In summary, this report provides strong evidence that sulindac can produce an isolated pulmonary hypersensitivity reaction. When pulmonary infiltrates develop in patients receiving sulindac therapy, a drug reaction should be considered as the possible cause.

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Myasthenia Gravis Presenting as Isolated Respiratory Failure*
Kevin M. Dushay, M.D.;† Joseph D. Zibtrak, M.D., F.C.C.P.;‡ and William A. Jensen, M.D., F.C.C.P.§

A patient with myasthenia gravis presenting as respiratory failure was unusual in his lack of peripheral neuromuscular involvement, negative results on many commonly used diagnostic tests, and lack of response to first-line therapeutic measures. Review of the pertinent literature revealed no previously described presentation of myasthenia gravis in this manner. (Chest 1990; 97:322-34)

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IF = inspiratory force; MEPF = miniature end plate potential

When pulmonary physicians evaluate patients with progressive respiratory insufficiency, it is important to consider neuromuscular disease in the differential diagnosis, as emphasized by the patient who is the subject of this report.

CASE REPORT

A 64-year-old water pipe installer was diagnosed as having obesity-hypoventilation syndrome associated with recurrent cor pulmonale. Three months earlier, he had presented to another hospital with peripheral edema and weight gain. Values of a room air blood gas analysis were as follow: PaO2, 61 mm Hg; PaCO2, 51 mm Hg; pH, 7.37. (Table 1) and the chest x-ray film showed a reduction in lung volumes interpreted as poor inspiratory effort. No other abnormalities were noted. Spirometry showed FEV1 of 2.30 (60 percent of predicted); FVC, 2.78 (54 percent); FEV1/FVC, .78; FEF25-75, 2.39 (68 percent) with no change after bronchodilator therapy. He was treated with diuretics and discharged with diagnoses of hypertension, restrictive lung disease of unspecified etiology, and chronic hypoxia.

Over the next six weeks, he noted increasing lethargy, weakness, dyspnea on exertion, pedal edema, cyanosis, and weight gain. On examination, a right sided S3 gallop, crackles at both lung bases, and 3+ pedal edema were noted. An arterial blood gas analysis on room air showed worsening CO2 retention and hypoxemia; spirometry was unchanged. In spite of treatment with diuretics and intravenous aminophylline, his dyspnea worsened, and he was transferred to the New England Deaconess Hospital.

On admission, he reported loud snoring, five to six years of daytime hypsomnolence, fatigue, and nocturnal apneic spells. In addition, he complained of a lump in his throat, some difficulty swallowing, and several episodes of diaplopia over the past two months. His medications were hydrochlorothiazide (Dyazide), diuretics, captopril, colchicine, and probenecid. He denied alcohol and cigarette use. On examination, he was tachypneic, and had diminished breath sounds at the right lung base without crackles or wheezes, an irregular rhythm without murmur or gallop, and a liver span of 8 cm. Laboratory test results were significant for the following: hematocrit, 50.6 percent; serum bicarbonate, 45 mEq/L; arterial blood gas on 1.5 L/min nasal cannula of PaO2, 91 mm Hg; pH, 7.33; PaCO2, 56 mm Hg; and chest x-ray film showing borderline cardiomegaly, normal pulmonary vasculature, and ascites at both lung bases. Spirometry showed FEV1, 1.62 (43 percent); FVC, 1.98 (42 percent); FEV1/FVC, .82; FEF25-75, 3.86 (43 percent); DCO, 17.78 (57 percent).

Over the next 24 hours, the patient deteriorated, developing respiratory distress and paradoxical abdominal motion without

---

Table 1—Arterial Blood Gas Determinations and Pulmonary Function Tests

<table>
<thead>
<tr>
<th>Date</th>
<th>PO2 mm Hg</th>
<th>PCO2 mm Hg</th>
<th>pH</th>
<th>FEV1 L</th>
<th>FVC L</th>
<th>FEV1/FVC Ratio</th>
<th>FEF25-75 L/s</th>
<th>TLC L</th>
<th>RV L</th>
<th>DCO ml/min/mm Hg</th>
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</thead>
<tbody>
<tr>
<td>5/8/87</td>
<td>61</td>
<td>51</td>
<td>7.37</td>
<td>2.20 (.56)</td>
<td>2.78 (.54)</td>
<td>78</td>
<td>2.39 (.68)</td>
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<td>1.78 (NA)</td>
<td>14.79 (NA)</td>
</tr>
<tr>
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<td>62</td>
<td>46</td>
<td>7.36</td>
<td>2.35 (NA)*</td>
<td>2.83 (NA)</td>
<td>82</td>
<td>2.93 (NA)</td>
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<td>1.78 (NA)</td>
<td>14.79 (NA)</td>
</tr>
<tr>
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<td>66</td>
<td>46</td>
<td>7.36</td>
<td>2.35 (NA)*</td>
<td>2.83 (NA)</td>
<td>82</td>
<td>2.93 (NA)</td>
<td>3.92 (NA)</td>
<td>1.78 (NA)</td>
<td>14.79 (NA)</td>
</tr>
<tr>
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<td>82</td>
<td>7.30</td>
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<td>2.83 (NA)</td>
<td>82</td>
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</tr>
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<td>1.98 (.43)</td>
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<td>17.78 (.57)</td>
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<tr>
<td>9/9/87</td>
<td>51</td>
<td>89</td>
<td>7.33</td>
<td>1.62 (.43)</td>
<td>1.98 (.43)</td>
<td>82</td>
<td>17.78 (.57)</td>
<td></td>
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</tr>
</tbody>
</table>

