


CASE REPORT

Open Access



SAPHO syndrome with pathological fractures of vertebral bodies: a case report

Yalong Li^{1,4†}, Guomin Liu^{1,4†}, Yian Zhao^{2,4}, Yungang Luo^{2,4*}  and Tiancheng Lu^{3,4*}

Abstract

Background: It's difficult to diagnose and treat synovitis-acne-pustulosis-hyperostosis-osteomyelitis (SAPHO) syndrome due to its rare and unknown pathogenesis. There is no effective treatment for SAPHO syndrome and the consequences of empirical treatment are unpredictable. This study reports a case of a young female diagnosed as SAPHO syndrome with pathological fractures of vertebral bodies.

Case presentation: A 29-year-old female complained of the right sternoclavicular joint and back pain accompanied limited activities and cutaneous lesions. Laboratory assays revealed abnormal inflammatory factors. Multiple imaging studies illustrated bone lesions and pathological fractures of vertebral bodies. A diagnosis of SAPHO syndrome was made. The patient was treated with Compound Troxerutin and Poreine Cerebroside Injection, non-steroidal anti-inflammatory drugs (NSAIDs), bisphosphonates, corticosteroids and the thoracolumbar brace. The patient was followed up for 6 months and showed improved results.

Conclusions: The case supports that multiple image inspections and laboratory tests contribute to diagnose SAPHO syndrome, and combination therapies of Compound Troxerutin and Poreine Cerebroside Injection, NSAIDs, bisphosphonates, corticosteroids and the thoracolumbar brace in the treatment of SAPHO syndrome with pathological fractures of vertebral bodies are crucial to regain health.

Keywords: SAPHO syndrome, Bisphosphonates, Osteomyelitis, Steroids, Multiple bone lesions

Background

SAPHO syndrome, an acronym for synovitis-acne-pustulosis-hyperostosis-osteomyelitis, is a rare disease with an estimated prevalence of 0.00144/100000 [1]. SAPHO syndrome was first introduced by Chamot in 1987 [2] and characterized by both cutaneous lesions and osteoarticular manifestations [3]. Besides, the latest study demonstrated that it can result in symptoms of depression [4]. There are few case reports which may be attributed to its extremely low prevalence and difficulty to diagnose or missed diagnosis. This study reports a case of young female diagnosed as SAPHO syndrome with pathological fractures of vertebral bodies.

Case presentation

A 29-year-old female complained of the right sternoclavicular joint and back pain accompanied limited activities and pustulosis-like rashes on the palms for 1 month without any clear predisposing cause. She took analgesic medicine by herself (an unknown analgesic), while without obvious effect. Physical examinations on admission revealed pustules on the palms and multi-erythematous nodules on the lower legs. There were also redness, swelling and tenderness in the right sternoclavicular joint area and tenderness in the lower back.

Laboratory assays revealed an elevation of the erythrocyte sedimentation rate (ESR, 87 mm/h, normal range 0–20 mm/h), levels of C-reactive protein (CRP, 28.30 mg/L, normal range 0–7.44 mg/L), prothrombin time (12.7 s, normal range 9.4–12.5 s), fibrinogen assay (5.13 g/L, normal range 2–4 g/L) and complement C4(40 mg/dL, normal range 16–38 mg/dL), and a slightly decline of hematocrit (33.9%, normal range 35–45%). In addition, rheumatoid factor(RF) and human leukocyte antigen B27(HLA-B27) tests were negative. The results for the remainder of her

* Correspondence: luoygjl@sina.com; tiancheng@jlu.edu.cn

[†]Yalong Li and Guomin Liu contributed equally to this work.

²Department of Stomatology, the Second Hospital of Jilin University, Changchun, Jilin 130041, People's Republic of China

³Life Sciences College, Jilin Agricultural University, Changchun, Jilin 130118, People's Republic of China

Full list of author information is available at the end of the article



biochemistry and hematology were within normal range, including immunoglobulins, antinuclear antibody (ANA) spectrum and tumor markers.

