dural success. While clinical improvement has been uniformly noted, it often has been tempered by the underlying disease processes. Complications that have been reported in the literature have included ventricular arrhythmias, compromise of arterial sidebranches, intimal flaps and arterial rupture, misplacement and migration of stents, and pulmonary edema.

In our patient, who presented with right-sided heart failure due to bilateral extrinsic compression of the PAs caused by extensive mediastinal lymphadenopathy due to adenocarcinoma of the lung, there were limited therapeutic options. The severe pulmonary hypertension appeared to represent an immediate threat to both the quality and quantity of this patient’s life. The angiographic appearance of the compressive lesions appeared to be amenable to stent placement. The patient was treated successfully with the placement, percutaneously, of bilateral PA stents. Although the natural course of the disease was not altered, he had significant symptomatic relief without adverse effects. Additionally, there was objective evidence of improvement.

In conclusion, this case suggests that in patients with mediastinal disease and pulmonary hypertension, evaluation should include careful examination of the mediastinum by CT scanning or MRI for possible PA compromise. Endovascular stenting is a feasible palliative management option in patients with right ventricular failure due to malignant extrinsic compression of the PAs.

REFERENCES

Pulmonary Alveolar Proteinosis*

Treatment by Bronchofiberscopic Lobar Lavage

Shih-Lung Cheng, MD; Hou-Tai Chang, MD; Hon-Ping Lau, MD; Li-Na Lee, MD, PhD; and Pan-Chyr Yang, MD, PhD, FCCP
The current mainstay of treatment for pulmonary alveolar proteinosis (PAP) is whole-lung lavage. Therapy with granulocyte-macrophage colony-stimulating factor is a possibility, although its long-term safety has not been determined. An alternative procedure is selected lobar lavage by fiberoptic bronchoscopy (FOB). We report here our experiences with lobar lavage by FOB in treating three patients with PAP. PAP was diagnosed in three patients (two men, one woman) who had dyspnea and hypoxemia after undergoing open-lung biopsy. The patients underwent lobar lavage by FOB under local anesthesia. The bronchoscope was wedged into a lobar bronchus. Approximately 2,000 mL warm normal saline solution was instilled via syringe in 50-mL aliquots through a fiberoptic bronroscope. After undergoing multiple lobar lavages, two patients showed clinical, physiologic, and radiologic improvement. The third patient, who had more advanced disease, showed improvement only in oxygenation. The major complications were severe cough and hypoxemia during lavage. Our experience suggests that bronchoscopic lobar lavage is simple and safe, and may find application in patients in whom a whole-lung lavage with generalized anesthesia may be hazardous, and in patients with less advanced disease whose proteinaceous substances can be removed with a small volume of lavage fluid. (CHEST 2002; 122:1480–1485)

Key words: bronchofiberscopic lobar lavage; pulmonary alveolar proteinosis

Abbreviations: DLCO = diffusing capacity of the lung for carbon monoxide; FOB = fiberoptic bronchoscopy; GM-CSF = granulocyte-macrophage colony-stimulating factor; LDH = lactate dehydrogenase; PAP = pulmonary alveolar proteinosis; TLC = total lung capacity

Pulmonary alveolar proteinosis (PAP), first described by Rosen and his associates in 1958, is a rare disease of unknown etiology that is characterized by the accumulation of proteinaceous material in the alveoli, leading to impairment in oxygen transfer across the involved alveoli. Although its exact pathogenesis is unclear, the condition has been associated with defective functions of alveolar macrophages, an abnormal structure of the surfactant protein, imbalance in the secretion of cytokines, and the defective expression of granulocyte-macrophage colony-stimulating factor (GM-CSF) or its receptors on alveolar macrophages and type-II pneumocytes. All of these hypothesized mechanisms may lead to abnormal catabolism and intra-alveolar accumulation of surfactant proteins. Because of the unknown pathogenesis, the most effective treatment for PAP is the mechanical removal of the proteinaceous material via whole-lung lavage. However, the severe hypoxemia in PAP patients and the difficulty of the technique have limited its application to medical centers and to more advanced cases. Seymour and colleagues have reported that 43% of their patients with PAP had clinical responses to recombinant GM-CSF therapy. However, there were some patients who did not respond and still needed to undergo whole-lung lavage. Another possible alternative treatment is multiple segmental or lobar lavage by fiberoptic bronchoscopy (FOB), which has been reported in only six cases, including two involving the use of potentially lung-damaging trypsin. Here, we report our experiences in treating three PAP patients with bronchoscopic lobar lavage, using only normal saline solution.

