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Clinical Case Studies

Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome presenting with a cervical vertebral fracture: A case report

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ABSTRACT

Background context: Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a rare condition that can be difficult to diagnose. There are no guidelines for the treatment of SAPHO syndrome, but newer modalities of medications show promising results. We present the case of a patient who presented with a pathologic fracture of her cervical spine who ended up being diagnosed with SAPHO syndrome.

Case: A 51-year-old female presented with severe neck pain and a rash on her hands and feet. Imaging showed a C5 vertebral compression fracture and multiple sites of bony involvement concerning for malignancy or widespread infection. The patient underwent corpectomy and fusion to address the instability and cervical stenosis and was started on immunomodulating therapy. Based on the biopsy findings showing left shifted bone marrow versus mild acute inflammation, and in conjunction with the cutaneous findings, the patent was diagnosed with SAPHO syndrome.

Outcome: At two year follow up, although posterior stabilization was required, her overall condition was improved. Nonetheless, she continued to have fatigue, malaise, and total body pain involving: the cervical spine, the mid thoracic spine, the left costal margin, bilateral sternoclavicular joints, and bilateral hips and knees.

Conclusion: SAPHO syndrome can mimic infection and neoplasia. It should be suspected in patients presenting with multifocal osteitis and associated rash. Accurate and timely diagnosis is paramount as the treatment of this condition may require immunomodulating agents.

Introduction

Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a rare condition considered as a type of seronegative spondyloarthritis [1–3]. The prevalence of SAPHO syndrome has been estimated as 1 in 10,000 previously, however, SAPHO syndrome is likely underdiagnosed [4–7]. There are no validated diagnostic criteria for SAPHO syndrome and no guidelines for treatment.

We present a rare case in which a patient presented with a pathological compression fracture of the cervical spine associated with spinal stenosis, severe neck pain, and associated rash on both hands and left foot, and multiple sites of osteitis. The patient was informed that her case would be submitted for publication and she provided consent.

Case presentation

A 51-year-old female presented to our emergency department with complaints of severe neck pain. She denied any trauma or injury. Her symptoms began four weeks prior to presentation and had progressively worsened since. She described the neck pain as burning/stabbing in quality; she also noted persistent dysesthesias and tingling along the left C6 distribution. She had initially seen a chiropractor and an acupuncturist for these symptoms. When the pain did not improve, an MRI was ordered by her chiropractor, and this showed a compression deformity of the C5 vertebral body (Fig. 1). Based on the above findings, the patient was instructed to present to the Emergency Department.

Upon presentation to the Emergency Department, she denied any fever, chills, night sweats, night pain, weight loss, or malaise. She had no prior history of inflammatory arthritis or skin diseases. Family history was significant for hand arthritis in her maternal grandmother and paternal aunt. Pertinent laboratory values were as follows: leukocyte count (WBC) 13.4 (normal 4–11 $\times 10^9$/L), hemoglobin (Hgb) 12.6 (normal 12–16 g/dL), erythrocyte sedimentation rate (ESR) 75 (normal 0–9 mm/h), and C-Reactive Protein (CRP) 0.7 (0.0–0.8 mm/dL). On physical examination, the patient had tenderness to palpation of the cervical and thoracic spine along with decreased cervical motion secondary

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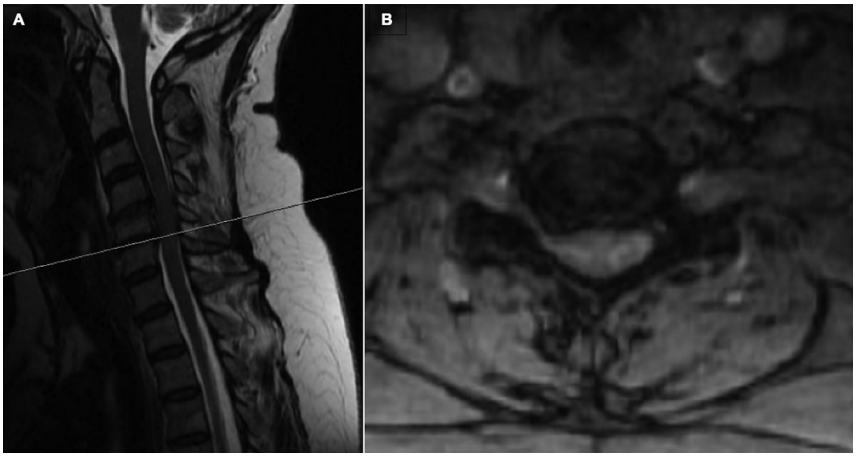

Fig. 1. Panel A shows a T2-weighted sagittal image and Panel B shows a T2-weighted axial image of the cervical spine demonstrating a compression deformity of the C5 vertebral body and moderate spinal canal stenosis.

