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CASE SERIES

Awareness of the Risk of Paradoxical Psoriasis in Patients with SAPHO Syndrome Undergoing Treatment with Secukinumab: A Case Series

Cheng Xu*, Xiayan Xu*, Yongmei Han

Department of Rheumatology, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, People's Republic of China

*These authors contributed equally to this work

Correspondence: Yongmei Han, Department of Rheumatology, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, 3#Qingchun East Road, Hangzhou, 310016, People's Republic of China, Email 3408235@zju.edu.cn

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Abstract: SAPHO syndrome is a systemic inflammatory disease characterized by skin lesions and inflammatory changes in the bones and joints. There is no consensus on the treatment strategy of SAPHO syndrome. For patients with refractory SAPHO syndrome, biological agents can be considered. We report three patients who responded poorly to conventional therapy, all of whom had paradoxical recurrence of pustulosis after receiving secukinumab, and whose paradoxical pustulosis resolved after adjustment to tofacitinib. We reviewed the literature and concluded that secukinumab may be potentially risky for the treatment of SAPHO syndrome. This paradoxical aggravation of the rash may be related to paradoxical psoriasis. The specific pathogenesis is not clear, and tofacitinib may be a remedy for this situation.

Keywords: SAPHO, PPP, IL-17, secukinumab, paradoxical psoriasis

Introduction

Synovitis, acne, pustular lesions, hyperostosis, and osteitis (SAPHO) syndrome is a systemic inflammatory disease characterized by skin lesions and inflammatory changes in the bones and joints. Due to the relatively low incidence of SAPHO syndrome, its pathogenesis remains not fully understood. The clinical features of SAPHO syndrome are characterized by lesions in the bones, joints, and skin, exhibiting considerable heterogeneity in presentation. Symptoms related to the bones and joints commonly involve the anterior chest wall and axial skeleton; however, other regions may also be affected. Cutaneous involvement primarily manifests as palmoplantar pustulosis but can also present with characteristics associated with acne and other dermatological conditions.[1] Currently, there is no consensus on the treatment of SAPHO syndrome. Treatment strategies are primarily based on seronegative spondyloarthritis or derived from case reports and single-center cohort studies. Traditional therapeutic approaches mainly include non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, methotrexate, sulfasalazine, cyclosporine A, and bisphosphonates.[2] The patients with SAPHO syndrome who are unresponsive to conventional treatment may consider the use of biological agents, and there have been reports on the efficacy of IL-17 monoclonal antibodies.[3] We observed three cases in which patients transitioned to IL-17 monoclonal antibody therapy after inadequate response to standard treatments. Surprisingly, our findings suggest that the effectiveness of IL-17 monoclonal antibodies in treating SAPHO syndrome may be contentious.

Case Reports

Case 1

The patient is a 42-year-old female who presents with a chief complaint of "recurrent pustular lesions on palms and soles for five years, along with chest and back pain for over two years". The skin rash is characterized by erythema and

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desquamation, localized to the palmar surfaces of both hands, the plantar surfaces of both feet, and both lower limbs. A dermatologist has diagnosed her condition as palmoplantar pustulosis. Musculoskeletal symptoms are noted in the anterior chest wall and sacroiliac joints, where significant pain is reported. The patient has no history of underlying diseases. Physical examination reveals pustular lesions on both hands, both feet, and bilateral calves. Tenderness is observed in the sternum and clavicular joint areas. The patient's serological tests for erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were within normal ranges, while HLA-B27 was negative. Imaging studies indicated abnormal uptake in the sternum, proximal bilateral clavicles, costovertebral joints, ribs, and sacroiliac joints on whole-body bone scintigraphy (Figure 1). After excluding other diseases, the patient was diagnosed with SAPHO syndrome and subsequently treated with celecoxib, mesalazine, thalidomide and halometasone. We conducted a follow-up for one year and found unsatisfactory results. In November 2023, the patient was treated with Secukinumab at a regimen of 150 mg weekly for weeks 0 through 4 followed by maintenance dosing of 150 mg every four weeks thereafter. The patient's joint pain symptoms showed significant improvement after the first administration; however, from the third month onward, there was a marked exacerbation of pustular lesions in both lower limbs. We attempted to adjust the dosage to 300 mg per administration. Unfortunately, there was no improvement in the pustular disease and the patient developed otitis media, leading to cessation of treatment. Subsequently, the patient received Adalimumab therapy (with a regimen of 40 mg every two weeks). After three months of treatment, there was still no improvement in skin rashes. Ultimately, we initiated Tofacitinib at a dose of 5 mg twice daily. One month later, an alleviation of skin rashes was observed (Figure 2a–c).