Materials and Methods

Three patients in whom PAP had been diagnosed by open-lung biopsy were enrolled in the study. Blood gases and pulmonary function were measured at the time of hospital admission (Table 1). Bronchoscopic lavage was performed under local anesthesia, with 2% xylazine given to the patient before and when needed during the FOB. No parenteral sedation or analgesia was used. While the patient breathed oxygen through a nasal cannula, a bronchoscope was passed through the nose and was placed in a segmental or lobar bronchus. We chose the lobes that showed the most severe changes from PAP on high-resolution CT scanning. Warm saline solution was instilled via a syringe in 50-mL aliquots into the lung and was removed by suction into a bottle. We used small aliquots of 50 mL because large volumes induced severe cough and were not tolerable to the patient. The returning lavage fluid was initially milky and gradually became clearer. We also applied a pair of portable ultrasonic vibrators on the patient’s chest wall for continuous vibration during lavage. In each procedure, one lobe on the same side was lavaged. The saline solution was instilled at the orifice of the chosen lobar bronchus, and all the segments were lavaged. The procedure lasted about 2 h and was stopped when the returning fluid became clear or the patient could no longer tolerate the discomfort. After 2 to 4 days, we performed the next lavage on the contralateral lung. The procedure was repeated two to five times (Table 1). We measured blood gas levels 2 to 3 days after each procedure, when the residual fluids in the lavaged lobes had been cleared. The baseline data for the three patients and the results of the lavage are listed in Table 1. The data on blood gas levels shown in the columns “After Lavage” in Table 1 were obtained 2 to 3 days after patients underwent the last lavage. Pulmonary function tests, chest radiographs, and measurement of hemoglobin, hematocrit, and lactate dehydrogenase (LDH) levels were performed until 2 weeks after the last lavage was performed. All the patients tolerated the procedure well. The major complications were severe cough and hypoxemia. The average of the lowest pulse oximetry values measured during the procedure was around 80%, with the patient breathing oxygen at 6 L/min through a nasal cannula. All the patients remained hemodynamically stable during the lavage procedure.
Table 1—Laboratory Data and Pulmonary Functions of Three Patients With PAP Before and After FOB Lavage*

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th></th>
<th>Case 2</th>
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<th>Case 3</th>
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<tbody>
<tr>
<td></td>
<td>Before Lavage</td>
<td>After Lavage</td>
<td>Before Lavage</td>
<td>After Lavage</td>
<td>Before Lavage</td>
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</tr>
<tr>
<td>Hb, g/dL</td>
<td>16</td>
<td>13.8</td>
<td>14.6</td>
<td>14.7</td>
<td>17.4</td>
<td>15.7</td>
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<tr>
<td>Hct, %</td>
<td>47.2</td>
<td>41.2</td>
<td>42.8</td>
<td>43.1</td>
<td>48.8</td>
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<tr>
<td>LDH, IU/L</td>
<td>1114</td>
<td>642</td>
<td>604</td>
<td>530</td>
<td>1105</td>
<td>872</td>
</tr>
<tr>
<td>PaO2, mm Hg</td>
<td>54.7</td>
<td>82.5</td>
<td>70.3</td>
<td>109.7</td>
<td>49.1</td>
<td>80.3</td>
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<tr>
<td>PaCO2, mm Hg</td>
<td>27.7</td>
<td>37.7</td>
<td>35.3</td>
<td>35.2</td>
<td>33.2</td>
<td>36.6</td>
</tr>
<tr>
<td>FEV1 L</td>
<td>1.60</td>
<td>2.31</td>
<td>1.60</td>
<td>2.42</td>
<td>1.71</td>
<td>1.77</td>
</tr>
<tr>
<td>% predicted</td>
<td>57.8</td>
<td>85.6</td>
<td>62.0</td>
<td>88.7</td>
<td>57.5</td>
<td>59.6</td>
</tr>
<tr>
<td>FVC L</td>
<td>1.58</td>
<td>2.65</td>
<td>2.33</td>
<td>2.78</td>
<td>1.94</td>
<td>1.92</td>
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<tr>
<td>% predicted</td>
<td>59.1</td>
<td>85.4</td>
<td>79.0</td>
<td>89.0</td>
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<td>53.3</td>
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<tr>
<td>TLC L</td>
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<td>3.93</td>
<td>3.49</td>
<td>3.96</td>
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<td>2.92</td>
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<tr>
<td>% predicted</td>
<td>64.9</td>
<td>93.5</td>
<td>76.2</td>
<td>94.2</td>
<td>62.2</td>
<td>55.9</td>
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<tr>
<td>Dlco mL/min/mm Hg</td>
<td>12.2</td>
<td>19.3</td>
<td>17.5</td>
<td>20.3</td>
<td>10.93</td>
<td>9.99</td>
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<tr>
<td>% predicted</td>
<td>51.2</td>
<td>79.9</td>
<td>80.8</td>
<td>82.5</td>
<td>42.8</td>
<td>39.2</td>
</tr>
</tbody>
</table>

