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CASE REPORT

Scleroderma with pulmonary nodules on CT scan: a rare case presentation

Imranullah Khan, Saif Ullah, Muhammad Zarak Khan, Shandana Khan

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Author Information

From: Department of Pulmonology, Rehman Medical Institute, Peshawar, Khyber Pakhtunkhwa, Pakistan

Dr. Imranullah Khan
Assistant Professor

Dr. Saif Ullah
Trainee Medical Officer
(Corresponding Author)
saif.ullah@rmi.edu.pk

Dr. Muhammad Zarak Khan
House Officer

Dr. Shandana Khan
House Officer

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ABSTRACT

A case is presented of a 30 year old gentleman, driver by occupation, who presented as an outdoor patient with pulmonary symptoms accompanied by left sided chest pain, other systemic complaints, and significant weight loss of 33 kgs over past few months associated with loss of appetite. Past history was significant for abdominal tuberculosis in 2014. He also gave history of alopecia and photophobia. On examination, chest was bilateral clear on auscultation and rest of the organ system findings were unremarkable. CBC showed anemia. Other baseline investigations were normal. Chest X-ray was done which showed bilateral asymmetrical irregular nodules in all lung zones. CT chest (without contrast) showed bilateral discrete peripheral nodules in upper and mid zones with hilar lymphadenopathy and mild pericardial effusion.

Image guided biopsy report showed inconclusive, non-specific chronic inflammation with fibrosis along with foci of excessive proliferation of atypical pneumocytes. Patient underwent Open lung pleural biopsy under general anesthesia, which revealed features seen in collagen vascular disease. Hence further clinical and serological evaluation was done which revealed Scl-70 of 11.06 (positive).

Patient was administered steroids. Interval regression of pulmonary nodules were noted after 4 months of commencement of steroids on subsequent CT chest films. Patient also showed significant clinical improvement and is currently under the treatment of Rheumatologist.

Keywords: Scleroderma; Lung Nodules; Lung Adhesions; Biopsy.

The authors declared no conflict of interest. All authors contributed substantially to the planning of research, data collection, data analysis, and write-up of the article, and agreed to be accountable for all aspects of the work.

INTRODUCTION

Systemic sclerosis (SSc) is a rare, autoimmune, heterogeneous connective tissue disorder which predominantly involves the skin. Other crucial manifestations are multi-organ dysfunction, vascular abnormalities and immune dysfunction. In early phases, the skin exhibits non-pitting edema, ulcerations of finger tips, Raynaud's phenomenon followed by skin thickening and fibrosis. Systemic sclerosis affects the lungs, heart, kidneys, musculoskeletal system and gastrointestinal tract.[1]

Both genetic and environmental triggers activate molecules and signaling pathways that contribute to the pathogenesis of scleroderma, these include, transforming growth factor-β (TGF-β) and WNT/β-catenin signaling pathways, signal transducer and activator of transcription 3 (STAT3), platelet-derived growth factor (PDGF), endothelin 1, interleukin 6, interleukin 13, autoantibodies, and numerous biologically active substances. 42% of patients with SSc are found to have Anti-ubiquitin antibodies and are associated with anti-histone antibodies. The latter might be positively correlated with the severity of pulmonary fibrosis in patients with SSc.[2]

Post-translational modifications such as acetylation, phosphorylation and ubiquitination play a key role in regulation of these pathways, serving as possible targets for the treatment of systemic fibrosis.[2]

Ubiquitination is a process by which target protein is covalently bound to ubiquitin (a protein molecule that modifies other proteins for degradation) by activating (E1), conjugating (E2) and ligating (E3) enzymes to form polyubiquitin chains which are recognized by the 26S proteasome complex and degraded into individual amino acid.[2]

Diagnostic criteria of scleroderma do not require histopathology findings and is usually not performed however skin biopsy is taken to rule out similar diseases i.e. scleroderma and sclero-myxedema, etc.[3]