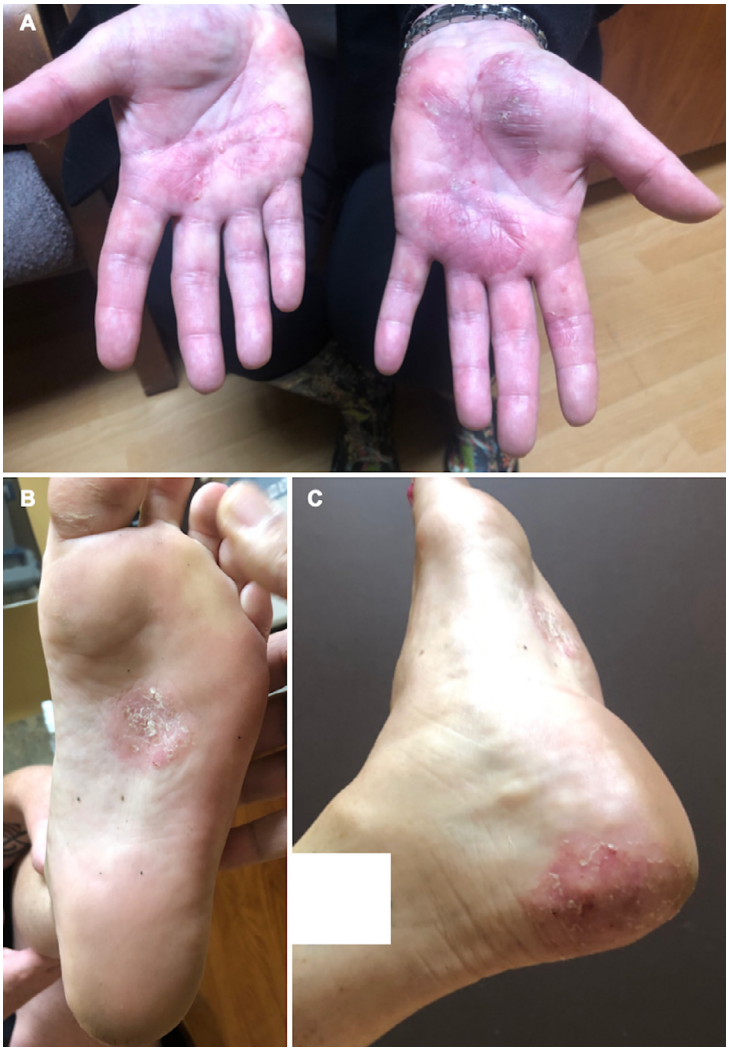

Fig. 2. Panel A shows a photograph of both hands and Panel B shows photographs of the patient's left foot showing palmoplantar pustulosis.

to pain. She was neurologically intact to motor and sensory function and was normoreflexic. She was found to have lesions on the palmar aspects of both of her hands and the plantar aspect of the left foot (Fig. 2).

A contrast enhanced magnetic resonance imaging (MRI) of the cervical, thoracic, and lumbar spine demonstrated a C5 compression deformity with moderate spinal canal stenosis at that level. Prevertebral enhancement was also noted anteriorly from C2–5 and anterior epidural enhancement of the ventral thecal sac at the C5 level (Fig. 3). T3 and T7 vertebral bodies also showed enhancement.

Computed tomography (CT) scans of the chest, abdomen, and pelvis were negative for neoplasm or nidus of infection and confirmed the C5 compression deformity (Fig. 4). A calcified nodular lesion was found in the left hemithyroid. Bone Single-photon Emission Computed Tomography (SPECT) scan performed showed increased activity in the C5, T7, and T11 vertebral bodies, as well as increased activity in bilateral 1st

