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Treatment for Sapho Syndrome: A Multimodality Therapy

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ABSTRACT

SAHPO syndrome is a heterogenous auto-inflammatory disease. There are many alternative drugs with various responses. but the treatment remains a challenge. This article is aimed to update the drugs and treatments applied to SAPHO syndrome.

Keywords: SAPHO syndrome; Treatment; Biological agents

Abbreviations: SPA: Spondyloarthritis; AS: Ankylosing Spondylitis; PSA: Psoriatic Arthritis; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; BPs: Bisphosphonates; TNF-α: Tumor Necrosis Factor A; GCs: Glucocorticoids; CDMARDs: Conventional Disease-Modifying Anti-Rheumatic Drugs; IL: Interleukin; JAKI: Janus Kinase Inhibitor; MTX: Methotrexate; LEF: Leflunomide; SASP: Sulfasalazine; HCQ: Hydroxychloroquine

Introduction

SAPHO syndrome, which represents synovitis, acne, pustulosis, hyperostosis and osteomyelitis, is a rare auto-inflammatory disease. To date, most studies on the treatment of SAPHO syndrome are case reports or case series. Few randomized clinical trials have been undertaken on the effectiveness of different therapies. The published clinical trials have problems such as small enrollment sample size and lack of placebo negative control. As a result, no consensus has been reached on the treatment of SAPHO syndrome. The aim of this article is to update the drugs and treatments applied to SAPHO syndrome.

Principles of Treatment

The primary aim of treatment is improving the clinical symptoms, including ostealgia and cutaneous lesions. Secondly, treatment should focus on preventing the progression of joint involvement and articular degeneration, thereby improving quality of life in the long term. Considering the negative immune indices such as the rheumatoid factor, and relative high incidence of axis and sacroiliac joint involvement, SAPHO syndrome is to some extent regarded as a subset of spondyloarthritis (SpA), which has certain overlaps with classic ankylosing spondylitis (AS) and psoriatic arthritis (PsA)[1]. SAPHO syndrome shares some clinical features with AS in terms of ankylosis, enthesitis as well as responses to non-steroidal anti-inflammatory drugs (NSAIDs), bisphosphonates (BPs) and tumor necrosis factor α (TNF-α) blockade, while it also resembles PsA in skin lesions and response to TNF-α blockade. These resemblances provide some inspiration for the treatment of SAPHO syndrome. At present, alternative pharmaceutical treatments of SAPHO syndrome include NSAIDs, glucocorticoids (GCs), antibiotics, conventional disease-modifying anti-rheumatic drugs (cDMARDs), BPs, TNF α inhibitors, interleukin (IL)-6 receptor antagonist, Janus kinase inhibitor (JAKi), IL-17 /23 antagonist, and IL-1 antagonist, which would be elaborated later in the article.

NSAIDs

NSAIDs are generally regarded as the first-line medication for pain relief and symptoms controlling in the treatment of SAPHO syndrome. NSAIDs work quickly and remarkably for patients at diagnostic stage of disease. This phenomenon indicates the similarity between SAPHO syndrome and SpA. However, NSAIDs monotherapy has shown limited effect with the process of drug withdrawal [2], or in patients with extensive osteomyelitis [3].

GCs

Systematic or intra-articular GCs work quickly but transiently [4]. Relapse tends to occur when treating cutaneous lesions and appear to be even more serious than before at the process of drug withdrawal [5]. Therefore, GCs are not first recommended. Taking adverse effects into consideration, course of GCs application is preferably on moderate dose in short term.

Antibiotics

Infection of Propionibacterium acnes is thought to be a possible pathogenetic factor, especially for patients with severe acne [6]. Antibiotics, such as clindamycin, azithromycin, and in particular tetracyclines, are reported successful in treating some cases of rash, but show little efficiency in other symptoms. In our cohort, skin involvement of SAPHO syndrome mainly manifests as palmoplantar pustulosis, in which condition antibiotics show curative effect but not as dramatically as in the treatment of acne. Besides, clinicians should be aware of the side effects of minocycline, such as vertigo or hyperpigmentation [7].

