SAPHO syndrome with rapidly progressing destructive spondylitis: two cases treated surgically

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Abstract The authors present two cases of synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome with rapidly progressing destructive spondylitis treated surgically. The spinal lesions in SAPHO syndrome generally have a good prognosis and rarely cause the structural destruction or neurological deterioration. Case 1: a 63-year-old female had palmoplantar pustulosis for 2 years. At first, she only felt a pain in the nape with no inducing factor. Two months later, she had incomplete quadriplegia (ASIA scale C). Magnetic resonance imaging showed destruction of C4–C7, kyphotic deformity, and severe compression of the spinal cord. Decompression and reconstruction surgery using anterior and posterior approach improved her paralysis. Case 2: a 69-year-old female complained of persistent back pain. Magnetic resonance imaging revealed spondylitis of T7–T9. Although there were no typical skin lesions, we diagnosed SAPHO syndrome by hyperostosis of the sternocostoclavicular joint and sacral joint. Destruction with kyphotic deformity of the spine progressed gradually for 3 months. Curettage and reconstruction surgery using thoracic endoscope relieved her pain and prevented the destruction of the spine. The histopathology of the specimen obtained surgically showed non-specific inflammation in both cases. Spondylitis in

SAPHO syndrome may cause severe destruction and kyphotic deformity followed by paralysis.

Keywords SAPHO syndrome · Spondylitis · Paralysis

Introduction

In 1987, Chamot et al. [1] suggested the concept of synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome to describe a number of peculiar bone, joint and skin lesions. SAPHO syndrome is defined as the presence of any one of the following four: osteoarticular manifestation of severe acne, osteoarticular manifestation of palmoplantar pustulosis (PPP), hyperostosis, or chronic recurrent multifocal osteomyelitis. The following osteoarticular features should be excluded: infectious disease, diffuse idiopathic skeletal hyperostosis (DISH), and osteoarticular manifestations of retinoid therapy [7]. The sternocostoclavicular lesion is the most frequent site of the disease (63–90%), followed by the sacroiliac joint (40–52%) and the spine (33–52%) [7, 12, 17]. The spinal lesions in SAPHO syndrome generally have a good prognosis and rarely cause neurological deterioration [17]. SAPHO syndrome is well known to dermatologists and rheumatologists, but not to neurosurgeons and orthopaedic surgeons. We report two cases of SAPHO syndrome with rapidly progressing destructive spondylitis treated surgically.

Case 1

A 63-year-old female had PPP from 61 years old presented at first with a pain in her nape with no inducing factor.

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Conservative treatment could not improve her pain. Then hypesthesia and muscle weakness of her upper arm, mainly on the right side, appeared and worsened. She was admitted and underwent treatment for pyogenic spondylitis in another hospital. Two months later, she was unable to walk. Since her paralysis did not improve, but rather got gradually worse, she consulted our hospital. When she consulted to our hospital, she had incomplete quadriplegia (ASIA scale C). The area of hypesthesia and muscle weakness spread under C5 neural level. She had had no fever up in this course. C-reactive protein was 0.67 mg/dL and erythrocyte sedimentation rate was 31 mm/h, which indicated slight inflammatory reaction. Other laboratory data were normal including a tumor marker. Xp showed destruction of cervical spine through C4–C7 and kyphotic deformity (Fig. 1). MRI showed severe destruction of vertebrae from C4 to C7 and severe compression of the spinal cord (Fig. 2). The posterior elements showed abnormal signal intensity and the anterior ligament thickened. Also, abnormal signal intensity was detected in inferior anterior part of the T5 vertebra and superior anterior part of the T6 vertebra. For diagnosis and decompression, we performed the operation 3 months after her first symptom appeared. The spinal cord was decompressed using the anterior approach. A discectomy was performed on C3/4, C4/5, C5/6, and C6/7, and then a spondylectomy was performed on C4, C5, and C6. We resected the median parts of these vertebrae and the lateral parts were left intact. These discs were fragile and the anterior parts of these vertebrae were almost completely destroyed. Adhesion between the lesion site and the dura matter was not so severe. We distracted C3 and C7 vertebral body using a vertebral distractor to correct the spinal