Approximately 70%-85% of patients with scleroderma present pulmonary manifestations.[4] The most common presentation of scleroderma is Interstitial Lung Disease (ILD) and occurs most commonly in patients with diffuse (rather than limited) cutaneous systemic sclerosis, anti-Scl-70, anti-topoisomerase I antibody, and in the absence of anti-centromere antibody. All patients with systemic sclerosis require extensive clinical assessment: respiratory symptoms, a high-resolution computed tomography (HRCT) chest scan, and pulmonary function tests. An increased extent of lung fibrosis on HRCT and a low forced vital capacity (FVC) are predictors of early mortality. Current treatment options for progressive SSc-ILD include immunosuppressant therapies: cyclophosphamide and mycophenolate mofetil. Both hematopoietic stem cell transplantation (HSCT) and lung transplantation are successful treatment modalities in patients with severe or a rapidly progressive disease.[5]

Common pulmonary manifestations include lung fibrosis with Non-Specific Interstitial Pneumonia (NSIP) being more common than Usual Interstitial Pneumonia (UP), Pulmonary Arterial Hypertension (PAH), and lung cancer. Predominant CT findings in cellular NSIP include ground glass opacity in posterior and subpleural regions whereas irregular reticulation with traction bronchiectasis is a common CT finding in fibrotic NSIP; honeycombing is an uncommon and limited finding. Scleroderma may present as PAH which appears as main and proximal pulmonary artery enlargement on chest X-ray and CT chest. An uncommon pulmonary manifestation of scleroderma is lung cancer which occurs mostly in association with lung fibrosis.[6]

The prevalence of PAH in scleroderma is 8% to 12% and is a factor for poor prognosis. It is the leading cause of death in scleroderma patients, therefore such patients should be commenced on aggressive treatment from the start and early transplantation should be considered in such patients.[7]

CASE PRESENTATION

We present a case report of 30 year old gentleman, driver by occupation, who presented on April 18, 2019 as an outdoor patient with chief complaints of left sided chest pain for 4 months, shortness of breath on exertion for 4 months, cough for 3 months, and fever for 1 month. Chest pain was gradual in onset and radiated to the abdomen and back. It was initially intermittent, later became persistent with severity of 7-8 on pain scale, relieved by bending and lying down and accompanied by palpitations. Fever usually occurred in the evenings and would persist till night, associated with sweating and body aches, relieved with anti-pyretics. Dry, continuous cough was present for last 3 months without hemoptysis. Weakness, mild bone pain, dysuria and significant weight loss of 33 kgs over past few months (85 kg to 52 kg) associated with loss of appetite were also reported.

Past history was significant for abdominal tuberculosis in 2014 which was treated properly with anti-tuberculous drugs for 9 months with improvement over time. A history of alopecia and photophobia was also given; however, there was no history of skin rash or oral ulcers, and no history of pets or cattle exposure as well. He never smoked during his lifetime. No history of alcohol use or I/V drug abuse was reported. Travel history was insignificant.

On General Physical Examination, patient was well-oriented in time, place, and person with GCS 15/15. Chest was bilateral clear on auscultation. Normal heart sounds. Abdomen was soft, non-tender with bowel sounds audible. Skin and extremities were normal. Vitally patient was stable. Other base line investigations were normal (Table 1).

Table 1: Base line investigations done

Complete Blood Count	
Hemoglobin	10.2 mg/dl
WBC	12.2 x 10 ^ 3/uL
MCV	68.7 fL
MCH	19.4 pg
MCHC	28.2 g/dl
Neutrophils	81%
Lymphocytes	14%
ESR	22mm/hr

Radiological studies

Chest x-ray radio film showed bilateral asymmetrical irregular nodules in all lung zones as shown in Figure 1.

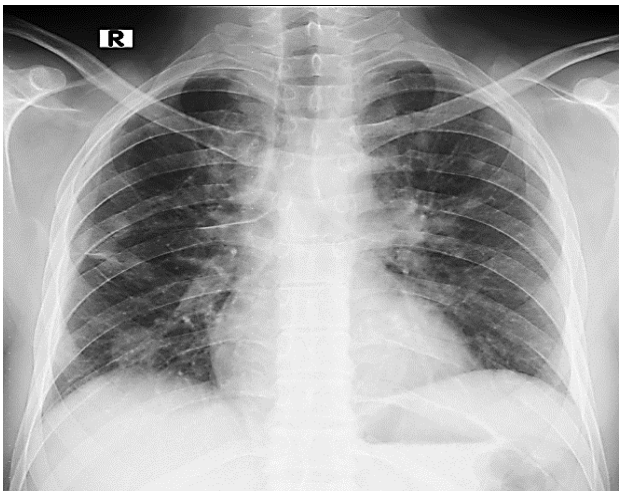

Figure 1: Bilateral asymmetrical irregular nodules in all lung zones.

