

Erasmus Syndrome: An Underrecognized Entity

Síndrome de Erasmus: Uma Entidade Pouco Reconhecida

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ABSTRACT

We present a case of a 33-year-old male who worked as a plumber and a locksmith. The patient presented with diffuse myalgia and asthenia, skin sclerosis and puffy fingers, Raynaud's phenomenon, exertional dyspnea and erectile dysfunction. The presence of specific autoantibodies enabled the diagnosis of systemic sclerosis. Chest-computed tomography revealed upper lobe consolidation. After extensive evaluation, the multidisciplinary interstitial lung disease team concluded that the patient also had advanced silicosis. After a year, there was significant clinical, radiologic, and functional deterioration of the lung disease. The patient was referred for lung transplant. Silica inhalation is the cause of silicosis but is also implicated in the development of systemic sclerosis (Erasmus syndrome). Although they share a common risk factor, it is rare to find both diseases co-existing. We present this case of a young patient where both diseases presented aggressively in order to raise awareness to this association.

Keywords: Connective Tissue Diseases; Lung Diseases, Interstitial; Silicosis; Scleroderma, Systemic

RESUMO

Apresentamos o caso de um homem de 33 anos que trabalhava como canalizador e serralheiro. Apresentava mialgias e astenia, esclerose cutânea e *puffy fingers*, fenómeno de Raynaud, dispneia de esforço e disfunção erétil. A presença de autoanticorpos específicos permitiu o diagnóstico de esclerose sistémica. A tomografia computadorizada de tórax revelou consolidações dos lobos superiores. Após extensa avaliação, o grupo multidisciplinar de doenças do interstício concluiu que o doente tinha também silicose avançada. Após um ano, houve agravamento clínico, radiológico e funcional significativo da doença pulmonar. O doente foi encaminhado para transplante pulmonar. A inalação de sílica é a causa da silicose, mas também está implicada no desenvolvimento da esclerose sistémica (síndrome de Erasmus). Embora tenham um fator de risco comum, é raro encontrar as duas doenças simultaneamente. Apresentamos o caso de um doente jovem em que ambas as doenças se apresentaram de forma agressiva para alertar sobre esta associação.

Palavras-chave: Doenças Pulmonares Intersticiais; Doenças do Tecido Conjuntivo; Escleroderma Sistémico; Silicose

INTRODUCTION

Silicosis is caused by the inhalation of free crystalline silica and is one of the most important occupational diseases worldwide. Its presentation, clinical course and severity are variable.¹ In most severe cases, there is disease progression into large fibrotic masses with upper-lobe predominance, which is known as progressive massive fibrosis.¹⁻³ A lesser-known association is the one between silica exposure and the development of systemic autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, antineutrophil cytoplasmic antibody-related vasculitis and systemic sclerosis (SSc).⁴⁻⁶ The rare occurrence of SSc developing after silica exposure is termed Erasmus syndrome.⁷

CASE REPORT

A 33-year-old Caucasian male presented with a history of diffuse myalgia and asthenia, edema of the hands with associated pain and Raynaud phenomenon, exertional dyspnea (mMRC 1- shortness of breath when hurrying or walking up a slight hill) and new-onset erectile dysfunction. He was a light smoker (ten packs a year), worked as a plumber and a locksmith, and had a family history of rheumatoid arthritis in a grandmother and a cousin. On clinical exami-

nation, the patient was eupneic with a peripheral resting oxygen saturation of 96%; he had skin sclerosis and puffy fingers (Fig. 1). Bloodwork revealed an elevated erythrocyte sedimentation rate of 32 mm, positive ANA antibodies (fine speckled) with a titre 1:320, anti-SSA-52kDa and Scl-70 with a strong titre. Radiography of the hands showed joint space narrowing of the interphalangeal joints.

A diagnosis of SSc was made, and given the severity of the symptoms, the patient was admitted to the ward and started on intravenous immunoglobulin. During the admission, further investigation was undertaken. Videocapillaroscopy was suggestive of secondary Raynaud's, sclerodermic pattern in early stage, and the echocardiogram showed good ventricular function and no signs of pulmonary hypertension. The chest radiography done upon admission (Fig. 2) showed bilateral upper lobe opacities and left pleural effusion.