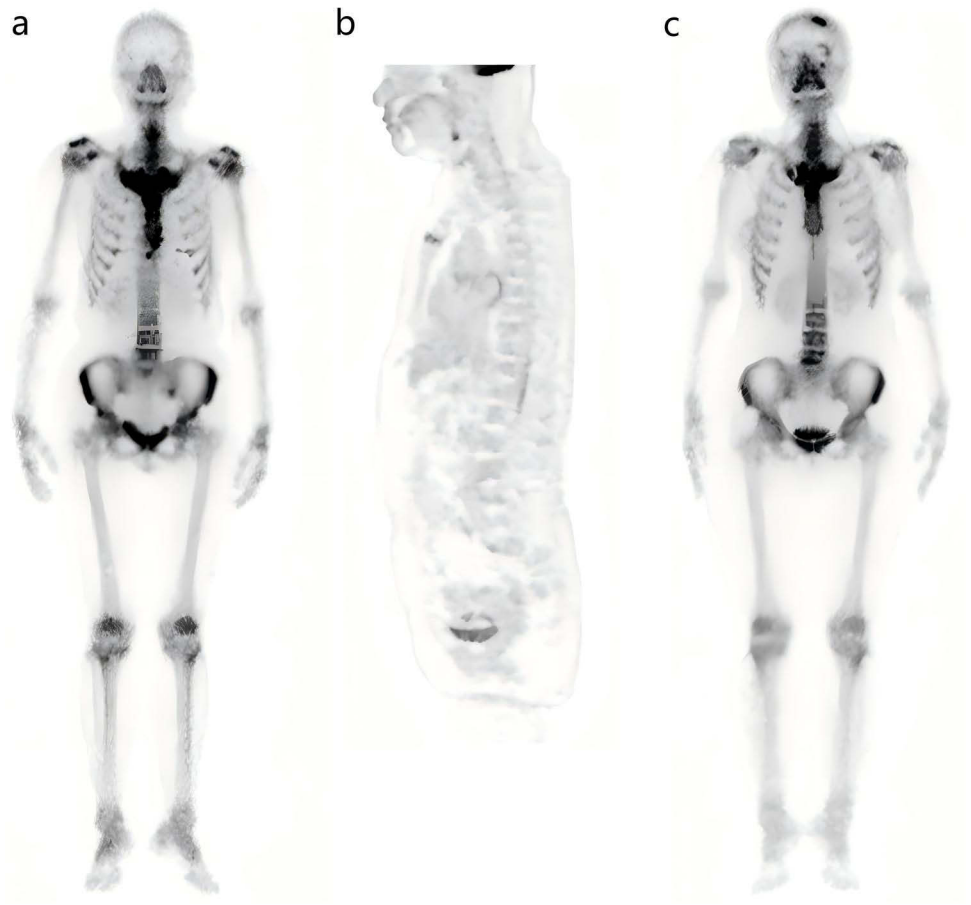

Figure 1 Patient 1 (**a**) and Patient 3(**c**) exhibited characteristic involvement of the sternum and rib joints, demonstrating a classic "horn sign". PET-CT demonstrated increased metabolic activity in the bilateral sternoclavicular joints, sternum in patient 2(**b**).