CT chest (without contrast) showed bilateral discrete peripheral nodules in upper and mid zones with hilar lymphadenopathy and mild pericardial effusion as shown in Figures 2-5.

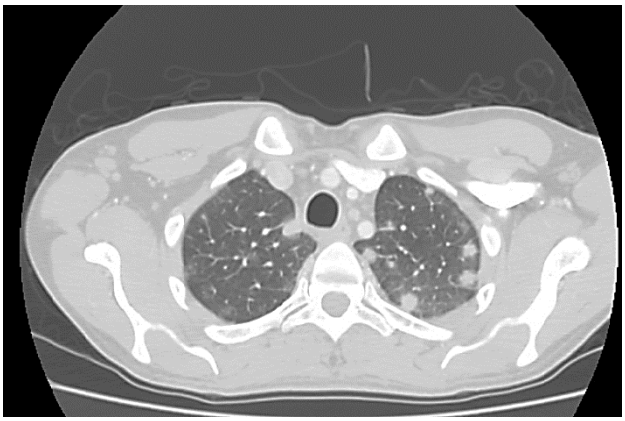

Figure 2: Bilateral discrete peripheral nodules in upper and mid zones with hilar lymphadenopathy and mild pericardial effusion.

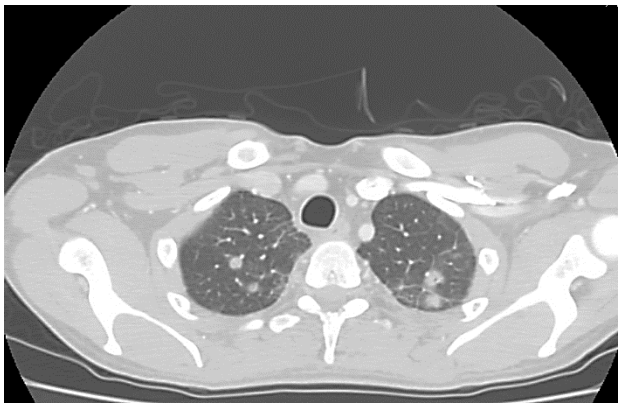

Figure 3: Bilateral discrete peripheral nodules in upper and mid zones with hilar lymphadenopathy and mild pericardial effusion.

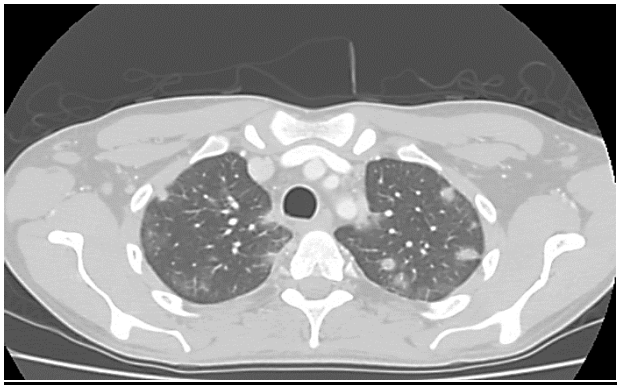

Figure 4: Bilateral discrete peripheral nodules in upper and mid zones with hilar lymphadenopathy and mild pericardial effusion.

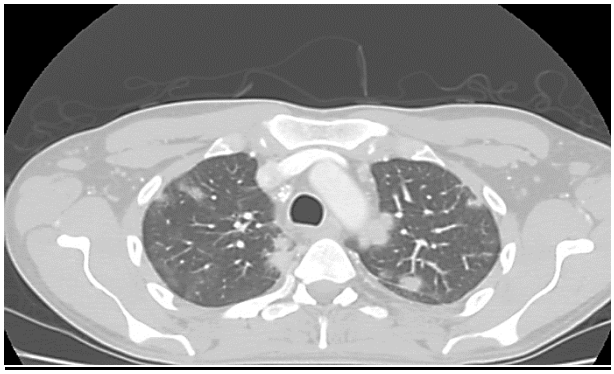

Figure 5: Bilateral discrete peripheral nodules in upper and mid zones with hilar lymphadenopathy and mild pericardial effusion.