alignment with the aid of a fluoroscope. After the deformity was corrected, we reconstructed the spine using autologous iliac bone and a plate. Simultaneously, posterior stabilization from C3 to C7 using wavy wire with facet fusion was performed. As for the specimens obtained surgically, culture was sterile and histopathology demonstrated no malignant cells but many infiltrated cells, which were mainly lymphocytes. Postoperative ^{99m}Tc bone scintigraphy showed abnormal high uptake of sternocostoclavicular joint, sacroiliac joint, bilateral wrist joints, and vertebrae of L4 and L5 in addition to middle thoracic and the operated cervical spine. After the pathological analysis and the bone scintigraphy examination, the diagnosis of SAPHO syndrome was made from her typical skin lesion and multifocal osteoarticular lesion, including the spine. Postoperatively, she was able to walk with one cane with slight spasticity. Approximately 1 year after the operation, bony fusion was achieved and all the implants were removed. At the time of the final follow-up, 2 years and 3 months later, the patient's sensory disturbance had considerably decreased, with only a slight hypesthesia on her right hand remaining.

Case 2

A 69-year-old female felt back pain with no inducing factor. Conservative treatment did not improve her pain. Her spinal MRI demonstrated spondylitis of T7–T9 and a spinal tumor at the T12 level. She consulted our hospital. A detailed medical interview revealed her past history of medication for sternoclavicular arthritis at age 64 years. She suffered from keratosis diagnosed by a dermatologist in both hands

Fig. 1 Case 1: **a** Preoperative Xp showing destruction of C4–7 and kyphotic deformity, **b** postoperative XP showing posterior decompression and reconstruction using wavy wire, and anterior reconstruction using autologous iliac bone and plate

Fig. 2 Case 1: **a** T1 weighted image showing low signal intensity, **b** T2 weighted image showing severe compression of the spinal cord. Not only the C4–7 vertebrae but also their posterior elements show abnormal signal intensity

for more than 10 years. At first examination, she had no abnormal neural sign with her severe back pain. Her body temperature was 36.1°C. The laboratory examination demonstrated only slight inflammatory reaction. C-reactive protein was 2.52 mg/dL, WBC was 4,560/μl, erythrocyte sedimentation rate was 32 mm/h. Blood culture, tumor marker, PCR of tubercle bacillus, and β -D-glucane were all negative. MRI showed compressed vertebrae at T7, 8, and 9 and kyphotic deformity with the center of collapsed T8 vertebra (Fig. 3). These compressed vertebrae showed abnormal irregular intensity with T1 low signal, T2 iso-high irregular, and contrast enhancement. Abnormal signal intensity could be seen in the anterior part of T10 and T11 vertebrae. There was an oval tumor posterior of the spinal cord at T12 level with contrast enhancement. Sagittal CT view demonstrated severe destruction with marginal

sclerosis at T7 and T8 vertebra (Fig. 4). Irregular sclerotic change existed through the T9 vertebra to T11, accompanied with erosive change at each end plate. The disc heights at these levels were decreased. To make a diagnosis, we performed CT-guided biopsy of the T8 vertebra where the destruction was the most severe 1 month after her first symptom appeared. Histopathology demonstrated only non-specific inflammation; culture of this specimen was negative. Prophylactically we administered antibiotics in case the amount of specimen might be insufficient or the spot of biopsy might be inappropriate. We treated her back pain conservatively with non-steroidal anti-inflammatory drugs and body brace. ^{99m}Tc bone scintigraphy, which was performed to evaluate the extent of the lesion, showed abnormal high uptake in bilateral sternocostoclavicular joint and bilateral sacroiliac joint in addition to destructive

Fig. 3 Case 2: **a** T1 weighted image, **b** T2 weighted image, **c** T1 weighted, fat suppression, gadolinium enhanced image. Images show the compressed vertebrae of T7, 8, and 9 and kyphotic deformity with the center of collapsed T8 vertebra. These compressed vertebrae show abnormal irregular intensity with T1 low signal, T2 iso-high irregular, and contrast enhancement. Abnormal signal intensity can be seen in the anterior part of T10 and T11 vertebrae

