Ulcerative Colitis as the Rarer Phenotype of Inflammatory Bowel Disease to Coexist with Psoriatic Arthritis: A Case Report

Eka Benhardi Layadi[1], Rabbinu Rangga Pribadi[1], Ening Krisnuhoni[2], Emiliana Kartika[1], Friska Wilda Wijaya[1], Oemar Ichsan[1]*

[1] Division of Gastroenterology, Pancreatobiliary, and Digestive Endoscopy, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia – Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
[2] Department of Anatomical Pathology, Faculty of Medicine Universitas Indonesia – Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

**** Corresponding Author:***
Rabbinu Rangga Pribadi, MD. Division of Gastroenterology, Pancreatobiliary, and Digestive Endoscopy, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia – Dr. Cipto Mangunkusumo Hospital. Jl. Diponegoro no. 71, Jakarta 10430, Indonesia. Email: rabbinurangga@gmail.com.

ABSTRACT

Psoriatic arthritis (PsA) has been linked to various diseases associated with immune dysregulation, such as Inflammatory Bowel Disease (IBD). Numerous studies have shown strong correlation between PsA and one of the phenotypes of IBD, Crohn's disease. On the other hand, the studies regarding the association of PsA with ulcerative colitis (UC) are less robust and have conflicting findings. We herein report a case of 56-year-old woman with a history of psoriatic arthritis, who developed chronic diarrhea and significant weight loss. The colonoscopy and histopathologic findings were suggestive of pancolitis with backwash ileitis, from which the working diagnosis of ulcerative colitis was carried out. The patient fit the typical epidemiological profile of a PsA patient with concomitant UC, but some aspects of the clinical features observed in this case, such as the development of anterior uveitis was rarely documented in similar studies. A conducted bidirectional meta-analysis also showed that there were more cases where UC preceded the diagnosis of psoriasis, which makes the late development of UC in this case atypical. Due to the uncommon nature of the concurrent development of these two disease entities in this case, this study could provide additional insights to the association of PsA and UC.

Keywords: *psoriatic arthritis, psoriasis, ulcerative colitis, inflammatory bowel disease.*

INTRODUCTION

Psoriasis is a chronic inflammatory disease of the skin that is often accompanied with concurrent systemic manifestations.[1] The prevalence of psoriasis varies greatly across countries, ranging between 0.09% and 11.4%.[2] Furthermore, the pathogenesis of psoriasis is multifactorial, involving a complex interplay between immune system dysregulation and genetic association.[3]

One of the conditions that commonly affects 30% of psoriasis patients is psoriatic arthritis (PsA).[4,5] PsA is part of the spondyloarthropathy (SpA) spectrum, which affects both peripheral and axial joints. The prevalence of PsA is roughly equal in men and women.[6,7] PsA has a potential to cause irreversible damage to the joints involved, which is linked to the deterioration of functional

capacity and marked impairment of psychosocial status in patients with psoriasis.[8] Moreover, PsA is also associated with increased mortality from cardiovascular disease by many studies.[9] The diagnosis of psoriatic arthritis may pose challenges, but an instrument such as CASPAR (Classification Criteria for Psoriatic Arthritis) criteria can help in diagnosing PsA with 98.7% specificity and 91.4% sensitivity.[10] Biologic agents, combined with disease-modifying antirheumatic drugs (DMARD) have been the mainstay of treatment for PsA.[11]

Inflammatory bowel disease is an inflammatory disease that is characterized by chronic relapsing inflammation of the digestive tract. This condition encompasses two phenotypes, Crohn's disease (CD) and ulcerative colitis (UC).[12] Ulcerative colitis is characterized by inflammation within the mucosa and submucosa of the colon.[13] The exact cause of IBD remains largely unknown, but recent research has shown that an individual's genetic susceptibility, the influence of the external environment, intestinal flora dysbiosis, and abnormal immune responses can cumulatively orchestrate the pathogenesis of IBD.[14]

Individuals with psoriasis are at greater risks of developing various diseases, making psoriasis a disease entity associated with many multisystem comorbidities.[15] IBD was one of the commonly identified comorbidities associated with psoriasis and the incidence of IBD in psoriasis is higher in CD compared to UC in multiple studies.[15,16] Furthermore, CD also shows strong positive correlation with psoriasis, while on the contrary, some studies including a large scale study failed to identify the association of UC to psoriasis.[15] In addition, a study conducted by Li et al. showed that when psoriasis was complicated with arthritis, the risk for developing CD increased significantly with a relative risk of 6.43, while the risk for developing UC was comparable to general population.[16]

Many studies have shown that the coexistence of psoriasis, especially when complicated with PsA and UC are less common than CD. The unusual coexistence of these two disease entities in this case drives the authors to explore this case further and connect the clinical characteristics of these two diseases in a more detailed manner. To the best of our knowledge, this is the first case report of PsA and UC in Indonesia.