Bronchoscopy

Bronchoalveolar lavage gram stain revealed few puss cells, numerous RBCs, moderate epithelial cells, few gram positive cocci, few gram negative rods and numerous gram positive rods. Culture report revealed growth of *Chryseobacterium meningosepticum*. Patient was treated with antibiotics, but no improvement was noted.

Image guided biopsy

Image guided biopsy report showed non-specific chronic inflammation with fibrosis along with foci of excessive proliferation of atypical pneumocytes. Hence the report was inconclusive.

Open lung biopsy

Patient underwent Open lung pleural biopsy under general anesthesia. Patient was cleaned and draped under strict aseptic condition. Camera port was inserted in right 6th intercostal space in posterior axillary line. Utility port was created through right 5th intercostal space in line of nipple and expanded. Lung adhesions were freed, and lung nodules were identified and biopsied. One nodule was taken from the right upper lobe next to hilum and one nodule taken from the right posteromedial segment of the lower lobe. Station lymph node was identified and biopsied as well.

Lung was washed with copious normal saline. Wound was closed in reverse order. 28 Fr chest tube was placed basally through the camera port, and antiseptic dressing was done. The specimens were sent for histopathology.

Postoperatively, patient was administered Inj. Augmentin 1.2 g IV q8h, Inj. Toradol 30 mg IV q12h, Inf. Provas1g IV q12h, Inf. Risek 40mg IV q24h.

Open lung biopsy revealed portion of lymphoid tissue with collections of carbon pigment containing macrophages with small number of needle birefringent silica crystals. There was no evidence of granuloma or malignancy. These features are seen in collagen vascular disease. Hence further clinical and serological evaluation was done.

Table 2: Autoimmune profile of patient.

ANA Profile	
U1-RNP Antibodies	< 0.5 U/ml (negative)
SS-B/La Antibodies	0.70 U/ml (negative)
SS-A/Ro Antibodies	< 0.2 U/ml (negative)
Sm- Antibodies	<0.2 U/ml (negative)
Serum p-ANCA	1.14 (negative)
Serum c-ANCA	4.40 (negative)
Scl-70	**11.06 (positive)**

Based on opinion of combined multidisciplinary team, patient was administered steroids. Interval regression of pulmonary nodules were noted after 4 months of commencement of steroids on subsequent Chest X-ray radiofilms as shown in Fig 6 and CT chest films as shown in Figure 7-9. Also, patient showed significant clinical improvement and is currently under the treatment of Rheumatologist.

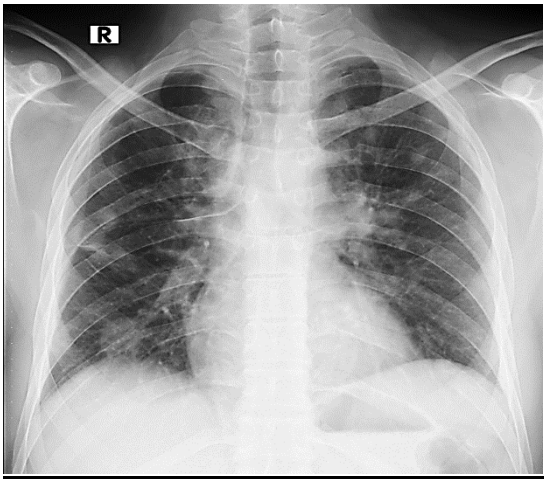

Figure 6: Bilateral irregular nodules have improved comparatively after steroid therapy.

