SHORT COMMUNICATION
https://doi.org/10.1590/1806-9282.20210377

Pulmonary rehabilitation: a unfairly forgotten therapeutic tool even in the worst scenarios

Joana Paixão[1]*, Joana Cascais Costa[1], Cidália Rodrigues[2], Filipa Costa[2], Leonor Aleluia[1,3]

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease that can affect almost every organ or system. Pleuropulmonary involvement, often underdiagnosed, occurs in about 60–80% of SLE cases[1]. Shrinking lung syndrome (SLS) is one of its rare, although debilitating, complications occurring between 0.5–1.1% of patients[2]. It is characterized by progressive unexplained dyspnea, chest pain, elevated hemidiaphragm, and reduced lung volumes with restrictive pattern on pulmonary function tests (PFTs), but without parenchymal anomalies[2]. Despite being more prevalent during the later stages of the disease, it can manifest at any stage of SLE, even with inactive disease (in more than half of patients, according to SELENA-SLEDAI scores) and usually without prior or simultaneous involvement of other organs[3].

It has been rarely described in other autoimmune disorders and is more prevalent in women (with ratio 6:1)[3]. Differential diagnoses include restrictive respiratory defect due to pulmonary fibrosis, obesity, diaphragmatic palsy, and central nervous system disorders[4]. There are no definite criteria for SLS diagnosis, and it usually relies on the association of reduced lung volumes and restrictive defects on PFTs, together with the exclusion of other causes[4].

Even though its pathophysiology remains unknown, because pleuritic chest pain is a prominent feature of SLS, it has been hypothesized that pleural effusion and inflammation could reduce diaphragmatic mobility. This would inhibit deep inspiration, resulting in chronic lung hypo-inflation, consequently leading to parenchymal remodeling with changes in elasticity and decrease in lung compliance[5,6].

Although the therapeutic approach does not gather consensus, the first-line treatment usually includes corticosteroids with or without immunosuppressants[1,2]. In their review, Duron et al. concluded that there was no prognostic difference between patients receiving isolated steroids or steroids associated with immunosuppressants[4]. Theophylline and beta-agonists alone or in combination with glucocorticoids have been also employed to increase diaphragmatic strength[7,8]. Although the SLS mechanism is poorly understood, there have also been positive outcomes with rituximab and belimumab as B cells may play an important role in SLS pathophysiology[9,10].

Surprisingly, no published literature on SLS patients makes any consistent reference to the benefits of respiratory pulmonary rehabilitation programs as a crucial component of any chronic lung disease management.

DESCRIPTION

The authors present the case of a 57-year-old female, with past medical history significant for SLE with 12 years duration, secondary antiphospholipid syndrome, and chronic pulmonary embolism. In a routine consultation, she had complains of progressive worsening of dyspnea on minor exertion (mMRC grade 2) and intermittent pleuritic chest pain over the past four months, with no extra-thoracic manifestations of SLE, namely, arthralgia or cutaneous involvement. At that time, her therapy consisted of daily prednisolone 10 mg/day, hydroxychloroquine 400 mg/day in addition to azathioprine 50 mg thrice a day, formoterol twice a day, and rivaroxaban 20 mg/day.

The chest X-ray showed small lungs and bilateral elevation of the diaphragm, with no evidence of pleuroparenchymal changes. For better clarification, the patient underwent chest computed tomography to assess the eventual pulmonary

[1]Centro Hospitalar e Universitário de Coimbra, Serviço de Medicina Interna – Coimbra, Portugal.
[2]Centro Hospitalar e Universitário de Coimbra, Serviço de Pneumologia – Coimbra, Portugal.
[3]Centro Hospitalar e Universitário do Algarve, Hospital de Faro, Unidade de AVC – Faro, Portugal.
*Corresponding author: jipaixao13@gmail.com
Conflicts of interest: the authors declare there are no conflicts of interest. Funding: none.
Received on April 14, 2021. Accepted on May 02, 2021.