Computerized tomography (CT) scans of the thoracic(T) and lumbar spine revealed multiple vertebral lesions (T8–11 and T2 vertebral bodies) while without the sternum and sternoclavicular joints (Fig. 1). Magnetic resonance imaging (MRI) scans of thoracic spine and ankle demonstrated multiple vertebral lesions (T4, T8–11 and L2 vertebral bodies), right ankle arthritis and pathological fractures (T9–10 vertebral bodies) (Fig. 2 and Fig. 3), same as CT scans. We diagnosed the patient with SAPHO syndrome. For further diagnosis, a whole body bone scan (WBS) was performed 4 h following the injection of 20 mCi ^{99m}Tc -methylene-diphosphonate(Fig. 4). Anterior and posterior views of the WBS illustrated intense uptake at the proximal end of the right clavicle, left first front rib, T8–11 vertebral bodies, right ankle joint and pubic symphysis. The thoracolumbar Single-Photon Emission Computed Tomography (SPECT)/CT fusion imaging showed a low density of bone in the same location and different levels of radioactivity uptake around the lesioned bone (Fig. 5). Pathological section of tibial lesions demonstrated massive neutrophil infiltration in bone marrow(Fig. 6).

A diagnosis of SAPHO syndrome was made. For the vertebral fractures, the patient was treated conservatively with the thoracolumbar brace and bed rest for 3 months. Besides, the patient was treated with dynastat (80 mg, BID) until the pain eased or disappeared and Compound Troxerutin and Poreine Cerebroside Injection(10 ml, BID)for improving blood circulation on the fourth and tenth days. And Technetium [^{99}Tc] Methylendiphosphonate Injection

(^{99}Tc -MDP, Product Name: Yunke Injection, 3 sets, QD)in combination with betamethasone sodium phosphate injection (20 mg, QD) was introduced on the tenth day for treating SAPHO syndrome. The patient experienced a moderate decrease in the intensity of the pain without any anodyne. On the seventeenth day, betamethasone sodium phosphate injection (12 mg, QD) was introduced again. There were normal ESR (8 mm/h) and CRP (0.36 ng/L), improved dermatoses and no relapse of joint pain on the eighteenth day. The patient was discharged on the twentieth day. During the 6-month telephone follow-up of the patient (phones are followed up every half month), there was no relapse of joint pain according to the patient's description, however, the patient refused to review for economic reasons.

Discussion

Chamot et al. [2] first proposed the SAPHO syndrome and the initial diagnostic criteria in 1987. SAPHO syndrome is at present considered a rare disease and sufficient data on its prevalence are unavailable, while for the lack of correct diagnosis, its actual prevalence may be underestimated. SAPHO syndrome has a female predominance among patients [5, 6], especially younger than 30 years old [5]. Despite all of this, it is considered that SAPHO syndrome may present at any age [5–7], even in an only 15-month-old childhood [8]. The etiopathogenetic mechanism of SAPHO syndrome, although having been proposed involving bacteriologic, immunologic and genetic factors [3] such as autophagy, interleukin-1(IL-1), Forkhead Box O1(FoxO1) and propionibacterium (*Cutibacterium*) acnes [9], remains poorly understood.

The most frequently mentioned diagnostic criteria for SAPHO syndrome was proposed by Kahn and Khan [10]

