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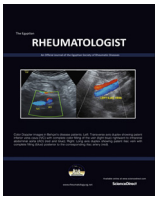

Original Article

Pulmonary manifestations in Egyptian patients with systemic sclerosis

Eman A. Hafez, Sherin H. Hamza *, Caroline S. Morad, Ahmed A. Abd Alkader

Internal Medicine Department-Rheumatology Division, Ain Shams University, Egypt

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ABSTRACT

Aim of the work: To study the occurrence of interstitial lung disease (ILD) and pulmonary hypertension (PH) in a cohort of Egyptian systemic sclerosis (SSc) patients and their relation to clinical variables.
Patients and methods: Thirty SSc patients underwent pulmonary function tests (PFTs), plain chest X-ray and chest high-resolution computed tomography to assess parenchymal abnormality and maximum fibrosis score (Fibmax). Transthoracic echocardiography to screen for evidence of pH. Nailfold capillary microscopy examination for recognizing nailfold capillary abnormalities and staging, skin thickness assessment by modified Rodnan's skin score (MRSS).
Results: The mean age of the patients was 40.97 ± 12.63 years; 22 females and 8 males and disease duration was 9.65 ± 8.18 years. 17(56.7%) patients had diffuse cutaneous systemic sclerosis (dcSSc) and 13 (43.3%) localized cutaneous (lcSSc). All patients showed restriction in the PFTs. ILD was present in 83% and PH in 17%; ground-glass opacity in 83.3%, septal thickening in 56.7%, honeycombing in 43.3%, bronchiolectasis in 23.3% and consolidations in 20% of the patients. ILD was significantly more in dcSSc than in lcSSc ($p = 0.025$). PH was present in 29.4% of the dcSSc patients but in none of the lcSSc patients. MRSS was significantly higher in patients with pulmonary affection than those without ($p = 0.016$) and in patients with ILD and PH than those with ILD alone. A significant correlation was found between the Fibmax and MRSS ($r = 0.87$, $p < 0.0001$). Predictors of ILD were disease duration >11 years, forced vital capacity (FVC) <80%, and MRSS > 20.
Conclusion: ILD is a frequent finding and PH is common in SSc patients especially the dcSSc subtypes. Disease duration, decline in FVC and increased skin thickness are associated with an increased risk of ILD.

1. Introduction

Systemic sclerosis (SSc) is a multisystem autoimmune disease of unknown etiology, characterized by endothelial dysfunction resulting in vasculopathy of small vessels, and dysfunction of fibroblasts with resultant excessive collagen production and fibrosis [1]. Fibrosis of internal organs can involve different body systems, including skin, pulmonary, cardiac, and gastrointestinal systems [2].

The pulmonary system is frequently involved in SSc and causes a significant increase in morbidity and mortality. Involvement can affect all parts of the respiratory tract including the blood vessels, lung parenchyma, airways, pleura, and respiratory muscles [3]. It is estimated that 80% of patients with SSc have some degree of pulmonary affection. This makes pulmonary system the second most commonly affected visceral system after the esophagus. Furthermore, pulmonary involvement predicts a poorer prognosis and is now considered the leading cause of death among patients with SSc [4].

Interstitial lung disease (ILD) is the most common type of pulmonary affection in SSc, about 90% of patients will have evidence of ILD on high resolution computed tomography (HRCT) of the chest and about 40–75% will have restrictive abnormalities in pulmonary function tests (PFTs) [1]. It develops insidiously and eventually progresses to fibrosis. Since lung fibrosis is an irreversible process, early diagnosis is mandatory to decrease morbidity and mortality. Assessment of ILD in SSc focuses on early detection, assessment of severity, and definition of progression and is best performed by regular PFTs [2]. HRCT is the most sensitive and specific tool for detecting and describing any ILD present in SSc [1].

Pulmonary hypertension (PH) is defined as an elevation in the mean pulmonary artery pressure greater than 25 mmHg at rest. It can occur in all forms of SSc and is associated with early mortality. The prognosis of SSc-associated PH is poorer than that of idiopathic PH [1,2]. The prevalence of SSc-PH is variable and is dependent upon the method of detection and the population studied. It has been reported to range from 21 to 26.7% when transthoracic echocardiography (TTE) is used as a screening tool [5,6].

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* Corresponding author.
E-mail address: drsherinehosny@hotmail.com (S.H. Hamza).

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The aim of the present work was to study the occurrence of ILD and PH in a cohort of Egyptian patients with SSc and their relation to the extent of skin affection and other clinical variables.

