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Case Report

Psoriatic arthritis with hyperuricemia: A case report

Nurrachmat Mulianto, Irene Ardiani Pramudya Wardhani

Department of Dermatology and Venereology, Dr. Moewardi General Hospital/ Faculty of Medicine Sebelas Maret University Surakarta, Indonesia.

Abstract Psoriatic arthritis (PsA) has a clinical picture that resembles other arthritic diseases and is accompanied by other co-morbidities such as hyperuricemia. The diagnosis of PsA needs to be established as early as possible to reduce the morbidity of the sufferer. A 52 year old woman came with complaints of pain in her fingers and wrist since two years ago. The patient has a history of psoriasis vulgaris for three years but is not taking medication regularly. The patient had his complaints checked, stated that he had gout, complaints improved but came and went. On examination of the dermatological status of the posterior truncus and manus region bilaterally and the lower extremity region, multiple erythematous papules and plaques were seen with thin scales on it. On the 2nd and 3rd digits of the right manus and 3rd digit of the left manus there is edema. Dermoscopic examination, bilateral manus x-ray and bilateral genu support the picture of PsA. The blood laboratory examination revealed hyperuricemia. Based on The Classification Criteria for PsA (CASPAR) a total of 5 points was obtained. Patients were given methotrexate tablets 7.5 mg per week orally, folic acid, sodium diclofenac, zinc and narrow band ultraviolet B phototherapy (NBUVB) 330mj/cm^2 per week which was increased by 10% from the minimal erythema dose (MED) per session with a satisfactory response.

Key words
Psoriatic arthritis; Hyperuricemia; CASPAR.

Introduction

Psoriasis is an autoimmune disease characterized by skin inflammation, epidermal hyperplasia. In psoriasis there is an increased risk of comorbid diseases including destructive arthritis and cardiovascular morbidity as well as psychosocial challenges. Psoriasis arthritis (PsA) is a progressive inflammatory musculoskeletal disease that occurs in about one-third of psoriasis sufferers and is characterized by a variety of clinical features such as peripheral arthritis, spondyloarthritis, enthesitis and dactylitis.[1]

Orbai and Flynn reported the prevalence of PsA in the general population worldwide of 0.02% to 0.25%, while the prevalence of PsA in psoriasis patients was 2.7 cases per 100 patients worldwide, most often found in adults with an average mean 39.2 years and no difference between men and women.[1] Ohara *et al.* (2015) in Japan reported the prevalence of PsA in psoriasis sufferers in Asia was 10%.[2] Lai *et al.* (2018) in Hong Kong reported that hyperuricemia was found in 13% to 40.7% of PsA sufferers and 20% in Asia.[3] Data on the prevalence of PsA in Indonesia both in the general population and in psoriasis sufferers and the prevalence of hyperuricemia in PsA sufferers in Indonesia have never been reported.

Risk factors for PsA include severe psoriasis, nail psoriasis, obesity, the presence of human leukocyte antigen-B27 (HLA B-27) on genetic examination, uveitis, comorbidities with cardiovascular disease and hyperuricemia,

Address for correspondence
Dr. Irene Ardiani Pramudya Wardhani
Department of Dermatology and Venereology, Dr. Moewardi General Hospital/ Faculty of Medicine Sebelas Maret University Surakarta, Indonesia.
Email: ireneardiani@gmail.com

smoking, alcohol consumption and environmental factors such as trauma, stress and infection.[4,5] Gottlieb *et al.* (2006) in the United States reported that as many as 6% to 39% of PsA sufferers had a previous history of psoriasis of the skin.[6]

Clinical manifestations that arise in PsA include cutaneous manifestations such as psoriasis of the scalp, groin, nails and severe psoriasis. In the subclinical stage there are non-cutaneous manifestations such as joint pain, fatigue and stiffness in the joints, whereas in the clinical stage clinical symptoms may appear in the form of arthritis, dactylitis, enthesitis, spondyloarthritis and musculoskeletal changes seen on radiographic examination.[6,7] Hyperuricemia is a common pathological condition found in psoriasis sufferers and is characterized by excess production or underexcretion of uric acid which is a product of purine catabolism which is excreted physiologically in the urine.[8] Hyperuricemia can lead to gouty arthritis which has clinical manifestations similar to PsA and is accompanied by the formation of gouty tophi.[3] In psoriasis, there is excess turnover of keratinocytes which results in excess uric acid production and can eventually trigger PsA.[9] The diagnosis of PsA is based on anamnesis, physical examination, determination of the classification criteria for psoriatic arthritis (CASPAR) and examination of rheumatoid factor and x-rays.[10,11]

