

Severe excessive dynamic airway collapse in a patient with primary Sjögren's syndrome

Sophie Ismael¹, Delphine Wermert², Kim-Diep Dang-Tran³, Marion Venot¹, Jean-Yves Fagon¹,
Jean-Luc Diehl^{1,4}

1 Service de Réanimation Médicale, Hôpital Européen Georges Pompidou,
Assistance Publique – Hopitaux de Paris, 20 rue Leblanc, 75015 Paris, France.

2 Service de Pneumologie, Hôpital Européen Georges Pompidou,
Assistance Publique – Hopitaux de Paris, 20 rue Leblanc, 75015 Paris, France.

3 Service de Radiologie, Hôpital Européen Georges Pompidou,
Assistance Publique – Hopitaux de Paris, 20 rue Leblanc, 75015 Paris, France.

4 INSERM U765, Faculté de Pharmacie and Faculté de Médecine, Université Paris Descartes,
Sorbonne Paris Cité, Paris, France.

The authors have disclosed no conflicts of interest.

Analysis and interpretation of the data: SI, DW, KDDT, MV, JYF, JLD

Drafting the manuscript for important intellectual content: SI, KDT, JLD

Key words: respiratory failure, expiratory dynamic airway collapse, Sjögren's syndrome,
bronchoscopy, lung cysts, inspiratory and expiratory CT

Abstract

Airway and cystic lung diseases can be observed in patients with Sjögren's syndrome. We report such a patient suffering of respiratory failure due to recurrent episodes of right pneumothorax, with the need of invasive mechanical ventilation. Despite thoracic drainage and adequate pneumothorax management, the patient could not be weaned from the respirator. Fiberoptic bronchoscopy revealed severe central excessive dynamic airway collapse of the lower part of the trachea and proximal bronchi. The severity of airway collapse was maximal at the intermediate bronchus level, with a near complete obstruction during expiration. Inspiratory and expiratory CT studies confirmed the fiberoptic findings and suggested a possible expiratory posterior compression of the intermediate bronchus by parenchymal lung cysts. Stenting was considered, but the patient died from ventilator-associated pneumonia before the realization of the procedure. This case is the first description of severe central excessive dynamic airway collapse in a patient with primary Sjögren's syndrome complicated by diffuse airway and cystic lung disease.

Introduction

Primary Sjögren's Syndrome (PSS) is one of the most frequent autoimmune diseases. Its prevalence, the second one after rheumatoid disease, is estimated up to 4% of the population (1-4). PSS is mainly characterised by a sicca syndrome (persistent symptoms of dryness of eyes and mouth), which can be associated with extra glandular manifestations. Despite a generally poor expression, clinical pulmonary involvement can affect up to 22 % of the PSS patients and is associated to reduced quality of life and increase in mortality (4). There is a broad spectrum of pulmonary manifestations, including airway diseases (mainly lymphocytic bronchial inflammation and xerotrachea) and interstitial diseases (mainly nonspecific interstitial pneumonia, usual interstitial pneumonia and organizing pneumonia) (5-7). Pulmonary cysts have also been increasingly described, with prevalence up to 46% (5, 7-13).

We report here the case of a 57 year-old woman suffering from severe respiratory insufficiency related to lung involvement of PSS, mainly characterized by diffuse airway and cystic lung diseases. A severe excessive dynamic airway collapse (EDAC) of central airways was observed, which was maximal at the intermediate bronchus level. EDAC was probably secondary to a PSS-related airway disease, with a possible accessory role of a posterior compression exerted by the cysts in some bronchial areas. To the best of our knowledge, such a feature has never been described in PSS patients. This case stands as an example of severe respiratory manifestations of PSS and raises some important diagnostic and therapeutic questions.

Case Report

A 57-year-old woman with a longstanding history of PSS was referred to our ICU for a severe respiratory distress related to a right pneumothorax. The PSS was diagnosed 25 yrs ago. At this time, the patient suffered from a sicca syndrome, polyarthralgias and already a severe

pulmonary involvement. A labial salivary gland biopsy showed a sialadenitis with a focus score superior to 1. At this time, CT scan studies displayed large areas of emphysema and cysts predominantly in the right lower lobe. A low-dosage systemic corticosteroid regimen was administered since the diagnosis of the PSS.