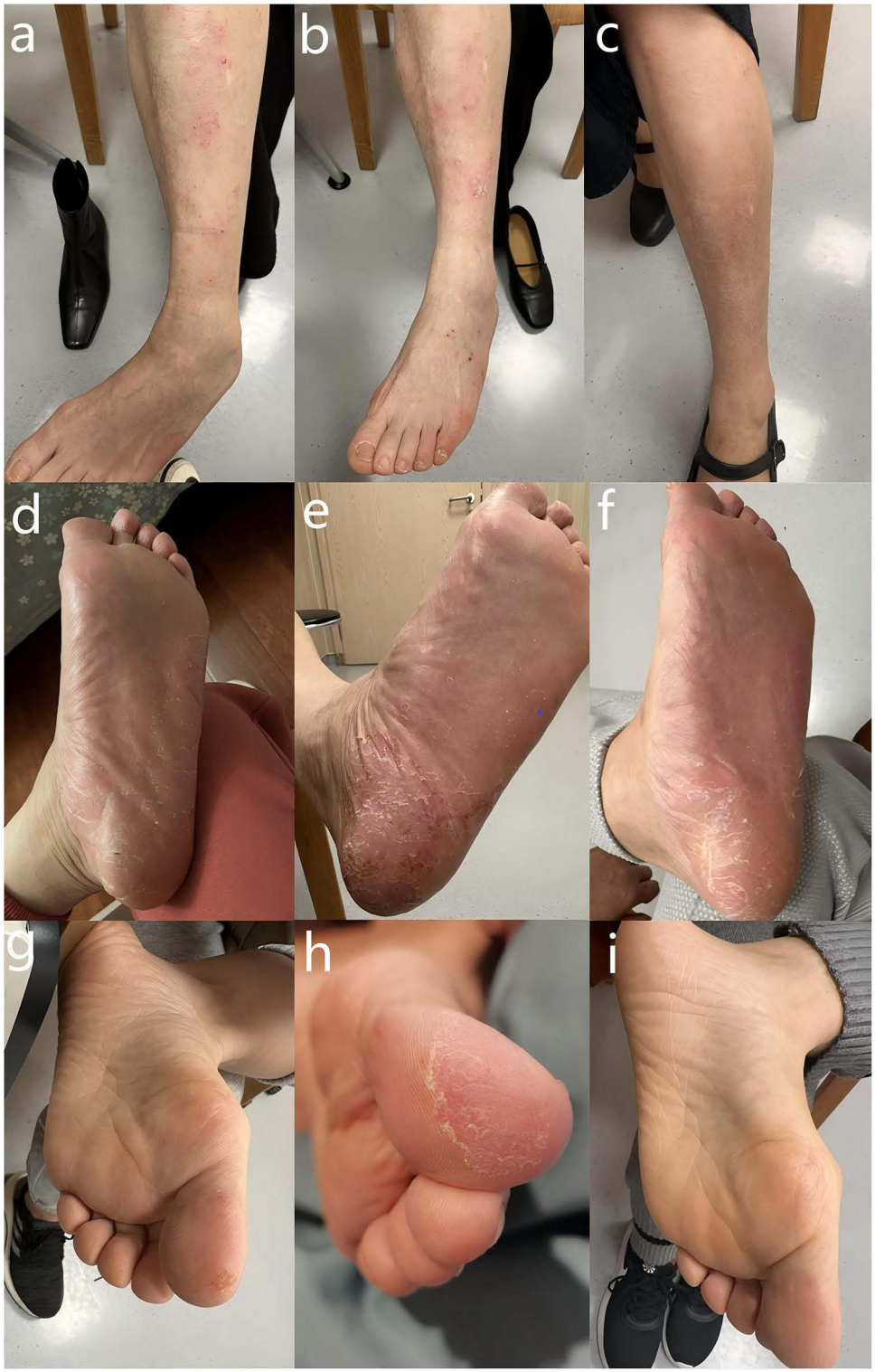

Figure 2 The transformation of the rash of three patients(**a-c** represent Patient 1; **d-f** represent Patient 2; and **g-i** represent Patient 3) before treatment with secukinumab, after treatment with secukinumab, and after treatment with tofacitinib is shown.