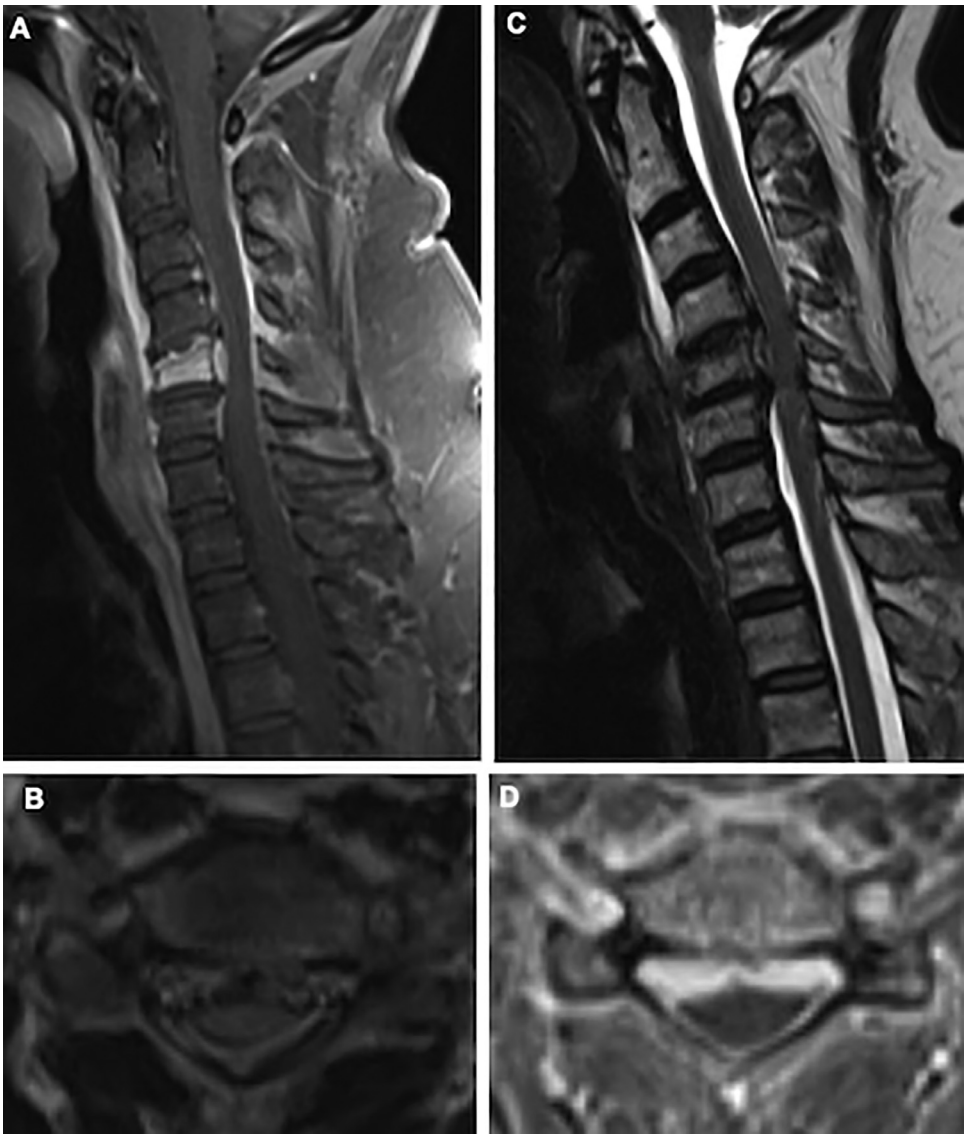

Fig. 3. Panel A shows a T1-weighted contrast enhanced sagittal image, Panel B shows a T2-weighted axial image at C5 level, Panel C shows a T2-weighted sagittal image, and Panel D shows a T1-weighted contrast enhanced axial image at C5 level demonstrating the C5 compression deformity with moderate spinal canal stenosis at that level, and prevertebral enhancement anteriorly from C2–5 and epidural enhancement posterior to the C5 vertebral body.

rib costochondral joints (Fig. 5). Sacroiliac joints were not reactive on SPECT and appeared normal on radiographs.

A transpedicular bone biopsy of T7 was performed which showed hyper cellular marrow with mild reactive changes of the marrow. Image guided left thyroid nodule fine-needle aspiration performed showed benign follicular epithelium with scattered colloid and blood showing degenerative changes (Thyroid Bethesda System: Category II: benign follicular nodule).

Initial treatment of the compression deformity of C5 was bracing with a hard cervical collar, but this did not ameliorate her pain. She was still dependent on intravenous morphine sulphate for pain control. Within a week of admission, the patient underwent anterior C5 corpectomy and fusion with cage placement (Fig. 6).

Samples of the C5 vertebral body, as well as the C4–5 and C5–6 vertebral disc were sent for pathology, which showed no malignancy. The C5 vertebral body pathology demonstrated moderate remodeling of bone spicules, consistent with the report of compression fracture. There was also diffuse fibrosis and serous atrophy of the marrow space, with the residual marrow being markedly hypocellular, and showing a moderate increase in plasma cells, and focally increased neutrophils that could represent either left shifted bone marrow or mild acute inflammation (Fig. 7).