Results of Pulmonary Function testing performed 5 yrs before admission were as follows: FVC: 1.52 L (54 % theoretical value), ERV: 0.11 L (12% theoretical value), IRV: 0.81 L, FEV₁: 0.85 L (35 % theoretical value), RV: 5.01 (287 % theoretical value). Six months before admission, arterial blood gases results while breathing room air were as follows: pH: 7.44, P_{aO2}: 63 mmHg and P_{aCO2}: 46 mmHg. Other biological explorations showed the presence of polyclonal hypergammaglobulinemia and of anti-SSA and anti-SSB auto-antibodies. Rheumatoid factor and anti-CCP (Anti-cyclic citrullinated peptide) auto-antibodies were not detected. CT scan study displayed a frank aggravation, with large bilateral cysts. Alpha-1 antitrypsin was within the normal range (1.55 g/l). There was no evidence for lymphangiomyomatosis or histiocytosis. The patient didn't suffer from renal insufficiency. She had lived alone, had a son and had no problem for daily living activity until the 6 months preceding ICU admission.

During this period, she had been hospitalised twice because of recurrent right pneumothorax requiring thoracic drainage. She also complained of a worsening dyspnea. The systemic corticoid regimen (prednisone, 12 mg per day) was continued, but with no adjunction of any other immune-suppressive agent. The patient was finally hospitalized in another institution for a respiratory distress secondary to an acute bacterial pneumonitis, and referred to our ICU 6 days later because of hypercapnic respiratory failure with the need of invasive mechanical ventilation. A chest CT study revealed diffuse pulmonary parenchymal cysts and a recurrent apical right pneumothorax, of favourable course after chest tube insertion. The ventilator settings were as follows: VC-CMV mode, Tidal volume: 8 mL/Kg, Respiratory rate: 12/min., applied

PEEP: 5 cmH₂O, with the aim to minimize the level of dynamic hyperinflation. No clinical, biological or CT arguments were found for systemic amyloidosis or an associated lymphoproliferative disorder. Persistent weaning difficulties were observed, as well as recurrent episodes of ventilator-associated pneumonia (VAP). Fiberoptic bronchoscopy-obtained BALs were performed as standard VAP diagnostic procedures in our institution (14). Bronchoscopies suggested an EDAC of proximal bronchi and of the lower part of the trachea, which was confirmed by a video-bronchoscopic examination. The severity of the airway collapse was maximal at the intermediate bronchus level, with a near complete obstruction during expiration (Fig. 1). Cartilagenous tracheal and bronchial structures were visually judged as normal. Inspiratory and expiratory CT analysis confirmed the fiberoptic bronchoscopy findings and suggested a possible expiratory posterior compression of the intermediate bronchus by parenchymal lung cysts (Fig. 2). We applied the multidimensional FEMOS classification system for patients with expiratory central airway collapse proposed by Murgu (15), and found the following results:

- Functional status: 4
- Extent of abnormality: 4
- Morphology: EDAC
- Origin: secondary
- Severity of airway collapse: 4

Even if the FEMOS classification is presented as a help to objectively stratify patients, it suggested in the present case the need for therapeutic interventions such as stent insertion, and/or reinforcement of immunosuppressive treatment, with the aim to wean the patient from mechanical ventilation (15). Stenting under rigid bronchoscopy was therefore considered, but the

patient died from recurrent ventilator-associated pneumonia before the realization of the procedure. An immediate stent implantation under flexible bronchoscopy could have been also considered, but such a method is actually not currently available in our institution.

Discussion

We report the first case of severe proximal EDAC in a patient suffering from severe PSS-related pulmonary involvement. The patient fulfilled the 2002 American-European Consensus Group European criteria for PSS (16). While clinical pulmonary involvement can affect up to 22 % of the PSS patients (4), pulmonary cysts have also been increasingly described, with prevalence up to 46% (5, 7-13). Using high-resolution CT studies, Lohrmann reported in 24 PSS patients a high prevalence (79%) of pathological findings, with almost half of the patients displaying thin-walled cysts (5).

Bonner and Kobayashi were the firsts to describe cases of bullae formation or lung cysts in relation with Sjögren's syndrome (8, 17), with the hypothesis that lung cysts could result from airways narrowing by peribronchiolar lymphoid cellular infiltration and/or amyloid deposition, with consequent air trapping. Such a view has been widely shared, even if a correlation between cystic lesions and airways obstruction was not always found (11). In fact, the exact mechanisms of lung cysts formation is still a matter of debate. The main advocated mechanism is therefore a partial airway obstruction, either caused by a peribronchial lymphoid cellular infiltration, as seen in lymphocytic interstitial pneumonia, or caused by an amyloid deposition, as seen in multinodular amyloidosis. These 2 conditions are known to be associated to Sjögren's syndrome. In our case, there was no argument for a multinodular amyloidosis.

