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CASE REPORT

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Rapidly progressing neurological disturbance due to intraspinal calcification in a patient with systemic sclerosis

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Abstract A 53-year-old woman with diffuse cutaneous systemic sclerosis (dsSSc) who developed muscle weakness in her lower extremities was admitted to our hospital. Computed tomography (CT) of her thoracic spine showed paraspinal and intraspinal calcifications producing severe spinal stenosis. After admission, her neurological symptoms, including muscle weakness and sensory disturbance, rapidly progressed and finally her lower extremities became completely paraplegic. After initiation of diltiazem and bucillamine, her neurological disturbance showed a marked improvement. A CT scan of the thoracic spine after medication showed dominant decrements in both intraspinal and paraspinal calcifications.

Key words Bucillamine · Diltiazem · Intraspinal calcification · Paraspinal calcification · Systemic sclerosis

Introduction

Neurological manifestations in patients with systemic sclerosis (SSc) are a relatively rare complication and encompass trigeminal neuropathy, carpal tunnel syndrome, autonomic neuropathy, polyneuritis, mononeuritis multiplex, and subacute combined degeneration of the spinal cord. Recently, SSc patients with neurological symptoms caused by compression, with paraspinal and intraspinal calcifications, have been reported, but the number of such cases is still limited. Here we report a case of a SSc patient who showed a rapidly progressing course of motor and sensory disturbance due to dominant intraspinal and paraspinal calcification. Treatment of the calcification with diltiazem and bucillamine led to a decrease in the bulk of the calcinosis in the intraspinal and paraspinal spaces, and a remarkable improvement in her neurological symptoms.

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Case report

A 53-year-old woman with diffuse cutaneous SSc (dsSSc) was admitted to our hospital with an increasing weakness and numbness of her bilateral lower extremities. She first noticed a weakness in her left leg when she stepped down the stairs 2 weeks before admission. Since then, the weakness of her lower extremities had been progressing rapidly, and she could not stand up at the time of admission. She also complained of severe numbness of both lower extremities. The patient had had a history of SSc for 10 years. At the age of 43 years, she showed Raynaud's phenomenon and scleroderma involving the trunk, face, and limbs, and was diagnosed as having SSc. At this time, she had been treated with D-penicillamine (300 mg/day). Other manifestations of SSc included peripheral calcinosis, telangiectasias, polyarthralgia, esophageal hypomotility, and mild lung fibrosis. Multiple ulcerations of the fingertips also occurred. An evaluation at the time of the initial diagnosis revealed positive anti-Scl-70 antibodies.

At physical examination on admission, her temperature was 37.6°C, pulse 80 per min, regular, and blood pressure 140/80 mmHg.

A neurologic examination revealed diffuse muscle weakness bilaterally in her lower extremities: anterior tibialis muscle (graded 2/5), bilateral gastrocunemius muscle (graded 2/5), bilateral iliopsoase muscle (graded 2/5), quadriceps muscle (graded 2/5). A severe disturbance of light touch sensations and a pain sensation below the fourth and fifth thoracic dermatomes were observed. The position and

