

# Symptoms of Shrinking Lung Syndrome Reveal Systemic Lupus Erythematosus in a 12-Year-Old Girl

Holger Meinicke, MD,<sup>1</sup> Andrea Heinzmann, MD,<sup>1</sup> Julia Geiger, MD,<sup>2</sup>  
Reinhard Berner, MD,<sup>3</sup> and Markus Hufnagel, MD<sup>1\*</sup>

**Summary.** While pleuropulmonary involvement in systemic lupus erythematosus (SLE) is a common occurrence, shrinking lung syndrome (SLS) is a rare complication of SLE, particularly in children. We report on a teenager girl with a primary SLE diagnosis, which was based upon clinical, imaging, lung-function and histological findings ascertained to be compatible with SLS. Following a pneumonia, the patient developed inflammatory residues in the lower lobes, an event that probably caused diaphragmatic immobility and subsequently led to SLS. Treatment response to steroids, cyclophosphamide and hydroxychloroquine in this case was excellent, and efficacy was more profound than previously has been reported in the literature with respect to pediatric patients. This case report argues that prognosis of SLS in SLE is likely to be favorable when the diagnosis is made early and the disease is treated appropriately. **Pediatr Pulmonol.** 2013; 48:1246–1249. © 2012 Wiley Periodicals, Inc.

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## INTRODUCTION

Shrinking lung syndrome (SLS) is a rare, and probably under-diagnosed, complication of systemic lupus erythematosus, particularly in children. Symptoms consist of progressive dyspnea and pleuritic chest pain. Physical examination is often unremarkable. Upon chest X-ray, lung fields may be reduced, but otherwise appear normal. Pulmonary function tests show a restrictive pattern, usually without decreased DLCO/Va (i.e., diffusing lung capacity for carbon monoxide corrected for alveolar volume). On high-resolution CT scans, evidence of interstitial lung disease is lacking. Ultrasound imaging may be helpful to document decreased movements of the diaphragm. In our case we focus on three key findings: I. The patient's SLS symptoms, in combination with characteristic immunological and other clinical aspects, led to the diagnosis of SLE. II. Prior to the patient's SLS symptoms, she suffered from mycoplasma pneumonia, which may have triggered the pathogenetic process in the development of SLS. III. Treatment response to steroids, cyclophosphamide and hydroxychloroquine was excellent.

<sup>1</sup>Department of Pediatrics and Adolescent Medicine, University Medical Center Freiburg, Freiburg, Germany.

<sup>2</sup>Department of Radiology, University Medical Center Freiburg, Freiburg, Germany.

<sup>3</sup>Department of Pediatrics, University Hospital Carl Gustav Carus Dresden, Dresden, Germany.

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\*Correspondence to: Markus Hufnagel, MD, Department of Pediatrics and Adolescent Medicine, University Medical Center Freiburg. Mathildenstr. 1, D-79106 Freiburg, Germany.  
E-mail: markus.hufnagel@uniklinik-freiburg.de

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## CASE REPORT

A 12-year-old girl presented to our pediatric rheumatology outpatient clinic with a 6-month history of recurring episodes of activity-limiting dyspnea, fatigue, fever, and intermitting ptosis of the right eye. In her previous medical history, she had been diagnosed with ANA-positive oligoarticular juvenile idiopathic arthritis at the age of eight. Prior to her more recent deterioration, she had an acute febrile infection with tonsillitis and *Mycoplasma pneumoniae* positive pneumonia with tachypnea, dyspnea, and non-pleuritic chest pain, as well as pleural and pericardial effusions. Her *M. pneumoniae* diagnosis was based upon positive DNA results for *M. pneumoniae* by PCR in a nasopharyngeal aspirate, as well as upon elevated *M. pneumoniae* antibody titers against IgA, IgM, and IgG by ELISA. She recovered quickly after intravenous antibiotic therapy and effusion drainage by pericardial puncture. No other relevant pathologies, comprising thrombotic disorders or asthma, had been present in her or her family history.

Inspection of her oral cavity revealed a painful mucous ulcer. Additionally, her respiratory rate was elevated (30/min) with mild dyspnea, oxygen saturation was 99% on room air. On auscultation, her lung fields were clear. Further examination revealed swelling and effusion of her distal interphalangeal joint on the middle fingers of both hands, as well as on her left elbow.