CASE ILLUSTRATION

A 58-year-old woman was first diagnosed with psoriatic arthritis in 2002 at the age of 40, with complaints of debilitating pain and swelling in several joints, especially the finger joints and area of both heels, which worsened over weeks. Concurrent with the pain in the joints, patient also noticed the appearance of red, scaly patches on her skin all over her body. The patient stated that she had never experienced these symptoms before and that no family members had these symptoms or that they had been diagnosed with psoriasis. The patient denied a history of smoking and excessive alcohol consumption. The patient also had a history of cataract on the right eye as a complication of chronic anterior uveitis and she also underwent intraocular lens replacement surgery for her right eye.

The physical examination showed multiple erythematous plaques covered with hard scales on scalp, lower arms, chest, back, and knees with a total of more than 10% of her body surface area on the first presentation. There were edema and swelling of the fingers, yellow discoloration and onycholysis of the nails were later documented. The patient also stated that these symptoms negatively affect her daily activities and mental health. There were no remarkable results of the patient's blood panel and she tested negative for rheumatoid factors. The radiological examination of the hands later on was suggestive of arthritis, but specific signs for PsA such as bone proliferation and pencil-in-cup deformity were not identified. Furthermore, the patient fulfilled 5 of the CASPAR criteria with arthritis, negative rheumatoid factor, skin lesions, psoriasis nail, onycholysis and oil spot. Therefore, the confirmation of psoriatic arthritis as the working diagnosis was carried out. The patient was treated with methotrexate and marked decrease in Psoriasis Area and Activity Index (PASI) scores were documented. The patient achieved remission with her symptoms of psoriasis and PsA until today with methotrexate

12.5 mg per week.

In 2017, the patient had complaints of unresolving bloody diarrhea and significant weight loss. She reported passing ten to twelve liquid stools a day, with occasional appearance of blood and mucus around the stools. She also felt feverish at times, although she did not measure her body temperature with a thermometer. She was referred to gastroenterology clinic and was scheduled for a colonoscopy. The colonoscopy findings showed evidence of colitis with grossly hyperemic and edematous mucosa of sigmoid colon extending to the caecum and terminal ileum, which was suggestive of pancolitis with backwash ileitis. Some aphthous ulcers with whitish base were also identified. The histopathological findings showed abundant deposition of chronic inflammatory cells in the lamina propria of the ileum mucosa. The colonic crypts were distorted and the lamina propria was also fully occupied with chronic inflammatory cells. From the colonoscopy findings and the histopathological findings, the diagnosis of ulcerative colitis was carried out.

The patient was given mesalazine for the treatment of UC and her symptoms resolved. She achieved remission for both UC and PsA with mesalazine 1,000 mg twice a day and methotrexate 12.5 mg per week. The patient is also prescribed with folic acid 5 mg per week for additional supplementation and topical steroid for her skin lesions. The prognosis of this patient was good, as shown in disease remissions without biologic agents nor invasive interventions needed. The patient was also counselled to build adequate awareness with the disease course. The patient also routinely visited the outpatient department of Gastroenterology Cipto Mangunkusumo National General Hospital, as shown in the medical record data. The patient admitted that she adhered to medications given as per advised on every consultation and reported no adverse events of medications administered during the disease course.

