thus suggesting that expiratory CT scans may complement functional evaluation for detecting small airways obstruction. In fact, if major indexes of airway obstruction were unimpaired in our four patients, indexes of small airways obstruction (FEF25–75, MEF50, and MEF25) were often impaired (Table 1). In particular, MEF25 was decreased in three patients and at the lower normal limits in the remaining patient. Interestingly, this finding agrees with that of Hansell et al10 of an independent association between the extent of decreased attenuation and decreased MEF25 values in 45 patients with sarcoidosis. It agrees also with that of Lucidarme et al21 of a significant negative correlation between air-trapping scores and MEF25 in 74 patients with suspected chronic airway disease. Thus, if the wide range of normal values limits the use of MEF25 in clinical practice, these observations support the old contended view that MEF25 is fairly sensitive for detecting small airways obstruction.

In conclusion, when pulmonary sarcoidosis is not advanced, as is the case in our four patients, an HRCT mosaic pattern may be seen that is associated with diffusion impairment. These alterations may be partially reversible under steroid treatment. Major indexes of airway obstruction may be normal, and indexes of airflow obstruction at low lung volumes may show limited or borderline reduction. This emphasizes the complementary role of HRCT in the evaluation of potential airflow obstruction when the results of spirometry are normal.

REFERENCES

16 Miller NL, Miller RR. Diseases of the bronchioles: CT and histopathologic findings. Radiology 1995; 196:3–12
19 Sharma OP. Functional impairment in sarcoidosis. Sarcoidosis 1988; 5:11–12

Bilateral Phrenic Paralysis in a Patient With Systemic Lupus Erythematosus*

Karen Hardy, MD, FCCP; Isabelle Henry, MD; Valérie Attali, MD; Jacques Cadranel, MD, PhD; and Thomas Similowski, MD, PhD

Respiratory manifestations of systemic lupus erythematosus (SLE) are frequent. They include respiratory muscle abnormalities, which have been implicated in the pathogenesis of the “shrinking lung syndrome” (SLS). We report the case of a patient with this syndrome, in whom diaphragmatic paralysis due to demyelinating phrenic lesions was diagnosed at the same time as SLE. Follow-up studies showed a favorable clinical and diaphragmatic outcome with corticosteroid therapy, but little change in spirometry.

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try. It is concluded that severe diaphragm palsy is possibly due to phrenic nerve lesions in SLE, and that the link between diaphragm dysfunction and the SLS is probably not a straightforward one.

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Key words: diaphragm; magnetic stimulation; phrenic nerve; respiratory muscles; respiratory paralysis; systemic lupus erythematosus

Abbreviations: CMS = cervical magnetic stimulation; EMGdi = surface diaphragm electromyogram; ES = electrical stimulation; Pn,t = mouth pressure twitch; SLE = systemic lupus erythematosus; SLS = shrinking lung syndrome

Pulmonary abnormalities are frequent in systemic lupus erythematosus (SLE),1 including pleuritis, interstitial pneumonitis, bronchiolitis, pulmonary vasculitis, and pulmonary hypertension. Pulmonary embolism is commonly associated with the antiphospholipid syndrome. The “shrinking lung syndrome” (SLS; lung volume reduction without parenchymal abnormalities, restrictive ventilatory defect, preserved carbon monoxide transfer coefficient) is a rare manifestation of SLE. Respiratory muscle weakness seems frequent, with controversial findings about diaphragm dysfunction.²,³ We describe the 2-year follow-up of diaphragm function in a case of SLE presenting with the SLS and bilateral phrenic nerve paralysis.

