

Research Article

Shrinking Lung Syndrome in Systemic Lupus Erythematosus



Haidy M. Osman¹, Gihan M. Omar¹, Nadia F. Elameen², Abdel-Nasser A.¹

¹Department of Rheumatology and Rehabilitation, Minia University, Egypt.

²Department of Radiology, Minia University, Egypt.

DOI: 10.21608/MJMR.2022.130642.1072

Abstract

Shrinking lung syndrome (SLS) is a rare complication of systemic lupus erythematosus (SLE), however it was also reported with other connective tissue diseases (CTDs). It is characterized by its low prevalence with higher incidence in females patients. Although it is much more frequent in advanced stages of the disease, rarely, SLS may be the presenting manifestation of SLE. It was found that it mostly occurs in patients without previous or concomitant major organ involvement, moreover in inactive stages of the disease. Progressive exertional dyspnea accompanied by pleuritic chest pain are considered the dominant symptoms in SLS. Pulmonary function tests (PFTs) with reduced lung volumes and radiographic finding of elevated diaphragmatic copula are the characteristic features in SLS. There are no standardized guidelines for the treatment of SLS in SLE. However, the majority of patients showed good response on medium to high doses of glucocorticoids. Moreover, an immunosuppressive agent should be added if the patient fails to improve on steroids alone.

Key words: Systemic lupus erythematosus, shrinking lung syndrome, pulmonary function tests.

Introduction

Shrinking lung syndrome (SLS) is a rare complication mainly associated with SLE, however it was also reported in patients with other connective tissue diseases (CTDs), including Sjögren syndrome, systemic sclerosis, rheumatoid arthritis and undifferentiated connective tissue disease⁽¹⁾. It is characterized by its low prevalence, estimated between 0.5% and 1.1% in the general lupus population^(2, 3). However, a study by Deeb et al.,⁽⁴⁾ involved 1439 SLE patients and reported a prevalence of 1.5%. A much higher incidence was reported by Gheita et al.,⁽⁵⁾ as SLS was present in 8 patients (17.02%) out of 47 SLE patients complaining of dyspnea. SLS was considered in those with exertional dyspnea, restrictive pulmonary function tests (PFTs) and elevated copula of the diaphragm. Casey et al.,⁽⁶⁾ recorded 10 (4.44%) cases with SLS out of 225 SLE patients. It may complicate SLE at any time over its course,

ranging from as early as 1 month to 35 years after disease onset. Although it is much more frequent in advanced stages of the disease, rarely, SLS may be the presenting manifestation of SLE^(7, 8, 9).

This complication is more common in SLE patients of female sex, with a female-to-male ratio of 17:1. The major symptom of SLS is progressive exertional dyspnea of variable severity, accompanied by pleuritic chest pain in three quarters of patients. This complication usually occurs in patients without previous or concomitant major organ involvement other than SLS, and, in more than half of the patients, in inactive stages of the disease, according to SELENA-SLEDAI scores⁽¹⁰⁾.

Case presentation

We are presenting a case of a 25-years-old SLE female patient presented with erythematous

photosensitive skin rash, oral ulcers, polyarthritis, anemia, lymphopenia, Positive antinuclear and anti-double stranded DNA antibodies. She was diagnosed with SLE and treated with corticosteroids, hydroxychloroquine and azathioprine, but she was not compliant on her treatment. 2 years after lupus diagnosis, she presented to our rheumatology clinic with progressive shortness of breath of 4 months duration. At time of admission the patient was vitally stable, dyspneic at rest, with decreased air entry at lung bases, malar rash, oral ulcers and polyarthritis of hand and wrist joints bilaterally. Her laboratory work showed: normocytic, normochromic anemia, normal white cell count (5.8), normal platelets, elevated erythrocyte sedimentation rate (40 mm/hr), normal liver and renal function, normal CPK, positive antinuclear antibody (ANA) titer of 1:80 (homogenous), and a highly positive double-stranded DNA titer (> 200), mild albuminuria in simple urine, normal C3 and C4 levels and negative antiphospholipid antibodies. Chest radiography (CXR) showed elevated cupula of diaphragm and markedly decreased lung volumes (Fig. 1a), however high-

resolution chest computed tomography (HRCT) showed normal parenchyma. She was found to have restricted PFTs (forced expiratory volume 1 (FEV1) 39%, forced vital capacity (FVC) 40%; total lung capacity (TLC) 40%) and normal carbon monoxide diffusion capacity (DLCO) denoting extra-pulmonary cause (table 1). When repeating PFT in supine position there was further decrease in FVC by 25%. According to these findings, she was diagnosed as SLS which was confirmed by decreased diaphragmatic excursion by M-mode ultrasound. Treatment was started with prednisolone 60mg/day, azathioprine (100 mg/day) and hydroxychloroquine (200 mg twice daily) for 2 weeks. Unfortunately, her dyspnea progressed and PFT showed deterioration (FEV1 31%, FVC 30%; TLC 30%) (table 1). So, the next decision was to start Rituximab 1 gm twice, 15 days apart which showed dramatic improvement in dyspnea after 1 week of the first cycle. Steroid was gradually tapered with improvement of pulmonary symptoms, function test and CXR showed less elevation of the diaphragm (Fig. 1b).

