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Medicine

PITYRIASIS RUBRA PILARIS TYPE I ASSOCIATED WITH CIRRHOSIS OF THE LIVER

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ABSTRACT:
PITYRIASIS RUBRA PILARIS (PRP) IS AN INFLAMMATORY SKIN DISEASE WITH POLYMORPHIC CLINICAL FEATURES, CONSISTING OF KERATOSIC FOLLICULAR PAPULES, YELLOW-ORANGE PALMOPLANTAR KERATODERMA ASSOCIATED WITH ERYTHEMATOUS OR ERYTHEMATOUS-SQUAMOUS PLAQUES, WHICH INTERSPERSED WITH AREAS OF HEALTHY SKIN. WE PRESENT THE CASE OF A 72-YEAR-OLD MAN IN WHICH THE DIAGNOSIS OF PRP REQUIRED ADDITIONAL EXPLORATIONS, FOR EXCLUDING NEOPLASIA OR OTHER INFLAMMATORY DISEASE. FINDING CONCOMITANT LIVER DISEASE REQUIRED A REASSESSMENT OF THERAPY.

KEYWORDS: A PITYRIASIS RUBRA PILARIS, ASSOCIATED CONDITIONS, TREATMENT.

INTRODUCTION

Pityriasis rubra pilaris is a rare condition, characterized by the appearance of follicular hiperkeratotic papules, associated with erythematous or erythematous-squamous plaques, which intersperse with areas of healthy tissue and yellow-orange palmoplantar keratoderma[6]. There are variations in the incidence depending on the race, in the UK there are 1 case

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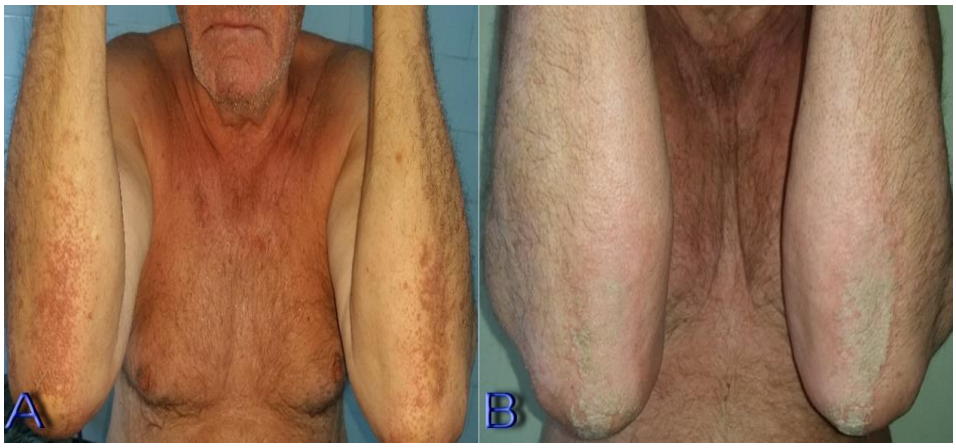
[6] Fuchs-Telem D., Sarig O., van Steensel M., Isakov O., Israeli S., Nousbeck J., Richard K., Winnepenninckx V., Vernooij M., Shomron N., Uitto J., Fleckman P., Richard G., Sprecher E. Familial Pityriasis Rubra Pilaris Is Caused by Mutations in CARD14. The American of Human Genetics, 13 July 2012, Volume 91 (1): 163–170.