She had mild hemolytic anemia (10.1 g/dl) with increased numbers of reticulocytes. Hematological tests showed an elevated platelet count (488,000/ $\mu$ l), as well as D-dimers (4.96 mg/L). Immunologic analysis revealed positive ANA titers (1:3,200, normal <1:50) with positive staining for anti-SS-A/Ro and anti-SS-B/

La, elevated anti-dsDNA (101 IU/ml), and elevated C3d levels (22.8 mg/L, normal <9 mg/L). The patient's urine was unaffected.

Chest radiography demonstrated enlargement of the cardiac silhouette, diminished lung volume, and elevated hemidiaphragms (Fig. 1). Ultrasound of the diaphragms confirmed severely reduced movement on both sides. The patient's thoracic-computed tomography scan (CT) excluded pulmonary thromboembolism, but showed thoracic lymphadenopathy and post-inflammatory residues in both lower lung fields (Fig. 2). Pulmonary function testing, including forced expiratory volume in 1 sec (FEV1, 34% of predicted value), forced vital capacity (FVC, 27%), and total lung capacity (TLC, 59%), was indicative of a restrictive ventilatory disorder.

Subsequent to this, a diagnosis of shrinking lung syndrome in association with systemic lupus erythematosus was made fulfilling 6 of the 11 American College of Rheumatology criteria for SLE (i.e., arthritis, oral ulcers, hemolytic anemia, positive ANA, and dsDNA titers as well as serositis).

As base therapy, the patient initially was treated with high doses of methylprednisolone (30 mg/kg/d i.v. for 4 days), followed by cyclophosphamide (according to the NIH protocol, 500 mg/m<sup>2</sup>, every 4 weeks for 6 months), together with oral prednisone and hydroxychloroquine. Ovarian protection was assured by a GnRh analog. Following this treatment regime, our patient progressively felt better and her dyspnea disappeared, with lung function tests improving continuously (Table 1) and getting nearly normal after 1 year. Additionally, anti-dsDNA titers became negative and C3d levels returned to normal. Movement of both hemidiaphragms was fully restored. Subsequently, her



Fig. 1. Chest X-ray shows typical diaphragmatic elevation and basal atelectasis.

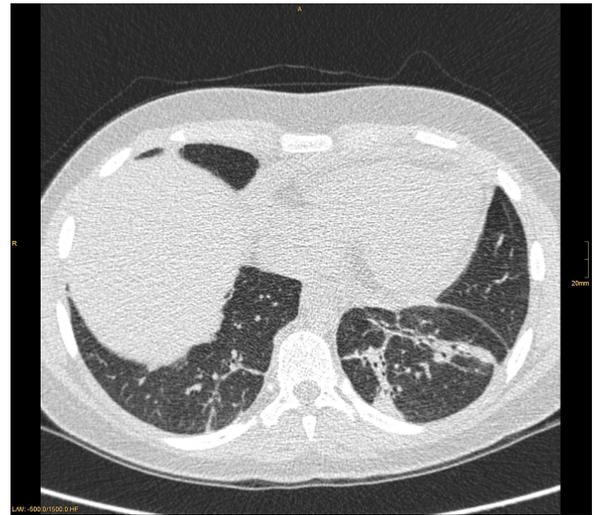


Fig. 2. CT scan reveals basal atelectasis, affecting predominantly the left lower lobe and leading to volume loss.

**TABLE 1—Results From Pulmonary Function Tests Over a 90-Week-Period**

Weeks after admission	FEV1 (% pred)	FVC (% pred)	TLC (% pred)	DLCO/Va (% pred)
0	44	37	59	Not possible
6	65	68	61	Not done
8	67	64	66	Not done
12	65	62	66	79
16	67	66	71	Not done
20	74	70	77	67
30	78	76	76	78
40	85	80	86	Not done
60	97	97	90	99
90	99	97	92	Not done

FEV1, forced expiratory volume in 1 sec; FVC, forced vital capacity; TLC, total lung capacity; DLCO/Va, diffusing lung capacity for carbon monoxide corrected for alveolar volume.

steroid dose was reduced to 7.5 mg/day and maintenance therapy with mycophenolate-mofetil was started (initially 500 mg/day, increased to 1,750 mg/day within 2 weeks).