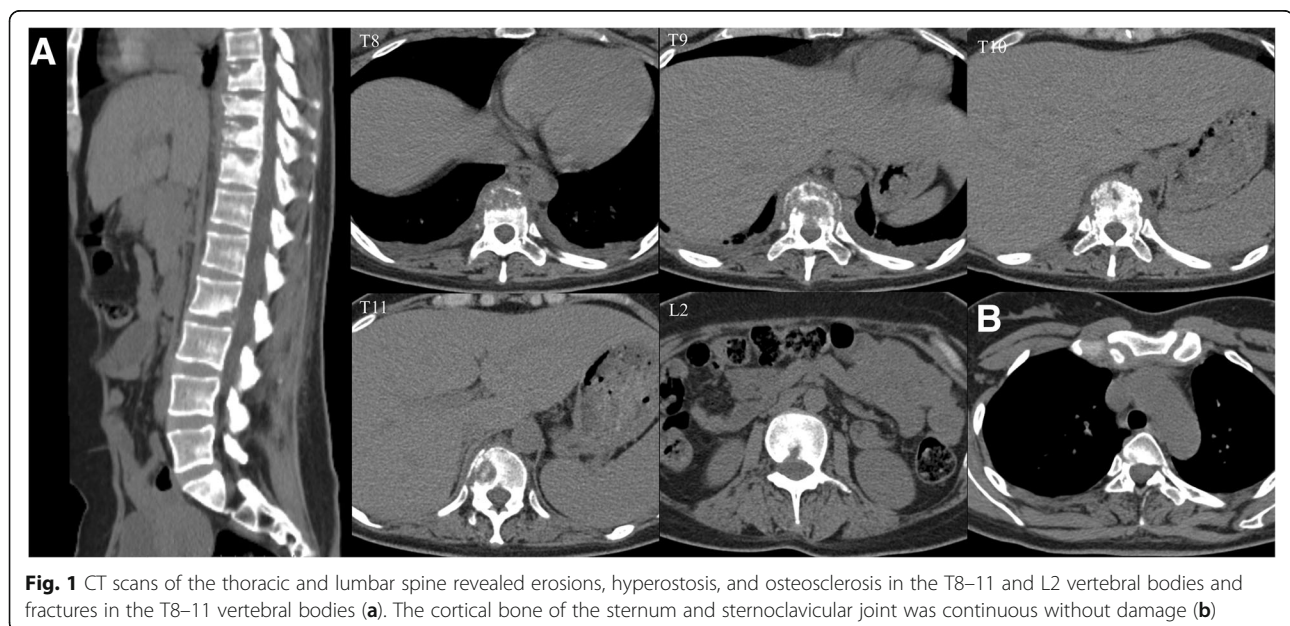


Fig. 1 CT scans of the thoracic and lumbar spine revealed erosions, hyperostosis, and osteosclerosis in the T8–11 and L2 vertebral bodies and fractures in the T8–11 vertebral bodies (a). The cortical bone of the sternum and sternoclavicular joint was continuous without damage (b)