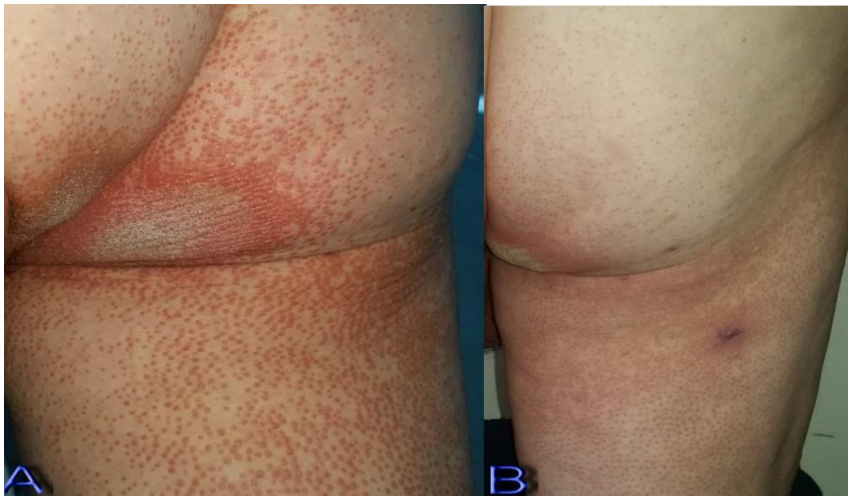
reported for 5000 inhabitants and in India 1 case for 50,000 inhabitants. Both sexes are equally affected regardless of age, and family spread is only sporadic (up to 6.5%). Type I PRP although it responds well to retinoids treatment may have a reserved prognosis due to associated comorbidities[7].

CASE REPORT

A 72-year-old patient, from rural environment, non-smoking, is admitted in the Dermatology Clinic for a rash consisting of follicular hiperkeratosic papules and erythematous plaques covered by white scales, with psoriasiform aspect, some coalescent in placards with imprecisely delimited margins, located on the trunk and limbs, lesions that appeared two months ago (figure 1, 2, 3).



(figure 1) Isolated follicular hyperkeratotic papules which in evolution forming psoriasiform erythematous plaques in classic adult type I pityriasis rubra pilaris. **A**, clinical aspect at admission. **B**, aspect 2 months after initiation of treatment with retinoids.



(figure 2) Follicular hyperkeratotic papules on the down half of the body. **A**, clinical aspect at admission. **B**, aspect 2 months after initiation of treatment with retinoids.

[7] Virendra N Sehgal, Govind Srivastava, Sunil Dogra. Adult onset pityriasis rubra pilaris. IJDVL, 2008, Volume 74 (4): 311-321

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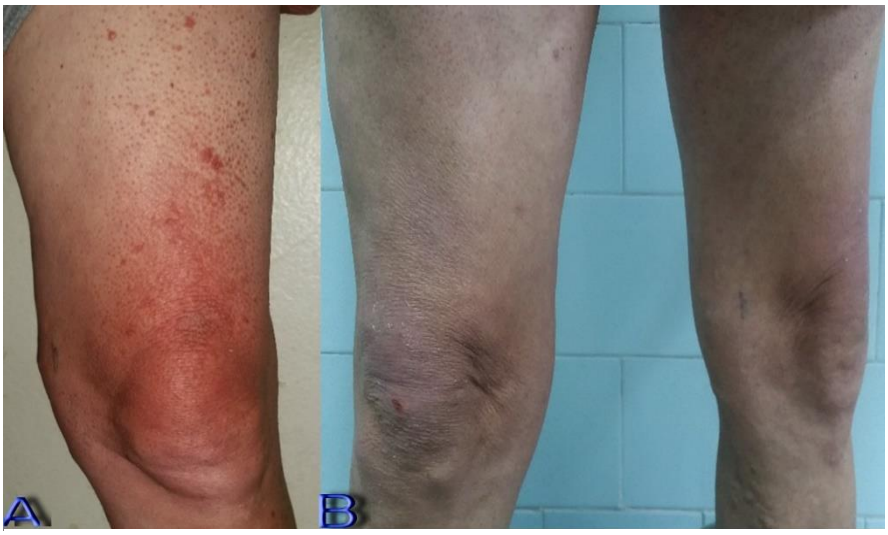
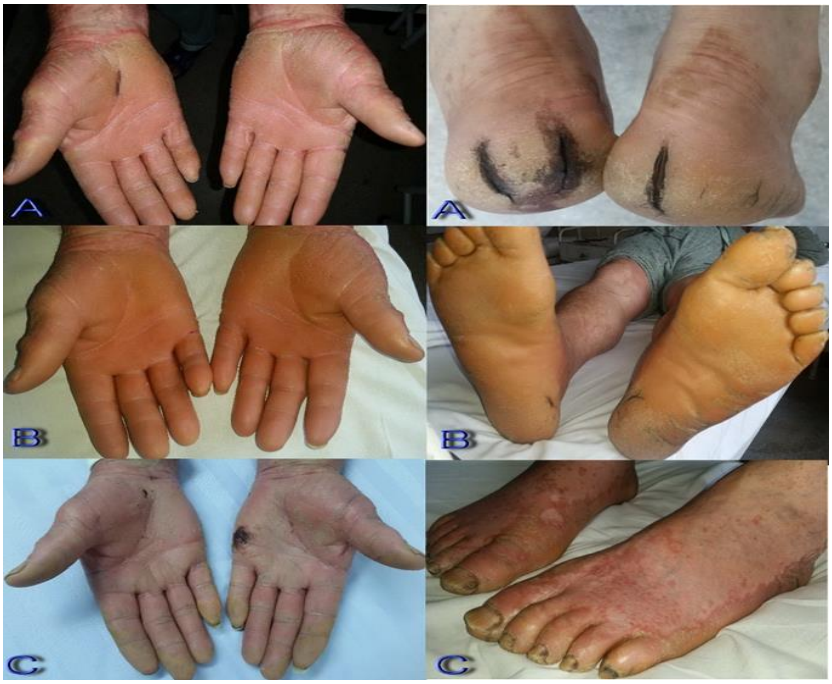