## DISCUSSION

In this report, we present a rare pulmonary complication of SLE in a pediatric patient—the shrinking lung syndrome, first described in 1965.<sup>1</sup> The condition is characterized by recurrent and progressive dyspnea, pleuritic chest pain, observation of a restrictive pattern in lung function testing, and elevated diaphragms with reduced movement. In most cases, clinical examination and chest radiographs show reduced, but otherwise unaffected, lung volume and normal pleural spaces.

Our patient presented with SLS symptoms of dyspnea – absence of chest pain together with reduced lung fields and elevated hemidiaphragms. Though she had had ANA-positive oligoarthritis and developed serositis prior to her SLS symptoms (the latter primarily was attributed to a mycoplasma infection), only the pulmonary complication of her SLS, in combination with an oral ulcer and additional immunological findings (positive anti-dsDNA, anti-SS-A/Ro, and anti-SS-B/La antibodies), confirmed the diagnosis of SLE.

To our knowledge, to date only six cases of SLS in children have been described in the English-language literature.<sup>2</sup> More recent publications describe children in an age-range similar to that of our patient: a 14-year-old boy<sup>3</sup> and a 12-year-old girl.<sup>4</sup>

Different hypothetical pathomechanisms of SLS involve a diaphragm dysfunction as a consequence of pleural inflammation or pleural fibrosis<sup>5</sup> or a respiratory myopathy including inspiratory and expiratory muscles.<sup>6</sup> Others postulate that an abnormal chest wall expansion<sup>2</sup> possibly due to pleural thickening<sup>7</sup> or fibrotic changes<sup>8</sup> is the likely etiology for the restrictive

pattern. Whereas one group found demyelinating phrenic nerve lesions as the cause of this diaphragmatic paralysis,<sup>9</sup> others<sup>10</sup> conclude that it is unlikely to be caused by phrenic neuropathy. Taken together, the pathophysiology of SLS is still uncertain.

Our case supports the hypothesis of diaphragmatic immobility caused by an inflammatory process. The patient began complaining of dyspnea after resolution of pneumonia but prior to onset of her SLS symptoms which included complicating pleuritis and pleural and pericardial effusion. In the CT scan of her thorax, inflammatory residues were clearly detected in both lower lung fields. Hence, a potential and comparable<sup>4</sup> pathogenetic sequence could be conceived as follows: after an infection triggers an ongoing immune process in the area of the lower lungs, consecutive scarring at the zone of apposition between the parietal and diaphragmatic pleura develops, leading to subsequent impairment of the diaphragmatic motion.

Successful therapies of pediatric SLS have been reported with the use of corticosteroids in combination with different immunosuppressive agents, including cyclophosphamide, methotrexate, and azathioprine.<sup>11</sup> Some publications have reported on remarkable improvements in lung function tests through the use of theophylline,<sup>12</sup> beta-agonists,<sup>13</sup> and rituximab.<sup>14</sup> Under the therapy of high-dose methylprednisolone and following intravenous cyclophosphamide pulses monthly for 6 months, together with daily oral prednisone, our patient improved significantly and her dyspnea fully abated.

Even if the long-term prognosis of SLS in SLE seems to be favorable<sup>6,15</sup> all pediatric patients who have been reported upon to date<sup>3,4</sup> continued to show more profound lung function impairment than that of our patient. Apart from considerable weight gain due to corticosteroid therapy, our patient has not complained of any limitation in daily life, including physical activity. Her pulmonary function test underlines this excellent recovery. Despite the overall positive outcome reported, it is critical to note that the restrictive lung disorder of SLS occasionally can be fatal.<sup>16</sup> As of yet, our patient has had no kidney involvement, a factor that improves her long-term prognosis with respect to SLE.

In conclusion, this case report should highlight the facts that SLS may also be a first sign of SLE in children and may probably be caused by basal pneumonia. If SLS is diagnosed early and treated appropriately with potent immunosuppressive therapy, the prognosis in children seems likely to be favorable.

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