Osteopetrosis in a Patient of Systemic Sclerosis Sine Scleroderma: A Rare Association

Saroj K. Pati1 Praveen Raja1 Ajoy K. Behera2 T.G. Ranganath2 Narendra K. Bodhey1

1 Department of Radiodiagnosis, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India
2 Department of Radiodiagnosis, Department of Pulmonary Medicine, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India

Indian J Radiol Imaging 2021;31:1019–1022.

Address for correspondence Narendra K Bodhey, MD, DNB, Professor and Head, Department of Radiodiagnosis, All India Institute of Medical Sciences, Raipur - 492 099, Chhattisgarh, India (e-mail: narendrakhb2001@yahoo.co.in).

Abstract

Systemic sclerosis is a connective tissue disorder of unknown etiology. Although it is a multisystemic disorder, skin thickening is considered a hallmark of the disease. It usually involves the lungs, gastrointestinal, and musculoskeletal systems. However, a rare subset of systemic sclerosis, systemic sclerosis sine scleroderma, is characterized by internal organ involvement and positive serologic markers with the total or partial absence of cutaneous manifestations. We present a rare association of osteopetrosis in a case of systemic sclerosis sine scleroderma, in a 22-year-old male patient, who presented with pulmonary symptoms as his chief complaints, unreported so far in literature.

Keywords
► interstitial lung disease
► osteopetrosis
► rugger jersey spine
► systemic sclerosis sine scleroderma

Introduction

Systemic sclerosis is a rare generalized connective tissue disorder of unknown etiology and unclear pathogenesis. It is generally accepted that the disease is characterized by widespread fibrosis of the skin and internal organs, vascular abnormalities, and immune disturbances.1 Skin involvement in systemic sclerosis is considered as a cardinal feature often presenting as skin thickening.2 Skeletal involvement in systemic sclerosis is commonly seen that includes demineralization, arthritis and systemic inflammation, hyperostosis of the phalangeal tuft, and the resorption of bone at various sites, including the carpal bones, distal radius, and ulna.3 Here, we present a rare association of osteopetrosis in a patient with rare variant of systemic sclerosis: systemic sclerosis sine scleroderma (ssSSc). This association is unreported till date to the best of our knowledge as searched in the PubMed and other Internet search engines.

Case Report

A 22-year-old male patient was presented with complaints of shortness of breath, dry cough, and fever on and off for the last 4 months. No similar complaints in the past were observed. Patient was a nonsmoker and nonalcoholic. On examination, pulse rate was 102/min; blood pressure was 114/76 mm Hg; oxygen saturation was 96% at room air, and respiratory rate was 20/min. On respiratory examination, bilateral basal crepitations were present. Other systemic examination was unremarkable.

Patient was referred to us for further evaluation of his pulmonary complaints. Chest radiograph revealed ill-defined reticulonodular opacities in bilateral lung parenchyma predominantly in mid and lower zone in an asymmetrical distribution. Visualized bones including spine appear increased in density (► Fig. 1). For further evaluation of interstitial changes noted in the chest radiograph, high-resolution computed tomography of the chest was done. On the lung window, it revealed reticular opacities predominantly in form of interlobular and intralobular septal thickening in subpleural and peripheral regions of all lobes of both lungs with associated early honeycombing and subtle bronchiectatic changes. Peripheral areas of ground glass opacities were also seen predominantly in the basal segments of bilateral lower lobes.
Above findings are suggestive of interstitial lung disease, possibly nonspecific interstitial pneumonia (NSIP) pattern (► Fig. 2). On mediastinal window, patulous esophagus is noted (► Fig. 3A and C). All major thoracic vessels including pulmonary vessels appear unremarkable. On bone window, dorsal spine reveals increase in density of both superior and inferior endplates of all the visualized vertebrae giving the appearance of rugger jersey spine (► Fig. 3B). Thoracic cage including visualized scapula and humerus shows generalized increase in density. This prompted us to do a skeletal survey. Radiograph of dorsolumbar spine reveals similar rugger jersey spine appearance in the other vertebrae also (► Fig. 4A and B). In anteroposterior view of pelvic radiograph, there is a generalized increase in bone density. In addition, both femurs in its visualized extent reveal narrowing of medullary space with increase in cortical thickness and density (► Fig. 4C). In contrast, radiograph of wrist including forearm appears unremarkable (► Fig. 4D). Above skeletal survey findings are suggestive of osteosclerosis.