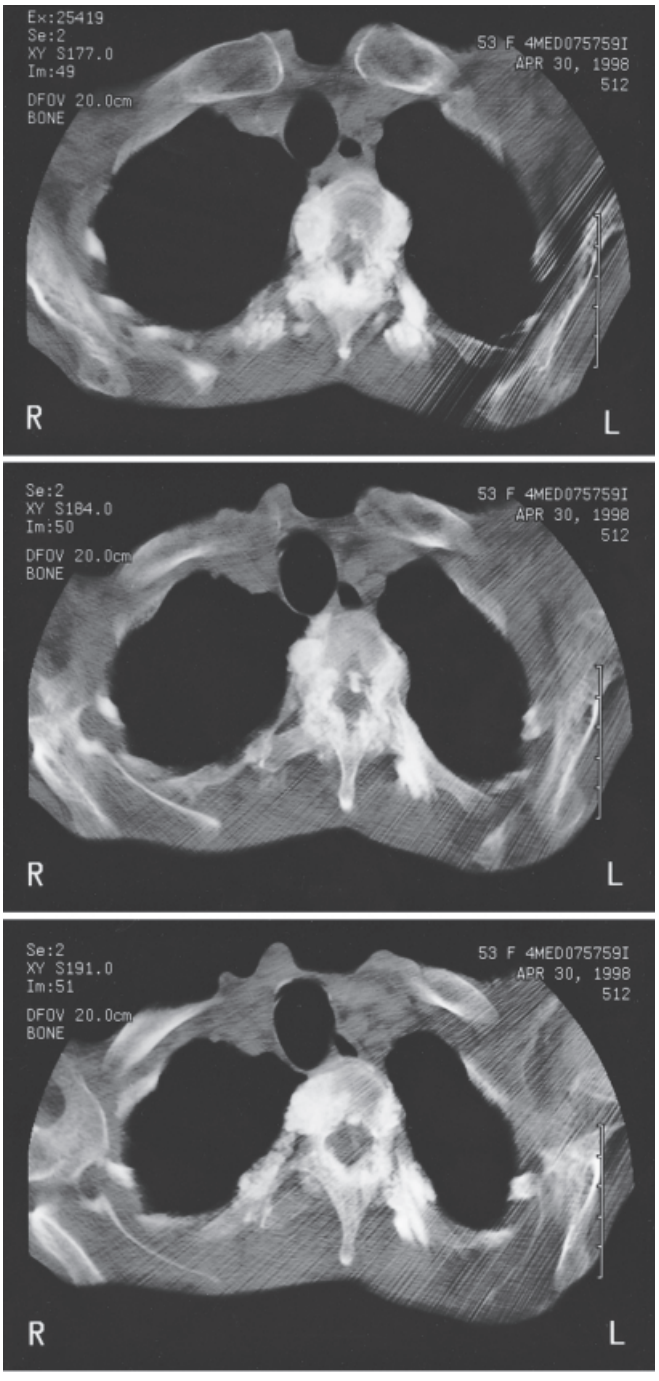

Fig. 1. Computed tomography (CT) scan at the Th5–6 level, demonstrating calcific masses around the facet joint, and paraspinal as well as intraspinal calcific masses producing spinal stenosis

vibration senses on her lower extremities were also disturbed. The deep tendon reflexes of the lower extremities were increased to 2+ bilaterally, but extensor toe signs were negative.

Thoracic spine radiographs showed extensive soft tissue calcification. Computed tomography (CT) of the thoracic spine showed paraspinal and intraspinal calcium deposits (Fig. 1). The paraspinal calcifications were concentrated in the intervertebral spaces. There was tumoral calcinosis at the Th4–Th5, Th5–Th6, and Th6–Th7 facet joints, producing significant spinal stenosis in conjunction with disc bulging at Th4–Th5 and Th5–Th6. Intraspinal calcifications were not seen at the cervical and lumber spine level.

Roentgenograms of the hip joints revealed severe calcification around the left femoral head with destruction, and marked articular narrowing accompanied by intraarticular calcification. Roentgenograms of both hands also revealed severe soft tissue calcification around the fingers.

Laboratory data showed a white blood cell count of 10600/μl. Hemoglobin was 11.0 g/dl and platelet count was 41.2×10^4/μl. C-reactive protein (CRP) was 3.4 mg/dl and erythrocyte sedimentation rate (ESR) was 36 mm/h. Serum calcium was 9.0 mg/dl and phosphorus was 2.8 mg/dl. Serum HS-PTH level was 460 pg/ml, and INTACT-PTH was 25 pg/ml. Antinuclear antibody was positive, 1:2560, with a homogenous and speckled pattern. Anti-Scl 70, antisingle-strand DNA, and anti-SS-A antibodies were positive. Other autoantibodies, including antidouble-stranded DNA, anti-RNP, anti-Sm, anti Jo-1, anti-SS-B, anticentromere, rheumatoid factor, anticardiolipine β2GP1, and peripheral antineutrophil cytoplasmic (MPO-ANCA) antibodies could not be detected.