(figure 3) Erythematous macules, psoriasiform plaques, follicular hyperkeratotic papules isolated and grouped. **A**, clinical aspect at admission. **B**, aspect 2 months after initiation of treatment with retinoids.

Bilateral palmar and plantar had a diffuse hyperkeratosis with painful fissures on the surface, occurring two weeks before the lesions on the trunk and limbs. The fingernailsof the hands and feet were thickened, there were no injuries to the mucous. (figure 4)



(figure 4) Waxy, diffuse, yellowish palmar and plantar keratoderma with deep fisssures in PRP type 1. **A**, clinical aspect at admission. **B**, aspect 1 month after initiation of treatment with retinoids. **C**, aspect 2 months after treatment.

From medical history we noticed: hypertension, atrial fibrillation, dyslipidemia.

Background medication: Indapamide LPH 1.5mg, p.o., b.i.d., Trimetazidine LPH 35mg p.o., b.i.d., Monopril 10mg p.o., b.i.d., Spironolactone 25mg p.o., q.d., Carvedilol 6.25mg p.o., b.i.d., Atorvastatin 20mg p.o., q.d.

Clinical examination: patient with good general condition, with obesity grade I (BMI = 32.74), pain in the lumbar spine, abdomen enlarged by volume through adipose tissue.

Laboratory explorations: Mild thrombocytopenia (136000/µl), blood count, GOT, GPT, glycemia, cholesterol, triglycerides, urea, creatinine, within normal limits, anti-HCV antibodies and negative HBs antigen. Urinalysis revealed: increased number of leukocytes, erythrocytes present, relatively frequent flat epithelium.

Abdomino and pelvic Ultrasound: Liver with anteroposterior diameter of left lobe 8.5cm, anteroposterior diameter of right lobe 18 cm, slightly increased consistency without localized processes. Gallbladder with thickened walls with sludge in the infundibular area, without calculi, portal vein with normal diameter, right kidney normal, homogeneous spleen. Left kidney with cyst at the level of the lower cortical pole with 3.2 cm diameter. Intensely hyperecogenic norm-sized pancreas. No fluid in the peritoneal cavity.

Pulmonary X-ray: Nothing active pleuro-pulmonary. Cord with increased transverse diameter.

