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GRAND ROUNDS

Rheumatoid arthritis-associated spinal neuroarthropathy with double-level isthmic spondylolisthesis

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Abstract

Introduction To the best of our knowledge, there has been no report regarding rheumatoid arthritis associated with spinal neuroarthropathy and combined double-level isthmic spondylolisthesis. Here, we report a rare case of spinal neuroarthropathy with double-level isthmic spondylolisthesis in a rheumatoid arthritis (RA) patient.
Case summary A 56-year-old female patient under medical treatment for RA during the last 13 years presented aggravating radiating pain to her right lower extremity and a limping gait developed 4 months ago. The disease activity of RA had remained low for a long time. Serial radiographs during last 8-year follow-up showed progressive dislocation at L4–L5 and L5–S1 with double-level isthmic spondylolisthesis and severe destructive status at the last follow-up. The patient underwent decompression and circumferential fusion with sacropelvic fixation and acceptable reduction was obtained.
Conclusion A RA patient with double-level isthmic spondylolisthesis showed a progressive destructive lesion. In addition to clinical presentations, the imaging findings were very similar to ones of spinal neuroarthropathy. The authors conclude that this Grand Round case probably had SNA secondary to RA and that this, combined with two-level isthmic spondylolisthesis, resulted in her rapidly progressing destructive lumbar lesion.

Keywords Rheumatoid arthritis · Spine · Charcot · Neuroarthropathy · Double-level · Isthmic spondylolisthesis

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Case presentation

Eight years ago, the patient visited our institute for mild low back pain and radiating pain to right lower extremity lasting 1 year. Visual analog scale (VAS) for back pain was 3 and VAS for leg pain was 2. She had been diagnosed with RA 5 years before the first visit to our spine center. At the time of diagnosis, serum rheumatoid factor had increased to 35.1 IU/mL (reference: <15.0) but C-reactive protein (CRP) was within the normal range. She has been undergoing medical treatment with methotrexate and methylprednisolone. She had no other diseases including diabetes mellitus. Initial lumbar spine radiographs showed double-level isthmic spondylolisthesis at L4–L5 and L5–S1 and suboptimal coronal imbalance (Figs. 1a, 2a). Because the symptoms were tolerable, she underwent conservative treatment and annual follow-ups were recommended.

