Clinical Case Report

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Long-term remarkable remission of SAPHO syndrome in response to short-term systemic corticosteroids treatment in an immunoglobulin E elevated patient

A case report

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Abstract

Rationale: Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a rare auto-inflammatory disease with no standardized treatment. Systemic corticosteroids are only transiently effective, but long-term use would bring complications and would not bring long-term remission. Bone scintigraphy is a first-line method for systematic evaluation of osteoarticular lesions but seems to show an "imprinting" pattern.

Patient concerns: A 31-year-old female patient presented significant palmoplantar pustulosis and nail lesion as well as typical tracer accumulation feature on bone scintigraphy with normal hypersensitivity C-reactive protein and erythrocyte sedimentation rate, but an elevated serum immunoglobulin E level.

Diagnosis: The diagnosis was made by dermatological manifestations and classical sign in bone scintigraphy in accordance with the diagnostic criteria proposed in 1988.

Interventions: Methylprednisolone was given with a primary dose of 40 mg/day for 1 week followed with a subsequent 20 mg/day oral prednisone for another 1 week and then reduced in a rate of 5 mg/week until the eventual cessation.

Outcomes: Long-term remarkable remission on clinical manifestations, MRI performance, and quantitative analysis of bone scintigraphy was achieved.

Lessons: Identification of specific subtype of SAPHO patient according to skin and nail manifestations as well as immunoglobulin E level may guide the selection of short-term systemic corticosteroids strategy, leading to remarkable long-term remission. Besides, the lesions on bone scintigraphy can hardly disappear in SAPHO patients, and instead, the quantitative analysis of bone scintigraphy and MRI performances may better reflect the change of disease condition and serve as indicator for treatment efficiency.

Abbreviations: ESR = erythrocyte sedimentation rate, hsCRP = hypersensitivity C-reactive protein, IgE = immunoglobulin E, MRI = magnetic resonance imaging, PPP = palmoplantar pustulosis, SAPHO = synovitis, acne, pustulosis, hyperostosis, and osteitis.

Keywords: bone scintigraphy, corticosteroids, immunoglobulin E, remarkable remission, SAPHO syndrome

1. Introduction

Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a rare auto inflammatory disease with no standardized treatment. The systemic corticosteroids are transiently effective in the majority of patients, but the long-term use would bring certain complications and would not avoid further disease recurrence.[1] Bone scintigraphy is the first-line method for systematic evaluation

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LW, CL, and MY contributed equally to this study.

The work has not been published elsewhere, nor is it currently under consideration for publication elsewhere.

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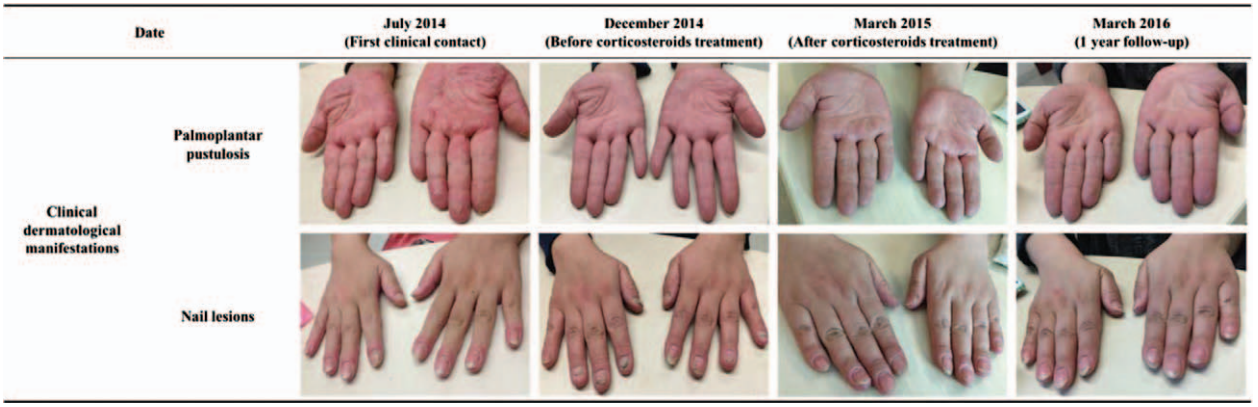

Figure 1. The dynamic change of clinical dermatological manifestations including palmoplantar pustulosis and nail lesions of the reported synovitis, acne, pustulosis, hyperostosis, and osteitis patient before and after the short-term systemic corticosteroids treatment. The palmoplantar pustulosis was continuously significant and her nail lesions aggravated after the first clinical contact. Lesser clinical dermatological manifestations were observed after a short-term systemic corticosteroids treatment and completely disappeared on March 2015.