CASE REPORT

Presentation

A 36-year-old patient was admitted in November 1996 with a 8-month history of arthralgia, slowly worsening dyspnea (leading to resting breathlessness and severe orthopnea), oscillating fever, and weight loss (~ 10 kg). Temperature was 39°C, and results of clinical examination showed an inspiratory inward motion of the abdomen suggesting severe diaphragm dysfunction, but were otherwise normal. Chest radiography showed a bilateral reduction in lung volume with a bilaterally elevated diaphragm. CT disclosed only minimal right pleural thickening. BAL findings were normal. Results of blood gas analysis and pulmonary function tests are given in Table 1. Laboratory tests revealed a mild hypochromic and microcytic anemia, with slightly elevated ferritin level suggestive of chronic inflammation, a positive immunofluorescence for antinuclear antibodies (> 1/1,000 UI/mL), proteinuria of 1 g/d without hematuria, and no other abnormalities whatsoever. Serum creatine phosphokinase and aldolase levels were normal, as was a comprehensive electromyographic examination of upper and lower limbs.

Phrenic Nerve-Diaphragm Studies

Phrenic nerve stimulation was performed using transcutaneous electrical stimulation (ES; bipolar electrode delivering square wave pulses of 0.1-ms duration and of an intensity adjusted to obtain a supramaximal response, applied at the posterior border of the sternocleidomastoid muscle, at the level of the cricoid cartilage; expected phrenic nerve conduction time approximately 7 ms) and cervical magnetic stimulation (CMS; Magstim 200; Magstim; Sheffield, UK) [90-mm circular coil delivering a maximal output 2.5 T] placed over the spinous process of the seventh cervical vertebra; expected normal phrenic nerve conduction time approximately 6 ms].⁴,⁵ Surface diaphragm electromyogram (EMGdi; two pairs of skin-taped silver cup electrodes placed in the sixth to eighth right and left intercostal spaces on the mid-clavicular line) [Neuropack; Nihon Kohden; Tokyo, Japan], mouth pressure twitch (Pn,t; Validyne DP45, ± 50 cm H₂O; Validyne Engineering; Northridge, CA) and changes in abdominal circumference (mechanical strain gauge) were recorded. Initially, the EMGdi response to CMS was abolished on the left

Table 1—Clinical and Functional Follow-up Information*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Diagnostic</th>
<th>2 mo</th>
<th>6 mo</th>
<th>8 mo</th>
<th>12 mo</th>
<th>22 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exertional dyspnea Treatment</td>
<td>Severe</td>
<td>None</td>
<td>None</td>
<td>Moderate</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>CS, 1 mg/kg</td>
<td>CS, 15 mg</td>
<td>CS, 5 mg</td>
<td>CS, 15 mg</td>
<td>Cy, 150 mg</td>
<td>Cy, 100 mg</td>
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<tr>
<td>Pulmonary function tests</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vital capacity†</td>
<td>45</td>
<td>40</td>
<td>38</td>
<td>38</td>
<td>37</td>
<td>41</td>
</tr>
<tr>
<td>FEV₁/vital capacity†</td>
<td>88</td>
<td>87</td>
<td>80</td>
<td>81</td>
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<td>80</td>
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<tr>
<td>Total lung capacity†</td>
<td>52</td>
<td>62</td>
<td>60</td>
<td>68</td>
<td>68</td>
<td>55</td>
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<td>Gas exchange</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KCO, mmol/min/kPa/L₄</td>
<td>1.7</td>
<td>1.7</td>
<td>1.8</td>
<td>1.8</td>
<td>1.6</td>
<td>2</td>
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<tr>
<td>PaO₂, mm Hg</td>
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<td>83</td>
<td>80</td>
<td>92</td>
<td>82</td>
<td>93</td>
</tr>
<tr>
<td>PaCO₂, mm Hg</td>
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<td>41</td>
<td>42</td>
<td>34</td>
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<td>7.43</td>
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<td>Diaphragm function</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tidal inspiratory abdominal displacement</td>
<td>Deflation</td>
<td>Expansion</td>
<td>Expansion</td>
<td>Expansion</td>
<td>Expansion</td>
<td>Expansion</td>
</tr>
<tr>
<td>CMS Pn, t, cm H₂O</td>
<td>−1</td>
<td>−2.5</td>
<td>−7</td>
<td>−5</td>
<td>−6.5</td>
<td>−20</td>
</tr>
<tr>
<td>CMS right PNCT, ms</td>
<td>15</td>
<td>10</td>
<td>6.5</td>
<td>7.5</td>
<td>6.9</td>
<td>6.9</td>
</tr>
<tr>
<td>CMS left PNCT, ms</td>
<td>Abolished</td>
<td>9</td>
<td>7.5</td>
<td>9.8</td>
<td>10.9</td>
<td>6.9</td>
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<tr>
<td>ES right PNCT, ms</td>
<td>15.5</td>
<td>7.5</td>
<td>7.5</td>
<td>7.5</td>
<td>7.6</td>
<td></td>
</tr>
<tr>
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<td>Abolished</td>
<td>7.4</td>
<td>7.4</td>
<td>6.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*CS = corticosteroids; Cy = cyclophosphamide, daily doses; PNCT = phrenic nerve conduction time; KCO = coefficient of carbon monoxide transfer.
†Values are given in percent predicted, with ethnic correction.
‡Values are given in absolute percentages.
¶Predicted value, 1.6; blood gases correspond to room air breathing.
side and attenuated and delayed on the right side (Fig 1). CMS was associated with a Pm,t value of 1 cm H₂O (normal value 10 cm H₂O according to Hamnegard et al.), which was probably due to extradiaphragmatic muscle contraction because of a concomitant decrease in abdominal circumference suggesting a complete absence of diaphragm mechanical efficiency.