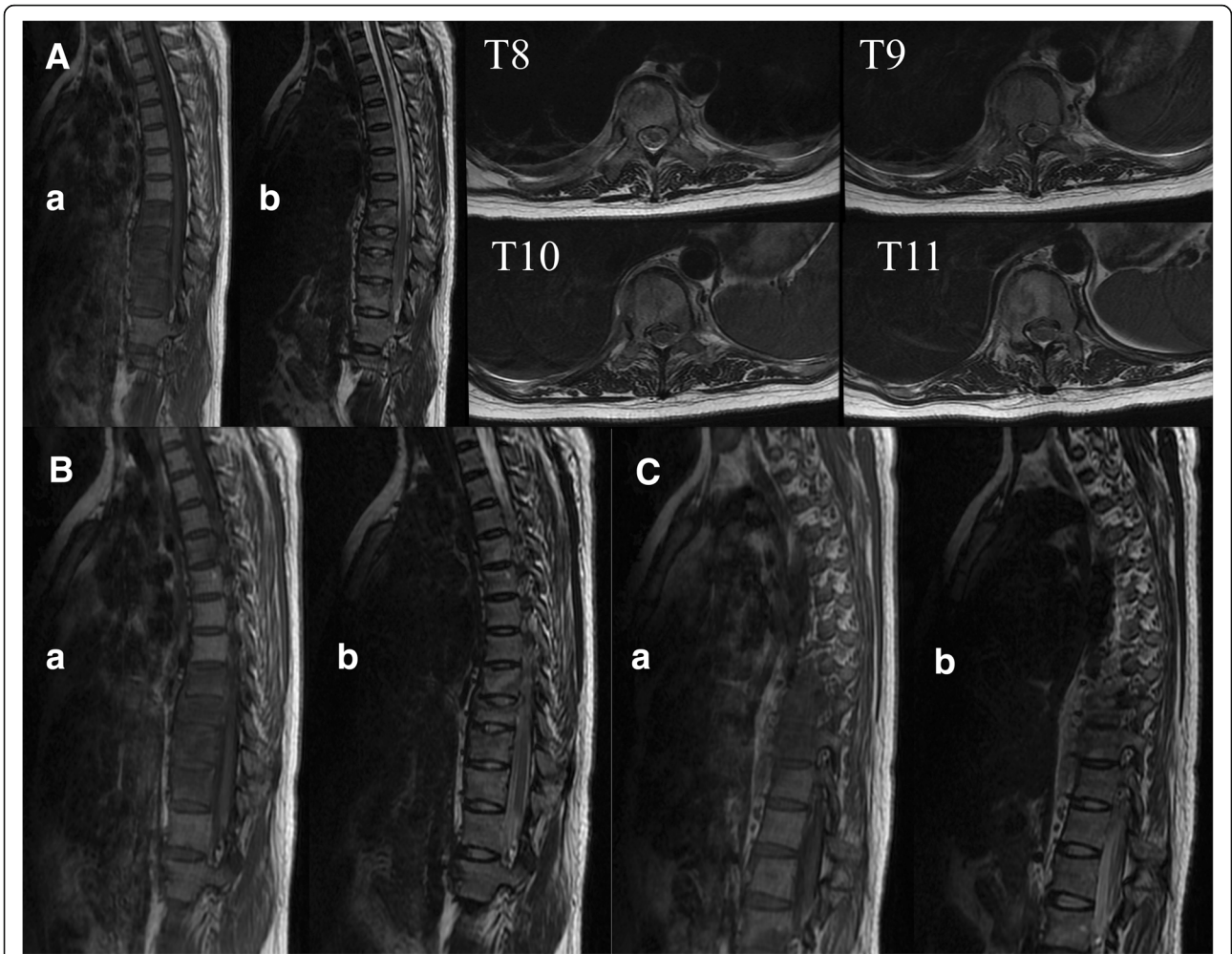


Fig. 2 MRI scans of the thoracic showed superior end plate compression deformity in the T4 (**b**) and T8–11 vertebral bodies (**a**). In addition, diffused inflammatory bone changes were also noted in the T4 (**b**), T8–11(**a**) and L2 (**c**) vertebral bodies that were hypointense on the T1-weighted image (**a**) and hyperintense on the T2-weighted image (**b**)

in 1994 (Table.1), and the more precise diagnostic criteria was modified by Kahn in 2003 [11] (Table.2). It's difficult, however, to