Case 2

The patient is a 60-year-old female who presents with a chief complaint of "recurrent chest and back pain for 7 years, along with palmoplantar pustulosis for over 2 years". The patient's past medical history reveals skin manifestations consistent with palmoplantar pustulosis, localized to the palmar surfaces and the plantar aspects of both feet. However,

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there were no skin lesions observed at the time of consultation. Currently, joint pain symptoms are pronounced, particularly in the anterior chest wall, spine, and sacroiliac joint regions. There is no significant past medical history. Physical examination revealed no pustular lesions on both hands or feet. Tenderness was noted upon palpation of the sternum. Laboratory tests indicated an elevated ESR of 32 mm/hr (normal range: 1–20 mm/hr), while CRP levels remained within normal limits. HLA-B27 testing returned negative. Imaging studies via PET-CT demonstrated increased metabolic activity in the bilateral sternoclavicular joints, sternum, lumbar vertebrae, and sacroiliac joints (Figure 1). After excluding other diagnoses, the patient was diagnosed with SAPHO syndrome. She had previously been treated with celecoxib and adalimumab but discontinued adalimumab due to personal reasons. In April 2024, she was treated with secukinumab at a regimen of 150 mg weekly for weeks 0 through 4 followed by maintenance dosing of 150 mg every four weeks thereafter. The patient experienced significant improvement in her joint symptoms; however, after four months she developed new pustular lesions which necessitated discontinuation of this therapy. Subsequently, treatment was adjusted to tofacitinib at a dosage of 5 mg twice daily. One month later showed marked improvement in her rash without any adverse events reported (Figure 2d–f).

Case 3

The patient is a 41-year-old female who presents with a chief complaint of "recurrent chest and back pain for 2 years, along with palmoplantar pustulosis for over 1 year". One year ago, she was diagnosed by a dermatologist with pustular psoriasis affecting the palms and soles, as well as facial acne. At the time of consultation, there were no skin rash symptoms. However, she exhibited joint and bone-related symptoms in the anterior chest wall and sacroiliac joints. The patient has no significant past medical history. Physical examination revealed no pustular lesions on both hands or feet. There was positive tenderness upon palpation of the sternum. Laboratory tests show ESR at 47 mm/hr and CRP level at 108 mg/l. IgA levels were measured at 6.13 g/L, HLA-B27 tested negative. Imaging studies suggested abnormal uptake in bilateral sternoclavicular joints, sternum, skull bones, lumbar vertebrae, and sacroiliac joints during whole-body bone scintigraphy (Figure 1). After excluding other diagnoses, the patient was diagnosed with SAPHO syndrome. Previous treatments included celecoxib, thalidomide, and adalimumab but these yielded unsatisfactory results. In July 2024, treatment commenced with secukinumab at a regimen of 300 mg weekly for weeks 0 through 4 followed by maintenance dosing of 300 mg every four weeks thereafter. The patient's arthralgia showed significant improvement; however three months later she developed new pustules accompanied by desquamation on one side of her foot sole. Consequently, we adjusted her medication to tofacitinib at a dosage of 5 mg twice daily. One month later post-adjustment revealed an improvement in her skin rash without any adverse events reported (Figure 2g–i).

Discussion

Overall, the outcomes were unsatisfactory. Firstly, only the symptoms of the joints have improved, all three patients experienced anterior chest pain, which is a typical manifestation of SAPHO syndrome. Following treatment with secukinumab, there was a rapid and significant alleviation of these symptoms. Regarding the skin lesions, all patients exhibited varying degrees of palmoplantar pustulosis (Figure 3). However, during the course of secukinumab treatment, all patients developed new-onset pustular eruptions to varying extents, which was unexpected. Additionally, two adverse events occurred during this period.

The pathogenesis of SAPHO syndrome remains incompletely understood. Current evidence suggests that SAPHO results from a complex interplay among immune dysregulation, genetic susceptibility, and environmental factors.[4] Research indicates that patients with SAPHO syndrome exhibit an increase in TH17 cells in peripheral blood.[5,6] Abnormal levels of cytokines (such as IL-1, IL-8, IL-17, IL-18, and TNFα) suggest the involvement of the Th-17 pathway in the inflammatory process associated with SAPHO syndrome.[1] This suggests that IL-17 is a key cytokine involved in the immune pathways related to skin and bone arthritis inflammation in SAPHO syndrome.

Secukinumab is a monoclonal antibody that targets interleukin-17A (IL-17A) and has been approved for the treatment of plaque psoriasis and ankylosing spondylitis (AS). However, there are only a limited number of reports regarding the use of secukinumab in patients with SAPHO syndrome, and significant heterogeneity exists in terms of patient characteristics, treatment dosages, duration of therapy, and methods for evaluating efficacy. Consequently, no unified conclusions have been reached.