involvement. As shown in Figure 1, there were only residual linear opacities compatible with fibrotic bands/linear atelectasis with no other relevant parenchymal findings, nor pleural effusion, as commonly reported in SLS cases[11]. Fluoroscopy showed bilateral diaphragmatic paralysis. PFTs confirmed a restrictive ventilatory defect with her forced vital capacity (FVC) being 60.4% of predicted, low total lung capacity (TLC) being 60.3% of predicted, forced expiratory volume (FEV1) being 61.2% of predicted, functional residual capacity (FRC) being 59.8% of predicted, residual volume (RV) being 58.4% of predicted, reduced diffusing capacity for carbon monoxide (DLCO) being 56.8% of predicted, transfer coefficient of the lung for carbon monoxide (KCO) being 91.7% of predicted, and resting gas exchange without significant difference from the age predicted pO_2 being 80.3 mmHg. A 6-min walk test was performed, but the patient only tolerated two min due to excessive dyspnea and desaturation (completed only 142 m; 96–84% oxygen desaturation; maximum exertion on Borg Scale 10/10). Despite having an adequate cardiac response to effort on cardiopulmonary exercise testing (CPET), she presented an important ventilatory limitation (VO_2 17.8 mL/min/kg, 62% of predicted), as her respiratory reserve was depleted, due to a gas exchange compromise with consequent desaturation, probably potentiated by her pulmonary vasculopathy; subsequent lung ventilation-perfusion (V/Q) scintigraphy confirmed evidence of chronic pulmonary thromboembolism, although without pulmonary hypertension, and she began full dose rivaroxaban. As reported elsewhere, there was an unusual C-reactive protein elevation, not common on controlled SLE[12]. Considering all these results, SLS diagnosis was assumed, and she initiated aminophylline thrice a day. Noteworthy, as shown in Table 1, when aminophylline was discontinued due to iatrogenic tachycardia, the patient reported worsening of shortness of breath concomitantly with marked decline of her restrictive lung pattern (FVC=36.2%; TLC=40.7%; FEV1=40.3%; FRC=36.7%; RV=46%, of the predicted values). Despite increasing corticosteroid and azathioprine doses, her tolerance to efforts continued to diminish, and she was started on a pulmonary rehabilitation program, twice weekly, for the next five months. The patient performed aerobic exercise training, ventilatory control exercises, and strength training of the upper and lower limbs. She presented a progressive improvement in exercise tolerance with endurance testing showing a significant increase in exercise tolerated time (from 9:25–30 min). The respiratory complains as well as the sequential PFT of patient began to improve progressively (Table 1). At present, her mMRC is grade 1, TLC is 51.6% of predicted, and she completes 462 m on the 6-min walk test, considered a minimal clinically important difference (MCID)[13] with 97–91% oxygen saturation and a Borg Scale 3/10. She is currently maintained on azathioprine 200 mg twice a day and prednisolone 5 mg/day, after a gradual weaning period; aminophylline was also carefully reintroduced. Equally important as exertional tolerance is the unquestionable improvement of patient's quality of life, being now able to restore her professional and normal activities of daily living (ADL), as expressed on The London Chest ADL Scale (LCADL)[14] which score diminished from 26–17, also considered MCID. Furthermore, on the Hospital Anxiety and Depression Scale (HADS)[15], there was also a favorable evolution of clinical importance (Table 1).