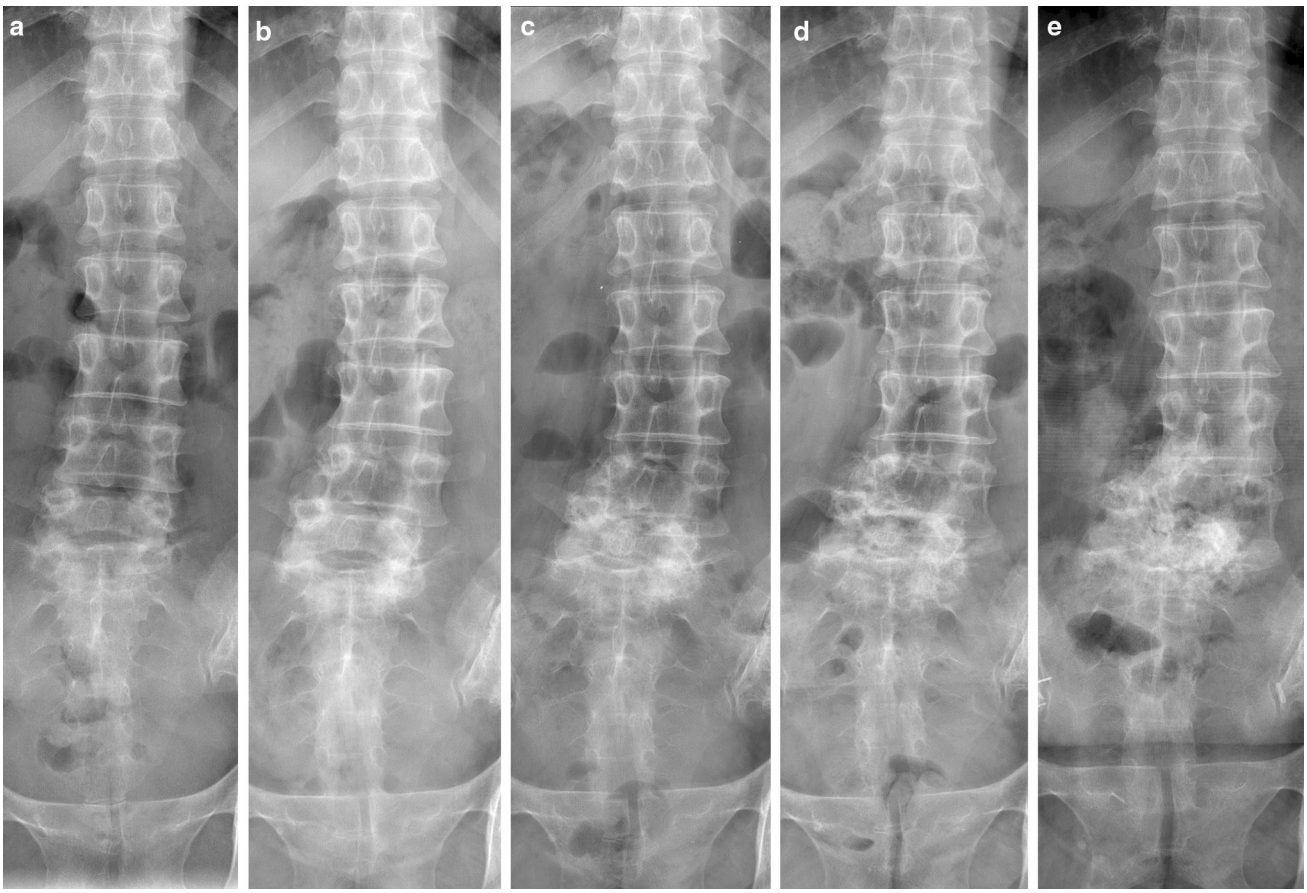

Fig. 1 Serial anteroposterior lumbar radiographs show progressive dislocation at L4–5 and L5–S1. **a** At initial visit 8 years before surgery, **b** 5 years before surgery, **c** 3 years before surgery, **d** 2 years before surgery, and **e** at the time of surgery

After 1 year from the initial visit, the back pain and radiating pain remained. On the follow-up radiographs, intervertebral disc space narrowing and lateral translation progressed (Figs. 1b–d, 2b–d). On the laboratory examination, erythrocyte sedimentation rate (ESR) and CRP were within the normal limit. The author recommended surgical treatment because of progression of spondylolisthesis, but the patient refused it due to little pain and a fear of surgery. Thereafter, she presented minimal back pain and radiating pain (VAS 1–2) consistently during the following 8 years, although radiographs showed gradual progression of dislocation and collapse at L4–L5 and L5–S1.

At the age of 56, she presented right buttock pain and radiation to right lower extremity lasting 4 months (VAS 6). She also showed neurogenic claudication and a limping gait by weakness of the right lower extremity. Radiographs showed severe destructive dislocation and collapse at L4–L5 and L5–S1 (Figs. 1e, 2e). ESR and CRP were kept within normal limit constantly. At this time, her simple disease activity index for RA was 4.1, which meant low disease activity [1]. She showed destruction at both wrist joints. Also, symptomless basilar impression was identified incidentally. Computed tomography (CT) showed intervertebral vacuum phenomenon and severe destruction of the entire endplates (Fig. 3). Magnetic resonance imaging (MRI) showed endplate destruction, intradiscal gas, facet involvement, and concomitant spinal stenosis (Fig. 4). Serologic test showed no evidence of syphilis.