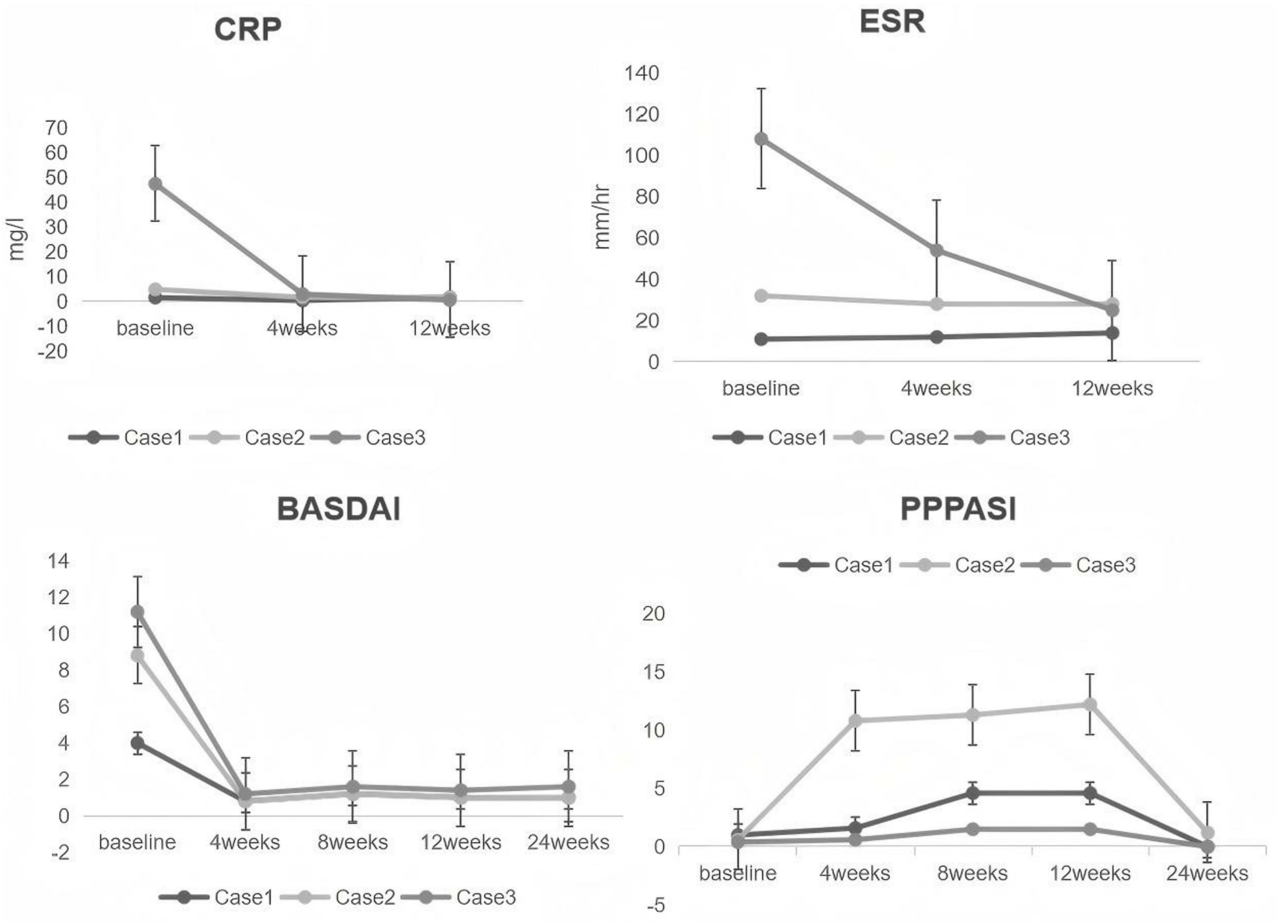

Figure 3 CRP, ESR and BASDAI were significantly improved during secukinumab treatment, but the PPPASI score was increased to varying degrees.