*Value not available.
Table 2 — Weaning Mechanics and Interventions

<table>
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<tr>
<th>Date</th>
<th>Vr, L</th>
<th>Vc, L</th>
<th>IF, cm H2O</th>
</tr>
</thead>
<tbody>
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</tr>
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<td>.400</td>
<td>.800</td>
<td>-16</td>
</tr>
</tbody>
</table>

muscle weakness elsewhere. An arterial blood gas analysis on 1.0 L/min was PaO2 45 mm Hg; PaCO2 103 mm Hg; pH 7.26. Pulmonary mechanics results disclosed: tidal volume of 200 ml, vital capacity of 1.0 L, and inspiratory force of ~11 cm H2O. A standard edrophonium (Tensilon) test was performed with no change in IF or VC. The patient was intubated and mechanical ventilation begun (Table 2).

Electrolytes, ESR, CT scan of the head, noninvasive venous studies of the lower extremities, repeat edrophonium test, electro- myogram including cranial nerves, and repetitive nerve stimulation of brachial plexus, median, ulnar, and spinal accessory nerves all were subsequently normal. Studies for heavy metal exposure were negative. During this period, the patient complained of intermittent vertical diplopia, but dysconjugate gaze was not observed.

Because of persistent clinical suspicion of myasthenia gravis, an empiric trial of neostigmine, 0.25 mg every four hours, was begun. While the patient’s baseline pulmonary mechanics (TV 250 ml; Vc 800 ml; IF ~8 cm H2O) were unchanged after four hours, his diplopia had resolved. Neostigmine was therefore continued and after 48 hours, respiratory mechanics had improved. When neostigmine was discontinued, mechanisms deteriorated significantly. Neostigmine was therefore re instituted at an increased dose (0.5 mg q4h) with definite improvement in respiratory mechanics.

Myasthenia gravis was confirmed when an antistriated muscle antibody titer was reported at 1:80 and an acetylcholine receptor antibody titer was reported at greater than 1:30 (normal <1:0.8). Neostigmine was increased to 1.0 mg q4h and prednisone 60 mg po qd was added. However, only with the institution of plasmapheresis was he successfully extubated.

DISCUSSION

Myasthenia gravis can frequently be complicated by respiratory failure. However, myasthenic involvement limited solely to the muscles of ventilation has not been reported in well-characterized patients. In retrospective series of 22 myasthenics requiring mechanical ventilation reported by Gracey et al, only four presented in this manner. None was described as having isolated respiratory failure. The conclusions of two earlier series by Ferguson et al (31 patients) and Ashworth and Hunter (13 patients) were similar. The latter specifically stated that, “respiratory failure was never the first symptom of the disease.” Factors leading to respiratory failure in these reports included myasthenic crisis, cholinergic crisis, brittle crisis, steroid induced crisis, postoperative state, and other medical conditions typically requiring mechanical ventilation not unique to myasthenia gravis. Only a single case report was found describing a patient who initially presented with ocular myasthenia and later returned with isolated respiratory failure.

Unlike previously described cases, our patient’s myasthenic involvement was limited to the ventilatory musculature, and multiple tests commonly used to confirm clinical suspicion of myasthenia gravis were negative. It is possible that 10 mg of edrophonium was an inadequate test dose for assessing improvement in respiratory mechanics—though Osserman and Genkins’ 1966 review of the edrophonium test stated less than 0.5 percent of cases require more than 10 mg to produce a response. Standard repetitive nerve stimulation and electromyography also were not helpful. Ultimately, serologic studies confirmed the diagnosis. Despite conventional treatment with acetylcholinesterase inhibitors and steroids, respiratory insufficiency persisted and extubation was not possible. Plasmapheresis, as reported by Pinching and Peters, and others, was then employed with success.

CONCLUSIONS

This case of myasthenia gravis was unusual in three respects: the patient presented with what appeared to be primary respiratory failure of unknown etiology; associated symptoms of myasthenia were suggested by history but could not be verified by objective means. Diagnosis was difficult despite a correct clinical impression in that several edrophonium trials as well as other standard tests for myasthenia gravis were negative. Treatment following diagnosis with accepted firstline agents, acetylcholinesterase inhibitors and corticosteroids, failed to produce an adequate response such that plasmapheresis was required before the patient could be weaned from ventilatory support.

This case illustrates the need to consider myasthenia gravis, as well as other motor neuron disorders, in evaluating individuals presenting with acute respiratory failure. The former should be aggressively pursued beyond conventional firstline tests, since diagnosis can be difficult and effective treatment is available.