Fig. 4 Case 2: **a** Preoperative sagittal CT image showing lytic change with marginal sclerosis mainly at T7 and T8 vertebra. Irregular sclerotic change in vertebrae exists through T9–T11, accompanied with erosive change at each end plate. Disc height of T8/9, T9/10, and T10/11 is decreased. **b** Postoperative sagittal CT image showing curettage of the destroyed vertebrae of T7 and T8, and reconstruction using autologous iliac bone

thoracic spine (Fig 5a). CT examination demonstrated hyperostosis in the sternocostoclavicular joint and sacroiliac joint. Her back pain persisted and kyphotic deformity progressed gradually for 2 months after our first examination. For definite diagnosis and prevention of progression of destruction, we performed an operation 3 months after her first symptoms appeared. We used an anterior approach with a thoracic endoscope in order to execute a less invasive

surgery and to identify the specimen definitely. The pleura, the anterior longitudinal ligament, and the periosteum were adhered at the lesion level. In the vertebral lesions, lytic fragile parts and sclerotic hard parts were mixed. We curetted the lesion as much as possible, and reconstructed it with the autologous iliac bone. The histopathology of the specimen obtained surgically showed non-specific osteomyelitis that was an infiltration of inflammatory cells and

Fig. 5 Case 2: **a** ^{99m}Tc bone scintigraphy showing abnormal uptake of sternocostoclavicular joint and sacroiliac joint in addition to thoracic spine. **b** Axial CT image showing hyperostosis and arthropathy of the sternoclavicular joint. **c** Axial CT image showing sacroilitis with erosion and osteosclerosis

Fig. 6 Case 2: HE staining of the curetted vertebra. It shows infiltration of inflammatory cells mainly lymphocyte and abnormal fibrous hypertrophy among the trabecular bone

abnormal fibrous hypertrophy among the trabecular bone (Fig. 6). There were neither atypical cells nor bacteria and the culture was sterile, and PCR for tuberculosis was negative. Although there were no typical skin lesions, we diagnosed SAPHO syndrome based on the examination of hyperostosis of the sternocostoclavicular joint and sacroiliac joint, and non-specific osteomyelitis of the thoracic spine. We thought the spinal tumor at the T12 level was a neurinoma unrelated to the upper T7–11 lesion. And a careful follow-up was planned. We planned a second stage operation to stabilize the spine posteriorly if her kyphotic deformity progressed. However, up to the time of the final follow-up, 1 year and 7 months after the operation, the kyphotic deformity had not progressed severely. Though she sometimes complained of back pain, there were no neurological symptoms.

Discussion

Two types of skin disease, PPP and acne, are included in the diagnostic criteria of SAPHO syndrome [1]. However, it is possible to diagnose SAPHO syndrome with specific osteoarthritic manifestation without skin manifestation like in case 2. Hayem et al. [7] analyzed 120 patients with SAPHO syndrome. They reported that the skin lesion was found to be PPP in 55% of the patients, severe acne in 25%, and nothing in 16%. They also reported that the first skin manifestation antedated the first osteoarthritic manifestation in 39%, whereas the opposite occurred in 32%, skin and osteoarthritic manifestations developed simultaneously in 29% [7]. Kahn et al. [9] described two cases of SAPHO syndrome in which more than a 20-year interval existed between the onset of skin lesion and the bone involvement. Taking into account a detailed medical history, especially past symptoms such as skin trouble or anterior chest wall pain, can sometimes be useful in diagnosing SAPHO syndrome.

The MRI features of spondylitis of SAPHO syndrome are as follows: the lesions begin at vertebral end plates [4] or enthesis and related tissues [12], spread through the vertebral corner [11], and rarely invade the disc [10]. Normally this progress of the lesion is very slow. However, when this progress is very rapid, as in these two cases, the MRI features of SAPHO syndrome become vague. It becomes very difficult to make a diagnosis with MRI only. On the other hand, SAPHO syndrome is an inflammatory disease whose main targets are bone and joint. ^{99m}Tc bone scintigraphy is most useful to evaluate the area of lesions. In these two cases, ^{99m}Tc bone scintigraphy demonstrated a typical pattern of SAPHO syndrome, which helped us to make the diagnosis. Diagnosis of SAPHO syndrome is based on exclusion of various manifestations, such as infectious diseases, tumorous diseases (e.g., metastatic tumor, sarcoma, or lymphoma), DISH, and retinoid therapy related manifestations. However, the accuracy rate of CT-guided biopsy for spinal infections or tumors is only about 70% [14]. Takeuchi et al. [15] reported that [(18)F]fluorodeoxyglucose positron emission tomography was useful for differentiating from multiple metastatic bone tumors. Court et al. [2] described a case of a SAPHO syndrome in which percutaneous biopsies and thoracoscopic biopsies were needed to be done two times to make the final diagnosis. When a result of biopsy is negative and a typical lesion of SAPHO syndrome, like hyperostosis or skin manifestation is absent, only the disease course may make it possible to diagnose SAPHO syndrome.