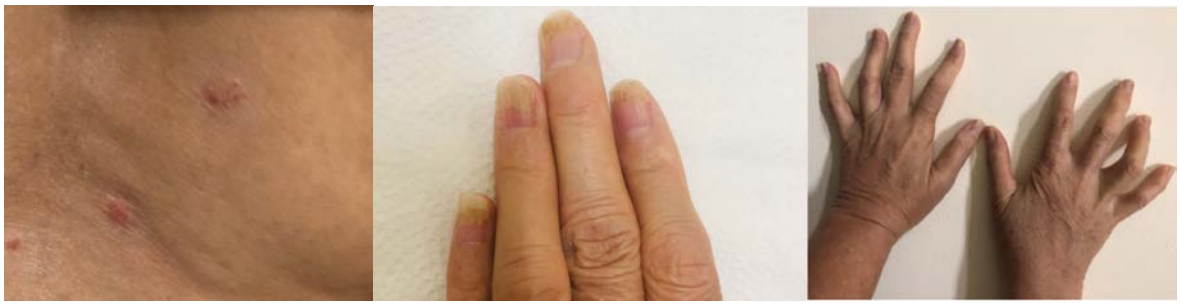

Figure 1. Discreetly distributed erythematous nummular plaques on back region with fine scales after treatment (left); Psoriatic nail with onycholysis and oil spot (middle); Deformity of the distal interphalangeal joints which are the predilection sites for psoriatic arthritis (right)

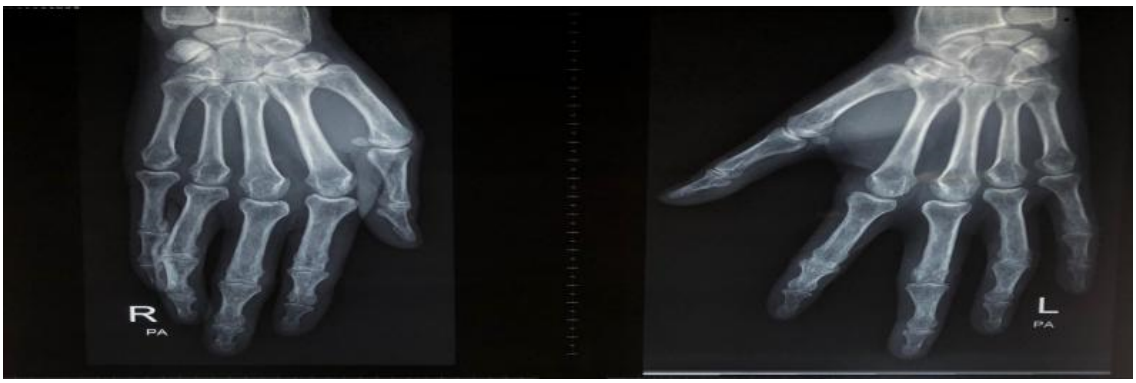

Figure 2. Radiography of the hands showed interphalangeal space narrowing which indicated arthritis, classic findings of pencil in cup deformity and bony proliferation were not found in this case

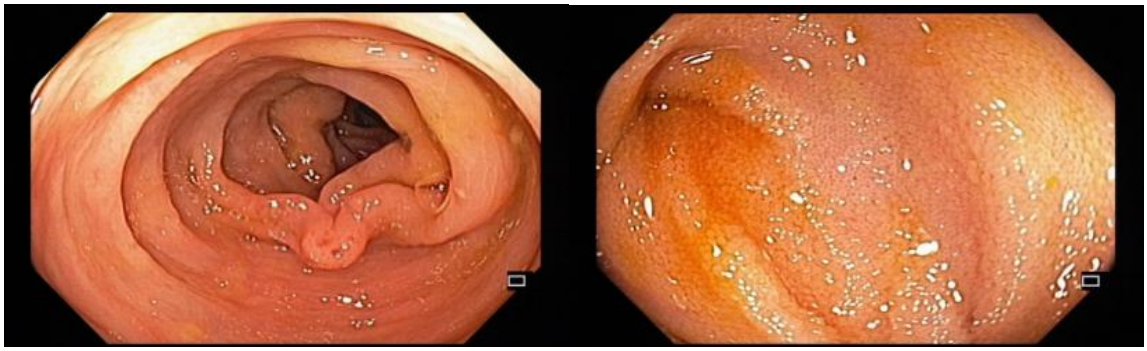

Figure 3. Hyperemic and edematous colonic mucosa with some aphthous ulcers (left), extending up to the terminal ileum (right), suggestive of pancolitis with backwash ileitis