Treatment of PsA can be carried out based on the European League against Rheumatism (EULAR) algorithm or the Group for Research and Assessment of Psoriasis and PsA (GRAPPA) which aims to suppress PsA inflammation until remission occurs. Medical treatment includes administration of disease-modifying antirheumatic drugs (DMARDs) such as methotrexate (MTX), corticosteroids and topical therapy for psoriasis, while non-medical treatment that can be given includes physical therapy.[1]

Case report

A 52-year-old woman came to the Dermatology and Venereology Polyclinic at RSUD Dr. Moewardi Surakarta with complaints of pain in the joints of the fingers of both hands and wrists and ankles that have been coming and going since 2 years ago. The patient initially complained of reddish spots which were getting thicker and thicker and accompanied by scales, itchy and intermittent since 3 years ago. The patient then went to a skin and genital specialist at a hospital and was diagnosed with psoriasis. The patient was referred to the Skin and Venereology Polyclinic at RSUD Dr. Moewardi, was examined and diagnosed with psoriasis vulgaris then given injection of methotrexate at a dose of 10 mg/week for 5 weeks, continued 7.5 mg/week for 3 weeks, continued 5 mg/week for 3 weeks, continued orally 5 mg/week for one year, a concoction cream containing 4% salicylic acid and 0.05% clobetasol propionate ointment applied 2x a day, albumin vaseline applied 2x a day, black shampoo 3x a week, NBUVB phototherapy 500mj/cm2 once a week. Complaints improved but came and went, the patient then stopped taking treatment for one year because he did not feel significant improvement and felt weak while taking the drug.

In the previous medical history, similar complaints were found two years before the patient was examined, the patient began to complain of pain in the joints of the fingers of both hands, especially in the morning, feeling stiff and followed by wrists and feet. The patient did not seek treatment for this complaint but because the joint pain was getting worse, the patient then returned to the Dermatology and

Venereology Polyclinic at RSUD Dr. Moewardi Surakarta. The patient claimed to have a history of high uric acid levels and routinely went to an internal medicine specialist at a private hospital and was given meloxicam tablets and methylprednisolone tablets but the patient forgot the dose. The patient denied any history of diabetes mellitus, hypertension, drug allergies, food allergies or atopy. Family history of disease found complaints of joint pain in the patient's mother but was never examined. History of gout, diabetes mellitus, hypertension, drug allergies and atopy in the family was denied. The patient is a housewife who manages a boarding house in her home. The patient lives with her husband and working daughter.

On physical examination, the general condition of the patient looked moderately ill, compos mentis, blood pressure 120/80 mmHg, pulse 80x/minute, respiration 20x/minute, temperature 36.5oC, height 160 cm, weight 65 kg, body mass index (BMI) 25.4 (overweight) and visual analog scale pain score (VAS) 3. On examination of the dermatological status of the bilateral trunkus posterior et manus region and lower extremity region, multiple erythematous papules and plaques were seen with thin scales on it. On the 2nd and 3rd digits of the right manus and 3rd digit of the left manus there is edema **(Figure 1)**. On bilateral dermoscopy examination of the digiti manus et pedis region, hyperkeratosis, onycholysis and pitting nails were seen **(Figure 2)**. Based on the history and physical examination of the patient, our differential diagnosis was psoriasis arthritis, rheumatoid arthritis and gouty arthritis.