Lesions were found to be more advanced in the anterior parts than the posterior parts of the vertebral body in these cases. Adhesion to the related tissues was also more severe in front of the vertebrae. These surgical aspects of spinal pathology correspond to past studies, which suspected the main spinal lesions of SAPHO syndrome would be in the enthesis and related tissues [12] or the anterior vertebral corner [11]. Spinal lesions were very fragile, resembling somewhat the spinal pathology of rheumatoid arthritis.

However, unlike rheumatoid arthritis, these lesions included some sclerotic hard parts. There was no incidence of pus, like that found in pyogenic spondylitis, nor a tendency to bleed, such as found in metastatic spinal tumor.

Because the spondylitis of SAPHO syndrome has an insidious onset and repeated recurrence and remission, lesions progress accompanied with marginal sclerosis. So the structural destruction of the spine in SAPHO syndrome is very rare. If the speed of destruction by inflammation is faster than that of sclerotic reaction, the spinal structure would break. In case 2, vertebral collapse got worse rapidly in about 3 months, and reconstruction surgery was needed. We strongly suspected spondylitis related SAPHO syndrome, because preoperative CT-guided biopsy showed negative results for metastatic tumor or infection. Also, preoperative bone scintigraphy showed typical high uptake in the sternocostoclavicular joint and sacral joint, which was reflected by hyperostosis. However, we performed a curative and diagnostic operation because of the following: her worsening destructive kyphotic deformity, the possibility that the amount of biopsy might not be sufficient to make a definite diagnosis, or that the causative species were not detected in normal culture, such as attenuated virulent species, e.g., fungus or atypical mycobacterium, and the absence of typical skin lesion of SAPHO such as pustulosis or acne. Due to the possibility of pyogenic spondylitis and the unnecessary of spinal alignment correction, it was decided that autologous bone graft without any instrumentation would be adequate. As she had no neurological symptom other than back pain, we might have treated her conservatively for a while. In the Japanese language literature, Fujii et al. [5] reported a case of SAPHO syndrome with paraplegia due to progressive kyphosis of 7 years. Moreover, Hitachi et al. [8] reported an autopsy case of SAPHO syndrome in which the patient died of respiratory failure. Progression of kyphotic deformity and expansion restriction of 17 years induced respiratory impairment and failure [8]. It has not been clarified when the reconstructive operation should be done.

There are only a few reports of SAPHO syndrome with neurological deficit. In the English language literature, Deltombe et al. [3], reported a case of SAPHO syndrome with an ankylosed spine disclosed by cervical spinal cord injury. Mulleman et al. [13] reported a case of right upper limb paresis due to ossification of the posterior longitudinal ligament of the cervical spine with SAPHO syndrome. In the Japanese language literature, there are two papers including the case report described above [5] and our report of case 1 [16]. In the French language literature, Gedouin et al. [6] reported a case of progressive paralysis in an 11-year-old girl with chronic recurrent multifocal osteomyelitis included in SAPHO syndrome. To our knowledge, case 1 is the first report of rapidly progressing quadriplegia

within 3 months without trauma. We performed a radical operation with an anterior and posterior approach because the spinal lesion with kyphotic deformity was severe and wide through C4–C7. In the posterior approach, a more rigid system such as lateral mass or pedicle screws might be more suitable to achieve rigid stability. However, due to our limited experience in using such cervical screws at that time, we opted to use wavy wire as well as facet fusion. Her paralysis improved by early decompression and reconstruction surgery, and she was able to walk with one cane.