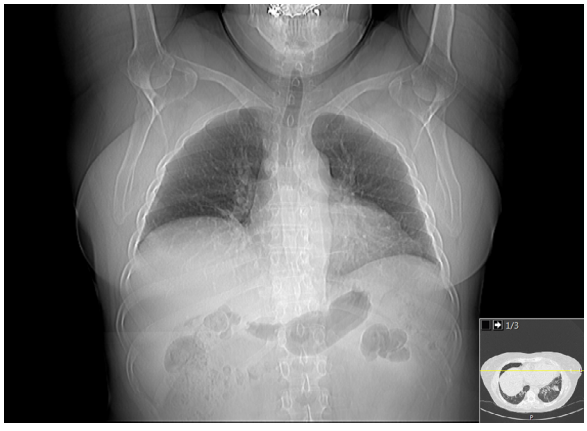

Figure 1. Chest computed tomography shows elevated hemidiaphragms with reduced lung volume, residual linear opacities compatible with fibrotic bands/linear atelectasis in medium lobe, anterior segment of the left upper lobe and lower lobes; right accessory tracheal bronchi directing toward the right upper lobe, with no other parenchymal relevant findings.

CONCLUSIONS

Shrinking lung syndrome is a rare lupus pulmonary manifestation of uncertain etiology whose diagnosis relies on the association of restrictive pulmonary capacity without interstitial lung disease, pleural effusion, or phrenic nerve palsy. Dyspnea, pleuritic chest pain, and elevated diaphragm should raise suspicion for this diagnosis[16]. In most cases, it has a favorable long-term prognosis if detected early and treated properly to avoid irreversible restrictive disturbances sequelae; however, in some case series, only 20% of patients normalize pulmonary function[9,16], while rest of them show only functional improvement or even stabilization of lung function[17].

Table 1. Evolution of the most important parameters.

	Before pulmonary rehabilitation	After aminophylline discontinuation	After pulmonary rehabilitation
FVC (% of predicted)	60.4	36.2	49.7
FEV1 (% of predicted)	61.2	40.3	54.2
TLC (% of predicted)	60.3	40.7	51.2
RV (% of predicted)	58.4	46	60.6
DLCO (% of predicted)	56.8	**	**
KCO (% of predicted)	91.7	**	**
pO_2 (mmHg)	80.3	77.4	77.5
VO_2 (ml/kg/min; % of predicted)	17.8 (62)	–	–
6-min walk test (m)	142	–	462*
Exercise tolerated time (min)	9:25	–	30*
Borg Scale	10	10	3
mMRC	2	3	1
LCADL	26	–	17*
HADS	16	–	12*

FVC: forced vital capacity; TLC: low total lung capacity; FEV1: forced expiratory volume; RV: residual volume; DLCO: reduced diffusing capacity for carbon monoxide; KCO: transfer coefficient of the lung for carbon monoxide; mMRC: modified medical research council dyspnea scale; LCADL: the London chest activities of daily living scale; HADS: hospital anxiety and depression scale. *Considered minimal clinically important difference (MCID). **Not calculated because of low volumes.

This case report is noteworthy, not only due to the rarity of this syndrome and the clear advantages of multidisciplinary management, but also essentially to stress out the core importance of pulmonary rehabilitation as a non-pharmacological tool that unquestionably reinforces therapeutic armamentarium not only on lupus shrinking lung syndrome but also on any chronic lung disease.

AUTHORS' CONTRIBUTIONS

JP: Writing – original draft, Writing – review & editing. **JCC:** Writing – original draft, Writing – review & editing. **CR:** Writing – original draft, Writing – review & editing. **FC:** Writing – original draft, Writing – review & editing. **LA:** Writing – original draft, Writing – review & editing.