Further consultative review of the C5 tissue confirmed the impression of chronic osteitis, and given the multifocality of the lesions and other associated findings, chronic multifocal osteitis as a part of the SAPHO syndrome was favored by the pathologist. Of note, prior to the pathology being confirmed the patient had been seen by dermatology and was diagnosed with dyshidrotic eczema and prescribed a variety of moisturizing creams, which did not improve her symptoms. After the diagnosis of SAPHO syndrome, dermatology changed the diagnosis to Psoriasis as a part of SAPHO syndrome and suggested that it should improve with her SAPHO treatment prescribed by rheumatology.

At her 8-week post-operative visit she complained of left sided rib pain, bilateral clavicular pain, along with polyarticular joint pain. She had a recurrence of the desquamative pustular rash on bilateral palms and left heel. Radiographs of the cervical spine performed at the 8-week visit showed posterior migration of the interbody cage along with compression of the C6 superior endplate (Fig. 8). Dual energy x-ray absorptiometry (DEXA) scan performed at this time, placed her in the osteopenia category with a *T*-score of −0.9 and −1.2 and a *Z*-score of −0.1 and −0.7 in the left hip and the lumbar spine respectively. The patient had no change in neurologic status and was noted to have full strength and sensation in bilateral upper and lower extremities. A CT scan of the cervical spine performed at 10 weeks post-op demonstrated stable posterior

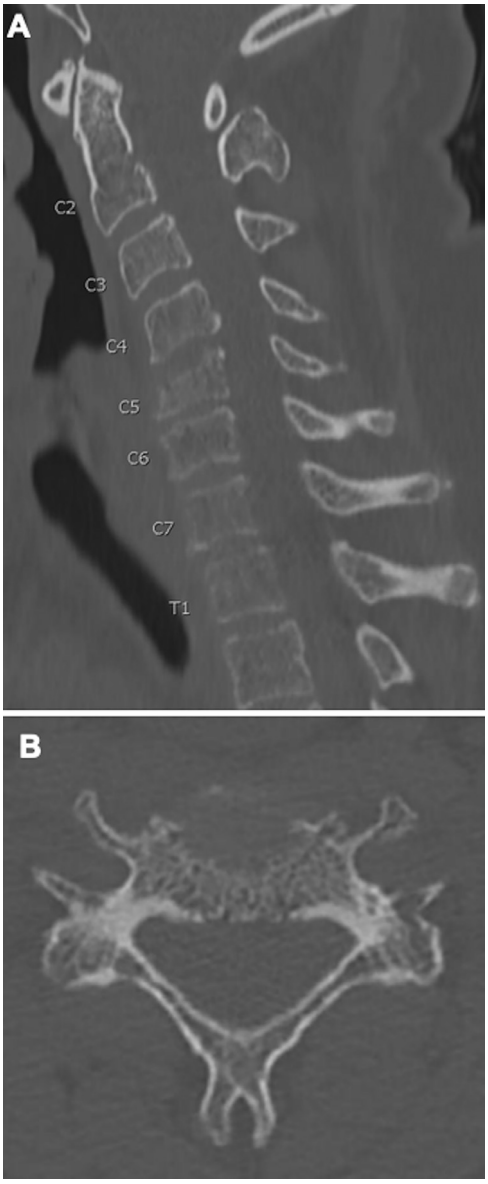

Fig. 4. Panel A shows a sagittal cut and Panel B shows an axial cut of a cervical spine CT scan showing a compression deformity of C5 vertebral body with an associated kyphotic deformity at the C4–5 level.

angulation of the C5 intervertebral body cage. Twelve weeks after the anterior cervical surgery, a posterior cervical segmental instrumentation and fusion was performed using lateral mass screws from C4 to C6 (Fig. 9).

Post-operatively the patient recovered appropriately, and her instrumentation has remained stable with circumferential arthrodesis at C4–6 levels. Medically, she continued to be followed as an outpatient by the Rheumatology service who started her on adalimumab (Humira) and methotrexate combination therapy, as well as alendronate (Fosamax). Of note, HLA-B27 testing done at her rheumatology visit post-op was negative. At two year follow up, her overall condition has improved, however, she continues to have fatigue, malaise, and total body pain involving: the cervical spine, the mid thoracic spine, the left costal margin, bilateral sternoclavicular joints, and bilateral hips and knees. She was recently changed from Adalimumab to Certolizumab due to the incomplete response but there is still no information on how her symptoms have responded to this change.