On bilateral human X-ray examination we found mild osteoporosis, whereas on bilateral genu we found early stage osteoarthritis which could be an early sign of PsA **(Figure 3)**. In laboratory

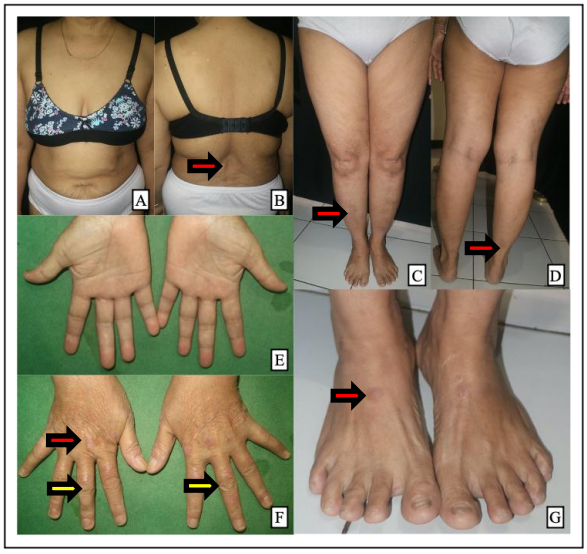


Figure 1 A-G. Examination of the dermatological status of the posterior truncus region, bilateral manus, bilateral lower limb and pedis regions showed multiple erythematous papules and plaques accompanied by thin scales on it (red arrows), digiti region 2 and 3 right manus and digital 3 manus left we found edema (arrow yellow).

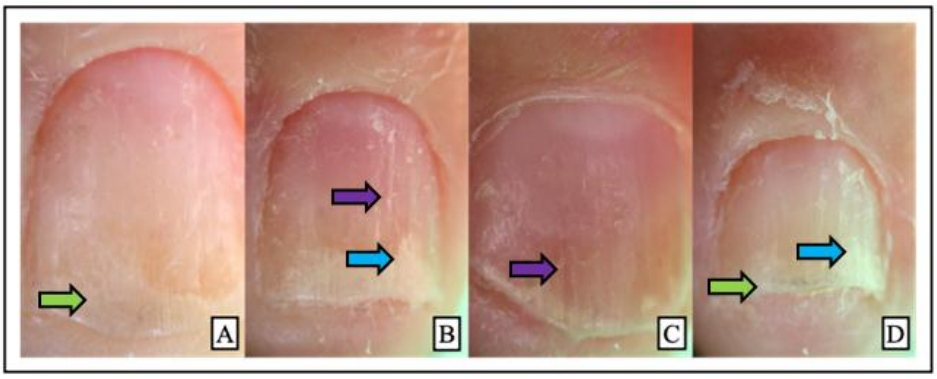


Figure 2 A-D Dermoscopy examination in the region of digits 1 and 5 of the right manus as well as digits 1, 4 and 5 of the left manus showed onycholysis (green arrows), on the left digits 3 and 4 manus there were pitting nails (purple arrows) and hyperkeratosis (blue arrows).

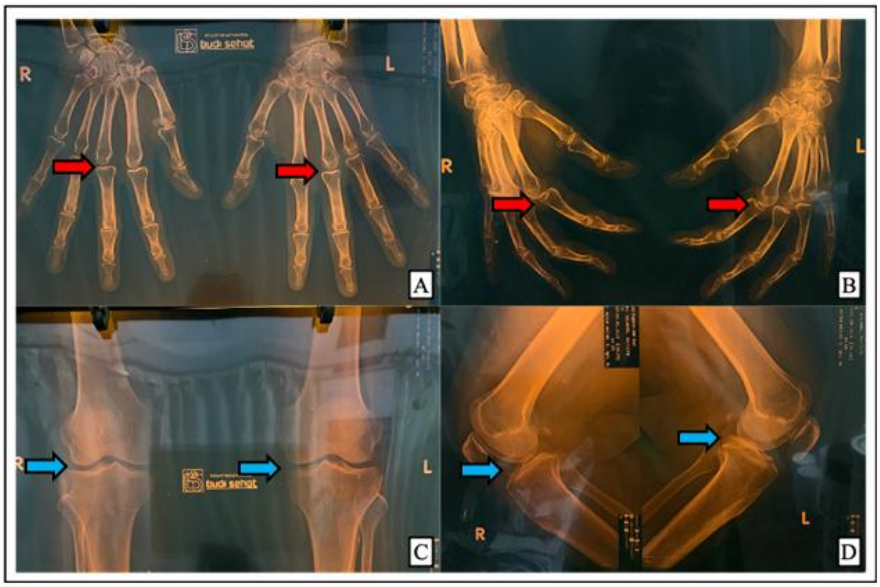


Figure 3 Radiological examination results. A, Bilateral manus showing mild osteoporosis (red arrow). B. Bilateral genu showing early-stage osteoarthritis (blue arrows).