cDMARDs

cDMARDs, such as methotrexate (MTX), leflunomide (LEF), sulfasalazine (SASP), and hydroxychloroquine (HCQ), have been widely used in clinical practice. cDMARDs are usually recommended as second-line options and the response to cDMARDs varies in different patients. MTX is the anchor drug for RA, which is an auto-immune disease mainly affecting the synovial tissue of peripheral small joints [8]. Since axis joints are more frequently involved in the SAPHO syndrome due to its auto-inflammatory nature, MTX can't play the role of "anchor drug" in SAPHO syndrome. However, for patients with peripheral joints involvement and relatively low levels of inflammatory biomarkers, administration of MTX could be helpful [9]. LEF is an efficacious and safe therapeutic option for the treatment of both joint and skin symptoms in PsA, which is reported by a multinational randomized clinical trial in 2004 [10]. LEF is reported to successfully improve the cutaneous lesions and swelling sternocostal joints in a patient with SAPHO syndrome [11]. Considering the similarity in clinical features between SAPHO syndrome and PsA, LEF is likely to work well in patients with nail lesions. SASP, HCQ are also treatment options for SAPHO syndrome. However, controversial results have been reported in previous studies [2,12-14].

BPs have consistent activity of inhibiting activity of osteoclast and anti-inflammatio [15]. Use of intravenous BPs (especially pamidronate) has been reported, demonstrating partial or full remission of clinical symptoms, including ostealgia, cutaneous lesions [16,17]. Our center also the significant improvement in ostealgia, palmoplantar pustulosis, and bone marrow edema in vertebrae and sacroiliac joints, which is found by magnetic resonance imaging (MRI). This finding has been accepted and not published.

Anti-TNF-α Therapy

Use of TNFi has been frequently reported, showing effects on osteoarticular and cutaneous involvement. However, about 17% of patients with administration of anti-TNF-α therapy developed new paradoxical skin lesions during treatment, which may present as psoriasiform scaly plaques or pustular lesions. These TNFi-induced psoriasiform lesions were undistinguishable from de novo psoriasis [18]. The dose, period of treatment, and plan of drug withdraw of anti-TNF therapy require further investigation.

Il-6 Receptor Antagonist

Considering the possible risk of inducing new rash, attention was turned to other biological agents. Immunohistochemical staining was performed on two patients' bone tissue. Based on the previous successful treatment of IL-6 inhibitor tocilizumab[19] and high level of IL-6 expression and low level of TNF-α, we tentatively prescribed tocilizumab. However, the effect is unsatisfactory [20]. Our research once again verified that SAPHO syndrome may be analogue of SpA, as two randomized placebo-controlled clinical trials demonstrated that IL-6 inhibitor was not an effective treatment for patients with AS [21].

JAK inhibitor

The efficacy of JAK inhibitor tofacitinib in managing PsA has been assessed in clinical trials [22,23]. Inspired by these findings, our center tentatively treats refractory SAPHO with tofacitinib. Responses in clinical symptoms, inflammatory parameters and magnetic resonance imaging all demonstrated amelioration [24].

Other biological Agents

Biologics targeting the IL-17/IL-23axis is a milestone in treatment of PsA. [25] Since SAPHO syndrome is to some degree a special type of axis PsA, IL-17/23 antagonist is a promising option for SAPHO syndrome. But responses to IL-17/23 antagonist range from dramatic remission [26] to almost no improvement except for skin lesions[27]. IL-1 inhibitor is also used for SAPHO syndrome, showing remarkable improvement in osteoarticular involvement, while its effect on cutaneous lesions are relatively poor. [26] IL-1 plays the pivotal role in the pathogenesis of most auto-inflammatory diseases. [28] There are two reports on the successful treatment of SAPHO syndrome withIL-1 receptor antagonist, anakinra [29,30]. Patients in the two reports all received anti IL-1 agents after failing

to response to TNF-inhibitors. However, follow-up results of these patients in the long term are still unavailable.

Conclusion

There are many alternative drugs for clinicians to treat SAPHO syndrome. NSAIDs are the first-line drugs. GCs, antibiotics, cDMARDs and BPs presents variable efficacy for different symptoms. Biological agents, including TNFi, JAKi, IL-17/23i and IL-1i, bring new choices and hope to the treatment for this disease. SAPHO syndrome is a heterogeneous disease with various clinical features. It remains a challenge for clinicians to choose the appropriate treatment based on individual differences.