Table (1): Pulmonary function test follow up results of the case

Pulmonary function tests	Normal values (% of the predicted)	On 1st presentation	After starting prednisolone	after rituximab
FVC	>80%	39%	31%	69%
FEV1	>80%	40%	30%	65%
TLC	>80%	40%	30%	70%
DLCO	>80%	normal	normal	normal

FVC: Forced vital capacity, FEV1: Forced expiratory volume 1, TLC: Total lung capacity, DLCO: Diffusion lung capacity for carbon monoxide.

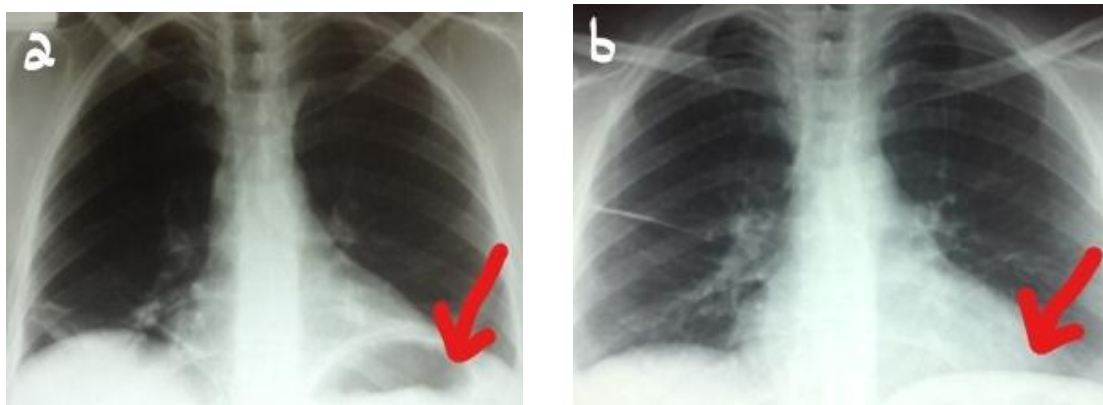


Figure (1) Chest X-ray with elevated copula of diaphragm before (a) and after (b) treatment

Discussion

An important diagnostic delay is observed in the clinical practice, indicating that SLS is still an under-recognized pulmonary complication of SLE. Patients should be considered to have an

SLS if they have: a compatible clinical picture (progressive exertional dyspnea of variable severity with or without pleuritic chest pain); lung volume reduction and restrictive ventilatory defect in PFT; and no evidence of parenchymal lung disease or vascular pathology on imaging (chest x-ray and thoracic high-resolution computed tomography [HRCT]) findings⁽¹⁾.

Despite its rarity, SLS should be considered in the differential diagnosis of lupus patients with dyspnea and/or pleuritic chest pain. In many ways, it represents a diagnosis of exclusion. In this sense, the recommended first-line procedures for diagnosis should include chest x-ray and thoracic HRCT, along with pulmonary and diaphragmatic function tests. The most distinctive findings of this entity were elevated unilateral or bilateral hemi diaphragms with reduced lung volumes, a restrictive ventilatory defect in PFT with reduced TLC and DLCO in absence of parenchymal lung disease or vascular pathology on imaging techniques⁽¹¹⁾.

Historically, Gibson et al.,⁽¹²⁾ measured trans-diaphragmatic pressure in those patients with SLS and found extra pulmonary volume restriction and inability of the diaphragm to generate normal pressure. The weakness of inspiratory and expiratory muscles could contribute to the cause of this syndrome. Controversially, other authors have found normal diaphragmatic strength in 12 patients with SLS, suggesting that a primary disorder of this muscle is an unlikely explanation. Phrenic neuropathy, pleural inflammation, adhesions and pain may also play a role in the pathogenesis of SLS⁽⁸⁾.

The evaluation of diaphragm dome motion by M-mode ultrasonography or dynamic contrast-enhanced lung MRI might be a useful second-line tool to reinforce clinical suspicion in cases of diagnostic difficulty. On the contrary, the diagnostic usefulness of the electromyography seems poor^(11,13).

There are no standardized guidelines for the treatment of SLS in SLE. According to the available experience, the majority of patients should be initially treated with medium or high doses of glucocorticoids⁽¹⁰⁾.

An immunosuppressive agent in conjunction with steroids should be used if the patient fails to improve, and it is advisable from the

beginning of the treatment in patients with severe clinical and functional decline, but there are no randomized controlled trials to provide data concerning their efficacy. The most widely used drugs were azathioprine and cyclophosphamide, with variable success⁽¹⁰⁾. Further, RTX was used in severe or refractory SLS (9 patients), with effectiveness and good safety profile in all cases^(14, 15). Based on this preliminary experience, RTX might emerge as the first-choice immunosuppressant, particularly in patients with severe or refractory disease, although larger-cohort studies must be performed in this field to confirm the efficacy of RTX in SLS. Theophylline and beta-agonists, alone or in combination with glucocorticoids, have also been suggested with the intent to increase diaphragmatic strength, but evidence of beneficial effects is lacking⁽¹⁵⁾. Recently, one case report showed good response to belimumab⁽¹⁶⁾.