We found a decrease in hemoglobin level of 8.3 g/dL (normal value: 12.0 – 16.0 g/dL), a decrease in hematocrit of 25.3% (normal value: 36.0 – 46.0%) , decrease in the number of erythrocytes 2.73 x 106 cells/uL (normal value: 4.00 - 5.20 x 106 cells/uL), increase in the sedimentation rate of 115 mm/hour (normal value: 20 mm/hour), increase eosinophils 5% (normal value: 1 – 3%), decrease in monocytes 1.9% (normal value: 2 – 8%). Examination of rheumatoid factor <8 (negative) IU/mL (normal value: <8 IU/mL), so as to rule out the diagnosis of rheumatoid arthritis. On examination of uric acid levels, the results showed an increase of 9.7 mg/dL (normal value: 2.4 – 6.1 mg/dL) and on the high sensitivity C-reactive protein (hs-CRP) examination we got increased results 1.17mg/dL (normal value: <0.85 mg/dL), thus not being able to rule out the differential diagnosis of gout arthritis. We consulted the department of internal medicine sub-rheumatology and then diagnosed with psoriatic arthritis and gout arthritis.

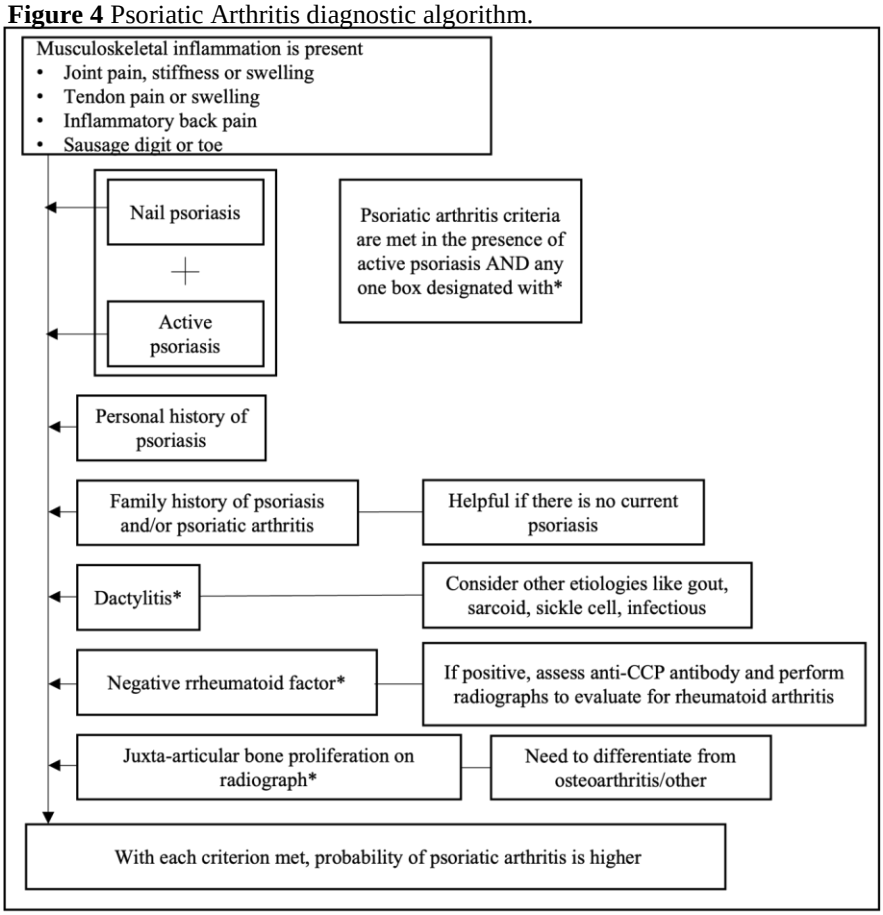
Based on t*he Classification Criteria for PsA* (CASPAR) **(Table 1)** we got 2 points for history of current psoriasis, 1 point for nail dystrophy typical of current psoriasis (onycholysis, nail pitting and hyperkeratosis), 1 point for negative