The chest computed tomography (CT) (Fig. 3) revealed areas of upper lobe consolidation, micronodular ground-glass opacities with a lower lobe predominance and a left pleural effusion.

The patient then underwent bronchoscopy which showed no endoscopic abnormalities. Bronchoalveolar

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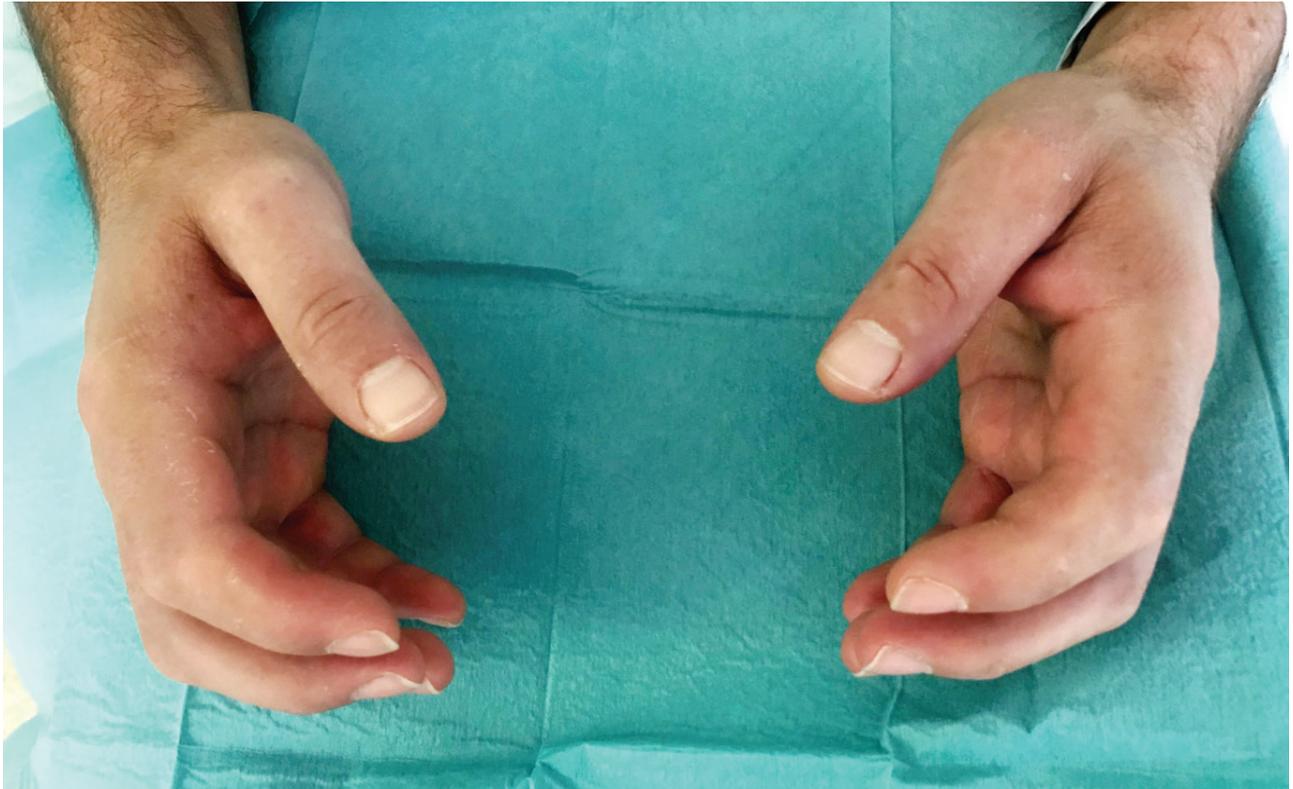


Figure 1 – Patient's hands showing skin sclerosis and puffy fingers

lavage (BAL) showed lymphocytosis (24%) with a normal CD4+/CD8+ and CD4+CD103+/CD4+ ratios and negative culture test. A Mantoux test was performed with 10 millimeters. Pulmonary function tests (PFT) revealed a moderately severe restrictive pattern and a moderate decrease in the diffusing capacity of carbon monoxide. In the six-minute walk test, the patient had a starting peripheral oxygen saturation of 96% and a minimum saturation of 94%. He walked 600 m and ended the test with extreme fatigue and moderate dyspnea.