Nerve conduction studies (NCV) were performed on the left side only because of patient intolerance, but the left peroneal and sural sensory nerves and motor nerves were delayed. Motor NCV in the left peroneal was 40 m/s, and sensory NCV in the left sural was also delayed to 31 m/s. After admission, the patient complained of increasing bilateral leg pain, numbness, and decreasing touch, vibratory, and position sense. She became unable to move her legs herself on the 7th day after admission, and developed urinary incontinence on the 21st day after admission. Her serum CRP level rose to 7.6 mg/dl. The progress of the weakness, neurological findings, polyarthralgia, femoral joint pain, high fever, elevation of CRP, and negative bacterial culture of urine, blood, and sputa suggested a deterioration of the systemic sclerosis rather than an infection.

For her paraplegia, we considered removing the calcific masses surgically, but the patient refused to have an operation. On the 24th day after admission, treatment with diltiazem (300 mg/day) and bucillamine (200 mg/day) was initiated, and the prescription of D-penicillamine was stopped because it was having no effect. On the 38th day after admission, she noticed a slight improvement in the motor and sensory functions of her lower extremities. From then on, the patient's leg movements were markedly improved, and the incontinence was resolved. A CT scan after 40 days of treatment showed a remarkable decrease in the paraspinal and intraspinal calcification at the thoracic spine level (Fig. 2). Her serum CRP level decreased to 1.3 mg/dl 90 days after admission. Finally, she was able to use a wheelchair by herself, and was able to go home. Her muscle strength also improved: bilateral anterior tibialis muscle (graded 4/5), bilateral gastrocunemius muscle (graded 4/5), bilateral iliopsoase muscle (graded 3−/5), bilateral quadriceps muscle (graded 3/5).