make a diagnosis in certain case, such as no skin lesions [12]. Not only the history and clinical signs play a crucial role in diagnosis, but also imaging findings and

laboratory tests. Some studies have demonstrated that erythrocyte sedimentation rate and CRP may be elevated [13] for SAPHO syndrome, and our report also confirmed this. Besides, we had not detected any autoantibodies, including RE, HLA-B27, immunoglobulin and ANA spectrum.

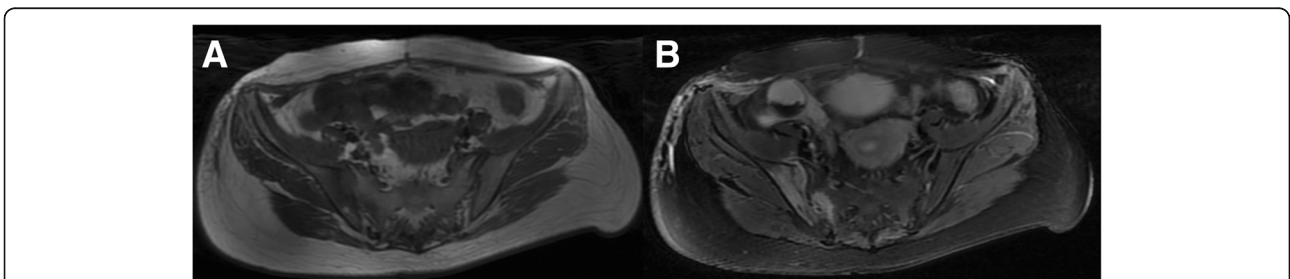
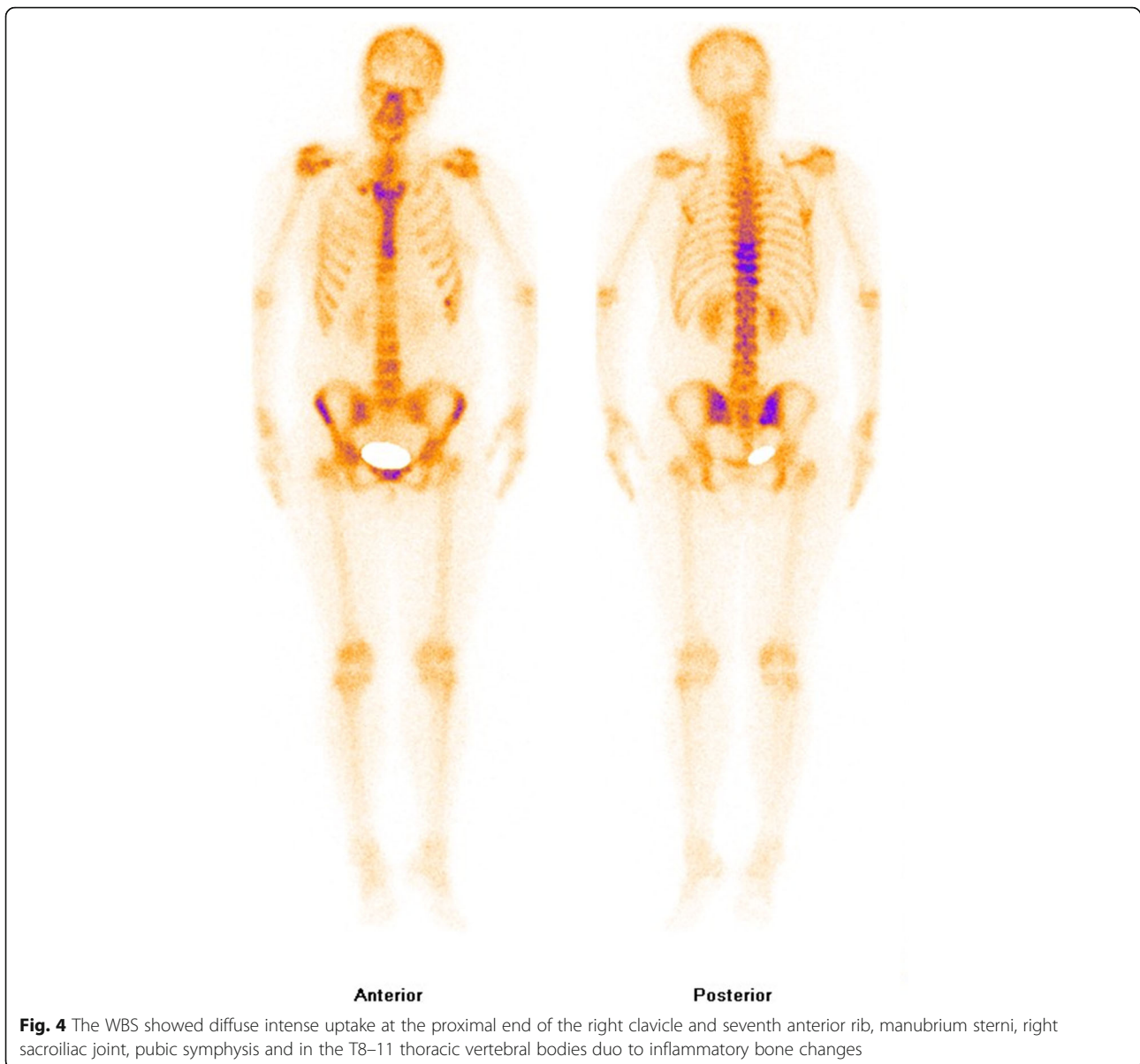