Wang et al conducted a single-center study involving four cases of SAPHO syndrome to assess the efficacy of secukinumab. After six months of follow-up, notable improvements were observed in both imaging results and clinical symptoms related to joints and skin manifestations among the patients. Regarding adverse events, three patients reported infections including otitis media, tonsillitis, herpes zoster, and fungal external ear infection.[7] Additionally, there have been case reports of successful treatment of joint pain and pustular psoriasis in patients with SAPHO syndrome using secukinumab. Ji et al reported a case involving a 24-year-old female patient with SAPHO syndrome who achieved complete relief from arthralgia and palmoplantar pustulosis following IL-17 therapy.[8] Fan et al reported a case of a 31-year-old female patient with SAPHO syndrome, in which the condition worsened despite treatment with adalimumab. Then, followed treatment with secukinumab, the patient's symptoms showed significant improvement.[9] Sun et al reported a case of a 31-year-old male patient primarily affected by mandibular involvement in SAPHO syndrome. Following treatment with secukinumab, the patient's joint symptoms improved; however, no information was provided regarding the condition of the skin.[10] Xia et al reported a case of a 29-year-old female patient diagnosed with SAPHO syndrome, who achieved complete resolution of joint symptoms and skin rash following treatment with ixekizumab.[11] However, not all studies report successful outcomes regarding the use of IL-17 in the treatment of SAPHO syndrome. Wendling et al documented six patients with SAPHO syndrome who did not respond to conventional treatments and subsequently received targeted therapy with IL-23 and IL-17. The average duration of treatment was 5.5 months; only one patient exhibited improvement in joint symptoms, while three patients showed improvements in skin symptoms. Notably, two patients developed paradoxical psoriasis during the course of treatment.[12] Li et al reported on seven cases of patients with SAPHO syndrome treated with secukinumab. Unfortunately, all patients developed atypical skin lesions within four weeks of treatment. Notably, all patients experienced significant improvement in paradoxical psoriasis within 12 weeks after discontinuing the IL-17 inhibitor and initiating oral tofacitinib therapy.[13] D'Ignazio et al reported a SAPHO syndrome patient in which the patient's

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palmoplantar pustulosis did not improve following treatment with infliximab. Subsequent adjustment to secukinumab therapy also failed to yield improvement, it is noteworthy that the patient's PPP ultimately resolved after receiving brodalumab treatment.[14] The above data on the treatment of SAPHO syndrome with IL-17 have been summarized in Table 1.

Table 1 Summary of the Results of IL-17 Treatment of SAPHO Syndrome

	Age (y)/ Sex	Disease Duration (y)	Treatment Before IL-17	Osteoarticular Pain	Rash	Osteoarticular Outcomes	Rash Outcomes	Adverse Events
Lun Wang et al[7]	30/F	0.7	NSAID	ACW, spine, sacroiliac region, and shoulder	PPP	Remission	Alleviation	Otitis media; Tonsillitis
	51/M	1.0	NSAID	ACW, spine, sacroiliac region, shoulder, and hip	PPP, PV	Remission	Alleviation	None
	49/F	12	TNFi, THD, SASP,NSAID	ACW, spine, and shoulder	PPP, PV	Remission	Alleviation	Herpes zoster
	42/F	4	NSAID	ACW, spine, sacroiliac region, and shoulder	PPP, PV	Remission	PPP, alleviation; PV, resolution;	Fungal external otitis;Dyslipidemia
Ji Q et al[8]	24/F	1	MTX, cyclosporine	Bilateral sternoclavicular joint	PPP	Remission	Remission	None
Fan D et al[9]	31/F	2 (months)	glucocorticoids, TNFi	Spine, sternoclavicular joints, and sacroiliac joints	PPP	Remission	Remission	None
Sun B et al[10]	31/F	9	pamidronate, tofacitinib and TNFi	Left jaw	NA	Remission	NA	None
Xia R et al[11]	29/F	3	acitretin	Sternoclavicular joint	PPP	Remission	PPP, remission	None
Wendling D et al[12]	37/F	3	MTX,TNFi	ACW	PPP	No improvement	PPP, Improvement	None
	64/M	5	MTX,SASP, TNFi	ACW,arthritis	PPP	No improvement	PPP, remission	None
	46/F	5	MTX,SASP, anakinra,TNFi	ACW,arthritis,SPA	PPP	No improvement	No improvement	ParadoxicalPsoriasis
Li Y et al[13]	39/F	NA	NA	NA	PPP	No improvement	No improvement	PPP aggravated
	58/M	NA	NA	NA	PPP	Improvement	No improvement	Sterile pimples eruption
	54/F	NA	NA	NA	PPP	No improvement	No improvement	Sterile pimples eruption
	43/M	NA	NA	NA	PPP	No improvement	No improvement	PPP aggravated
	50/M	NA	NA	NA	PPP	Improvement	No improvement	PPP aggravated
	31/F	NA	NA	NA	PPP	Improvement	No improvement	PPP aggravated; alopecia areata
	37/F	NA	NA	NA	PPP	No improvement	No improvement	PPP aggravated;new developed sterile pimples
D'Ignazio E et al[14]	38/M	NA	MTX,anakinra, TNFi	ACW	PPP	Remission	No improvement	None