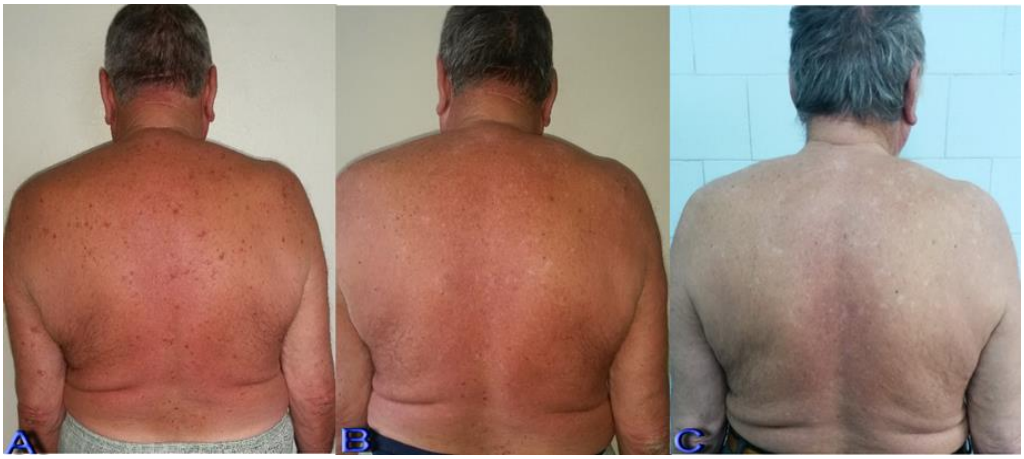
Otorhinolaryngology exam: Left ear plug. Right otomycosis. Perforation of the right eardrum. It is practiced local toilet. Spraying with iodized boric acid is practiced.

During the hospitalization were performed two skin biopsies: from the level of the right calf – the posterior region and from the dorsal face of the right forearm.

The histopathological examination reveals: Epidermis with focal acanthosis, orthokeratosis that alternating horizontal and vertical with parakeratosis, hipergranulosis, thickening of the rete ridges, follicular hyperkeratosis, dilation of the infundibule of the hair follicle, discrete spongiosis. Underlying chronic perivascular inflammatory infiltrate, collagen degeneration.

Based on the anamnesis, clinical features, laboratory and histopathological examinations, we have established the diagnosis of classical type I PRP.

Treatment with acitretin at a dose of 50 mg/day was initiated for 3 weeks, with the dose lowered to 30 mg/day for 3 weeks and then 20 mg/day for 2 weeks. (figure 5)



(figure 5) Erythematous slightly scaling eruption with a tendency to erythroderma. **A**, clinical aspect at admission. **B,** aspect 1 month after initiation of treatment with retinoids. **C**, aspect 2 months after treatment.

The evolution was favorable, with the remission of palmoplantar hyperkeratosis, persisting a desquamative erythema on the dorsal face of the hands and a desquamative cheilitis, for which he is undergoing emollient treatment. For pecuniary reasons the patient discontinued therapy with acitretin.

2 months after discontinuation of acitretin therapy, the patient was hospitalized for recurrence of lesions.

Laboratory exams have revealed the persistence of thrombocytopenia (121700/µl), increased GOT (53U/L), slightly elevated triglycerides (152 mg/dl) and increased tumor markers AFP (8.60 IU/mL) and CA 19-9 (65.20 IU/mL).

Abdominal and pelvic ultrasound reveals an enlarged liver of volume with left lobe of 8.3 cm, right lobe 16 cm, inhomogeneous, pseudo-nodular structure, with hyperechogenic nodules up to 6 mm on a possible cirrhotic liver, a relaxed gallbladder without calculi, CBP 5 mm, VP 10 mm, intense hyperechogenic pancreas, anteroposterior diameter in the body 27 mm, normal kidneys size, without calculi, without dilations, normal vascularization, spleen 10.5 cm, urinary bladder normal.

The Internal Medicine consult recommends the extension of investigations: upper endoscopy, abdominal CT scan, colonoscopy and reassessment with the results obtained.

Upon discharge the patient there was recommended systemic treatment with acitretin at a dose of 30 mg/day for two months and hepatoprotective medication. For palmoplantar region we prescribed an ointment with salicylic acid 5% and urea 10%. Also, there were indicated a hypolipemic hygienic-dietary regimen, prohibition of alcohol consumption, regular control of lipid profile and transaminases and conducting investigations in the gastroenterology clinic.

After 2 months, at the admission to the Gastroenterology Clinic, the patient diagnosed with: alcoholic cirrhosis of the liver, chronic liver failure, esophageal varices with bleeding, high blood pressure, congestive heart failure, atrioventricular block grade 1.