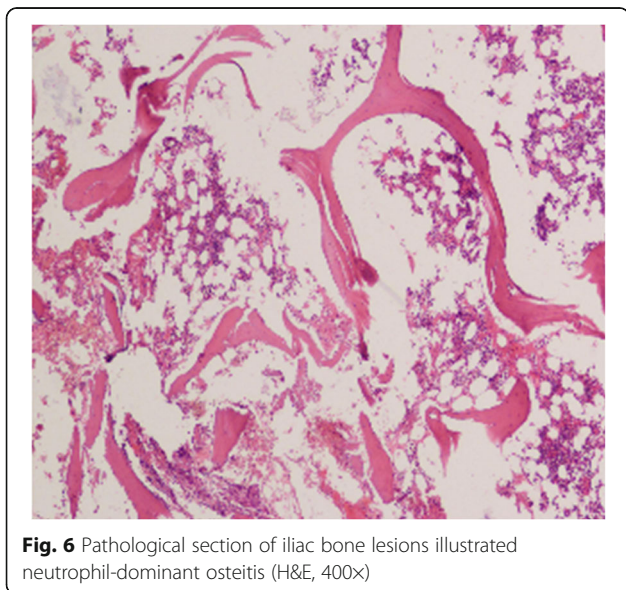
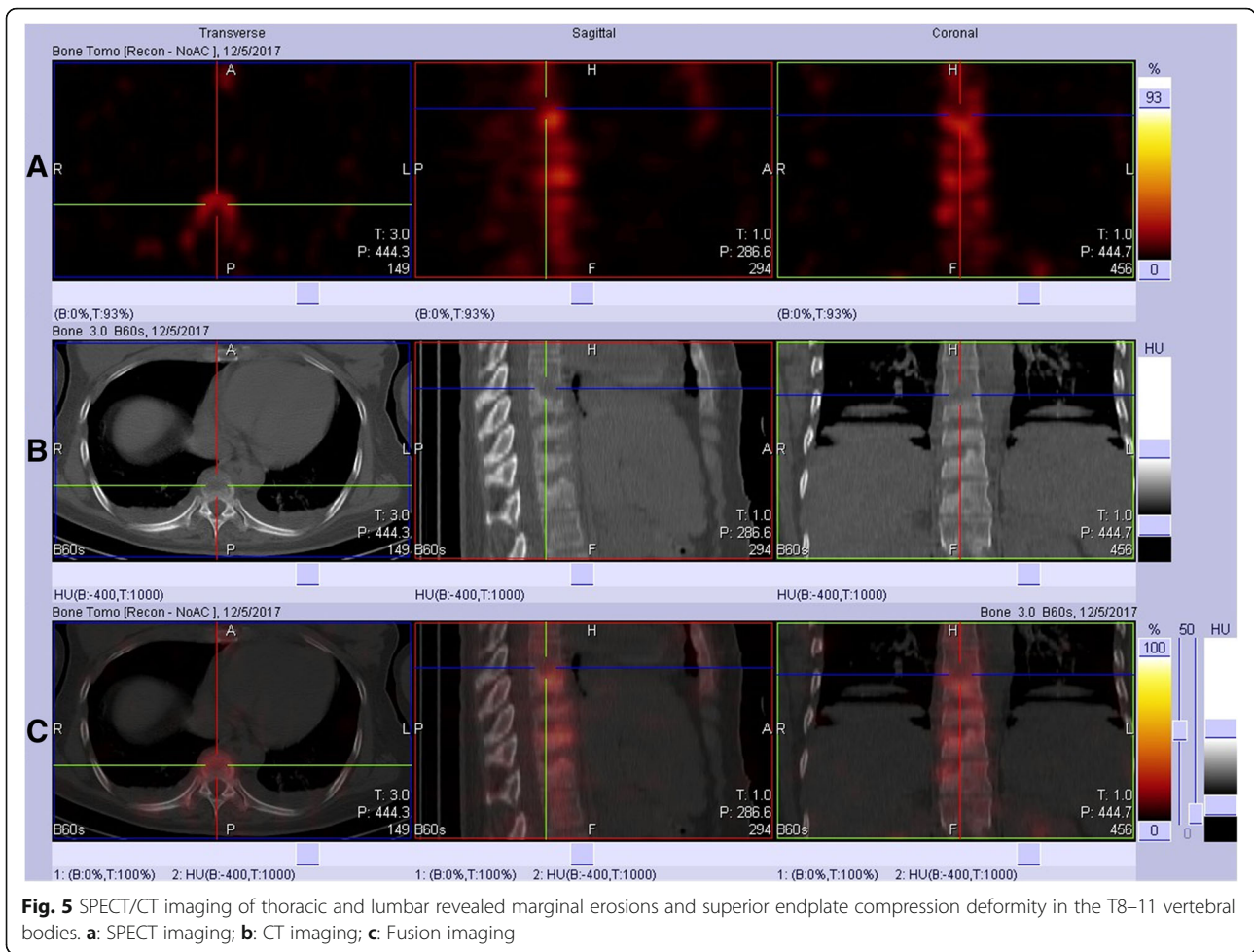
Fig. 3 Axial MRI scans of the sacroiliac joints illustrated inflammatory bone changes at the right sacroiliac joint that were hypointense on the T1-weighted image (**a**) and hyperintense on the T2-weighted image (**b**)