Historical review of the condition, diagnosis, pathology

Spinal neuroarthropathy (SNA), also known as neuropathic spinal arthropathy and Charcot spine, is an uncommon condition defined as an aseptic and rapidly progressive destruction of the spine following the loss of innervation for any reason. This process damages the disc, endplate, and facet joints and can result in dislocation of the spine like our case. The final status is severe destruction, collapse, and instability of the involved segment [2]. Neuropathic joint destruction was first described by Charcot as a feature of tertiary syphilis, though the main cause today is diabetes [2, 3], while other causes include syringomyelia,

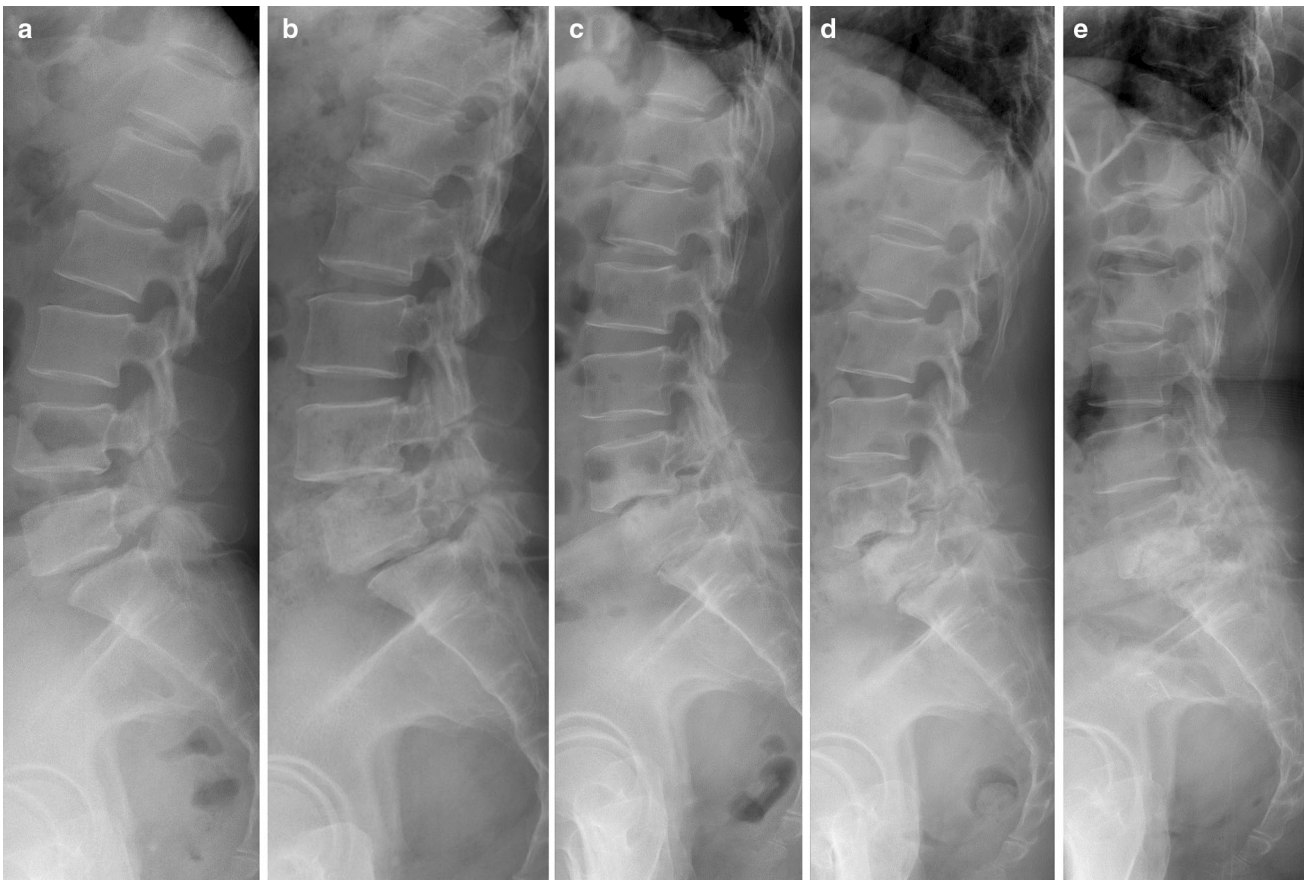

Fig. 2 Serial lateral lumbar radiographs show progressive endplate destruction and collapse of the intervertebral disc space. **a** Double-level isthmic spondylolisthesis at L4–5 and L5–S1 at initial visit 8 years before surgery, **b** 5 years before surgery, **c** 3 years before surgery, **d** 2 years before surgery, and **e** at the time of surgery