Table 1. CASPAR criteria.[1]

Criteria	Point	Case
1. Psoriasis		
a. Recent ilness	2 points	2 points
b. Personal history	1 point	-
c. Family history (first or second degree relatives)	1 point	-
2. Recent onychodystrophy specific for psoriasis (onycholysis, *pitting nail*, hyperkeratosis)	1 point	1 point
3. Negative reumathoid factor	1 point	1 point
4. Dactylitis on recent illness or personal history	1 point	1 point
5. Juxtaarticular new bone formation	1 point	-
Total	**7 point**	**5 points**

Description: A classification of PsA is met if the final score is equal to or more than 3 points. Specificity is 98.7% and sensitivity is 91.4% against the criterion standard, which is a diagnosis established by the rheumatologist.

Figure 4 Psoriatic Arthritis diagnostic algorithm.



result on rheumatoid factor test and 1 point for dactylitis, giving a total result of 5 points for CASPAR criteria. On the CASPAR criteria, a result of 3 points can meet the PsA criteria. Based on the history, physical examination and supporting examinations, our patient was diagnosed with PsA accompanied by hyperuricemia. Then we gave the patient therapy with methotrexate tablets 7.5 mg per week orally, folic acid 1 x 1 mg per day orally on days other than the day of taking methotrexate (7.5 mg/week), diclofenac sodium 2 x 50 mg per day if pain, zinc 3 x 20 mg per day and narrow band ultraviolet B phototherapy (NBUVB) 330mj/cm2 per week which is increased by 10% from the minimal erythema dose (MED) per session. Therapy from the department of internal medicine is given colchicine 1 x 0.5 mg per day and allopurinol 2 x 100 mg per day.

Evaluation in the first month after the patient's therapy found clinical improvement but the patient felt the side effect of nausea while taking the drug so we gave ranitidine 2 x 150 mg per day before meal, we did not get new lesions or other complaints. Evaluation in the second month after the patient's therapy found clinical improvement in the form of a decrease in pain intensity with a decrease in the VAS score to 1, improvement of skin lesions and loss of edema in digits 2 and 3 of the right manus and 3rd digit of the left man so that we will continue the therapy.

Discussion

Psoriasis arthritis is an inflammatory joint disease associated with psoriasis and usually has a negative rheumatoid factor. Incidence of PsA tends to increase in individuals over 30 years of

age with onset ranging from 30 to 55 years of age and can affect men and women in equal proportions.[12] Cantini *et al.* (2010) in Italy reported that around 70% of cases of PsA develop cutaneous lesions before the onset of joint symptoms, while 15% experience arthritis about 1 year before skin involvement and another 15% have simultaneous skin and joint disease.[12] PsA symptoms began to be felt by patients one year after being diagnosed with psoriasis. This case is also in accordance with the literature where PsA is also commonly found in patients with a history of psoriasis for 3 years and fulfills 2 CASPAR criteria points for a history of psoriasis at this time.

Weight gain has been reported to increase the risk of developing PsA compared to individuals who have normal BMI.[13] Research by Li *et al.* (2012) in the United States reported an increased risk of overweight women or individuals suffering from PsA. Individuals with a BMI over 25 has increased susceptibility to suffer from inflammatory diseases such as psoriasis and PsA.[14] In individuals who have a BMI above normal, there is a decrease in plasma adiponectin levels and an increase in systemic inflammation and oxidative stress, which triggers the expression of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) which play a role in pathogenesis of PsA.[15] In this case, the patient has a BMI of 25.4 which belongs to the overweight group and is included in a group of individuals prone to suffering from psoriasis and PsA.