In view of the interstitial lung changes and the patulous esophagus, the treating physician was directed to investigate in the lines of systemic sclerosis. The laboratory investigations of the patient were positive for SCL-70 antibodies favoring a diagnosis of systemic sclerosis. Echocardiography revealed trivial tricuspid regurgitation (TR) with right ventricular systolic pressure (RVSP) of 43 mm Hg representing early pulmonary arterial hypertension. However, skin examination was unremarkable including the normalcy of the skin fold on dorsum of the wrist (► Fig. 5). In view of above findings and absence of skin involvement, the patient is diagnosed as a rare subset of systemic sclerosis; ssSSc. Moreover, renal blood parameters (serum urea: 15.21 mg/dL, serum creatinine: 0.85 mg/dL) including screening abdominal sonogram are unremarkable thereby excluding any renal pathology.
Osteopetrosis in a Patient of Systemic Sclerosis Sine Scleroderma

Pati et al.

Discussion

Systemic sclerosis is a chronic connective tissue disease that typically affects skin and internal organs to variable extent by widespread microvascular damage and excessive deposition of collagen. The main subsets of systemic sclerosis are limited cutaneous form, diffuse cutaneous form, and systemic sclerosis without skin involvement. Limited cutaneous form involves skin distal to elbow and knees only, whereas diffuse variety involves proximal extremities and/or trunk in addition to distal thickening. On the other hand, ssSSc, a rare subset of systemic sclerosis, is characterized by the presence of visceral involvement in the absence of skin manifestations. It is believed that some ssSSc cases remain under-diagnosed and considered to be various forms of idiopathic fibrosis of internal organs. The absence of skin involvement itself is probably the reason for under-diagnosis of ssSSc. Owing to the absence of skin changes, we would have also missed the case if the computed tomography (CT) findings of patulous esophagus would not have prompted the specific antibody tests.

Systemic sclerosis is characterized by three hallmark findings: signs of skin and/or internal organ fibrosis, signs of vasculopathy, and autoantibodies. Skin involvement is considered a cardinal feature of systemic sclerosis that often appears as skin thickening in the fingers of both the hands extending proximal to the metacarpophalangeal joints. The involvement of internal organs in the patients with ssSSc has been reported to be 79% for the gastrointestinal tract, 68% for pulmonary, and 9% for the heart. Others have reported that esophageal involvement was the most frequent (83%) and followed by pulmonary involvement (68%). Similar other studies also support involvement of gastrointestinal tract more frequent followed by pulmonary involvement in systemic sclerosis patients. Esophageal involvement is associated with dilation of esophagus with or without dysphagia. These can be readily visualized in esophagogram or CT scan.

Interstitial lung changes are most commonly presented as ground glass opacities and findings of fibrosis in form of reticular opacities, traction bronchiectasis, and honeycombing. Peripheral and subpleural distribution is more common involving predominantly lower lung zones as well as posterior lung fields. NSIP is more frequent as compared with usual interstitial pneumonia. Moreover, interstitial lung disease is included as a disease identification criterion in the American College of Rheumatology/European League against Rheumatism Collaborative Initiative joint classification.

Signs of vasculopathy include Raynaud’s phenomenon, digital vasculopathy, and pulmonary arterial hypertension. Multiple autoantibodies are described in the literature to be associated with systemic sclerosis. Most of these patients have positive antinuclear antibody by indirect immunofluorescence (85–90%). Among scleroderma-specific antibodies, antitopoisomerase (Scl-70) and anti-RNA polymerase III are more specific for diffuse variety, whereas anticentromere is more specific for limited variety.

The index case having strong positivity for SCL-70 immunoglobulin G and antinuclear antibodies, a NSIP pattern of interstitial lung disease, esophageal dilatation, without any skin involvement led to the diagnosis of ssSSC. The trivial TR on two-dimensional Echo with RVSP of 43 mm Hg could represent early pulmonary arterial hypertension. However, there is no evidence of Raynaud’s phenomenon or digital vasculopathy seen in our patient.

Skeletal involvement is common in systemic sclerosis. To quote Morrisroe et al—“Musculoskeletal involvement in systemic sclerosis occurs more frequently than expected, with a prevalence of 24% to 97%.” Both articular and nonarticular
involvements are described in the literatures. Common articu-
lar manifestations are arthralgia, synovitis, and flexion
contractures, while generalized and localized osteopenia,
acro-osteolysis and osteolysis in other body regions are
common nonarticular manifestation. Arthritis in this disor-
der often simulates rheumatoid arthritis except for distal
interphalangeal joint involvement. Exact etiopathogenesis of
bone involvement is unclear; however, it is postulated that
digital ischemia combined with retractile pressure of thick-
ened skin may predispose to distal tuft resorption.