of osteoarticular lesions and can also reveal some potential lesions without clinical manifestations in SAPHO patients.[2,3] However, according to clinical observations, the bone scintigraphy of SAPHO seems to show an "imprinting" pattern, representing a continuously irreducible accumulation number that is not correlated with the disease activity change. We present a report in which a long-term remarkable remission on both manifestations, MRI and quantitative analysis of bone scintigraphy, was achieved after short-term systemic corticosteroids treatment in an immunoglobulin E (IgE) elevated SAPHO patient.

2. Case report

A written informed consent was obtained from the patient for publication of this case report, and the study was approved by the Ethics Committee of Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences (Identifier: ZS-944).

A 31-year-old Chinese female patient noted skin itchy and wheals during the pregnancy after artificial insemination in November 2012. After the delivery in August 2013, she begun to have repeated folliculitis and later in May 2014, the palmoplantar pustulosis (PPP) appeared on both hands with the involvement of nails and pain at left sternoclavicular joint and left shoulder. The joint pain relived within 1 week in absence of treatment; however, her PPP symptoms aggravated 2 months later (Fig. 1). No family history of similar symptoms was reported.

On her first clinical contact in July 2014, blood analysis revealed that her hypersensitivity C-reactive protein (hsCRP) and erythrocyte sedimentation rate (ESR) were within the normal range. Her complete blood count, liver and renal function all revealed no significant abnormality. Rheumatoid factor, antinuclear antibody, and human leukocyte antigen B27 were all negative. Whole body bone scintigraphy using 99Tc-MDP showed multiple lesions with increased tracer accumulation in bilateral sternoclavicular joints and left first anterior rib, which are common tracer accumulation sites in the anterior chest wall of SAPHO patients.[4]

Based on her dermatological and osteoarticular manifestations as well as classic involvement of sternoclavicular joints on bone scintigraphy, the diagnosis of SAPHO syndrome was made, in accordance with the diagnostic criteria proposed in 1988.[2]

After the first clinical contact, her nail lesions aggravated and an elevated level of serum total IgE 3311.0 KU/L was found. Thus, considering her protruding nail lesions and high IgE level, methylprednisolone was later given on December 2014 in a dose of 40 mg/day for 1 week followed with a subsequent 20 mg/day oral prednisone for another 1 week and then reduced the dose in a rate of 5 mg/week until the eventual cessation after 3 weeks on January 2015.

Following the 5-week systemic corticosteroids treatment, all her PPP and nail lesions significantly relieved until they completely disappeared on March 2015 (Fig. 1). During the subsequent follow-ups, she did not suffer from any dermatological or osteoarticular manifestations and was recommended for a repeated bone scintigraphy on May 2018.

Although accentuated tracer accumulation on both sternoclavicular joints and left first anterior rib were still seen after 3-year remission period on bone scintigraphy, the quantitative concentration represented by the target-to-background ratio had decreased from 11.9 (30.9/2.6) to 5.4 (39.4/7.3) compared to the images of 2014, calculated on the total uptake of the region of interest including left sternoclavicular joint and first anterior rib, with the uptake of medial thigh soft tissues referring the background concentration (Fig. 2). To further evaluate the osteoarticular status, an MRI of anterior chest wall was done and no abnormal bone marrow edema signal was observed in the bilateral sternoclavicular joint (Fig. 2).

During remission, her blood analyses including ESR and hsCRP were all still within the normal range. No significant change of her complete blood count, liver, and renal function has been observed. Her serum total IgE level had once decreased to 610.0 KU/L in April 2015, just 3 months after the treatment (Fig. 3).

3. Discussion

This case provides new insight on clinical features, pathogenesis, diagnosis, and treatment of the SAPHO syndrome.