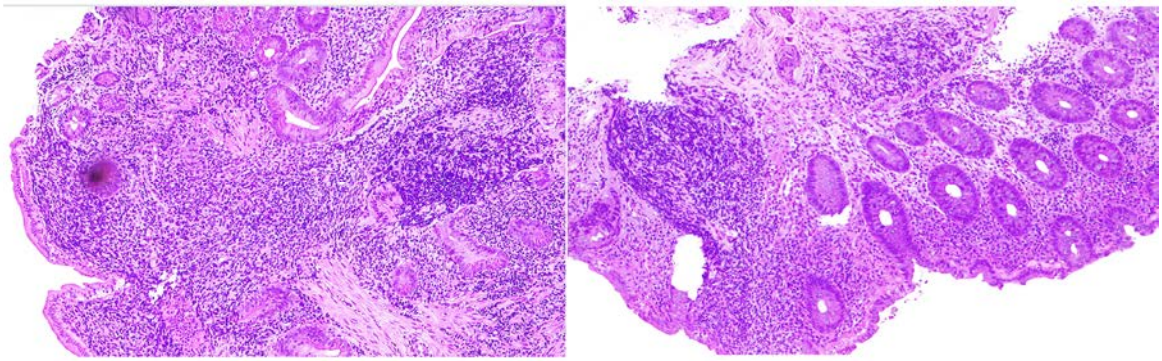

Figure 4. Histopathology (hematoxylin and eosin, original magnification of 100x). Deposition of chronic inflammatory cells in the lamina propria of the ileum mucosa (left); Distorted colonic crypts with deposition of chronic inflammatory cells (right)

DISCUSSION

Psoriasis and IBD share some common pathways in their pathogenesis, involving immune cells of Th17 and T-reg cells and various chromosomal loci which map for genes associated with innate and adaptive immunity.[17] The link between PsA (as part of the spondyloarthropathies spectrum) and IBD is presumed to lie in the proposed model of "the gut-synovium axis". Some studies have also hypothesized the upregulation of adhesion molecules such as E-cadherin and α-Eβ7 integrin, as an integral part of SpA development in IBD.[18]

According to the study conducted by Eppinga et al., it was reported that patients with psoriasis concurrent with UC were mostly female, with the median age of psoriasis diagnosis at 46 years old.[19] Compared to the coexistence of psoriasis and UC, patients with psoriasis concurrent with CD have younger onset of psoriasis with the median age of 28 years and were associated with greater disease severity. They also revealed that PsA patients were also more likely to have IBD than psoriasis-only patients.[19] A case control study conducted by Lolli et al. showed different results where IBD was associated with milder severity of psoriasis and lower incidence of PsA.[20] The contradictive findings from different studies suggested that the characteristic profiles of patients with psoriasis, especially PsA, concurrent with IBD need to be explored further. In this case, the patient fits the typical epidemiological profile from the sex and age of psoriasis diagnosis.

The patient also had a history of anterior uveitis. A study regarding this matter has shown that there were indeed substantial risks for PsA patients to develop uveitis and/or CD, but not for PsA and UC, which makes the development of uveitis in this case uncommon.[21] In cases of psoriasis concomitant with UC, nail manifestation was also rarely documented, even though nail manifestation is perceived to be a strong predictor of arthritis development in psoriasis.[19,22] Plaque-type psoriasis was reported as the most common cutaneous phenotype of

psoriasis to be documented in UC, followed by phenotypes of capitis, inverse, psoriatic palmar pustulosis, and lastly guttate.[19,20] Cutaneous manifestation usually precedes the diagnosis of PsA by an average of 10 years, while in this patient, cutaneous lesions and arthritis manifested simultaneously at diagnosis, which is rare.[7]

This patient had been diagnosed with psoriasis complicated with PsA for 15 years before the diagnosis of UC was carried out. The findings from a bidirectional meta-analysis of psoriasis and IBD conducted by Fragoulis et al. have shown that that there were more cases where UC preceded the diagnosis of psoriasis than the other way around, as the prevalence of UC in psoriasis (0.7%) was lower than the prevalence of psoriasis in UC (1.8%).[23] In support of that notion, CD was also more commonly observed with other spectrum of SpA (either axial and peripheral) other than PsA as well, rather than UC.[18]