Clinical manifestations that are often found in PsA include edema in the axial and peripheral joints, dactylitis, pain in the buttocks and coccyx and nail dystrophy, psoriasis lesions on the scalp, extensive psoriasis skin lesions and intergluteus or perianal lesions, while the clinical symptoms that appear are pain and swelling in the joints involved, especially in the morning.[16] Based on the results of the patient's history, we found complaints of pain in the joints of the fingers and wrists of both hands and feet, which was felt the most in the morning and appeared one year after the thick reddish spots accompanied by scales in the posterior truncus region, bilateral manus, inferior extremities and bilateral pedis according to the literature. On physical examination and dermoscopy, our patient found dactylitis in the form of edema in the right 3rd digit and left 3rd digit so that it meets 1 point of CASPAR criteria for dactylitis, onychodystrophy in the form of pitting nails, onycholysis and hyperkeratosis which is in accordance with the literature and fulfills 1 point of CASPAR criteria for onychodystrophy characteristic of psoriasis.

Patients with PsA have characteristic radiological features not seen in RA, namely increased osteolysis, a clearly visible “pencil-in-cup” deformity, ankylosis, spur formation, osteoporosis in the enthesitis area, paramarginal erosions and asymmetric sacroiliitis.[17] On bilateral manus/hand X-ray examination we found mild osteoporosis, whereas on bilateral genu/knee we found early stage osteoarthritis which is not typical for PsA radiology.

A negative result for rheumatoid factor meets CASPAR criteria for PsA.[1] In the laboratory examination, we found decreased hemoglobin levels, decreased hematocrit, decreased erythrocyte count, increased sedimentation rate, increased eosinophils, decreased monocytes, increased hs-CRP, negative results for rheumatoid factor which are in accordance with the literature and meet 1 point of CASPAR criteria. In this case, the diagnosis of PsA was made through physical examination, laboratory and radiological examination based on the PsA diagnosis algorithm. The patient had musculoskeletal inflammation, namely

dactylitis, nail psoriasis, negative rheumatoid factor making 5 points of CASPAR criteria so that the diagnosis of PsA could be established.

Hyperuricemia is a condition where uric acid levels in the blood exceed normal values which can be asymptomatic but can sometimes trigger gout arthritis due to the formation of gout crystals in the joints. Research by Ragaab *et al.* (2017) in France reported that only 5% of hyperuricemia sufferers with levels exceeding 9 mg/dL had gouty arthritis.[18] It mostly affects individuals who have a history of consuming excess alcohol, a BMI greater than 30, kidney disease or psoriasis.[19] In our patient we got hyperuricemia with blood uric acid level of 9.7 mg/dL (normal value: 2.4 – 6.1 mg/dL). In psoriasis, accelerated turnover of keratinocytes causes excessive accumulation of uric acid which is a metabolite of nucleic acids (purines) in the blood which further stimulates the activation of the innate immune system and triggers inflammation through the production of pro-inflammatory cytokines and triggers joint inflammation in patients of psoriasis.[20] Lai *et al.* (2018) in Hong Kong reported that 30.6% of PsA sufferers worldwide have asymptomatic hyperuricemia and Aljohani *et al.* (2017) in Canada reported that one third of PsA patients suffer from hyperuricemia and half suffer from persistent hyperuricemia.[5,23] This explains that the condition The hyperuricemia experienced by the patient was not related to gout arthritis(rewrite).

Management of PsA according to the guidelines of the Group for Research and Assessment of Psiariasis and PsA (GRAPPA) includes conservative therapy in the form of non-steroidal anti-inflammatory drugs (NSAIDs) or corticosteroids, physical therapy and topical therapy for psoriasis, accompanied by classic synthetic disease modifying first-line therapy. antirheumatic drugs (csDMARDs) such as methotrexate or targeted synthetic disease modifying antirheumatic drugs (tsDMARDs) such as apremilast, tofacitinib. Second-line therapy for PsA includes tumor necrosis factor inhibitors (TNF-I), interleukin 12/23 inhibitors (IL-12/23I), interleukin 17 inhibitors (IL-17I) and tsDMARDs. Third-line therapy for PsA includes replacement of TNF-I, IL12/23I, IL-17I and tsDMARDs.[1,12] In this case, our patient was given therapy according to the guidelines, namely csDMARDs methotrexate at a dose of 5 mg/week orally and NSAIDs diclofenac sodium 2 x 50 mg per day and colchicine 1 x 0.5 mg per day from the internal medicine department.