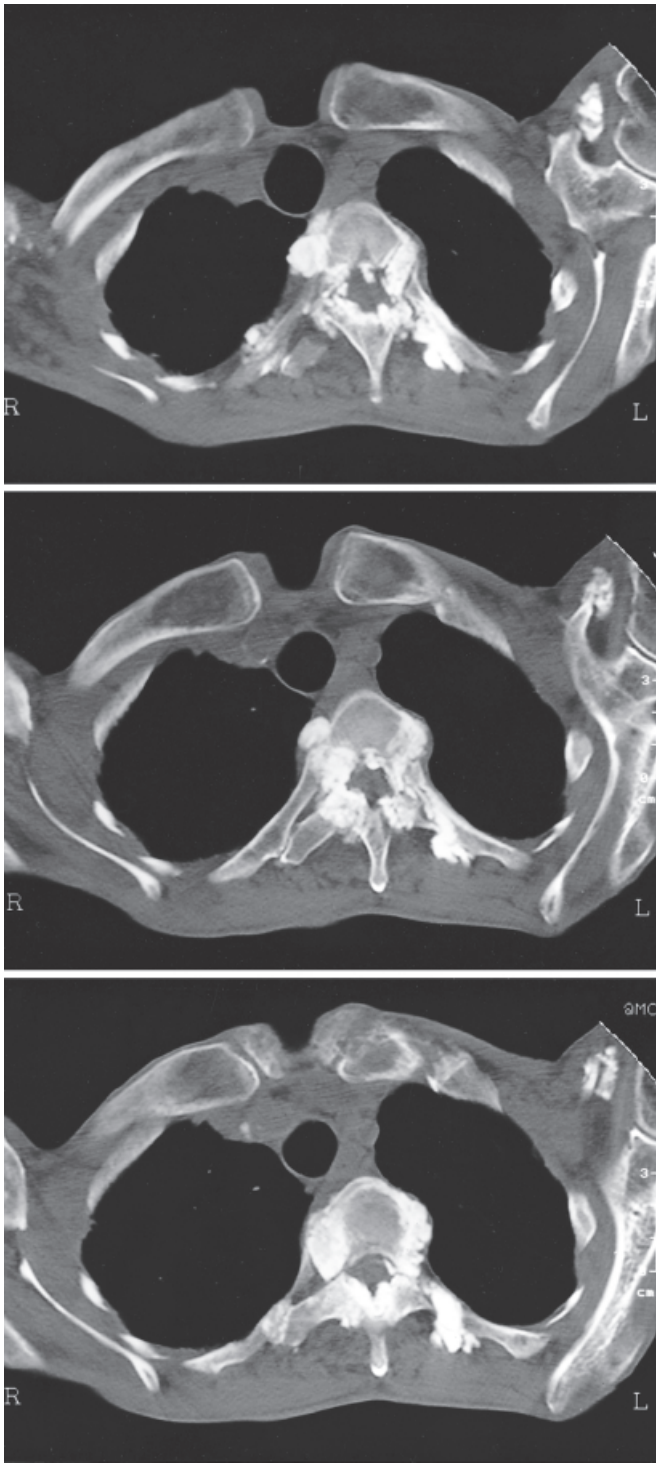

Fig. 2. CT scan at the Th5–6 level after treatment, showing decreasing paraspinal and intraspinal calcific masses

Discussion

Although soft tissue calcifications are a relatively common complication in systemic sclerosis, and are observed in 8.7%–27% of patients,[1,2] reports of intraspinal calcifications in SSc patients are still limited. Most of these reports show the involvement of the cervical spine[3–8] and the lumber spine.[7] Thoracic spine involvement was demonstrated in only one report.[9] In the present case, marked intraspinal calcification was limited to the thoracic spine level.

The pathogenesis of calcification is not fully understood, but it is generally accepted that local tissue factors are more important than a systemic derangement in calcium or phosphorus metabolism.[10] However, intraspinal calcification is generally seen in patients with severe subcutaneous calcification, as in the present case, and this suggests that there is some systemic derangement leading to the occurrence of calcification in different sites. Generally, calcinosis is more frequent in patients with extensive skin sclerosis, and it is also more common in female patients.[2]

In most previous cases of intraspinal calcification, the neurological symptoms progressed rapidly, and caused severe pain, numbness, or paraplegia. The present case also showed a very rapidly course, leading to complete paraplegia of both her lower extremities. Therefore, when patients with SSc show symptoms of disease of the spine, intraspinal and paraspinal calcification should be checked without delay.

Most of the reported cases have an operation such as a laminectomy, disckectomy, or excision of a calcific cyst,[3–5,7,8] but in our case, the patient refused to have an operation. We then gave her bucillamine and diltiazem orally. After the initiation of this treatment, the calcification masses gradually reduced, as seen on a thoracic CT scan, and the patient's motor and sensory functions were dramatically improved. This case also showed an elevation in the serum CRP level, and a suggestion of arthritis, particularly on her femoral joints. Because this severe femoral calcification and arthritis affected the dysfunction and numbness of her lower extremities, her weakness was not completely cured.

The patient's CRP level also decreased after treatment. Palmieri et al.[11] reported that diltiazem markedly reduced muscle Ca content in calcinosis, and to a certain extent would correct the cellular disorder, thus diminishing the accumulation of Ca deposits. However, other drugs seem to be ineffective for the treatment of calcification in SSc. For example, systemic steroids, intravenous chelating agents, ketogenic diets, and other dietary manipulations have been unsuccessful in the treatment of dystrophic calcification.[9] Bisphosphonates have also been unimpressive in clinical trials.[12,13] Probenecid, which increases urinary phosphate excretion, and warfarin, which blocks the formation of gamma-carboxyglutamic acid residues on proteins, have also been advocated.[12,13]