Discussion

Because of the heterogenous presentation, SAPHO syndrome can be difficult to diagnose [8,9]. It is not uncommon for the diagnosis to be delayed by several years, as symptoms are often wrongly attributed to other conditions before a correct diagnosis is made [7,10,11]. SAPHO syndrome can be considered as a subtype of seronegative spondyloarthropathy (SNSA) as it shares many of the clinical manifestations seen in SNSAs, but the taxonomic concept is controversial and most times is considered an undifferentiated spondyloarthropathy [3]. Chronic recurrent multifocal osteomyelitis (CRMO) and SAPHO syndrome are often grouped together as the same condition, as CRMO is thought by many to be a variant presentation of SAPHO syndrome [12,13]. SAPHO has a strong female predominance and it typically affects patients 30 to 50 years of age [7,10,11,14,15], whereas CRMO is usually seen in pediatric patients [16–18]. SAPHO tends to involve the axial skeleton while CRMO predominates in the extremities. There is still significant controversy regarding whether CRMO and SAPHO occur on a spectrum or are separate entities [19–21].

The most common presentations of SAPHO and CRMO mimic infection and neoplasia, and thus these conditions should be considered early in the differential diagnosis. The etiology of SAPHO syndrome is poorly understood. Theories involving bacteriologic, immunologic, and genetic factors have been proposed but none is universally accepted [22–24]. Palmoplantar pustulosis (PPP) is the most common skin manifestations and is seen in over 50% of patients diagnosed with SAPHO syndrome [14,15,25–27]. However, the correlation between cutaneous and musculoskeletal lesions is variable. Skin manifestations can appear before, after, or concurrently with the osteoarticular symptoms. It has been reported that in approximately 30% of cases, skin and musculoskeletal findings occur simultaneously [10,11].

Patients can present with only one site of osteoarticular involvement [16,28,29], however, in most cases there are multiple affected sites which may only be evident on imaging [2,6,14,30]. The anterior chest wall is the most commonly affected site [10,11,14,25], followed by the spine, primarily the thoracic spine [11,31–33]. As previously mentioned, SAPHO syndrome generally presents with more axial skeleton involvement as compared to CRMO which tends to involve the extremities more.

A high uptake of the sternoclavicular joints on bone scintigraphy called “bull’s head sign” is considered pathognomonic of SAPHO [34]. This finding was not present on our patient who only had low uptake on the right sternoclavicular joint (Fig. 5) . Affected areas can present with pain, tenderness, swelling, and limited range of motion [7,11,16]. At the time of presentation ESR is usually elevated while WBC count and CRP are normal [16,35].

Six radiological manifestations associated with the vertebral column have been documented in patients with SAPHO syndrome: vertebral body corner lesions, non-specific spondylodiscitis, osteodestructive lesions, osteosclerosis, paravertebral ossifications, and sacroilitis [6,11,30,31,36–38]. Vertebral body fractures secondary to SAPHO syndrome have been documented, with at least three documented case requiring surgical stabilization [39,40]. To the best of our knowledge, this is only the third reported case of cervical vertebral collapse in a patient with SAPHO syndrome requiring surgical stabilization. Borok et al. [41] reported the case of a 61 year old man with SAPHO syndrome who presented with C5–6 vertebral collapse and kyphotic deformity requiring surgical intervention. No mention is made of what surgery was done for that patient in the report. Takigawa et al. [42] reported the case of SAPHO syndrome in a 63 year old female with severe destruction of C4 to C7 associated with kyphosis, severe compression of the spinal cord, and incomplete quadriplegia (ASIA scale C). This patient was treated with anterior and posterior fixation. In our case, after the C5 corpectomy and anterior fixation, there was posterior migration of the interbody cage along with compression of the C6 superior endplate, likely due to potential involvement of the C6 superior vertebral body