A “bull’s head” appearance shown in bone scintigraphy is the characteristic of SAPHO syndrome [10], while bone scintigraphy in our case only revealed intense uptake at the proximal end of the right clavicle and manubrium sterni, which may be related to the patient was in the early stage of the disease. What’s more, SAPHO syndrome is heterogeneous, different patients may have different performance. In adult patients, the most frequent area are the anterior chest wall, accounting for 60–95%, especially in the costochondral, sternoclavicular, manubriosternal and costosternal junctions, and spine, accounting for 32–52%, most commonly in the thoracolumbar spine [14]. The radiological results of SAPHO syndrome comprise hyperostosis, osteolysis, osteitis, and osteosclerosis [3]. In this report, CT scans, MRI scans and SPECT/

CT fusion image demonstrated a detailed image of multiple bone destructions, vertebral fractures and sclerosis formation surrounding lesion bones. For the patient, the complaint of back pain and limited activities were due to vertebral fractures, which was resulted from osteolysis of T8–11 vertebral bodies. And the latest research showed that ultrasound can also contribute to the diagnosis of SAPHO syndrome [15]. For excluding malignancy, bone biopsy was performed. Infiltration of large numbers of neutrophils supports osteitis.

As far as we know, there is no effective treatment to cure SAPHO syndrome. Current treatment of this illness is mainly focused on relieving symptoms. NSAIDs are the first-line treatment. Several studies have supported the effectiveness of bisphosphonates, steroids, methotrexate, tumor



necrosis factor (TNF) inhibitors and so on as effective treatments [16–18]. While before we treated this patient, several reports had shown that some patients may develop or have paradoxical worsening of skin lesions after starting TNF inhibitors with unclear reasons [19, 20], which was confirmed by a recent array research [21]. In this study, conservative treatments including Compound Troxerutin and Poreine Cerebroside Injection, NSAIDs, bisphosphonates, corticosteroids and the thoracolumbar brace were applied to treat SAPHO syndrome and pathological fractures of vertebral bodies resulting from it, and the combination proved to be effective for this disease according to the observation results of the patient.

Table 1 Diagnostic criteria proposed by Kahn for SAPHO syndrome diagnosis, 1994 [10]

1. Chronic recurrent multifocal sterile and axial osteomyelitis, with or without dermatosis
2. Acute, subacute, or chronic arthritis associated with palmoplantar pustulosis, pustulous psoriasis, or severe acne
3. Any sterile osteitis associated with palmoplantar pustulosis, pustulous psoriasis, or severe acne

Table 2 Diagnostic criteria proposed by Kahn for SAPHO syndrome diagnosis, 2003 [11]

Inclusion criteria:

Bone–joint involvement associated with palmoplantar pustulosis and psoriasis vulgaris

Bone–joint involvement associated with severe acne

Isolated sterile* hyperostosis/osteitis (adults)

Chronic recurrent multifocal osteomyelitis (children)

Bone–joint involvement associated with chronic bowel diseases

Exclusion criteria:

Infectious osteitis

Tumoral conditions of the bone

Non-inflammatory condensing lesions of the bone

*Exception: growth of *Propionibacterium acnes*

Note: Table 1 and Table 2 should appear at the second paragraph of the 'Discussion' section

Conclusion

According to our study, multiple image examinations and laboratory tests are helpful for the diagnosis of SAPHO syndrome, and combination therapies of Compound Troxerutin and Poreine Cerebroside Injection, NSAIDs, bisphosphonates, corticosteroids and the thoracolumbar brace in the treatment of SAPHO with pathological fractures of vertebral bodies are vital for controlling the disease.

Abbreviations

ANA: Antinuclear antibody; BID: Twice a day; CRP: C-reactive protein; CT: Computerized tomography; FoxO1: Forkhead Box O1; IL-1: Interleukin-1; MRI: Magnetic resonance imaging; NSAIDs: Non-steroidal anti-inflammatory drugs; QD: Once a day; RF: Rheumatoid factor; SAPHO: Synovitis-acne-pustulosis-hyperostosis-osteomyelitis; SPECT/CT: Single-Photon Emission Computed Tomography; T: Thoracic; TNF: Tumor necrosis factor; WBS: Whole body bone scan

Acknowledgements

The authors would like to thank the participating patient, as well as the study nurses and colleagues who made this work possible.

Funding

This work was supported by *Jilin Provincial Development and Reform Commission of China (No. 2014G072; 3J115AK93429)*. Funding includes only the publication fee. No funding for the design of the study, the collection, analysis, and interpretation of data and for writing the manuscript was obtained.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

YL contributed to the design, data acquisition, analysis, and interpretation. YL and GL decided about final diagnosis, wrote the draft of the manuscript, participated in medical treatment and the follow-up of the patient. YZ participated in the follow-up of the patient. YL and TL completed all examinations, analyzed the data, helped to draft and finalize the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Second Hospital of Jilin University (registration number 138/2018). A written informed consent was obtained from the patient.

Consent for publication

Written informed consent for publication of this case report and any accompanying images was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details

¹Department of Orthopedics, the Second Hospital of Jilin University, Changchun, Jilin 130041, People's Republic of China. ²Department of Stomatology, the Second Hospital of Jilin University, Changchun, Jilin 130041, People's Republic of China. ³Life Sciences College, Jilin Agricultural University, Changchun, Jilin 130118, People's Republic of China. ⁴Jilin provincial Changbai mountain medicine anti-tumor engineering center, Jilin, People's Republic of China.