A surgical lung biopsy was proposed, but the patient refused to undergo surgery. The case was then presented to the multidisciplinary interstitial lung disease (ILD) team. The conclusion was that, given the history of occupational exposure to silica, the radiologic findings were consistent with progressive massive fibrosis, and in the absence of alternative differentials, a solid diagnosis of silicosis could be made.

The patient had clinical improvement, and immunosuppressive therapy was adjusted to mycophenolate mofetil 1000 mg twice daily plus prednisolone 5 mg daily. He was started on sildenafil 25 mg and bosentan 125 mg for the treatment of Raynaud's phenomenon and underwent treatment for latent tuberculosis. He was discharged from the hospital after which he remained clinically stable for several

months.

After about a year, the patient started to complain of worsening exertional dyspnoea and a weight loss of 11 kg in a few months. The PFTs (Table 1) showed worsening of the restrictive pattern with a decrease of the forced vital capacity (FVC) of 740 mL, which corresponds to 22%. The CT scan revealed progression of the fibrotic masses (Fig. 4). The symptoms associated with SSc remained stable.

The patient's attending physician in the Pulmonology Department advised him to undergo evaluation for lung transplantation and he was considered eligible for bilateral lung transplant, given the absence of significant calcification of the fibrotic masses and hilar lymphadenopathies. The patient is currently on the lung transplant waiting list.

DISCUSSION

SSc is an autoimmune connective tissue disease characterized by vasculopathy, progressive fibrosis with multi-organ involvement and the presence of specific autoantibodies.⁸ The association between SSc and silica was first described by Erasmus in 1957 with 17 cases of SSc in South African miners and has since been called Erasmus syndrome.⁷ Although little is known about the mechanisms by which silica exposure leads to the development of SSc, it has been proposed that silica leads to the activation of the



Figure 2 – Admission's chest radiography



Figure 3 – Thoracic computed tomography of the chest in June 2019

EDITORIAL
PERSPECTIVA
ARTIGO ORIGINAL
ARTIGO DE REVISÃO
CASO CLÍNICO
IMAGENS MÉDICAS
NORMAS ORIENTAÇÃO
CARTAS

Table 1 – Pulmonary function tests in June 2019 (left column) and July 2020 (right column)

	06/2019	07/2020
FVC	3.43 L (60%)	2.69 L (47%)
FEV1	2.66 L (57%)	2.01 L (43%)
FEV1/FVC	77	74
TLC	4.88 L (65%)	4.31 L (57%)
RV	1.32 L (70%)	1.32 L (70%)
DLCO	52%	45%

FEV1: forced expiratory volume in one second; FVC: forced vital capacity; TLC: total lung capacity; RV: residual volume; DLCO: diffusing capacity for carbon monoxide

innate immune system with lung inflammation, activation of the adaptive immunity and production of autoantibodies.⁴ Epidemiological studies confirmed this, and a 2009 meta-analysis concluded that exposure to silica may be associated with a 3.2-fold increase in the relative risk of SSc, while the absolute risk in the general population is less than 0.5%.⁶

In the case of this patient, with an established diagnosis of SSc and respiratory symptoms, we expected to find pulmonary complications. These typically present in the form of ILD as non-specific interstitial pneumonia or, less commonly, usual interstitial pneumonia,⁹ but none of these patterns fitted the radiologic findings on the CT scan. A mul-

tidisciplinary discussion of the case led to the diagnosis of silicosis. This disease can present as acute silicosis, developing within weeks to a few years after exposure to high concentrations of silica and with rapid onset of dyspnea, cough, weight loss and fatigue. Chronic silicosis develops more than ten years after exposure with slowly progressive symptoms. Progressive massive fibrosis is the most severe form and results from the coalescence of the silicotic nodules and consolidations into large fibrotic masses in the upper lung zones.^{2,3} As there is no effective treatment, efforts should be focused on its prevention, early diagnosis and swift elimination of further exposure. In end-stage disease, lung transplantation is a treatment option for selected patients.^{3,10}

We add this case to the small number of published case reports of silicosis and SSc co-existing in the same patient,^{11–15} with the aim of raising awareness to this association, and as a reminder that the same environmental and occupational exposures may be a risk factor for different diseases.