DISCUSSIONS

The etiology and pathogenesis of PRP remain still poorly understood. There is considered that exist a dysfunction in the metabolism of vitamin A, but the role of its deficiency remaining uncertain because the attempts to produce lesions by the lack of vitamin A were not conclusive. Acute upper respiratory tract infections are implicated as triggers for juvenile forms of PRP. Autosomal dominant genetic factors play an important role in PRP induction[8].

According to Griffits, PRP is classified according to the clinical features and evolution as follows:

Type I (adult, classic) – is the most common form. It affects the sexes equally, having peak incidence between 40 and 60 years. The rash at onset consists of erythematous macules, slightly squamous at the level of the head, neck, or upper trunk, followed by the appearance of new macules over the course in a few weeks. Then arise many erythematous perifollicular papules with central hyperkeratotic plug, initially isolated, which then will merge together. Interfollicular erythema occurs, and follicular lesions combine into erythematous plaques with a slight orange tinge that generalize. The face becomes evenly erythematous and can be observed the occurrence an ectropion. Erythroderma usually develops within 2-3 months. In

[8] Schäkel Knut. Pityriasis Rubra Pilaris In: Kang S., Amagai M, Bruckner A, Enk A, Margolis D, McMichael A, Orringer J (eds), Fitzpatrik's Dermatology in General Medicine, Nineth Edition, Mc Graw Hill Medical Companies, Inc., 2019, 498-503.

most cases, well-demarcated islands of healthy tissue about 1 cm in size remain a useful diagnostic sign. The nails are thickened and discolored distally, with longitudinal hemorrhagic striae; and compared to psoriasis, there is no dystrophy of the nail bed and pitting is minimal. Spontaneous resolution occurs in 60-80% of patients in 1-3 years, but the disease can persist indefinitely. The rash resembles seborrheic dermatitis as it resolves. Recurrences are rare[3].

Type II (adult, atypical) - Affects 5% of patients and presents as a prominent follicular hyperkeratosis in certain areas with lamellar scales in other locations, especially in the lower limbs. Often there are areas with changes of eczematous type[3].

Type III (juvenile, classic) - The onset is from 5 to 18 years. It resembles type I but can quickly develop an acute infection and spontaneous resolution is usually between 1-2 years. The evolution from type III to type IV and vice versa may occur.

Type IV (juvenile, circumscribed) - Onset by the age of 12 years. Patients have well-defined hyperkeratosis plaques with erythema of varying intensity located in the knees and elbows and several squamous erythematous macules sprinkled on the trunk or scalp, with certain cases also showing marked keratoderma of the palms and soles. The prognosis remains unclear but certain cases heal at the end of adolescence[3].

Type V (juvenile, atypical) – The familial form is often of this type and can overlap clinically with ichthyosis and erythrokeratoderma. Patients present erythema and hyperkeratosis at birth or in the first years of life. Follicular plugs and erythema suggest the diagnosis of PRP but keratoderma is common[3].

PRP type VI (PRP and immunodeficiency) - A PRP-like rash associated with HIV infection, which responds to antiretroviral therapy, is recognized[9]. The clinical manifestations are similar to those of type I but have increased severity and additional manifestations of acne conglobate, hidradenitis suppurative and lichen spinulosus[3]. Some authors still preferred the term follicular syndrome associated with HIV infection[10].

Differential diagnosis is made especially with psoriasis, from which it is clinically differentiated by:

1. the general condition of patients with PRP remains good in contrast to that of those who have psoriasis,
2. the"islands" of unaffected tissue are characteristic,
3. scarlet or orange color of the skin,
4. the absence of infiltration, lichenification and profuse lamellar squamous that are characteristic of psoriasis,
5. absence of oncolysis typical of psoriasis,
6. palmoplantar hyperkeratosis of yellow-orange color, without infiltration,
7. ineffective antihistamine and hormonal treatment[11].

Other differential diagnoses are follicular ichthyosis, variable erythrokeratodermia, follicular eczema, hair keratosis, chronic lichenoid pityriasis, nonbullous congenital ichthyosiform erythroderma, and for treatment-resistant cases - with HIV infection, T-cell lymphomas[3].