EDAC was evidenced in our patient, according to the definition proposed by Kalra and al., i.e. a pathological collapse and narrowing of the airway lumen by more than 50%, which is entirely due to the laxity of the posterior wall membrane with structurally intact airway cartilage (18). As suggested by Kalra, EDAC could have been suspected in our patient by difficulties in weaning from the mechanical ventilation and was evidenced by fiberoptic bronchoscopy with recording of short clips (18). CT studies performed during controlled mechanical ventilation with

end-inspiratory and end-expiratory pauses confirmed severe EDAC, which was maximal at intermediate bronchus level. Moreover, CT studies suggested some level of air trapping, particularly affecting cysts localized near to the posterior wall of the right main bronchus and of the intermediate bronchus. Therefore, we can hypothesize that the compression exerted by the cyst could have explained in part the higher severity of the right bronchus system collapse, as compared to the left one. Inspiratory and expiratory high-resolution CT studies were previously used by Meyer and al. to demonstrate air trapping in a patient with secondary Sjögren's syndrome, but without mention of airway collapse (9). A dynamic expiratory CT study could have displayed more precise informations, but was finally not considered for our patient, because of the difficulties related to the coupling of mechanical ventilation and CT-acquisitions and because of the already available results of the bronchoscopic examination (19). Therefore, one of the main interests of the CT study in our case was to appreciate the degree of compression exerted by the cysts.

We applied in our patients the FEMOS classification system proposed by Murgu as a help to define the need for therapeutic interventions such as stent insertion, and/or reinforcement of immunosuppressive treatment for PSS, with the aim to wean the patient from mechanical ventilation (15, 20) and found it to be of value for this purpose.

In conclusion, we report a PSS patient with severe pulmonary involvement characterized by severe EDAC, mainly in relation with a PSS bronchial disease, and cystic lung disease. Despite an unfavourable outcome, this case helps to discuss diagnostic and therapeutic strategies in such patients.

References

1. Thomas E, Hay EM, Hajeer A, Silman AJ. Sjögren's syndrome: a community-based study of prevalence and impact. *Br J Rheumatol* 1998;37(10):1069-1076.
2. Pillemer SR, Matteson EL, Jacobsson LTH, Martens PB, Melton LJ, O'Fallon WM, Fox PC. Incidence of physician-diagnosed primary Sjögren's syndrome in residents of Olmsted county, Minnesota. *Mayo Clin Proc* 2001;76(6):593-599.
3. Haugen AJ, Peen E, Hulten B, Johanessen AC, Brun JG, Halse AK, Haga HJ. Estimation of the prevalence of primary Sjögren's syndrome in two age-different community-based populations using two sets of classification criteria: the Hordaland Health Study. *Scand J Rheumatol* 2008;37(1):30-34.
4. Palm O, Garen T, Enger TB, Jensen JL, Lund MB, Aalokken TM, Gran JT. Clinical pulmonary involvement in primary Sjögren's syndrome: prevalence, quality of life and mortality – a retrospective study based on registry data. *Rheumatology* 2013;52(1):173-179.
5. Lohrmann C, Uhl M, Warnatz K, Ghanem N, Kotter E, Schaefer O, Langer M. High-resolution CT imaging of the lung for patients with primary Sjögren's syndrome. *Eur J Radiol* 2004;52(2):137-143.
6. Lazor R. Lung involvement in Sjögren's syndrome: interstitium, airways, or both? *Respiration* 2009;78(4):375-376.
7. Watanabe M, Naniwa T, Hara M, Arakawa T, Maeda T. Pulmonary manifestations in Sjögren's syndrome: correlation analysis between chest computed tomographic findings and clinical subsets with poor prognosis in 80 patients. *J Rheumatol* 2010;37(2):365-373.
8. Kobayashi H, Matsuoka R, Kitamura S, Tsunoda N, Saito K. Sjögren's syndrome with multiple bullae and pulmonary nodular amyloidosis. *Chest*. 1988;94(2):438-40.
9. Meyer CA, Pina JS, Taillon D, Godwin JD. Inspiratory and expiratory high-resolution CT findings in a patient with Sjögren's syndrome and cystic lung disease. *Am J Roentgenol* 1997;168(1):101-103.
10. Koyama M, Johkoh T, Honda O, Mihara N, Kozuka T, Tomiyama N, et al. Pulmonary involvement in primary Sjögren's syndrome. Spectrum of pulmonary abnormalities and computed tomography findings in 60 patients. *J Thor Imaging* 2001;16(4):290-296.