**Evolution**

Administration of prednisone, 1 mg/kg/d, brought a dramatic clinical improvement over 6 weeks. At 2 months, the EMGdi response had improved on both sides (Fig 1), with a normalized pattern of abdominal movement (expansion) and a slightly increased Pm,t (Table 1). Improvement was sustained at 8 months, after tapering of the dose of corticosteroids. Over 2 years, the evolution of the disease was generally favorable, although there were fluctuations leading to increased corticosteroid therapy and a resort to cyclophosphamide. Diaphragm function paralleled the clinical course, whereas findings of pulmonary function tests and chest radiographs were unchanged.

**Discussion**

This observation shows that a neuropathic process involving the phrenic nerve can be the source of SLE-associated diaphragm dysfunction. Although it seems to be the first such report with unambiguous electrophysiologic documentation, it should be noted that the two cases described by Stevens et al. in which SLE-associated respiratory muscle weakness was reversed by corticosteroid therapy, probably pertained to a similar mechanism.

**Methodologic Considerations**

Our diagnosis relies on surface EMGdi in response to CMS. Signal contamination could make this approach unreliable, but we and others have shown that surface electrodes can record uncontaminated diaphragmatic signals. In addition, in the present case, EMGdi patterns with CMS and ES were consistent (Table 1).

**Diaphragm Function and the SLS**

Wilcox et al. showed a restrictive ventilatory defect and decreased inspiratory muscle strength in 11 SLE patients. In nine cases, they found decreased diaphragm strength without phrenic nerve conduction abnormalities. All the patients had received corticosteroids, at higher dosages in the diaphragm dysfunction group. Conversely, Laroche et al. using bilateral ES in 12 patients with the SLS, failed to demonstrate diaphragm weakness. At first sight, our observation would support diaphragm dysfunction as the source of the SLS. Nevertheless, the course during treatment casts doubt on the link between diaphragm weakness and the restrictive ventilatory defect. Indeed, exertional dyspnea and diaphragm function in our patient fluctuated with exacerbations of the disease and the treatment (Table 1), whereas there was no clear increase in total lung capacity or vital capacity over time.

**SLE and Peripheral Nerve Lesions**

Peripheral neuropathy is described in SLE, involving the deposition of immune complexes and ischemic lesions. Demyelinating polyneuropathy has also been reported, with recurring episodes responding favorably to corticosteroids. This closely resembles our observation and those of Stevens et al. The phrenic nerves appeared to be the only involved nerves in our patient, a feature already reported in diabetes, possibly reflecting a particular nerve-fiber composition.