congenital pain insensitivity, and Guillain–Barré syndrome [4–6]. The diagnosis is based primarily on past history and imaging studies, however, the need to differentiate it from other diseases including spondylodiscitis, metastasis, or hemodialysis-induced destructive spondyloarthropathy might sometimes cause pathological examinations.

Neuropathic joints in patients with syphilis were described first by Charcot in nineteenth century. Appendicular joints are affected more commonly, however, an axial arthropathy were rarely reported since the first report in a patients with diabetes by Kronig [7].

Brower et al. reported two theories about the pathogenesis of the neuropathic joint: one, neurotraumatic and the second, neurovascular [8]. The former is that neuropathic joints come from loss of proprioception, which hinders protective function of paraspinal muscles against stress on the spine. Repeated microtrauma accumulates in the unprotected mobile joints and causes instability. This creates a vicious cycle eventually leading to destruction of joints. This excessive mobility is likely to occur adjacent to fixed segments. This is why SNA usually develops in the thoracolumbar or lumbosacral junction [7]. In this case, SNA developed in the lumbosacral junction with double-level isthmic spondylolisthesis, in which its intrinsic instability aggravated.

According to the neurovascular theory, loss of autonomic regulation of joints induces hyperemia and excessive inflammation through release of proinflammatory cytokines [9]. This results in osteoclast activation leading to osteolysis [9]. Both neurotraumatic and neurovascular pathomechanisms operate at the intervertebral articulation, causing progressive destruction of discovertebral and facet joints.

SNA is mainly associated with paraplegia from spinal cord injury, neurosyphilis, diabetes mellitus, and congenital insensitivity to pain. However, it was reported that RA might also induce peripheral neuropathy. Electrophysiological assessment shows that sensory and sensorimotor neuropathy are quite common (17–57%) in RA [10]. RA has a pathophysiology associated with proinflammatory cytokines [11]. Recent studies showed that proinflammatory cytokines, such as TNF-α and IL-1, have osteoclastogenic effects and are responsible for cytokine-mediated bone destruction in RA [12]. It seems that RA and SNA