Received: 4 August 2018 Accepted: 8 January 2019

Published online: 17 January 2019

References

- Mochizuki Y, Omura K, Hirai H, Kugimoto T, Osako T, Taguchi T. Chronic mandibular osteomyelitis with suspected underlying synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome: a case report. *J Inflamm Res*. 2012;5:29–35.
- Chamot AM, Benhamou CL, Kahn MF, Beranek L, Kaplan G, Prost A. Acne-pustulosis-hyperostosis-osteitis syndrome. Results of a national survey. 85 cases. *Rev Rhum Mal Osteoartic*. 1987;54(3):187–96.
- Rukavina I. SAPHO syndrome: a review. *J Child Orthop*. 2015;9(1):19–27.
- Lu J, Duan YP, Zuo ZT, Xu WR, Zhang XW, Li C, Xue R, Lu HZ, Zhang WH. Depression in patients with SAPHO syndrome and its relationship with brain activity and connectivity. *Orphanet J Rare Dis*. 2017;12(1):103.
- Hayem G, Bouchaud-Chabot A, Benali K, Roux S, Palazzo E, Silberman-Hoffman O, Kahn MF, Meyer O. SAPHO syndrome: a long-term follow-up study of 120 cases. *Semin Arthritis Rheum*. 1999;29(3):159–71.
- Colina M, Govoni M, Orzincolo C, Trotta F. Clinical and radiologic evolution of synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome: a single center study of a cohort of 71 subjects. *Arthritis Rheum*. 2009;61(6):813–21.
- Kerrison C, Davidson JE, Cleary AG, Beresford MW. Pamidronate in the treatment of childhood SAPHO syndrome. *Rheumatology (Oxford)*. 2004; 43(10):1246–51.
- Eleftheriou D, Gerschman T, Sebire N, Woo P, Pilkington CA, Brogan PA. Biologic therapy in refractory chronic non-bacterial osteomyelitis of childhood. *Rheumatology (Oxford)*. 2010;49(8):1505–12.
- Berthelot JM, Corvec S, Hayem G. SAPHO, autophagy, IL-1, FoxO1, and *Propionibacterium (Cutibacterium) acnes*. *Joint Bone Spine*. 2018;85(2):171–6.
- Kahn MF, Khan MA. The SAPHO syndrome. *Baillieres Clin Rheumatol*. 1994; 8(2):333–62.
- Hayem G. SAPHO syndrome. *Rev Prat*. 2004;54(15):1635–6.
- Duan N, Chen X, Liu Y, Wang J, Wang Z. Multimodal imaging findings of SAPHO syndrome with no skin lesions: a report of three cases and review of the literature. *Exp Ther Med*. 2016;12(4):2665–70.
- Song X, Sun W, Meng Z, Gong L, Tan J, Jia Q, Yu C, Yu T. Diagnosis and treatment of SAPHO syndrome: a case report. *Exp Ther Med*. 2014;8(2):419–22.
- Leone A, Cassar-Pullicino VN, Casale R, Magarelli N, Semprini A, Colosimo C. The SAPHO syndrome revisited with an emphasis on spinal manifestations. *Skelet Radiol*. 2015;44(1):9–24.
- Umeda M, Kawashiri SY, Nishino A, Koga T, Ichinose K, Michitsugu T, Shimizu T, Fukui S, Nakashima Y, Hirai Y, Iwamoto N, Aramaki T, Tamai M, Nakamura H, Origuchi T, Ueki Y, Kawakami A. Synovitis of sternoclavicular and peripheral joints can be detected by ultrasound in patients with SAPHO syndrome. *Mod Rheumatol*. 2017;27(5):881–5.
- Zwaenepoel T, Vlam K. SAPHO: treatment options including bisphosphonates. *Semin Arthritis Rheum*. 2016;46(2):168–73.
- Vekic DA, Woods J, Lin P, Cains GD. 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*. 2018;57(1):10–8.

18. Akçaboy M, Bakkaloğlu-Ezgü SA, Büyükkaragöz B, İsiyel E, Kandur Y, Hasanoğlu E, Buyan N. Successful treatment of a childhood synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO) syndrome with subcutaneous methotrexate: a case report. *Turk J Pediatr.* 2017;59(2):184–8.
19. Liew J, Xu TH, Chu CQ. Synovitis acne pustulosis hyperostosis osteitis (SAPHO) - paradoxical reactions and different responses to tumour necrosis factor inhibitors. *Rheumatology.* 2017;56(12):2239–41.
20. Massara A, Cavazzini PL, Trotta F. In SAPHO syndrome anti-TNF-alpha therapy may induce persistent amelioration of osteoarticular complaints, but may exacerbate cutaneous manifestations. *Rheumatology.* 2006;45(6):730–3.
21. Li C, Wu X, Cao Y, Zeng Y, Zhang W, Zhang S, Liu Y, Jin H, Zhang W, Li L. Paradoxical skin lesions induced by anti-TNF-alpha agents in SAPHO syndrome. *Clin Rheumatol.* 2018. <https://doi.org/10.1007/s10067-018-4083-5>.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