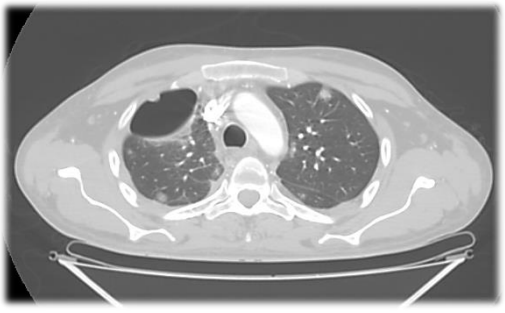

Figure 7: Pulmonary nodules decreases in size and number after steroid therapy.

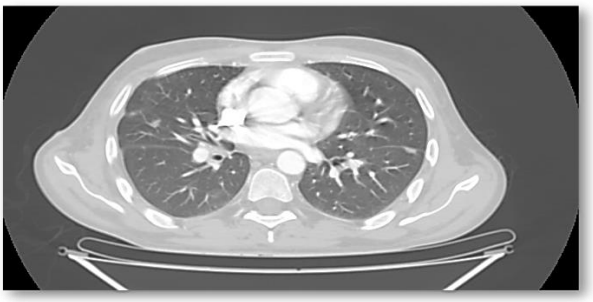

Figure 8: Pulmonary nodules decreases in size and number after steroid therapy.

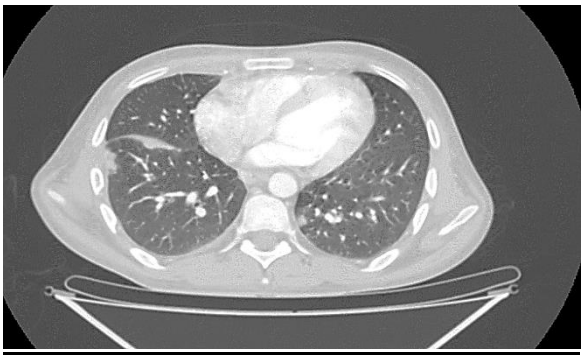

Figure 9: Pulmonary nodules decreases in size and number after steroid therapy.

DISCUSSION

Scleroderma with pulmonary involvement most commonly presents with Interstitial Lung Disease as reported in a study conducted by Vincent Cottin in France in 2019.[5] Similarly, according to a study conducted by A C Arroliga et al in Italy, interstitial lung disease and pulmonary vascular disease are the two most common pulmonary manifestations of scleroderma.[8]

In comparison, our case repot shows that scleroderma can also present as pulmonary nodules in patients with pulmonary involvement.

According to a study conducted by Tülay Kıvanç et al in Ankara, Turkey, cyclophosphamide and corticosteroid therapy administered to a patient with scleroderma and pulmonary nodules showed resolution of pulmonary nodules at the end of the first month of treatment upon subsequent chest computerized tomography. In unusual radiological findings suggesting pulmonary nodules, scleroderma should be kept in view as the etiological factor.[4]

Similarly, another study conducted by A C Arroliga et al in Italy, Both D-penicillamine and cyclophosphamide are successful treatment modalities for patients with interstitial lung disease. Pulmonary vascular disease in scleroderma can be best treated with Nifedipine.[8]

According to another study conducted by Lutz Wollin et al in Germany in 2019, Nintedanib inhibits a number of steps in the initiation and progression of lung fibrosis hence acting as anti-fibrotic agent in scleroderma patients with pulmonary manifestations.[9]

Our study showed similar results i.e. administering steroids led to significant clinical improvement in the patient as well as resolution of pulmonary nodules after 4 months of follow up chest CT. Therefore, steroids can be considered as a successful and reliable treatment option in patients with scleroderma having pulmonary manifestations.

CONCLUSION

Pulmonary involvement in sarcoidosis patients often goes undiagnosed due to the asymptomatic nature of lung involvement in its early stage, as well as other outcomes of their disease. Clinicians need to have a low threshold to look for Interstitial Lung Disease and Pulmonary Arterial Hypertension which are the leading causes of death in these patients. In unusual radiological findings suggesting pulmonary nodules, scleroderma should be kept in view as an etiologic factor.

Once diagnosed, therapy or enrolment in treatment is recommended, while lung transplant is an option in selected patients with advanced lung disease. Other non-pharmacological treatment interventions and goal-oriented measures that are not taken care in this case may affect outcome for patients with pulmonary manifestations of Systemic Sclerosis.

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