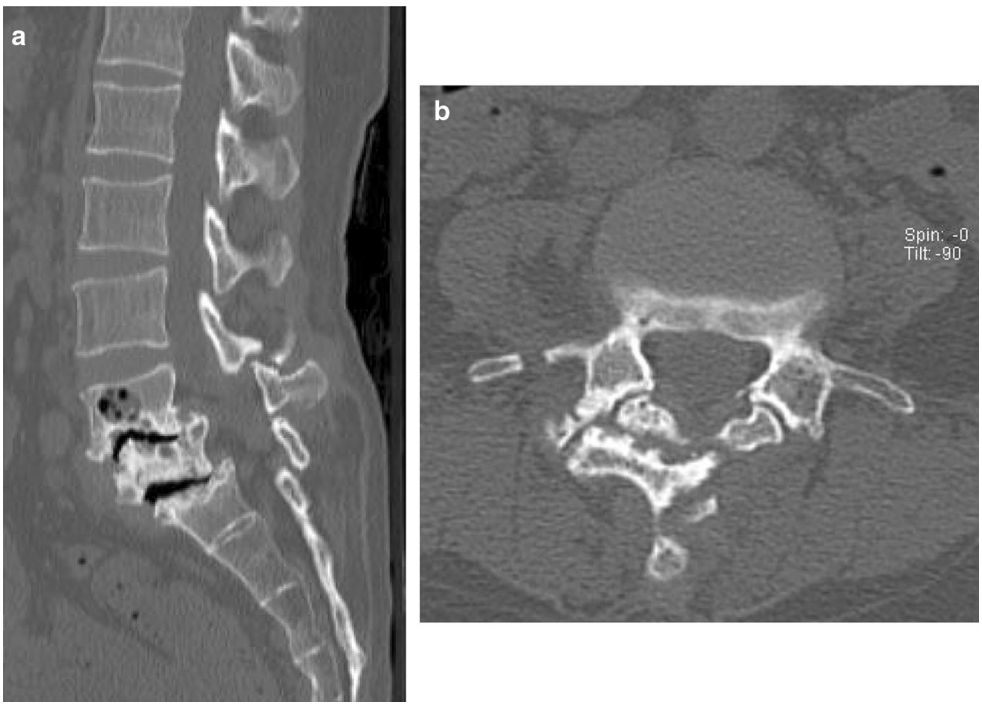

Fig. 3 Computed tomography with sagittal (**a**) and axial (**b**) scans shows intradiscal vacuum and destruction of endplates and facet joints

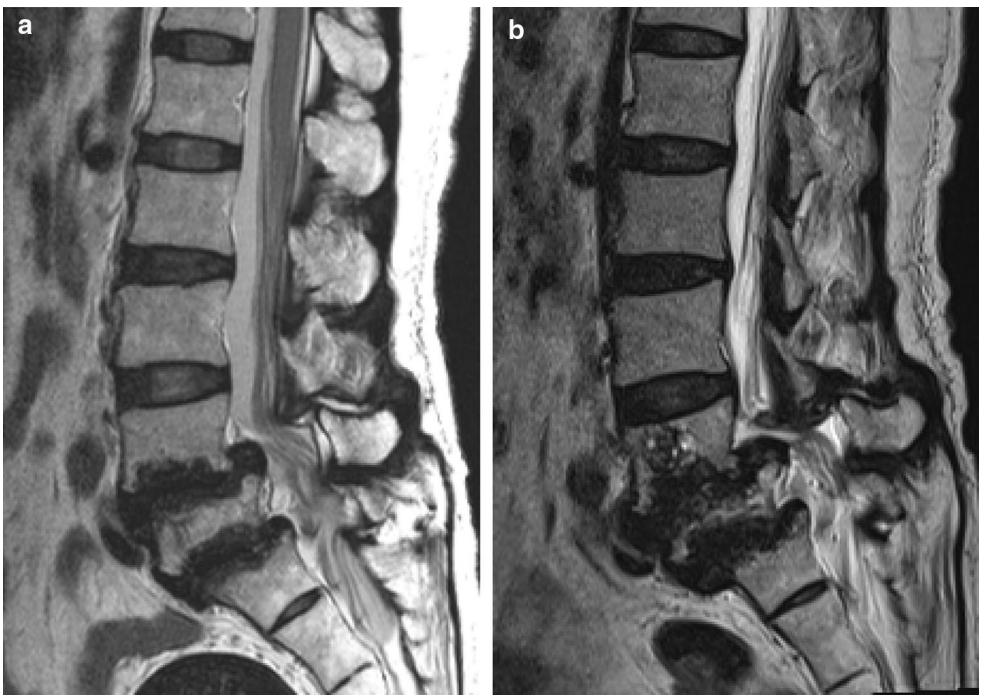

Fig. 4 Two MRIs with a 2-year interval show progression of destruction of endplates and disorganization of joints: **a** 2 years before surgery, and **b** at the time of surgery

with regard to the neurovascular theory share inflammatory pathophysiology.

Imaging studies for SNA are important for differentiation from other diseases. Typical findings of neuropathic joint are "six D's": distension, density, debris, disorganization, dislocation, and destruction [13]. However, most of such findings in SNA are nonspecific and appear at the later stage. The imaging findings suggestive of SNA are

intradiscal vacuum, bone debris, joint disorganization (spondylolisthesis and dislocation) [13]. CT and MRI can help differentiate SNA from other diseases including infection. Gadolinium enhancement in the periphery of the disc and diffusely in the vertebral bodies is suggestive of SNA, whereas the signal abnormalities are usually confined to the endplates in infection [13, 14]. Another important discriminator from infection is facet joint destruction in SNA [13, 14].