Patients with psoriasis and psoriatic arthritis experience changes in absorption of folic acid due to inflammation of the gastrointestinal tract and accelerated turnover of keratinocytes which causes an increase in the need for folic acid which plays a role in the synthesis of dioxyribonucleic acid (DNA). Deficiency of folic acid can cause side effects in administering methotrexate such as nausea, vomiting, hair loss and increased liver enzymes, therefore folic acid supplementation is needed.[21,22] Rai *et al.* (2016) in India reported that giving folic acid to psoriasis and psoriatic arthritis sufferers with a maximum dose of 5 mg/week given on days other than the day of taking methotrexate provided benefits in preventing the side effects of methotrexate in doses of up to 20 mg per week without reducing its efficacy.[23] In our patients, we gave folic acid 1 x 1 mg per day orally on a day other than the day of taking methotrexate (7.5 mg/week) according to the literature. Zinc is an important element that maintains the function of the immune system, growth, development, reproductive function and sensory function so that zinc deficiency is a problem that needs to be addressed. Zinc deficiency has been reported to be common in several skin diseases such as psoriasis, acne vulgaris, rosacea, and vitiligo. Giving zinc

tablets with a maximum dose of 120 mg per day for 6 months is reported to be beneficial for psoriasis and psoriasis arthritis patients as DMARDs and preventing disease severity.[24] In this case, our patient was given zinc supplementation in a dose of 3 x 20 mg tablets per day to prevent zinc deficiency.

Narrow band ultraviolet B has been shown to reduce the pro-inflammatory cytokines IL-12 and IL23/Th17 which play a role in the pathogenesis of psoriatic arthritis, so NBUVB therapy is beneficial in improving psoriasis and arthritis, The recommended initial dose for patients with Fitzpatrick skin type IV is 330 mJ/cm2 weekly and increased by 10% of the MED per session.[25] The patient in our case was given NBUVB phototherapy at an initial dose of 330mj/cm2 weekly and increased by 10% of MED per session.

Hyperuricemia in psoriasis and PsA sufferers can prolong the duration of the disease and exacerbate the degree of severity. Hyperuricemia that does not receive long-term therapy has a tendency to suffer from cardiovascular and metabolic diseases.[19] In this case the patient received allopurinol therapy 200 mg per day according to the literature. The patient experienced clinical improvement in the first month after therapy, a decrease in uric acid levels to 6.4 mg/dl which still exceeds the normal value (normal value: 2.4 – 6.1 mg/dl) and no side effects were reported by the patient. We then plan the patient for routine control and evaluation until complete remission is achieved. Diagnosis and management of PsA need to be done as early as possible. The diagnosis of PsA can be made using the CASPAR criteria. Appropriate management can reduce morbidity and disability in patients with PsA.

References

1. Orbai AM, Flynn JA. Psoriatic Arthritis and Reactive Arthritis. In: Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, McMichael AJ, *et al*., editors. Fitzpatrick's dermatology. 9th ed. New York: McGraw-Hill Education; 2019. p. 1126–45.
2. Ohara Y, Kishimoto M, Takizawa N, Yoshida K, Okada M, Eto H, *et al*. Prevalence and Clinical Characteristics of Psoriatic Arthritis in Japan. The Journal of Rheumatology. 2015;42(8):1–4.
3. Lai TL, Yim CW, Wong PY, Leung MC, Ng WL. Hyperuricemia in Asian psoriatic arthritis patients. International Journal of Rheumatic Diseases. 2018;41(2):1–7.
4. Ogdie A, Gelfand J. Clinical risk factors for the development of psoriatic arthritis among patients with psoriasis: A review of available evidence. Curr Rheumatol Rep. 2017;17(10):1–12.
5. Puig L. Cardiometabolic Comorbidities in Psoriasis and Psoriatic Arthritis. International Journal of Molecular Sciences. 2017;19(58):1–19.
6. Scher JU, Ogdie A, Merola JF, Ritchlin C. Preventing psoriatic arthritis: focusing on patients with psoriasis at increased risk of transition. Nature Reviews Disease Primers. 2019;10(8):1–14.
7. Tam LS, Leung YY, Li EK. Psoriatic arthritis in Asia. Rheumatology. 2009;48(12):1473–7.
8. Kwon HH, Kwon IH, Choi JW, Youn JI. Cross-sectional study on the correlation of serum uric acid with disease severity in Korean patients with psoriasis. British Association of Dermatologists. 2011;36(11):473–8.
9. Tsuruta N, Imafuku S, Yutaka Narisawa. Hyperuricemia is an independent risk factor for psoriatic arthritis in psoriatic patients. Journal of Dermatology. 2017;46(3):1–4.
10. Gottlieb AB, Mease PJ, Jackson M, Eisen D, Xia A, Asare C, *et al*. Clinical characteristics of psoriatic arthritis and psoriasis in dermatologists' offices. Journal of Dermatological Treatment. 2006;17(5):279–87.
11. Rymal E, Rizzolo D. Gout: A comprehensive review. Journal of the American Academy of Physician Assistants. 2014;27(9):1–6.
12. Cantini F, Niccoli L, Nannini C, Kaloudi O, Bertoni M, Cassara E. Psoriatic arthritis: a systematic review. International Journal of Rheumatic Diseases. 2010;13(1):300–17.

