected people, as well as elevations of IL-23/Th17. [15-18]

However, PRP has important histopathological features that facilitate the determination of the patient's diagnosis. Among them, orthokeratosis and parakeratosis in a board pattern, confluent or focused hypergranulosis, irregular acanthosis, thickened suprapapillary plaques, in addition to sparse perivascular lymphocytic and histiocytic involvement in the dermis layer, as well as follicular plugging with parakeratosis at the edges of the follicular orifice. Less classic findings, such as lichenoid infiltrate and dermal eosinophilia, may be present. [1]

Therapeutic management for PRP cases is usually challenging, with a gap in guidelines and algorithms for treatment, as well as efficient clinical studies to guide interventionist actions. [19-21] Among the options used in systemic therapy are oral retinoids, such as acitretin; immunosuppressive drugs, such as methotrexate, cyclosporine and azathioprine, especially in refractory cases; phototherapy and immunobiological products. [22 -25]

Promising results have been reported with the use of immunobiologicals, including Anti-TNF agents (Infliximab, Etanercept and Adalimumab); anti-IL 12/ IL 23 (risankizumab) and ILA 17 agents (Brodalumab, Guselkumab, Ustekinumab, Ixekizumab and Secukinumab). [25-35]

Despite the increasing indications for the use of immunobiologicals in this pathology, the intrinsic risks of their use must be considered, due to the immunological modulation/ suppression activity, which can cause a greater risk of developing serious infections and malignant diseases, like lymphomas. [36]

While the exact mechanism of action of MTX in inflammatory skin diseases like PRP remains unclear, it presumably depends primarily on two different effects. On the one hand, MTX acts as an antiproliferative agent as it depresses the mitotic rate of keratinocytes via induction of apoptosis of proliferating keratinocytes through oxidative stress. On the other hand, MTX has anti-inflammatory effects, especially via the reduction of pro-inflammatory cytokines, such as interleukin 1 (IL1) and tumor necrosis factor alpha (TNFα). In addition, an increase in the gene expression of the anti-inflammatory Th2 cytokines IL4 and IL10, a decrease in the gene expression of the pro-inflammatory Th1 cytokines IL2 and interferon gamma (IFNγ), or the induction of apoptosis in cells involved in the immune/ inflammatory reaction that may play a therapeutic role.[37]

In a literature review on MTX administration for PRP, doses ranging from 5 to 25 mg/week were found, depending on variables such as age (3-83 years) and patient weight. Studies with doses greater than 25 mg/week have not shown a benefit in terms of better results, but on the other hand, they have been associated with an increased risk of side effects.[37] Regarding the MTX dosage recommended in the PRP, it is important to note that the use is still off-label. However, based on the findings analyzed, we recommend the use of up to 25 mg/week, similar to the dose for the treatment of psoriasis, highlighting the individualities of each patient as well as their adaptation to the treatment.[38] After the clinical picture improves, the dose must be reduced to the lowest effective dose for maintenance therapy.

The management of PRP cases is often challenging, given the unsatisfactory outcome of some lines of treatment, the particularities of patients, as well as the high cost of the biological therapies currently used. The patient in the report, in line with some of the analyzed studies, employed the use of methotrexate in PRP therapy, obtaining promising results.

Thus, the use of MTX as the therapy of choice must be considered a prominent option in the therapeutic approach to the disease, as it has favorable outcomes that have optimized management and reduced adverse effects.

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