There has not been any documented endoscopic findings of patients with PsA concomitant with UC, but it has been suggested that isolated proctitis in UC has a scarce association with rheumatic manifestations. On the other hand, CD patients with evidence of colitis show more association with joint involvement compared to CD patients with findings of ileitis.[18] Aside from IBD, there are many common gastrointestinal diseases (celiac disease, esophagitis, irritable bowel disease) that are associated with psoriasis in other studies, and these findings highly suggest that psoriasis might have a concrete link to gut inflammation in general.[24] The results from a study conducted by Scarpa, et. al supported this notion by showing that the bowel mucosa of patients with PsA exhibit microscopic changes, even when appearing normal macroscopicallly and in absence of gastrointestinal symptoms.[25]

To the best of our knowledge, there has not been any study documenting the radiologic findings of PsA concurrent with IBD, but a large scale study conducted by Geijer et al. concluded that male PsA patients showed more pronounced radiological abnormalities than female patients.[26] In this case, the radiologic findings were suggestive of arthritis because of the narrowing of the interphalangeal joint spaces. But, classic radiological findings were not visualized.

To the best of our knowledge, there has been no published consensus on the most appropriate treatment options for PsA complicated with IBD, although these two entities share similar medications with overlapping effects on both diseases.[27] A study conducted by Eppinga et al. showed that most patients with psoriasis concomitant with UC were treated with sulfasalazine (64.3%), steroids (64.3%), and methotrexate (57.1%); while patients with psoriasis concomitant with CD were mostly treated with steroids (58.3%), azathioprine (50%), and Anti-TNFα (50%).[19] This patient was treated with methotrexate for PsA and sulfasalazine for UC, and administration of these medications exhibited favorable response and maintained remission in this patient. Furthermore, methotrexate was associated with improvement of PsA and maintenance of remission in CD, but studies have shown that methotrexate has no effects on maintaining remission in UC.[28] Mesalamine has been regarded as the first-line treatment for mild-to-moderate UC which has been documented by many studies to induce clinical response and maintain clinical remission in UC.[29] Although there are not enough data regarding the association of 5-ASA compound in PsA, sulfasalazine has been shown to improve symptoms and exhibited beneficial outcomes in patients with PsA as well. However, there was not any supporting evidence that sulfasalazine can halt the progression of joint damage in PsA.[30]

Emerging biologic agents, such as infliximab and adalimumab have been used to treat PsA concomitant with IBD as they share common predisposing genes and inflammatory pathways. However, there are less data on their efficacy on UC compared to robust evidences on CD. Certain biologic agents that were shown to exhibit favorable response in both PsA and UC are infliximab and adalimumab.[28] Besides the two favorable biologic agents that are beneficial to both PsA and UC, secukinumab, a biologic agent which is primarily used for PsA may aggravate IBD manifestations in some patients.[31]

CONCLUSION

PsA is commonly observed with IBD, especially with CD, while cases of UC concomitant with PsA are less documented. There was robust evidence regarding the association and correlation between PsA and CD from the clinical findings to treatment, while some studies showed conflicting findings with PsA and UC.