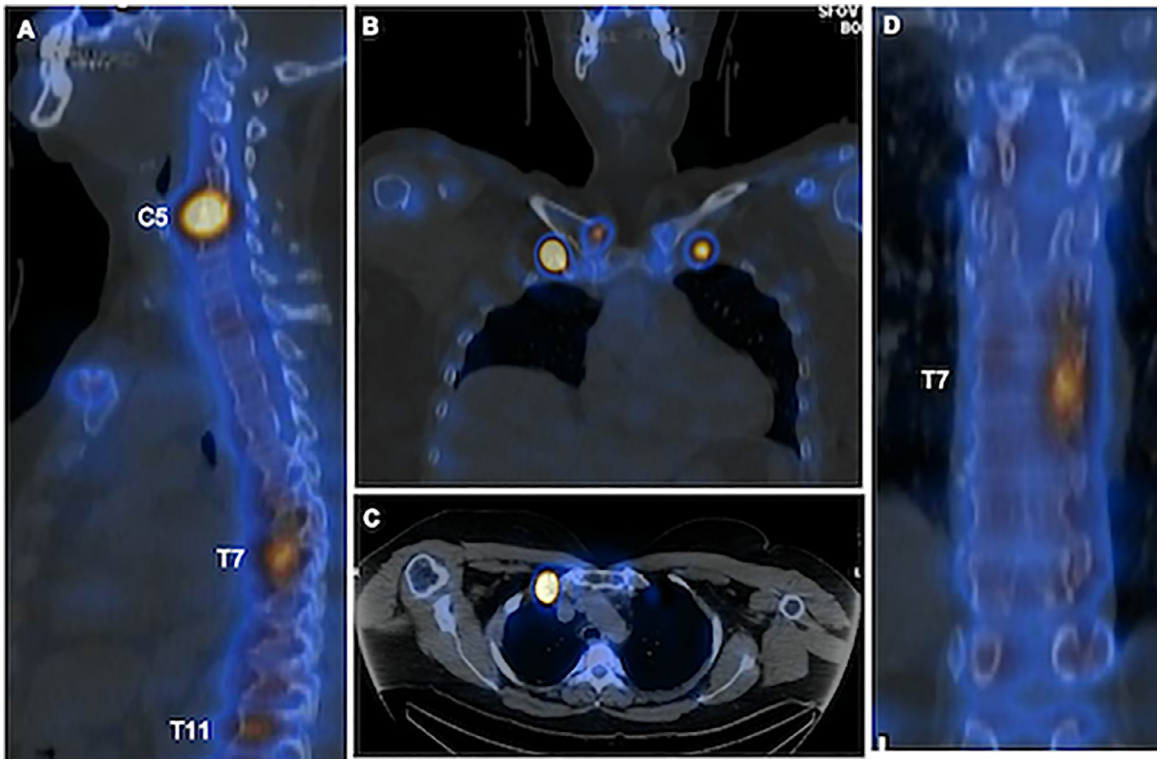

Fig. 5. Panel A shows a sagittal cut, Panel B shows a coronal cut, Panel C shows an axial cut, and Panel D shows a coronal cut of a whole-body Bone Single-photon Emission Computed Tomography (SPECT) scan showing increased activity in the C5, T7 and T11 vertebral bodies, as well as increased activity in bilateral 1st rib costochondral joints and right sternoclavicular joint.

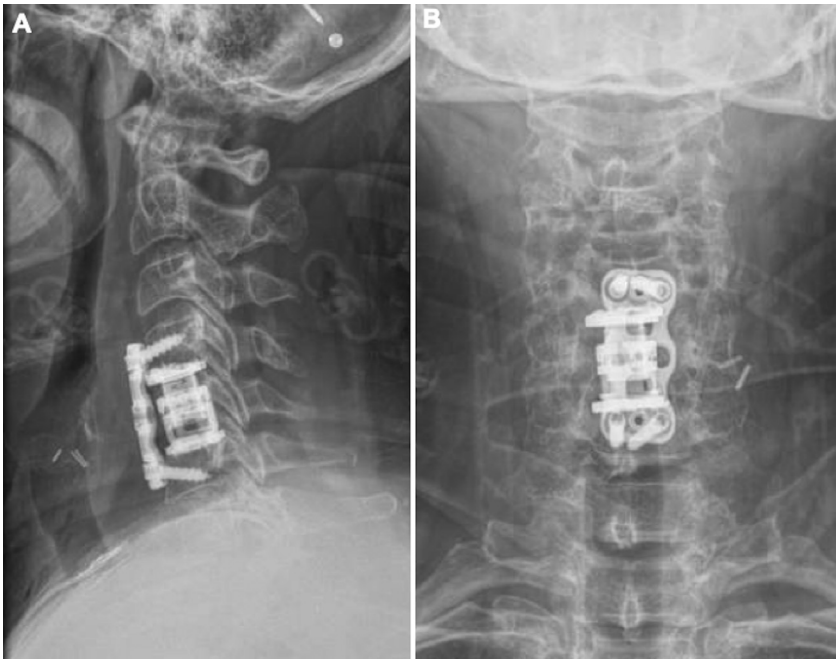

Fig. 6. Panel A shows the lateral and Panel B shows the AP postoperative radiographs showing good position of the implants after a C5 corpectomy, C4–5 and C5–6 discectomy and fusion with cage placement.