AUTHOR CONTRIBUTIONS

AM, IM: Draft of the manuscript.

SP, AB: Critical review of the manuscript and redrafting.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical

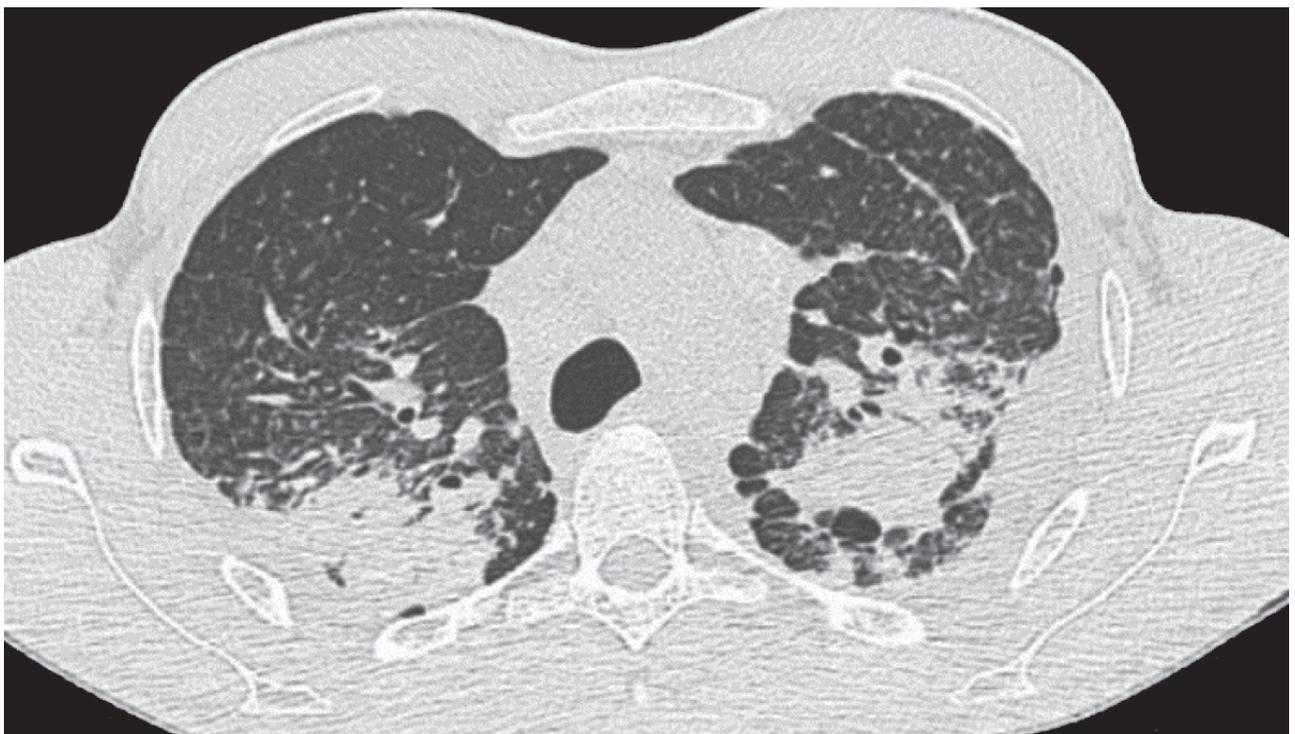


Figure 4 – Thoracic computed tomography of the chest in August 2020 showing worsening of the fibrotic masses

Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

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COMPETING INTERESTS

The authors have declared that no competing interests exist.

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