Playing an important role in type I hypersensitivit y, an elevated IgE level was always observed in various allergic diseases, such as asthma, allergic rhinitis, urticaria, and atopic dermatitis. which are considered to be the inflammatory condition irritated by external allergens.[5] The etiology of

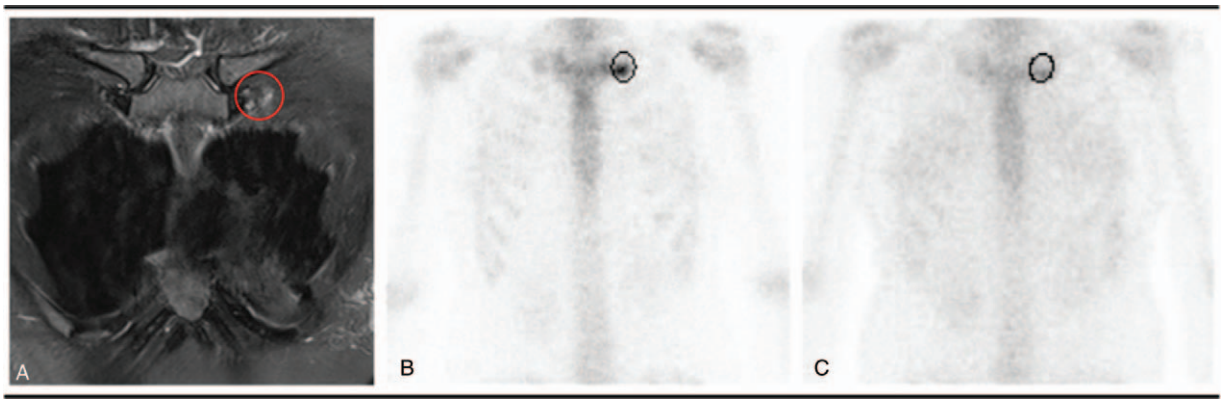

Figure 2. The magnetic resonance imaging and follow-up bone scintigraphy of anterior chest wall of the reported synovitis, acne, pustulosis, hyperostosis, and osteitis patient. (A) The oblique coronal T2-weighted imaging fat-suppressing sequence revealed mild hyperintensity in the left first costosternal joint (red circle), whereas there was no significant abnormality in the bilateral sternoclavicular joint. (B, C) The bone scintigraphy on July 2014 (B) and May 2018 (C) with increased tracer accumulation in bilateral sternoclavicular joints and left first anterior rib. The black circle refers to the region of interest combining the left sternoclavicular joint and first anterior rib.

SAPHO syndrome remains unclear, which might be a combination of genetic, infectious, and immunological components according to current evidence.[1,6] The high IgE level and its good response to corticosteroids shown in this case indicated a potential role of allergy (type I hypersensitivity) in the pathogenesis of SAPHO.

The present case has provided a credible example that further consolidates the "imprinting" hypothesis. The lesions on bone scintigraphy can hardly disappear in SAPHO patients even after long-term significant remission. Although tracer accumulations were continuously seen, the quantitative analysis did reveal decreased concentration on the region of interest which was further confirmed by MRI performance. Therefore, rather than the accumulation number, quantified accumulation concentration on serial bone scintigraphy and MRI can be used for dynamical assessment of disease activity and treatment efficiency. However, such "imprinting" pattern can also be taken advantage for disease diagnosis. As SAPHO is characterized by repeated episodes of remission and recurrences,[7] the skin lesions and osteoarticular symptoms can relief, even with normal ESR, hsCRP level, and imageology performances during remission period, thereby it would only be helpful for physicians to consider the diagnosis of SAPHO according to some typical patterns on bone scintigraphy, such as the involvement of bilateral sternoclavicular joints or the more specific "bull's head" pattern.

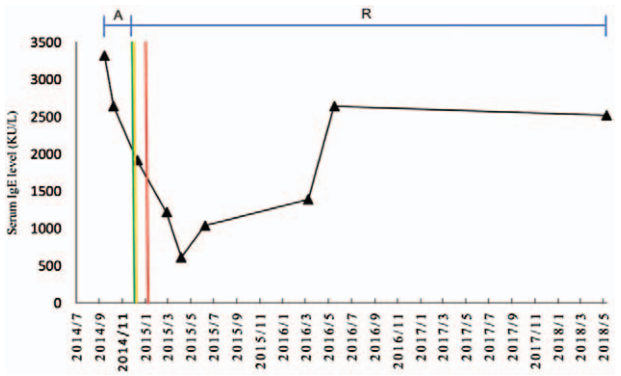

Figure 3. The serum IgE level change of the reported synovitis, acne, pustulosis, hyperostosis, and osteitis patient before and after the short-term systemic corticosteroids treatment. The green, yellow and red line indicate the administration, dosage reduction, and cessation of corticosteroids treatment, respectively. A and R indicate the period of aggregation and remission of nail lesions, respectively. Serum total IgE level had once decreased to 610.0 KU/L 3 months after the treatment.