However, skeletal survey in our case shows generalized
increased bone density in most of the bones and rugger
jersey appearance of the thoracolumbar spine representing
osteosclerosis. To the best of our knowledge supported by
the search on PubMed and other Internet search engines, osteo-
sclerosis is not yet reported to be associated with systemic
sclerosis.

Osteosclerosis can be seen in various conditions like
osteopetrosis, secondary hyperparathyroidism, heavy metal
poisoning, and blood dyscrasias. The fluorosis will show
heterogenous sclerosis to start with but not like that of a
rugger jersey spine and is associated with ossifying ends of
the ligaments and tendons. The sclerosis associated with
beryllium, lead, or bismuth poisoning shows sclerotic meta-
physial band along with relevant history. Blood dyscrasia
like myelofibrosis is usually associated with splenomegaly
and extramedullary hematopoiesis along with osteosclero-
sis. However, in our case, there was no such band or soft
tissue changes or relevant history leaving us with osteopet-
rosis as a more plausible diagnosis.

Osteopetrosis is a rare sclerosing bone dysplasia charac-
terized by reduced osteoclastic activity due to defect in
formation and function of osteoclast with resultant increase
in bone mass. Broadly, it comprises three types: infantile
malignant autosomal recessive form, intermediate autosoma-
ral recessive form, and the benign autosomal dominant
form. Clinical presentation of autosomal dominant form
varies from recurrent bone fractures to asymptomatic inci-
dental finding as in this index case. The rugger jersey spine
is considered as pathognomonic sign for osteosclerosis as-
associated with secondary hyperparathyroidism of chronic
renal failure. However, in our case, the serum calcium and
phosphorus were in normal range with no elevation of
serum parathormone levels thus excluding secondary hyper-
parathyroidism. Moreover, it may also be seen in other
diseases like osteopetrosis. It is a very rare and yet undocu-
ted association of osteopetrosis in a patient of ssSSc.

Conclusion
Even if the clinical cutaneous markers are absent, the pres-
eece of a patulous esophagus and interstitial lung changes
should lead us to investigate in lines of systemic sclerosis that
can result in diagnosis of rare variant of systemic sclerosis;
ssSSc. Moreover, presence of atypical skeletal changes in
form of rugger jersey spine leads us to do skeletal survey
resulting in diagnosis of osteopetrosis. This will initiate an
eyearly treatment thus reducing the morbidity and mortality.

Declaration of Patient Consent
The authors certify that they have obtained all appropri-
ate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial Support and Sponsorship
Nil.

Conflicts of Interest
There are no conflicts of interest.

References
1 van den Hoogen F, Khanna D, Fransen J, et al. Classification criteria
for systemic sclerosis: an ACR-EULAR collaborative initiative.
Arthritis Rheum 2013;65:2737–2747
2 Kucharz EJ, Kopeć-Mędrek M. Systemic sclerosis sine scleroder-
3 Morrisroe KB, Nikpour M, Proudman SM. Musculoskeletal mani-
41(03):507–518
4 Chilukuri B, Chinnadurai S, Mahendran B, Ramamoorthy R, Sel-
vakumar B, Sankaralingam R. ABO736 Systemic sclerosis sine
scleroderma: Characteristics of a south Indian cohort from a
5 Poormoghim H, Lucas M, Fertig N, Medsger TA Jr. Systemic
sclerosis sine scleroderma: demographic, clinical, and serologic
features and survival in forty-eight patients. Arthritis Rheum
2000;43(02):444–451
6 Marangoni RG, Rocha LF, Del Rio AP, Yoshinari NH, Marques-Neto
JF, Sampaio-Barros PD. Systemic sclerosis sine scleroderma: dist-
tinct features in a large Brazilian cohort. Rheumatology (Oxford)
2013;52(08):1520–1524
7 Chowaniec M, Skoczynska M, Sokolik R, Wiland P. Interstitial lung
disease in systemic sclerosis: challenges in early diagnosis and
management. Reumatologia 2018;56(04):249–254
8 Jun LIU, Jin LIU, Zhao FU, et al. The imaging value of bone turnover
9 Shingade RG, Suthar PR, Patel R. Osteopetrosis with typical
2015;4:36–38
10 Oon SF, Singh D, Tan TH, et al. Primary myelofibrosis: spectrum of
imaging features and disease-related complications. Insights
Imaging 2019;10(01):71
11 Wu CC, Econs MJ, DiMeglio LA, et al. Diagnosis and management
of osteopetrosis: consensus guidelines from the osteopetrosis
12 Patil K, Mahima VG, Raina A, Mutneja P. Osteopetrosis: A case
13 Wittenberg A. The rugger jersey spine sign. Radiology 2004;230
(02):491–492