In conclusion, spondylitis in SAPHO syndrome may cause severe destruction and kyphotic deformity followed by paralysis. Clinicians should know that SAPHO syndrome is one of the differential diagnoses of the destructive spondylitis.

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References

1. Chamot AM, Benhamou CL, Kahn MF, Beraneck L, Kaplan G, Prost A (1987) Acne-pustulosis-hyperostosis-osteitis syndrome. Results of a national survey. 85 cases. *Rev Rhum Mal Osteoartic* 54:187–196
2. Court C, Charlez C, Molina V, Clerc D, Miquel A, Nordin JY (2005) Isolated thoracic spine lesion: is this the presentation of a SAPHO syndrome? A case report. *Eur Spine J* 14:711–715
3. Deltombe T, Nisolle JF, Boutsen Y, Gustin T, Gilliard C, Hanson P (1999) Cervical spinal cord injury in sapho syndrome. *Spinal Cord* 37:301–304
4. Earwaker JW, Cotten A (2003) SAPHO: syndrome or concept? Imaging findings. *Skeletal Radiol* 32:311–327
5. Fujii T, Matsudaira K, Oda H, Seichi A, Nakamura K (2002) A case of SAPHO syndrome with paraplegia due to a thoracic kyphosis. *Ryumachi* 42:687–693
6. Gedouin JE, Violas P, Chapuis M, Bracq H (2001) Stiff painful spine in an 11-year-old girl with SAPHO syndrome. *Rev Chir Orthop Reparatrice Appar Mot* 87:830–834
7. Hayem G, Bouchaud-Chabot A, Benali K, Roux S, Palazzo E, Silbermann-Hoffman O, Kahn MF, Meyer O (1999) SAPHO syndrome: a long-term follow-up study of 120 cases. *Semin Arthritis Rheum* 29:159–171
8. Hitachi K, Yazawa Y, Suehara Y, Inoue H (2004) SAPHO (synovitis-acne-pustulosis hyperostosis-osteitis) syndrome; a report of autopsy case. *Seikei Geka* 55:159–162
9. Kahn MF, Bouvier M, Palazzo E, Tebib JG, Colson F (1991) Sternoclavicular pustulotic osteitis (SAPHO). 20-year interval between skin and bone lesions. *J Rheumatol* 18:1104–1108
10. Kayani I, Syed I, Saifuddin A, Green R, MacSweeney F (2004) Vertebral osteomyelitis without disc involvement. *Clin Radiol* 59:881–891
11. Laredo JD, Vuillemin-Bodaghi V, Boutry N, Cotten A, Parlier-Cuau C (2007) SAPHO syndrome: MR appearance of vertebral involvement. *Radiology* 242:825–831
12. Maugars Y, Berthelot JM, Ducloux JM, Prost A (1995) SAPHO syndrome: a follow-up study of 19 cases with special emphasis on enthesitis involvement. *J Rheumatol* 22:2135–2141

13. Mulleman D, Mammou S, Griffoul I, Goupille P, Valat JP (2005) Ossification of the posterior longitudinal ligament of the cervical spine and SAPHO syndrome. *J Rheumatol* 32:1361–1364
14. Sucu HK, Çiçek C, Rezanko T, Bezircioğlu H, Erşahin Y, Tunakan M, Minoğlu M (2006) Percutaneous computed-tomography-guided biopsy of the spine: 229 procedures. *Joint Bone Spine* 73:532–537
15. Takeuchi K, Matsusita M, Takagishi K (2007) A case of SAPHO (synovitis-acne-pustulosis-hyperostosis-osteomyelitis) syndrome in which [(18)F]fluorodeoxyglucose positron emission tomography was useful for differentiating from multiple metastatic bone tumors. *Mod Rheumatol* 17:67–71
16. Takigawa T, Sugimoto Y, Ikuma H, Masato T, Hashizume H (2005) Four cases of spondylitis with palmoplantar pustulosis. *Cent Jpn J Orthop Traumatol* 48:1053–1054
17. Toussiro E, Dupond JL, Wendling D (1997) Spondylodiscitis in SAPHO syndrome. A series of eight cases. *Ann Rheum Dis* 56:52–58