Information about the duration of applied treatment, particularly with respect to glucocorticoid regimen and tapering, was not specified in the revised articles. In addition, the dose and duration of corticosteroids required for controlling SLS have never been tested in a randomized trial design. So it must be individualized based on the clinical response and evolution of pulmonary and diaphragmatic function tests, but taking also into account the recommendations for a more rational prescription of glucocorticoids^(17, 18).

The overall response to treatment is positive. The great majority of patients had significant clinical improvement and stabilization, or mild to moderate improvement on PFT. Despite the persistence of a chronic restrictive defect in most of these patients, none required chronic home oxygen therapy, and death because of respiratory failure or associated complications was extremely rare, indicating a low-grade defect⁽¹¹⁾.

Conclusion

SLS represents a rare complication of SLE. Although uncommon, it is important to be aware of its presenting features and prognosis because if it is not treated promptly and aggressively, it can lead to chronic restrictive ventilator dysfunction. Further multicenter controlled studies are required to define the best

diagnostic and treatment options for this complication.

References

- 1 Borrell H, Narváez J, José Alegre J, Castellví I, Mitjavila F, Aparicio M, et al., Shrinking lung syndrome in systemic lupus erythematosus A case series and review of the literature. *Medicine*. 2016; 95:33.
- 2 Bertoli A, Vila L, Apte M, Fessler B, Bastian H, Reveille J, et al., LUMINA Study Group Systemic lupus erythematosus in a multiethnic US Cohort LUMINA XLVIII: factors predictive of pulmonary damage. *Lupus*. 2007; 16: 410–7.
- 3 Calderaro D and Ferreira G. Presentation and prognosis of shrinking lung syndrome in systemic lupus erythematosus: report of four cases. *Rheumatol Int*. 2012;32:1391–6.
- 4 Deeb M, Tselios K, Gladman D, Su J, Urowitz M. Shrinking lung syndrome in systemic lupus erythematosus: a single-centre experience. *Lupus*. 2018; 27: 365–371.
- 5 Gheita T, El-Mofty S, Fawzy S, El-Fishawy H. Shrinking lung syndrome in systemic lupus erythematosus patients with dyspnea. *The Egyptian Rheumatologist*. 2012; 34: 179–183.
- 6 Casey A, Perin M, Enghelmayer J, Legarreta C, Zenon F, Rossi P, et al., Shrinking lung syndrome (SLS) associated with systemic lupus erythematosus (SLE): A series of cases in a university hospital. *European Respiratory Journal*. 2019; 54: Suppl. 63, OA5329.
- 7 Al-Raquum H, Uppal S, Al-Mutairy M, Kumari R. Shrinking lung syndrome as a presenting manifestation of systemic lupus erythematosus in a female Kuwaiti. *Clin Rheumatol*. 2006; 25:412–4.
- 8 Toya S and Tzelepis G. Association of the shrinking lung syndrome in systemic lupus erythematosus with pleurisy: a systematic review. *Semin Arthritis Rheum*. 2009; 39: 30–7.
- 9 Pillai S, Mehta J, Levin T, Muzumdar H, Nandalike K. Shrinking lung syndrome presenting as an initial pulmonary manifestation of SLE. *Lupus*. 2014; 23:1201 3.
- 10 Stevens W, Burdon J, Clemens L, Webb J. The 'shrinking lungs syndrome': an infrequently recognised feature of systemic

- lupus erythematosus. Aust N Z J Med. 1990; 20:67–70.
- 11 Carmier D, Diot E, Diot P. Shrinking lung syndrome: recognition, pathophysiology and therapeutic strategy. *Expert Rev Respir Med.* 2011; 5:33–9.
 - 12 Gibson G, Edmonds J, Hughes G. Diaphragm function and lung involvement in systemic lupus erythematosus. *The American Journal of Medicine.* 1977; 63: 6: 926-932.
 - 13 Henderson L, Loring S, Gill R, Liao K, 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;40:273-81
 - 14 Langenskiöld E, Bonetti A, Fitting J, Heinzer R, Dudler J, Spertini F, et al., Shrinking Lung Syndrome Successfully Treated with Rituximab and Cyclophosphamide. *Respiration.* 2012; 84:144–149
 - 15 Toribio P, Córca Albani M, Pérez M, de la Serna A. Rituximab in the Treatment of Shrinking Lung Syndrome in Systemic Lupus Erythematosus. *Reumatol Clin.* 2014; 10: 5:325–327.
 - 16 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. doi:10.7759/cureus.8216.
 - 17 Ugarte A and Ruiz-Irastorza G. SLE: the changing prognosis. *Lupus.* 2016; 25: 1285–1287.
 - 18 Kasturi S. and Sammaritano L. Corticosteroids in lupus. *Rheum Dis Clin North Am.* 2016; 42:47–62.