and/or poor bone quality. This was addressed with segmental posterior fixation. As compared to the case presented by Takigawa et al. [42], our patient did not have as extensive involvement and kyphotic deformity. However, given the multifocal nature of SAPHO syndrome and in patients with poor bone quality, strong consideration should be given to primary anterior and posterior fixation in patients presenting with similar findings. Although the patients presented in these reports are older and could have poor bone quality, which would put them at risk for vertebral fractures and subsequent deformity, Li et al. [39] present the case of a 29 year old female with SAPHO syndrome presenting with multiple compression deformities of thoracic and lumbar vertebrae secondary to the syndrome.

There are no guidelines for the treatment of SAPHO syndrome, mainly due to the rarity of this condition [37]. Conventional treatments, including non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, antibiotics, bisphosphonates, and disease-modifying anti-

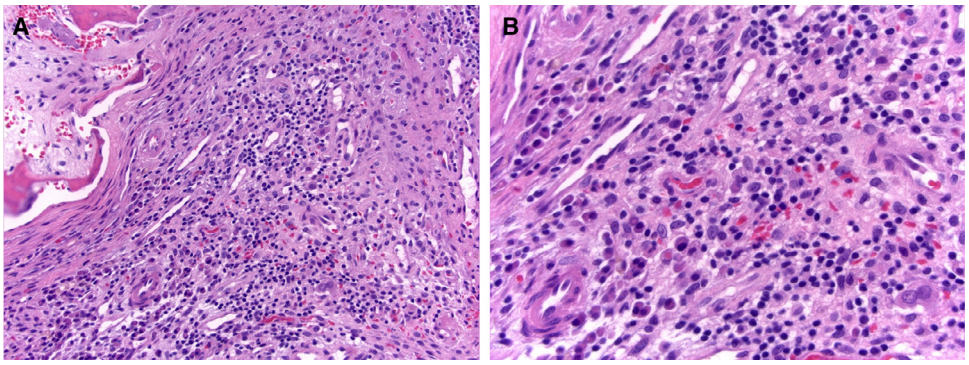

Fig. 7. Panel A shows an hematoxylin and eosin (H&E) stain at 200× of magnification demonstrating reactive bone on the left superior corner, with fibrosis and mixed inflammation. Panel B shows an H&E stain at 400× of magnification demonstrating a mixture of plasma cells and lymphocytes, with few intermixed histiocytes.

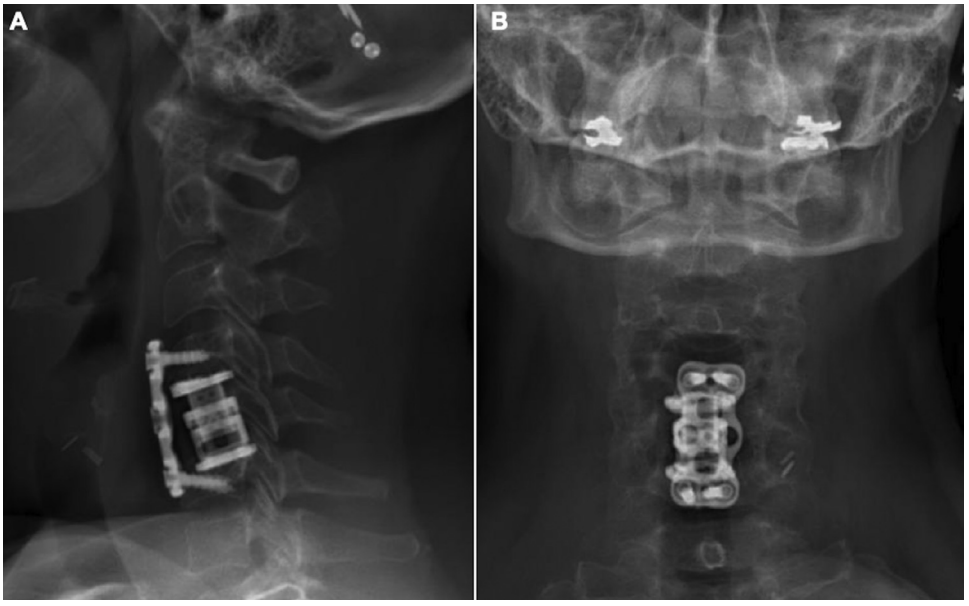

Fig. 8. Panel A shows the lateral and Panel B shows the AP 8-week postoperative radiographs showing posterior migration of the interbody cage along with compression of the C6 superior endplate.