REFERENCES

1. Affandi AM, Khan I, Saaya NN. Epidemiology and clinical features of adult patients with psoriasis in Malaysia: 10-year review from the Malaysian psoriasis registry (2007-2016). Dermatol Res Pract [Internet]. 2018 Apr 23 [cited 2020 Dec 19];2018. Available from: /pmc/articles/PMC5937568/?report=abstract
2. Mehrmal S, Uppal P, Nedley N, Giesey RL, Delost GR. The global, regional, and national burden of psoriasis in 195 countries and territories, 1990 to 2017: A systematic analysis from the Global Burden of Disease Study 2017. J Am Acad Dermatol. 2021;84(1):46–52.
3. Kim WB, Jerome D, Yeung J. Diagnosis and management of psoriasis [Internet]. Vol. 63. Canadian family physician. College of Family Physicians of Canada; 2017 [cited 2020 Dec 16]. p. 278. Available from: www.cfp.ca
4. Ritchlin CT, Colbert RA, Gladman DD. Psoriatic arthritis. In: Longo DL, editor. N Engl J Med [Internet]. 2017 Mar 9 [cited 2020 Dec 9];376(10):957–70. Available from: http://www.nejm.org/doi/10.1056/NEJMra1505557
5. Gottlieb AB, Merola JF. Axial psoriatic arthritis: An update for dermatologists [Internet]. Vol. 84. Journal of the American Academy of Dermatology. Mosby Inc.; 2020 [cited 2020 Dec 9]. p. 92–101. Available from: https://doi.org/10.1016/j.jaad.2020.05.089
6. Coates LC, Helliwell PS. Psoriatic arthritis: State of the art review [Internet]. Clinical medicine. Royal College of Physicians. 2017;17:65-70 [cited 2020 Dec 9]. Available from: /pmc/articles/PMC6297592/?report=abstract
7. Lloyd P, Ryan C, Menter A. Psoriatic arthritis: An update. Arthritis [Internet]. 2012;2012:1–6 [cited 2021 Jan 18]. Available from: https://www.hindawi.com/journals/arthritis/2012/176298/
8. Busse K, Liao W. Which psoriasis patients develop psoriatic arthritis? Psoriasis Forum [Internet]. 2010;16a(4):17–25 [cited 2020 Dec 19]. Available from: /pmc/articles/PMC4206220/?report=abstract
9. Veale DJ, Fearon U. The pathogenesis of psoriatic arthritis [Internet]. The Lancet. 2018;391:2273–84 [cited 2021 Jan 18]. Available from: http://www.thelancet.com/article/S0140673618308304/fulltext
10. Cather JC, Young M, Jan Bergman M. Psoriasis and psoriatic arthritis [Internet]. Matrix Medical Communications. 2017;10:S16–S25 [cited 2020 Dec 9]. Available from: /pmc/articles/PMC5367866/?report=abstract
11. Day MS, Nam D, Goodman S, Su EP, Figgie M. Psoriatic arthritis. Am Acad Orthop Surg [Internet]. 2012;20(1):28–37 [cited 2021 Jan 18]. Available from: http://journals.lww.com/00124635-201201000-00004
12. Fakhoury M, Negrulj R, Mooranian A, Al-Salami H. Inflammatory bowel disease: Clinical aspects and treatments [Internet]. Journal of Inflammation Research. 2014;7:113–20 [cited 2020 Dec 26]. Available from: /pmc/articles/PMC4106026/?report=abstract
13. Qin X. Why is damage limited to the mucosa in ulcerative colitis but transmural in Crohn's disease? World J Gastrointest Pathophysiol [Internet]. 2013;4(3):63 [cited 2021 Jan 10]. Available from: /pmc/articles/PMC3740262/?report=abstract
14. Zhang YZ, Li YY. Inflammatory bowel disease: Pathogenesis. World J Gastroenterol [Internet]. 2014;20(1):91–9 [cited 2020 Dec 25]. Available from: /pmc/articles/PMC3886036/?report=abstract
15. Takeshita J, Grewal S, Langan M, et al. Psoriasis and comorbid diseases Epidemiology. 2017 [cited 2021 Jan 17]; Available from: http://dx.doi.org/10.1016/j.jaad.2016.07.064
16. Li W, Chan AT, Han J-L, Qureshi AA. Psoriasis, psoriatic arthritis and increased risk of incident Crohn's disease in US women | Request PDF. Ann Rheum Dis [Internet]. 2012;72(7) [cited 2021 Jan 17]. Available from: https://www.researchgate.net/publication/230783788_Psoriasis_psoriatic_arthritis_and_increased_risk_of_incident_Crohn's_disease_in_US_women
17. Skroza N, Proietti I, Pampena R, et al. Correlations between psoriasis and inflammatory bowel diseases [Internet]. BioMed Research International. 2013;2013 [cited 2020 Dec 16]. Available from: /pmc/articles/PMC3736484/?report=abstract
18. Fragoulis GE, Liava C, Daoussis D, Akriviadis E, Garyfallos A, Dimitroulas T. Inflammatory bowel diseases and spondyloarthropathies: From pathogenesis to treatment. World J Gastroenterol [Internet]. 2019;25(18):2162–76 [cited 2021 Jan 17]. Available from: /pmc/articles/PMC6526158/?report=abstract
19. Eppinga H, Poortinga S, Thio HB, et al. Prevalence and Phenotype of Concurrent Psoriasis and Inflammatory Bowel Disease. Inflamm Bowel Dis [Internet]. 2017;23(10):1783–9 [cited 2021 Jan 18]. Available from: https://pubmed.ncbi.nlm.nih.gov/28617755/
20. Lolli E, Saraceno R, Calabrese E, et al. Psoriasis phenotype in inflammatory bowel disease: A case-control prospective study. J Crohns Colitis [Internet]. 2015;9(9):699–707 [cited 2020 Dec 17]. Available from: https://pubmed.ncbi.nlm.nih.gov/25908719/
21. Charlton R, Green A, Shaddick G, et al. Risk of uveitis and inflammatory bowel disease in people with