Bucillamine is one of the disease-modifying antirheumatic drugs and is commonly used for rheumatoid arthritis in Japan. Recently, we demonstrated the preventive effect of bucillamine on skin sclerosis.[14] We therefore selected bucillamine for the treatment of SSc with arthritis and calcification in this case instead of D-penicillamine. The successive treatment of intraspinal and paraspinal calcification with bucillamine and diltiazem in the present case seems to suggest that this combined therapy is useful for this condition. Although there are no previous reports of its effect in preventing calcification, we also consider that bucillamine

may have had an effect not only on the inflammation, but also on the calcification in this case. However, further study is needed to verify the usefulness of this therapy for the treatment of intraspinal and paraspinal calcification.

Although intraspinal and paraspinal calcification is not yet fully understood, we conclude that intraspinal calcification, which may lead to severe neurological disorders, is an important manifestation in SSc patients.

References

1. Bassett LW, Blocka KLN, Furst DE, Clements PJ, Gold RH. Skeletal findings in progressive systemic sclerosis (scleroderma). AJR 1981;136:1121.
2. Muller SA, Brunsting LA, Winklemann RK. Calcinosis cutis: its relationship to scleroderma. AMA Arch Dermatol 1959;80:15.
3. Schweitzer ME, Cervilla V, Manaster BJ, Gerharter J, Dalinka M, Peck WW, et al. Cervical paraspinal calcification in collagen vascular diseases. Am J Roentgenol 1991;157:523–5.
4. Pinstein ML, Sebes JI, Levanthal M, Robertson JT. Case report 579: progressive systemic sclerosis with cervical cord compression syndrome, osteolysis and bilateral facet arthropathy. Skeletal Radiol 1989;18:603–5.
5. Harverbush TJ, Wilde AH, Hawk WA. Osteolysis of the ribs and cervical spine in progressive systemic sclerosis (scleroderma). J Bone Joint Surg Am 1974;56:637–40.
6. Clement GB, Grizzard K, Vasey FB. Neuropathic arthropathy (Charcot joints) due to cervical osteolysis: a complication of progressive systemic sclerosis. J Rheumatol 1984;11:545–8.
7. Ward M, Cure J, Schabel S, Smith EA, Schumacher HR, Silver RM. Symptomatic spinal calcinosis in systemic sclerosis. Arthritis Rheum 1997;40:1892–5.
8. Petrocelli AR, Bassett LW, Mirra J, Gold RH, Brahn E. Scleroderma: dystrophic calcification with spinal cord compression. J Rheumatol 1988;15:1733–5.
9. Walden CA, Gilbert P, Rogers LF, Hendrix RW. Case report 620: progressive systemic sclerosis with paraspinous and intraspinous calcifications. Skeletal Radiol 1990;19:377–8.
10. Resnick D. Scleroderma (progressive systemic sclerosis). In: Resnick D, Niwayama G, editors. Diagnosis of bone and Joint disease, vol 2, 2nd ed. Philadelphia: WB Saunders; 1988. p. 1296–301.
11. Palmieri GMA, Sebes JI, Aelion JA, Moinuddin M, Ray MW, Wood GC, et al. Treatment of calcinosis with diltiazem. Arthritis Rheum 1955;38:1646–54.
12. Cram RL, Barmeda R, Geho WB, Ray RD. Diphosphonate treatment of calcinosis universalis. N Engl J Med 1971;285:1012–3.
13. Metzger AL, Singer FR, Bluestone R, Pearson CM. Failure of disodium etidronate on calcinosis due to dermatomyositis and scleroderma. N Engl J Med 1974;291:1294–6.
14. Ogawa T, Saito E, Ogawa K, Okada S, Ogura T, Kinoshita M. Bucillamine prevents skin fibrosis in the tight-skin mouse. Arthritis Rheum 1997;40 Suppl:297.