REFERENCES

1. Warrington KJ, Moder KG, Brutinel WM. The shrinking lungs syndrome in systemic lupus erythematosus. Mayo Clin Proc. 2000;75(5):467-72. https://doi.org/10.4065/75.5.467
2. Borrell H, Narváez J, Alegre JJ, Castellví I, Mitjavila F, Aparicio M, et al. Shrinking lung syndrome in systemic lupus erythematosus: a case series and review of the literature. Medicine (Baltimore). 2016;95(33):e4626. https://doi.org/10.1097/MD.0000000000004626
3. Deeb M, Tselios K, Gladman DD, Su J, Urowitz MB. Shrinking lung syndrome in systemic lupus erythematosus: a single-centre experience. Lupus. 2018;27(3):365-71. https://doi.org/10.1177/0961203317722411
4. Duron L, Cohen-Aubart F, Diot E, Borie R, Abad S, Richez C, et al. Shrinking lung syndrome associated with systemic lupus erythematosus: a multicenter collaborative study of 15 new cases and a review of the 155 cases in the literature focusing on treatment response and long-term outcomes. Autoimmun Rev. 2016;15(10):994-1000. https://doi.org/10.1016/j.autrev.2016.07.021
5. Pillai S, Mehta J, Levin T, Muzumdar H, Nandalike K. Shrinking lung syndrome presenting as an initial pulmonary manifestation of SLE. Lupus. 2014;23(11):1201-3. https://doi.org/10.1177/0961203314536248
6. Henderson LA, Loring SH, Gill RR, Liao KP, Ishizawar R, Kim S, et al. Shrinking lung syndrome as a manifestation of pleuritis: a new model based on pulmonary physiological studies. J Rheumatol. 2013;40(3):273-81. https://doi.org/10.3899/jrheum.121048
7. Muñoz-Rodríguez FJ, Font J, Badia JR, Miret C, Barberà JA, Cervera R, et al. Shrinking lungs syndrome in systemic lupus erythematosus: improvement with inhaled beta-agonist therapy. Lupus. 1997;6(4):412-4. https://doi.org/10.1177/096120339700600413
8. Van Veen S, Peeters AJ, Sterk PJ and Breedveld FC. The "Shrinking Lung Syndrome" in SLE, Treatment with Theophylline. Clin Rheumatol. 1993;12(4):462-5. https://doi.org/10.1007/BF02231771
9. Langenskiöld E, Bonetti A, Fitting JW, Heinzer R, Dudler J, Spertini F, et al. Shrinking lung syndrome successfully

treated with rituximab and cyclophosphamide. Respiration. 2012;84(2):144-9. https://doi.org/10.1159/000334947

10. Choudhury S, Ramos M, Anjum H, Ali M, Surani S. Shrinking Lung Syndrome: A Rare Manifestation of Systemic Lupus Erythematosus. Cureus. 2020;12(5):e8216. https://doi.org/10.7759/cureus.8216
11. Neto F, Lyra T, Mello R, Valois V, Albano T, Paiva A, et al. Shrinking lung detected on computed tomography: pictorial essay of the main findings of the image. Open J Med Imaging. 2018;8(2):17-24. https://doi.org/10.4236/ojmi.2018.82003
12. Smyth H, Flood R, Kane D, Donnelly S, Mullan RH. Shrinking lung syndrome and systemic lupus erythematosus: a case series and literature review. QJM. 2018;111(12):839-43. https://doi.org/10.1093/qjmed/hcx204
13. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166(1):111-7. https://doi.org/10.1164/ajrccm.166.1.at1102
14. Bisca GW, Proença M, Salomão A, Hernandes NA, Pitta F. Minimal detectable change of the London chest activity of daily living scale in patients with COPD. J Cardiopulm Rehabil Prev. 2014;34(3):213-6. https://doi.org/10.1097/HCR.0000000000000047
15. Puhan MA, Frey M, Büchi S, Schünemann HJ. The minimal important difference of the hospital anxiety and depression scale in patients with chronic obstructive pulmonary disease. Health Qual Life Outcomes. 2008;6:46. https://doi.org/10.1186/1477-7525-6-46
16. Allen D, Fischer A, Bshouty Z, Robinson DB, Peschken CA, Hitchon C, et al. Evaluating systemic lupus erythematosus patients for lung involvement. Lupus. 2012;21(12):1316-25. https://doi.org/10.1177/0961203312454343
17. Ciaffi J, Gegenava M, Ninaber MK, Huizinga TWJ. Shrinking lung syndrome: diagnostic and therapeutic challenges in 3 patients with systemic lupus erythematosus. J Clin Rheumatol. 2019. https://doi.org/10.1097/RHU.0000000000001132