psoriatic arthritis: A population-based cohort study. Ann Rheum Dis [Internet]. 2018;77(2):277–80 [cited 2021 Jan 23]. Available from: https://pubmed.ncbi.nlm.nih.gov/29092855/

22. Sobolewski P, Walecka I, Dopytalska K. Nail involvement in psoriatic arthritis [Internet]. Reumatologia. 2017;55:131–5 [cited 2021 Jan 22]. Available from: /pmc/articles/PMC5534507/?report=abstract
23. Alinaghi F, Tekin HG, Burisch J, Wu JJ, Thyssen JP, Egeberg A. Global prevalence and bidirectional association between psoriasis and inflammatory bowel disease—A systematic review and meta-analysis. J Crohn's Colitis [Internet]. 2020;14(3):351–60 [cited 2020 Dec 21]. Available from: https://academic.oup.com/ecco-jcc/article/14/3/351/5556860
24. Cottone M, Sapienza C, Macaluso FS, Cannizzaro M. Psoriasis and inflammatory bowel disease. Dig Dis [Internet]. 2019;37(6):451–7 [cited 2020 Dec 15]. Available from: https://www.karger.com/Article/FullText/500116
25. Scarpa Raffaele, Manguso Francesco, D'Arienzo Agesilao, D'Armiento Francesco Paolo. Microscopic inflammatory changes in colon of patients with both active psoriasis and psoriatic arthritis without bowel symptoms | Request PDF. J Rheumatol [Internet]. 2000;27(5):1241–6 [cited 2021 Jan 17]. Available from: https://www.researchgate.net/publication/12505183_Microscopic_inflammatory_changes_in_colon_of_patients_with_both_active_psoriasis_and_psoriatic_arthritis_without_bowel_symptoms
26. Geijer M, Lindqvist U, Husmark T, et al. The Swedish early psoriatic arthritis registry 5-year followup: Substantial radiographic progression mainly in men with high disease activity and development of dactylitis. J Rheumatol [Internet]. 2015;42(11):2110–7 [cited 2021 Jan 18]. Available from: https://pubmed.ncbi.nlm.nih.gov/26472410/
27. Haddad A, Zisman D. Comorbidities in patients with psoriatic arthritis. Rambam Maimonides Med J [Internet]. 2017;8(1):e0004 [cited 2020 Dec 16]. Available from: /pmc/articles/PMC5298365/?report=abstract
28. Mikhaylov D, Hashim PW, Nektalova T, Goldenberg G. Systemic psoriasis therapies and comorbid disease in patients with psoriasis: A review of potential risks and benefits [Internet]. Journal of Clinical and Aesthetic Dermatology. 2019;12:46–54 [cited 2021 Jan 18]. Available from: /pmc/articles/PMC6624011/?report=abstract
29. Ham M, Moss AC. Mesalamine in the treatment and maintenance of remission of ulcerative colitis [Internet]. Expert Review of Clinical Pharmacology. 2012;5:113–23 [cited 2021 Jan 24]. Available from: /pmc/articles/PMC3314328/?report=abstract
30. Kang EJ, Kavanaugh A. Psoriatic arthritis: latest treatments and their place in therapy. Ther Adv Chronic Dis [Internet]. 2015;6(4):194 [cited 2021 Jan 24]. Available from: /pmc/articles/PMC4480547/?report=abstract
31. Conforti C, Dianzani C, Zalaudek I, et al. Spotlight on the treatment armamentarium of concomitant psoriasis and inflammatory bowel disease: a systematic review [Internet]. Journal of Dermatological Treatment. 2020 [cited 2021 Jan 18]. Available from: https://pubmed.ncbi.nlm.nih.gov/33074781/