[9] M.R. Judge, W.H.I. McLean, C.S. Munro. Disorders of Keratinization, in Rook's Textbook of Dermatology, Vol. 1, 19.77-19.79.

[10] M.R. Judge, W.H.I. McLean, C.S. Munro. Disorders of Keratinization, in Rook's Textbook of Dermatology, Vol. 1, 19.77-19.79

[11] Kubanov A., Gallyamova Y. Diagnosis and Treatment of Pityriasis Rubra Pilaris, Serbian Journal of Dermatology and Venerology, 2011, Volume 6 (4): 167-173. DOI: 10.2478/sjdv-2014-0014.

Associated diseases

Associations with paraneoplastic dermatomyositis, inflammatory arthritis, viral hepatitis A have been described, and recently a case associated with lichen planus, universal alopecia, vitiligo and viral hepatitis C has been described[3,12,13].

Some authors consider PRP as paraneoplastic syndrome being cited associations with liver carcinoma, cholangiocarcinoma[14,15].

Treatment

Early treatment with retinoids seems to provide the greatest chance of cure for PRP. If treatment with retinoids does not give results, treatment with methotrexate should be considered.

The effectiveness of retinoids and methotrexatu is supported by numerous studies compared to other forms of treatment, including corticosteroids, vitamin A and cyclosporine, which were ineffective[16].

The most effective retinoid for the treatment of PRP is acitretin at a dose of 0.5-0.75 mg/kg/day, with the average daily dose varying between 25-50 mg/day. The improvement of the symptomatology is observed from the first month of treatment, but substantial improvements or even healing occur during the first 4-6 months. According to certain studies, the average duration of treatment is about 4 years[3,5].

Methotrexate can be a therapeutic alternative at a dose of 15-25 mg/week. The associating methotrexate (5-30 mg/week) with oral retinoids over a period of 16 weeks increases the therapeutic response but the combination may lead to increased hepatotoxicity.

The use of phototherapy (UVA) is controversial, with some cases evolving favorably, others worsening, no UVB is indicated.

In severe cases, an effective treatment option are immunomodulators: fumaric acid, TNFα antagonists, apremilast[3,5]. Recently, very good results have been reported with ustekinumab and secukinumab in cases with familial PRP, but also the appearance of follicular lymphoma in a case treated with adalimumab and methotrexate[17,18,19].

Used only as an adjunct, topical treatment during retinoid therapy increases the quality of life of patients. Emollient creams, ointments with salicylic acid 2-5 %, urea 10 %, calcipotriol, malic acid 1-20 % are used in the treatment of palmoplantar hyperkeratosis.

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[12] Erdem T, Atasoy M, Aliagaoglu C, Melikoglu M, Yildirim U. Pityriasis rubra pilaris in association with hepatitis A. Saudi Med J. 2006 Sep;27(9):1421-2.

[13] Cecchi R, Giomi A, Tuci F, Bartoli L, Seghieri G. Pityriasis rubra pilaris,lichen planus, alopecia universalis and vitiligo in a patient with chronic viral hepatitis C. Dermatology. 1994;188(3):239-40. PubMed PMID: 8186518.

[14] Sharma S, Weiss GR, Paulger B. Pityriasis rubra pilaris as an initial presentation of hepatocellular carcinoma. Dermatology. 1997;194(2):166-7. PubMed

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[19] Dhonncha N.E, Fadalla K, Moriarty B, Gibbons D, Collins CD, Fabre A, Collins P. High grade follicular lymphoma in a patient receiving adalimumab and methotrexate for pityriasis rubra pilaris. J Dermatolog Treat. 2017 Mar 7:1-7. doi: 10.1080/09546634.2017.1303572

CONCLUSIONS

PRP remains a condition that causes problems of diagnosis and treatment, with an important impact on the quality of life regardless of the clinical form. Retinoids remain an effective therapeutic option but require precautions in the presence of liver pathology.

The occurrence of PRP in an elderly patient requires further explorations to exclude an internal neoplasia or other inflammatory diseases.

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