11. Hubscher O, Re R, Iotti R. Cystic lung disease in Sjögren's syndrome. *J Rheumatol* 2002;29(10):2235-2236.
12. Jagirdar J, Chikkamuniyappa S, Sirohi D, McCarthy MJ, Peters JL. Cystic lung lesions in Sjogren syndrome: analysis of lymphocyte subsets in tissue with clinico-radiologic-pathologic correlation. *Ann Diagn Pathol* 2013;17(1):113-116.
13. Baqir M, Kluka EM, Aubry MC, Hartman TE, Yi ES, Bauer PR, Ryu JH. Amyloid-associated cystic lung disease in primary Sjögren's syndrome. *Respir Med* 2013;107(4):616-21.
14. Chastre J, Fagon JY. Ventilator-associated pneumonia. *Am J Respir Crit Care Med*. 2002;165(7):867-903.
15. Murgu SD, Colt HG. Description of a multidimensional classification system for patients with expiratory central airway collapse. *Respirology*. 2007;12(4):543-50.
16. Vitali C, Bombardieri S, Jonsson R, Moutsopoulos HM, Alexander EL, Carsons SE, et al. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. *Ann Rheum Dis*. 2002;61(6):554-558.
17. Bonner H, Ennis RS, Geelhoed GW, Tarpley TM. Lymphoid infiltration and amyloidosis of lung in Sjögren's syndrome. *Arch Pathol* 1973;95(1):42-44.
18. Kalra A, Abouzgheib W, Gajera M, Palaniswamy C, Puri N, Dellinger RP. Excessive dynamic airway collapse for the internist: new nomenclature or different entity? *Postgrad Med J*. 2011;87(1029):482-486.
19. Joosten S, MacDonald M, Lau KK, Bardin P, Hamilton G. Excessive dynamic airway collapse co-morbid with COPD diagnosed using 320-slice dynamic CT scanning technology. *Thorax* 2012;67(1):95-96.
20. Murgu SD, Cherrison LJ, Colt HG. Respiratory failure due to central airway collapse. *Respir care* 2007;52(6):752-754

Legends for Figures

Figure 1:

Still pictures of a video-bronchoscopic examination of the intermediate bronchus during inspiration (panel A) and expiration (panel B) under controlled mechanical ventilation. Severe EDAC was evidenced.

Figure 2:

Multidetector CT-scans under controlled mechanical ventilation during an end-inspiratory pause (panel A) and during an end-expiratory pause (panel B) confirming severe EDAC of the intermediate bronchus (blue arrow). Cysts localized near to the posterior part of the bronchus demonstrated some level of air trapping during expiration (red arrows), which probably participated to the magnitude of the bronchus collapse.

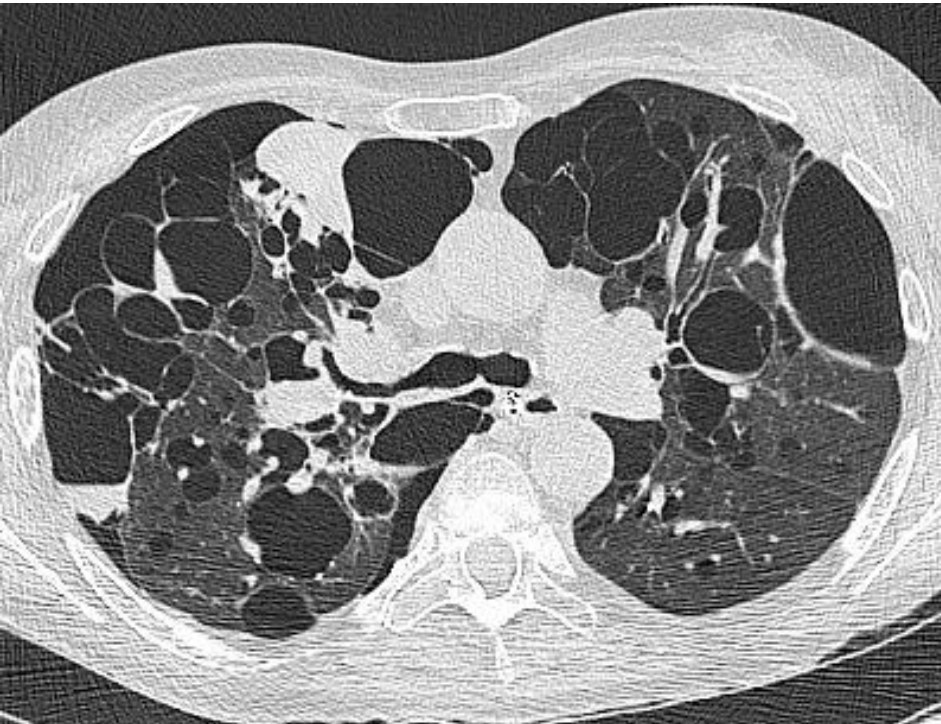
A



B



A



B