From this observation, and although the observed discrepancy between diaphragm function and pulmonary restriction leaves the pathophysiology of the SLS unexplained, we submit that phrenic nerve and diaphragm studies should be considered in SLE patients with dyspnea or a restrictive ventilatory defect and a normal chest radiograph.

**References**


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**Figure 1.** Electromyographic responses to CMS recorded with surface electrodes during the initial examination (left panel) and at 22 months (right panel).
Influenza Pneumonia in Lung Transplant Recipients*

Clinical Features and Association With Bronchiolitis Obliterans Syndrome

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Influenza infection is increasingly recognized to cause significant morbidity and mortality in the community, especially in pediatric patients and elderly persons. Influenza infection, however, has not been well described among thoracic organ transplant recipients. We present the first detailed clinical, radiographic, and histologic description of influenza pneumonia among three lung transplant recipients. The presentation varied considerably among the three patients and, in some cases, was atypical for influenza. Despite treatment, a persistent decline in pulmonary function occurred in all three patients after the acute illness. Interestingly, on follow-up biopsy specimens, each patient had histologic evidence of acute rejection and/or obliterative bronchiolitis. Additional research, therefore, is needed to clarify the relationship between influenza infection, acute rejection, and obliterative bronchiolitis.

Key words: allograft rejection; bronchiolitis obliterans syndrome; influenza; lung transplantation; obliterative bronchiolitis

Abbreviations: BMT = bone marrow transplant; BOS = bronchiolitis obliterans syndrome; CMV = cytomegalovirus; OB = obliterative bronchiolitis

Respiratory viruses are increasingly recognized to cause morbidity and mortality in the community. Influenza viruses, in particular, are among the most important seasonal respiratory pathogens. During the winter months, up to 10% of all patient visits to physicians are due to influenza-like illnesses. In addition, influenza may cause 10,000 to 40,000 deaths and >150,000 hospitalizations annually, especially in patients with preexisting medical conditions.

For editorial comment see page 997

Influenza-related illness has been described in immunocompromised persons, including solid-organ and bone marrow transplant (BMT) recipients. Between 6% and 29% of all acute respiratory infections in BMT patients are caused by influenza viruses. The incidence and significance of influenza infection after lung transplantation, however, remains unknown. In this article, we provide the first detailed description of the clinical presentation, radiographic features, histologic findings, and clinical outcomes of influenza pneumonia in three lung transplant recipients.

CASE 1

A 53-year-old African-American woman had received a bilateral lung transplant in October 1997 for end-stage sarcoidosis. Although she experienced a complicated posttransplant course characterized by severe reperfusion injury, she was discharged from the hospital with acceptable pulmonary function (FEV1 of 1.60 L or 60% predicted). The patient did well, with no episodes of allograft rejection or infection, and remained free from bronchiolitis obliterans syndrome (BOS). In April 1999, she presented with increasing shortness of breath, cough productive of yellow sputum, fatigue, and weakness. She was afebrile. Physical examination revealed diffuse rhonchi and wheezes throughout both lung fields, with decreased breath sounds at the right lung base. Chest radiography revealed homogeneous right-lower-lobe consolidation with small associated pleural effusion (Fig 1). She received 3 weeks of antibiotic treatment (cefazolin and ciprofloxacin) without improvement. Therefore, bronchoscopy was performed and the results revealed bilateral mucopurulent secretions without endobronchial lesions. Transbronchial biopsy was not performed because of hypoxemia during the procedure. Immunofluorescence staining of the lavage fluid returned positive for influenza A virus. Culture findings were negative for viruses, fungi, and bacteria. She was treated with a 2-week course of amantadine. Although the patient’s clinical condition and radiographic findings improved by discharge, her