2. Patients and methods

This was a cross-sectional, observational study involving 30 patients fulfilling 2013 ACR/EULAR classification criteria for scleroderma [7]. The patients were recruited from the rheumatology inpatient and outpatient clinic, Ain Shams University Hospitals. Patients with other connective tissue diseases, pulmonary malignancies and smokers were excluded. The study conforms to the 1995 Helsinki declaration and approved by the ethical committee of Ain Shams University Hospitals. Informed consent was obtained from all patients.

All patients were subjected to complete medical history taking and thorough clinical examination with special emphasis on skin manifestations (such as Raynaud's phenomenon, skin thickness, sclerodactyly, puffy fingers, calcinosis and digital tip ulcers), pulmonary, cardiac, gastrointestinal and musculoskeletal manifestations. Skin fold thickness was scored using modified Rodnan's skin score (MRSS) [8]. Laboratory investigations were performed including a complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) titer, serum creatinine and blood urea nitrogen (BUN), aspartate transaminase and complete urine analysis.

Pulmonary function tests were performed including forced vital capacity (FVC), forced expiratory volume in the first second of forceful exhalation (FEV_1) and FEV_1/FVC ratio [9].

Radiological assessment included plain chest X-ray and HRCT. Abnormal findings were recorded; and parenchymal ILD abnormalities were categorized in 5 categories as follows: no abnormal findings, ground-glass appearance, consolidations, septal thickening, bronchiolectasis, and honeycombing [10]. Images from the right and left lungs were each divided into 3 zones (upper, middle, and lower) and scored for the extent of pulmonary fibrosis using a 0–4 Likert scale (0%, 1–25%, 26–50%, 51–75%, and 76–100% involvement), then semiquantitative record for maximum fibrosis score (Fibmax) was done [11]. Transthoracic echocardiography (TTE) was used to screen for evidence of pH in the form of right ventricular systolic pressure (RVSP) of 35 mmHg or higher, dilated right ventricle (RV), and decreased RV function [1,12].

Nail fold capillary microscopic (NFCM) examination was done and staged as; *Early*: few giant capillaries and hemorrhages, well-preserved capillary architecture and no evident loss; *Active*: more giant capillaries and hemorrhages, moderate capillary loss and mild architecture derangement; *Late*: irregular capillary enlargement, few/absent giant capillaries and hemorrhages, severe

Table 1
Demographic data, clinical characteristics, maximum fibrosis score and nailfold capillary microscopy examination in the systemic sclerosis patients.

Variables Mean ± SD (range) or n (%)			SSc patients (n = 30)	
Age			40.97 ± 12.63 (22–65)	
Disease duration			9.65 ± 8.18 (1–28)	
Sex F (n = 22):M (n = 8)			2.75:1	
MRSS			23.03 ± 10.27 (6–45)	
Subtypes	lcSSc		13	(43.3)
	dcSSc		17	(56.7)
Clinical manifestations				
Skin	RP		29	(96.7)
	Puffy finger		28	(93.3)
	Digital tip ulcer		28	(93.3)
	Sclerodactyly		19	(63.3)
	Calcinosis		7	(23.3)
Pulmonary	Dyspnea	Grade I	4	(13.3)
		Grade II	10	(33.3)
		Grade III	12	(40)
		Grade IV	2	(6.7)
	Chest pain		10	(33.3)
	Cough		16	(53.3)
	Leathery crepitations		24	(80)
	Cyanosis		1	(3.3)
GIT	Lower dysphagia		13	(43.3)
	Reflux		25	(83.3)
Arthralgia			25	(83.3)
Cardiac (Arrhythmias)			7	(23.3)
Hypertension			6	(20)
HRCT Fibmax score			2.17 ± 1.26	
HRCT staging according to Fibmax score				
Stage 0			5	(16.7)
Stage 1			2	(6.7)
Stage 2			10	(33.3)
Stage 3			9	(30)
Stage 4			4	(13.3)
NFCM examination				
Findings	Dilated capillaries		28	(93.3)
	Mega/Giant capillaries		18	(60)
	Capillary hemorrhages		18	(60)
	Avascular area		13	(43.3)
Stages	Active		7	(23.3)
	Early		14	(46.7)
	Late		9	(30)

SSc: Systemic sclerosis, MRSS: modified Rodnan skin score, lcSSc: limited cutaneous systemic sclerosis, dcSSc: diffuse cutaneous systemic sclerosis, RP: Raynaud's phenomenon, GIT: gastrointestinal tract, HRCT: high resolution computerized tomography, Fibmax score: maximum fibrosis score, NFCM: nailfold capillary microscopy.

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