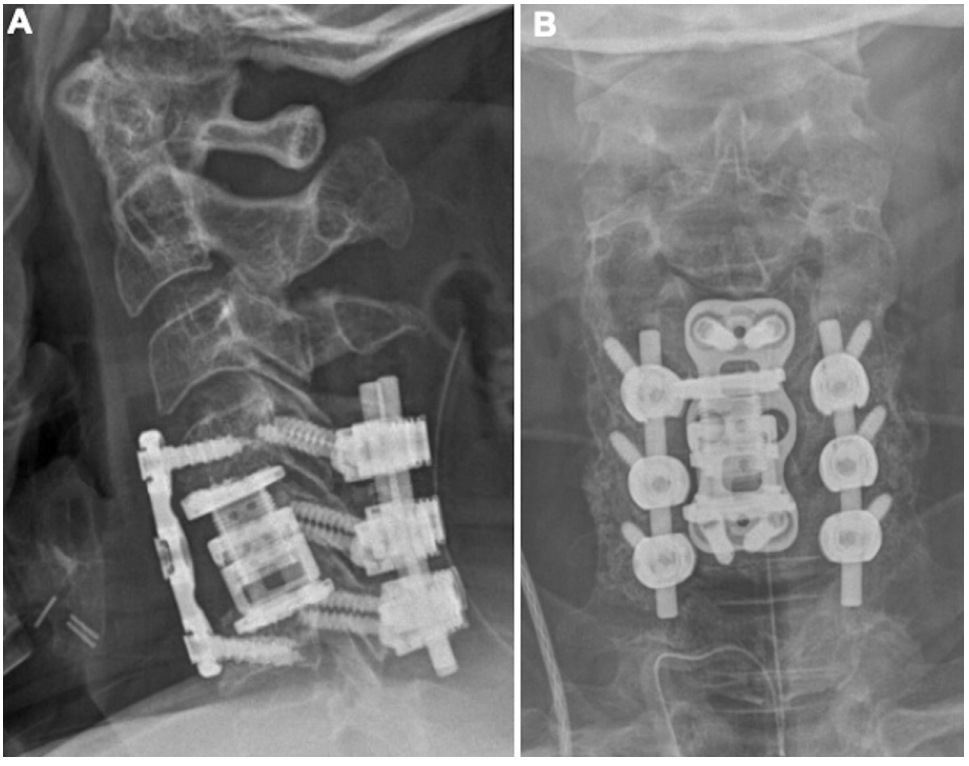

Fig. 9. Panel A shows the lateral and Panel B shows AP postoperative radiographs showing no change of the implants after posterior C4–6 instrumentation and fusion.

rheumatic drugs (DMARDs) have yielded suboptimal results [14,43]. Newer agents, like anti-tumor necrosis factor-alpha (anti-TNF- α) and interleukin-1 (IL-1) antagonists have shown promising results. Despite these newer drug modalities, some patients develop refractory conditions and a positive response is unable to be achieved [44,45]. Most current recommendations still suggest starting treatment with conventional treatments including NSAIDs, corticosteroids, and conventional DMARDs (Methotrexate, Azathioprine, etc.) with early addition of biologic agents (Infliximab, Adalimumab, etc.) in patients with no response or incomplete response to the conventional treatment [45,46]. Timely treatment should theoretically decrease the risk for further spondylitis, vertebral fractures, and subsequent deformity although there is still no evidence to support this.

Conclusion

The presentation of SAPHO syndrome can be highly variable which makes it difficult to diagnose in a timely manner. The most common presentations of SAPHO syndrome involving the spine can mimic infection and neoplasia and these conditions should always be ruled out. A timely diagnosis is paramount as appropriate treatment has the best chance to achieve clinical remission.

Statements

This is an original manuscript, to our knowledge there are no prior or duplicate versions of this manuscript that have been published or are in submission at other journals.

All authors have read and agree with this manuscript in its entirety.

There are no conflicts of interest with the authors concerning the context of this manuscript.

No funding was received from any entity in association with this study.

Patient informed consent

The authors declare that informed patient consent was not provided for the following reason: This retrospective study on coded data was exempt by the regional ethics board from seeking informed consent from patients without general consent or dissent.

Declarations of Competing Interests

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.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.xnsj.2021.100050.

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