Rationale for treatment

The treatment goal of SNA is to make unstable segments stable and to resolve neurologic symptoms. Long-term data of surgical management showed development of junctional SNA and late breakdown and a high rate of revision surgery [15, 16]. Meanwhile, Moreau et al. reported that the natural evolution of SNA could be less disabling than surgery and conservative treatment should be also considered [17]. However, surgical treatment is generally recommended and solid fusion has shown favorable outcomes [2, 18, 19]. To achieve solid circumferential fusion, three-column fixation with extensive debridement, bone grafting, and sacropelvic fixation is necessary [15, 16, 18, 19].

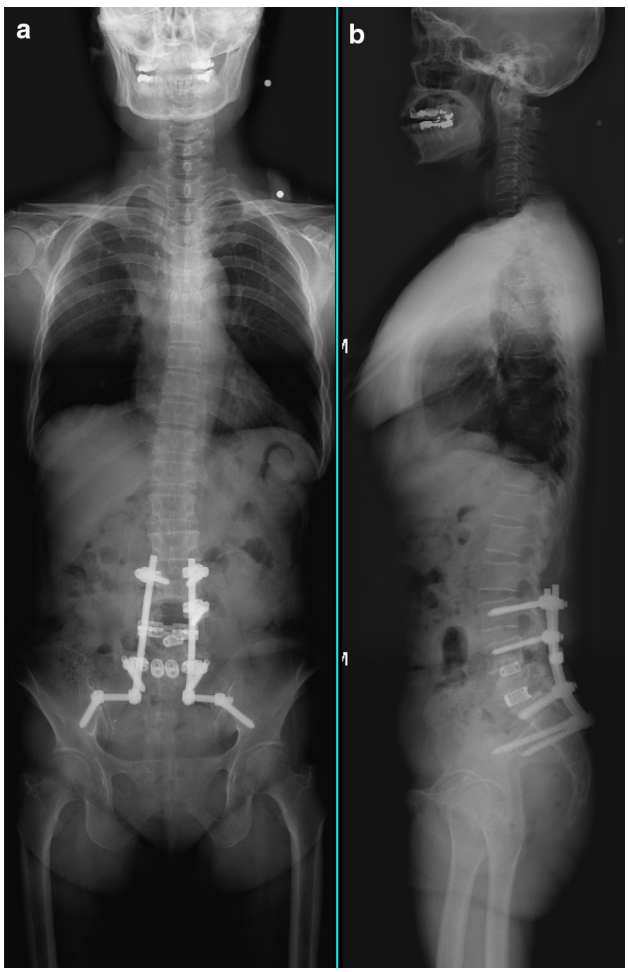

Fig. 5 Laminectomy, posterior pedicle fixation and posterior lumbar interbody fusion with sacropelvic fixation were performed. Postoperative anteroposterior (**a**) and lateral (**b**) plain radiographs of whole spine show acceptable reduction

Surgery

The patient underwent decompression and posterior screw fixation at L3–S1 with posterior interbody fusion at L4–L5 and L5–S1 (Fig. 5). Intervertebral disc space at L4–L5 was very narrow, and hence the author had no choice but to insert one small-diameter cage. Resected local bone and demineralized bone matrix were used for posterolateral fusion.

Outcome

Postoperatively, she wore rigid orthosis for 3 months and was followed up by 1 year and presented symptomatic relief (VAS for back and leg, 3 and 2, respectively) and minimal disability (ODI 24). At postoperative 1-year, electrophysiologic study was conducted at 31–34 °C room temperature with a Medelec Synergy EMG machine (Oxford, UK). It showed decreased conduction velocity and amplitude, which meant peripheral polyneuropathy.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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