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References

1. Rohekar G, RD Inman (2006) Conundrums in nosology: synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome and spondylarthritis. Arthritis Rheum 55(4): 665-669.
2. Hayem G (1999) SAPHO syndrome: a long-term follow-up study of 120 cases. Semin Arthritis Rheum 29(3): 159-171.
3. Hofmann (2017) Chronic Recurrent Multifocal Osteomyelitis (CRMO): Presentation, Pathogenesis, and Treatment. Curr Osteoporos Rep 15(6): 542-554.
4. Jung J (2012) Intra-articular glucocorticosteroid injection into sternocostoclavicular joints in patients with SAPHO syndrome. Semin Arthritis Rheum 42(3): 266-270.
5. Firinu D (2016) SAPHO Syndrome: Current Developments and Approaches to Clinical Treatment. Curr Rheumatol Rep18(6): 35.
6. Berthelot JM, S Corvec, G Hayem (2018) SAPHO, autophagy, IL-1, FoxO1, and Propionibacterium (Cutibacterium) acnes. Joint Bone Spine 85(2): 171-176.
7. Roberts G, HA Capell (2006) The frequency and distribution of minocycline induced hyperpigmentation in a rheumatoid arthritis population. J Rheumatol 33(7): 1254-1257.
8. Smolen JS (2017) EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis 76(6): 960-977.
9. Vekic DA (2018) SAPHO syndrome associated with hidradenitis suppurativa and pyoderma gangrenosum successfully treated with adalimumab and methotrexate: a case report and review of the literature. Int J Dermatol 57(1): 10-18.
10. Kaltwasser JP (2004) Efficacy and safety of leflunomide in the treatment of psoriatic arthritis and psoriasis: a multinational, double-blind, randomized, placebo-controlled clinical trial. Arthritis Rheum 50(6): 1939-1950.
11. Zhao Z (2011) Synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO) syndrome with review of the relevant published work. J Dermatol 38(2): 155-159.
12. Adamo S (2018) Successful treatment of SAPHO syndrome with apremilast. Br J Dermatol 179(4): 959-962.
13. Rukavina I (2015) SAPHO syndrome: a review. J Child Orthop 9(1): 19-27.
14. Colina M (2009) Clinical and radiologic evolution of synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome: a single center study of a cohort of 71 subjects. Arthritis Rheum 61(6): 813-821.
15. Amital H (2004) SAPHO syndrome treated with pamidronate: an open-label study of 10 patients. Rheumatology (Oxford) 43(5): 658-661.
16. Aljuhani F (2015) The SAPHO syndrome: a single-center study of 41 adult patients. J Rheumatol 42(2): 329-334.
17. Zwaenepoel T, K Vlam (2016). SAPHO: Treatment options including bisphosphonates. Semin Arthritis Rheum 46(2): 168-173.
18. Li C (2019) Paradoxical skin lesions induced by anti-TNF-alpha agents in SAPHO syndrome. Clin Rheumatol 38(1): 53-61.
19. Sato H (2017) Adult-onset Chronic Recurrent Multifocal Osteomyelitis with High Intensity of Muscles Detected by Magnetic Resonance Imaging, Successfully Controlled with Tocilizumab. Intern Med 56(17): 2353-2360.
20. Sun XC (2018) Failure of tocilizumab in treating two patients with refractory SAPHO syndrome: a case report. J Int Med Res.
21. Sieper J (2014) Assessment of short-term symptomatic efficacy of tocilizumab in ankylosing spondylitis: results of randomised, placebo-controlled trials. Ann Rheum Dis 73(1): 95-100.
22. Gladman D (2017) Tofacitinib for Psoriatic Arthritis in Patients with an Inadequate Response to TNF Inhibitors. N Engl J Med 377(16): 1525-1536.
23. Schwartz DM (2017) JAK inhibition as a therapeutic strategy for immune and inflammatory diseases. Nat Rev Drug Discov 16(12): 843-862.
24. Yang Q (2018) Case report: successful treatment of refractory SAPHO syndrome with the JAK inhibitor tofacitinib. Medicine (Baltimore) 97(25): e11149.
25. Lubrano E, FM Perrotta (2017) The role of IL-17 in the treatment of psoriatic arthritis. Expert Rev Clin Immunol 13(8): 815-821.
26. Daoussis D (2018) Biologics in SAPHO syndrome: A systematic review. Semin Arthritis Rheum.
27. Wendling D (2017) IL-23/Th17 targeted therapies in SAPHO syndrome. A case series. Joint Bone Spine 84(6): 733-735.
28. Aksentijevich I, MF McDermott (2017) Lessons from characterization and treatment of the autoinflammatory syndromes. Curr Opin Rheumatol 29(2): 187-194.
29. Colina M (2010) Dysregulation of P2X7 receptor-inflammasome axis in SAPHO syndrome: successful treatment with anakinra. Rheumatology (Oxford) 49(7): 1416-1418.
30. Wendling DC Prati, F Aubin (2012) Anakinra treatment of SAPHO syndrome: short-term results of an open study. Ann Rheum Dis 71(6): 1098-100.

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