The long-term remission on both clinical manifestations and imageology performance after a short-term systemic corticosteroids treatment is remarkable. As effective immunosuppressive drugs, corticosteroids are considered to be the cornerstone for both disease cure and symptom control in many immune diseases. The intra-articular corticosteroids can be transiently effective, but does not appear to reduce osteitis in SAPHO patients;[8] thus, systematic use might be more suitable for overall disease activity remission. However, the side effects of corticosteroids, especially systemic use, including cardiovascular diseases, metabolic disorders, osteoarticular lesions, and so on, have severely affected the long-term prognosis. Thus, systemic glucocorticoids treatment was not recommended in patients with axial spondyloarthritis[9] and can only be used with caution at the lowest effective dose in psoriatic arthritis management.[10] Short-term and low-dose usage of systemic corticosteroids might minimize their potential side effects and serve as a better solution, which was being gradually emphasized in the guidelines of some rheumatic immune diseases such as the EULAR recommendations for the management of rheumatoid arthritis.[11] Both a low inflammatory activity indicated by her normal ESR and hsCRP level and specific pathogenesis represented by her prominent nail lesions as well as elevated IgE level may contributed to such a significant response. Nail changes including pitting, ridging, hyperkeratosis, and onycholysis are mostly studied in psoriatic arthritis, which have been found to have a close relationship with joint involvement and disease severity.[12] However, the clinical significance and potential treatments of nail lesions have not been well illustrated in SAPHO patients. This case may deepen the understanding of nail involvement in SAPHO and further prompt disease subtyping according to skin and nail manifestations as well as ESR, hsCRP, and IgE levels, which would instruct subsequent use of systemic corticosteroids as a possible solution.

4. Conclusions

To the best of our knowledge, this is the first report of remarkable long-term remission of SAPHO syndrome after short-term systemic corticosteroids treatment. Identification of specific subtype of SAPHO patient according to clinical manifestations and IgE levels may guide the selection of such strategy. Besides, the lesions on bone scintigraphy can hardly disappear in SAPHO patients, whereas quantitative analysis of bone scintigraphy and MRI performances may better reflect the change of disease condition and monitor treatment efficiency.

Author contributions

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Visualization: Lun Wang, Hongli Jing.
Writing – original draft: Lun Wang.
Writing – review & editing: Chen Li, Meiyan Yu, Yihan Cao, Hongli Jing, Junqiu Li.

References

[1] Ferine D, Garcia-Larsen V, Manconi PE, et al. SAPHO syndrome: current developments and approaches to clinical treatment. Curr Rheum Rep 2016;18:35.
[2] Nguyen MT, Borchers A, Selmi C, et al. The SAPHO syndrome. Semin Arthritis Rheumatism 2012;42:254–65.
[3] Schaub S, Sirkis HM, Kay J. Imaging for Synovitis, Acne, Pustulosis, Hyperostosis, and Osteitis (SAPHO) syndrome. Rheum Dis Clin North Am 2016;42:695–710.
[4] Li C, Zuo Y, Wu N, et al. Synovitis, acne, pustulosis, hyperostosis and osteitis syndrome: a single centre study of a cohort of 164 patients. Rheumatology (Oxford, England) 2016;55:1023–30.
[5] Gould HJ, Sutton BJ, Beavil AJ, et al. The biology of IGE and the basis of allergic disease. Ann Rev Immunol 2003;21:579–628.
[6] Cianci F, Zoli A, Gremese E, et al. Clinical heterogeneity of SAPHO syndrome: challenging diagnose and treatment. Clin Rheumatol 2017;36:2151–8.
[7] Leone A, Cassar-Pullicino VN, Casale R, et al. The SAPHO syndrome revisited with an emphasis on spinal manifestations. Skeletal Radiol 2015;44:9–24.
[8] Jung J, Molinger M, Kohn D, et al. Intra-articular glucocorticosteroid injection into sternocostoclavicular joints in patients with SAPHO syndrome. Semin Arthritis Rheum 2012;42:266–70.
[9] van der Heijde D, Ramiro S, Landewe R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis 2017;76:978–91.
[10] Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. Ann Rheum Dis 2016;75:499–510.
[11] Smolen JS, Landewe R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis 2017;76:960–77.
[12] Williamson L, Dalbeth N, Dockerty JL, et al. Extended report: nail disease in psoriatic arthritis–clinically important, potentially treatable and often overlooked. Rheumatology (Oxford, England) 2004;43:790–4.