Abbreviations: ACW, anterior chest wall; NSAID, nonsteroidal antiinflammatory drugs; PPP, palmoplantar pustulosis; PV, psoriasis vulgaris; SASP, salicylazosulfapyridine; THD, thalidomide; TNFi, tumor necrosis factor inhibitor; MTX, methotrexate; SpA, spondyloarthritis; NA, Not available.

Additionally, Li et al articulated in their systematic review that IL-17 therapies for SAPHO syndrome may be associated with paradoxical exacerbation of skin rashes.[2]

The reasons for the phenomenon of exacerbated pustulosis occurring in SAPHO syndrome remain incompletely understood. A comparable situation can be traced in the treatment of psoriasis, where this specific occurrence is referred to as "paradoxical psoriasis".[15] A cohort study involving 13,699 patients with psoriasis out of a total of 24,997 cases exposed to biologics. The findings indicated that patients receiving interleukin-17 inhibitors had the highest risk of developing paradoxical psoriasis compared to other biologic therapies, followed by those treated with TNF-alpha inhibitors.[16] Research has reported that the overexpression of plasmacytoid dendritic cells (pDCs) secreting IFN-α is a major pathogenic event in the development of PPP induced by TNF-α. However, the pathological mechanisms by which IL-17 induces PP remain to be further elucidated. The pathogenesis of paradoxical psoriasis may be related to the imbalance of cytokines after blocking IL-17A, which may lead to the increase of upstream cytokines such as IL-23 and IFN-α. At present, the idea of IL-17 in the treatment of SAPHO syndrome is derived from the treatment of psoriasis and ankylosing spondylitis, and its dose, administration interval, and patient's immune tolerance still need to be further explored.[17] The available research on pyoderma gangrenosum (PP) in the context of SAPHO syndrome is extremely limited. Interestingly, the probability of developing PP with JAK inhibitors is very low, whether in the treatment of psoriasis or SAPHO syndrome, a finding that has been corroborated by our report. This observation provides new insights for future treatment options and more in-depth studies for patients with refractory SAPHO syndrome.

Conclusion

Our case series report highlights that the efficacy and safety of IL-17 for patients with SAPHO in real-world settings remain debatable. JAK inhibitors may represent a more favorable option for SAPHO. This conclusion serves as a cautionary note regarding our selection of biological agents for SAPHO syndrome and provides new insights into the exploration of its pathogenesis. Currently, this report is among the few available globally. However, it does have limitations; for instance, our sample size is limited due to the inherently low incidence rate of SAPHO syndrome. Additionally, we did not conduct an in-depth investigation into the reasons behind the paradoxical psoriasis that occurred during treatment. We hope that our findings will serve as a warning to clinicians when considering re-treatment options and offer researchers new directions for future studies.

Ethics Statement

Written informed consent was obtained from the patients for publication of their case details and accompanying images. Ethical approval was not required for this case report, and institutional approval for publication was also not applicable.