REFERENCES

Interstitial Pulmonary Disease Induced by Occupational Exposure to Paraffin*  

Jean-Louis Pujol, M.D.; Gilbert Barnéon, M.D.; Jean Bousquet, M.D.; François-Bernard Michel, M.D., F.C.C.P.; and Philippe Godard, M.D.

An occupational interstitial pulmonary disease was observed in a 59-year-old workman after five years of massive exposure to aerosolized paraffin. Histologic studies of open-lung biopsy showed a lipid pneumonia characterized by (1) alveolitis involving large lipid-laden macrophages and (2) interstitial fibrosis. Electron microscopy of AMs disclosed features of paraffin-laden cytoplasmic vacuoles. Successive treatments included prednisolone and cyclophosphamide. Despite these treatments and withdrawal from exposure, the pulmonary function became impaired progressively, resulting in restrictive syndrome and severe exertional dyspnea. Concomitantly, PMNs harvested by BAL increased, whereas initial lymphocytosis decreased. This is the first case observed of occupational interstitial fibrosis in which electron-microscopic findings clearly established a relationship with an exposure to paraffin. This observation also emphasizes the switch from alveolitis to fibrosis in the pathogenesis of interstitial pulmonary disease.  

(Chest 1990; 97:324-36)

Paraffin, a mineral oil, can induce alveolitis and interstitial fibrosis, possibly related to the activation of oil-laden AMs. This lipid pneumonia is usually related to repeated aspiration of paraffin-containing laxative or nasal drops. We report the first case of a workman suffering from an interstitial pulmonary disease related to occupational paraffin exposure.

CASE REPORT

A 59-year-old workman, a mild smoker, was admitted to the hospital in July 1984 for exertional dyspnea. He had been well until May 1984. He had no previous medical or surgical history and had never received long-term treatment. He had no history of asbestos exposure. Five years ago, he started to work for an automobile dealer. From 1979 to May 1984, the patient was chronically exposed to paraffin in cleaning new cars protected by paraffin, using hot water generated by compressed air jets. This technique aerosolized hot paraffin from car surfaces in a closed workshop (80 m²) without any ventilation and led to massive inhalation. He never used a mask to reduce inhalation, whereas the French legislation requires the use of such protective devices.

The findings from physical examination, cardiac function, routine biologic analyses, and chest x-ray films were normal. A CT scan showed (1) a diffuse interstitial process more pronounced in the periphery of the lower lobes and (2) right paratracheal hypodense (~40 UH) lymph node enlargement (Fig 1).

Hypoxemia and a slight decrease in the DSS were found. In contrast, other pulmonary function tests, including plethysmographic evaluation of compliances, were normal (Table 1).

A BAL was performed and showed an increase in total cell numbers and lymphocyte percentage. Light microscopy of a transbronchial biopsy showed mixed alveolitis involving both normal lymphocytes and AMs, some of them presenting unusual cytoplasmic vacuoles. Diagnostic investigations failed to demonstrate any evidence of systemic disease, of infectious or hypersensitivity pneumonitis, and the patient did not present any evidence of endogenous dislipidosis or gastroesophageal reflux.

In March 1985, a surgical open biopsy of the right middle lobe was performed. Light microscopy following hematoxylin-eosin, PAS, and trichrome stainings disclosed a uniform interstitial pneumonitis with fibrosis. The alveoli were filled with extracellular lipid droplets and large AMs containing lipid vacuoles. Some of them were multilined foam histiocytes (Touton giant cells). Lymphocytes were also involved in the alveolitis without granuloma organization. Some histiocytes were present in thickened interalveolar septum in which numerous collagen fibers were seen (Fig 2). Lipid pneumonia was diagnosed.

A new BAL was performed after the open-lung biopsy. Electron microscopy of the AMs disclosed an aspect of foam cells with cytoplasmic vacuoles of various sizes unstained by osmic acid, a specific feature of mineral oil (Fig 3).

A daily dose of prednisolone (1.5 mg/kg) was begun in March 1985. Then dosage was slowly decreased until a daily maintenance dosage of 0.5 mg/kg was reached. In November 1985, corticosteroids were discontinued because of clinical impairment. An immunosuppressive treatment by cyclophosphamide (2 mg/kg daily per os) was begun and maintained for four months. Cyclophosphamide induced neutropenia with digestive candidiasis. Despite therapy, dyspnea and pulmonary function became worse, and a restrictive syndrome occurred (Table 1). Diffusing capacity (49 percent) and static compliance (0.25 L/cm H₂O) decreased concomitantly. Serial cyto logic studies of BAL fluid demonstrated the progressive decrease of total cells and lymphocyte counts, which returned to subnormal values, whereas PMNs increased (Table 1). As no clinical benefit justified further active therapy, cyclophosphamide was discontinued, and only long-term oxygen therapy was maintained.

FIGURE 1. Computed tomographic scan shows diffuse interstitial process more pronounced in periphery of lower lobes.

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