13. Kumthekar A, Ogdie A. Obesity and Psoriatic Arthritis: A Narrative Review. Rheumatol Ther. 2020;20(6):1–10.
14. Li W, Han J, Qureshi AA. Obesity and risk of incident psoriatic arthritis in US women. Ann Rheum Dis. 2011;71(6):1267–72.
15. Queiro R, Lorenzo A, Tejón P, Coto P, Pardo E. Obesity in psoriatic arthritis. Medicine. 2019;98(28):1–6.
16. Krakowski P, Gerkowicz A, Pietrzak A, Krasowska D, Jurkiewicz A, Gorzelak M, *et al*. Psoriatic arthritis – new perspectives. Arch Med Sci. 2019;15(3):580–9.
17. Mease PJ, Armstrong AW. Managing Patients with Psoriatic Disease: The Diagnosis and Pharmacologic Treatment of Psoriatic Arthritis in Patients with Psoriasis. Adis. 2014;40(14):1–33.
18. Lai TL, Yim CW, Wong PY, Leung MC, Ng WL. Hyperuricemia in Asian psoriatic arthritis patients. International Journal of Rheumatic Diseases. 2018;15(6):1–7.
19. AlJohani R, Polachek A, Ye JY, Chandran V, Gladman DD. Characteristic and Outcome of Psoriatic Arthritis Patients with Hyperuricemia. jrheum. 2017;11(23):1–6.
20. Tsuruta N, Imafuku S, Narisawa Y. Hyperuricemiais an independent risk factor for psoriatic arthritis in psoriatic patients. Japanese Dermatological Association. 2017;10(11):1–4.
21. McDonald I, Connolly M, Tobin AM. A Review of Psoriasis, a Known Risk Factor for Cardiovascular Disease and Its Impact on Folate and Homocysteine Metabolism. Journal of Nutrition and Metabolism. 2012;96(5):1–4.
22. Schmajuk G, Tonner C, Miao Y, Yazdany J, Gannon J, Boscardin WJ, *et al*. Folic Acid Supplementation Is Suboptimal in a National Cohort of Older Veterans Receiving Low Dose Oral Methotrexate. pone. 2016;11(12):1–10.
23. Rai T, Singh SK. Role of Folic Acid Supplementation in Reducing Side Effects of Oral Methotrexate in Patients of Psoriasis: A Study. ijdd. 2016;2(2):83–6.
24. Mogaddam MR, Ardabili N safavi, Maleki N. The Effect of Oral Zinc Therapy in Psoriasis Patients with Serum Zinc De. Research square. 2021;15(3):1–13.
25. Farid A, Tawfik A, Elsioufy B, Safwat G. Narrow band ultraviolet B therapy deactivates Th1/Th17 pathway and activates Th2 cytokines secretion in Egyptian psoriatic arthritis patients. Journal of Radiation Research and Applied Science. 2020;13(1):356–61...