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Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Demirci Yildirim T, Sari İ. SAPHO syndrome: current clinical, diagnostic and treatment approaches. *Rheumatol Int*. 2024;44(11):2301–2313. doi:10.1007/s00296-023-05491-3
2. Li SWS, Roberts E, Hedrich C. Treatment and monitoring of SAPHO syndrome: a systematic review. *RMD Open*. 2023;9(4):e003688. doi:10.1136/rmdopen-2023-003688
3. Cheng W, Li F, Tian J, et al. New Insights in the Treatment of SAPHO Syndrome and Medication Recommendations. *J Inflamm Res*. 2022;15:2365–2380. doi:10.2147/JIR.S353539

4. Yang Y, Chen Q, Zhong W. The role of cytokines in the pathogenesis of SAPHO syndrome. *Front Immunol*. 2024;15:1427784. doi:10.3389/fimmu.2024.1427784
5. Firinu D, Barca MP, Lorrai MM, et al. TH17 cells are increased in the peripheral blood of patients with SAPHO syndrome. *Autoimmunity*. 2014;47(6):389–394. doi:10.3109/08916934.2014.906582
6. Zhang S, Li C, Zhang S, et al. Serum levels of proinflammatory, anti-inflammatory cytokines, and RANKL/OPG in synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome. *Mod Rheumatol*. 2019;29(3):523–530. doi:10.1080/14397595.2018.1469580
7. Wang L, Sun B, Li C. Clinical and radiological remission of osteoarticular and cutaneous lesions in SAPHO patients treated with secukinumab: a case series. *J Rheumatol*. 2021;48(6):953–955. doi:10.3899/jrheum.201260
8. Ji Q, Wang Q, Pan W, et al. Exceptional response of skin symptoms to secukinumab treatment in a patient with SAPHO syndrome: case report and literature review. *Medicine*. 2022;101(33):e30065. doi:10.1097/MD.0000000000030065
9. Fan D, Li F, Liu Z, Tang Z, Lv S. Successful treatment of refractory Synovitis, Acne, Pustulosis, Hyperostosis, and Osteitis (SAPHO) syndrome and paradoxical psoriasis with secukinumab: a case report. *Clin Cosmet Invest Dermatol*. 2024;17:547–552. doi:10.2147/CCID.S454057
10. Sun B, Cao Y, Wang L, Wang M, Li C. Successful treatment of refractory mandibular lesions in SAPHO syndrome with secukinumab. *Rheumatology*. 2021;60(1):473–474. doi:10.1093/rheumatology/keaa352
11. Xia R, Diao Z, Zhang Z, Liu J, Yin Z. Successful treatment of synovitis, acne, pustulosis, hyperostosis and osteitis syndrome with ixekizumab. *Clin Exp Dermatol*. 2022;47(5):978–980. doi:10.1111/ced.15087
12. Wendling D, Aubin F, Verhoeven F, Prati C. IL-23/Th17 targeted therapies in SAPHO syndrome. A case series. *Joint Bone Spine*. 2017;84(6):733–735. doi:10.1016/j.jbspin.2017.05.016
13. Li Y, Meng F, Jiang H, et al. Paradoxical skin lesions induced by IL-17 inhibitors in SAPHO syndrome. *J Dermatol Treat*. 2024;35(1):2295239. doi:10.1080/09546634.2023.2295239
14. D'Ignazio E, Trovato E, Cantarini L, Calabrese L, Frediani B, Gentileschi S. Clinical response to brodalumab in a patient affected by refractory SAPHO syndrome. *Clin Exp Rheumatol*. 2024;42(9):1887–1888. doi:10.55563/clinexprheumatol/qhq2o0
15. Abdelghaffar M, Kottilil S, Murphy MJ, Cohen JM, Damsky W. Paradoxical Psoriasis. *Dermatol Clin*. 2024;42(3):471–480. doi:10.1016/j.det.2024.02.011
16. Al-Janabi A, Alabas OA, Yiu ZZN, et al. Risk of paradoxical eczema in patients receiving biologics for psoriasis. *JAMA dermatol*. 2024;160(1):71–79. doi:10.1001/jamadermatol.2023.4846
17. Maronese CA, Valenti M, Moltrasio C, et al. Paradoxical psoriasis: an updated review of clinical features, pathogenesis, and treatment options. *J Investig Dermatol*. 2024;144(11):2364–2376. doi:10.1016/j.jid.2024.05.015

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