*Hb = hemoglobin; Hct = hematocrit.
†Two lavage cycles.
‡Four lavage cycles.
§Five lavage cycles.

Case Reports

Case 1

A 36-year-old man, a cigarette smoker of 20 pack-years, was brought to our emergency department due to progressive shortness of breath for 6 months and intermittent fever for 5 days. He had been a cement worker for 10 years. He was tachypneic and cyanotic. There were coarse rales over bilateral lower lung fields. A chest radiograph (Fig 1) disclosed diffuse alveolar infiltrates predominantly in the lower lobes. Arterial blood gas analysis on the patient’s arrival in the emergency department revealed a pH of 7.44, a PaO2 of 31.6 mm Hg, and a PaCO2 of 54.7 mm Hg while breathing room air. A pulmonary function test administered 4 days after emergency department admission showed that total lung capacity (TLC) was 64.9% and a diffusing capacity of the lung for carbon monoxide (DLCO) of 51.2% predicted. A high-resolution CT scan of the chest showed bilateral, diffuse, linear and reticular opacities. The diagnosis of PAP was made after open-lung biopsy. The patient underwent the first FOB lavage of the right lower lobe on the 10th day of hospitalization. Approximately 1,700 mL warm saline solution was instilled, and about 600 mL was aspirated. A similar procedure was performed 3 days later on the left lower lobe. Two days after the second FOB lavage was performed, the patient’s PaO2 improved to 82.5 mm Hg while breathing room air. The chest radiographic findings also showed partial clearing of the lung (Fig 1). The results of pulmonary function tests that were performed 12 days after the second lavage were nearly normal. The patient was discharged from the hospital and has remained asymptomatic (follow-up time, 12 months).

Case 2

A 42-year-old housewife, a lifetime nonsmoker, visited our outpatient clinic due to dry cough, chest tightness, and dyspnea on exertion for the past year. Physically, she was mildly tachypneic (respiratory rate, 22 breaths/min) but was not cyanotic. There were diffuse crackles over both lungs. Her chest radiograph revealed diffuse interstitial and alveolar infiltrates over the bilateral lower lung field. Her PaO2 at the time of hospital admission was 70.3 mm Hg while breathing room air. A pulmonary function test revealed a TLC of 76.2% and a DLCO of 80.5% predicted. PAP was diagnosed via open-lung biopsy. The patient subsequently underwent three FOB lavages for the left lower lobe, the right lower lobe, and the left lower lobe. The average volume of warm saline solution that was instilled was 2,050 mL, and that of the effluent fluid was 1,000 mL. After four lavages, her symptoms were relieved. The patient’s PaO2 was 109.7 mm Hg while breathing room air, the TLC was 94.2%, and the DLCO was 82.5% of the predicted value 14 days after she had undergone the final lavage. Opacities of the chest radiograph resolved partially. She was discharged from the hospital and has remained asymptomatic (follow-up time, 12 months).

Case 3

A 54-year-old man, a taxi driver who had consumed 30 pack-years of cigarettes but had not smoked for 3 years, had received a diagnosis of PAP 5 years before and had received whole-lung lavages several times thereafter. Dry cough and shortness of breath, however, recurred, and he was admitted to the hospital again in late September 2000. On examination, he was cyanotic with diffuse coarse crackles over both lungs. A chest radiograph showed diffuse alveolar infiltrates over both lungs. The PaO2 at the time of hospital admission was 49.1 mm Hg, and the PaCO2 was 33.2 mm Hg while breathing room air. The results of a pulmonary function test showed a TLC of 62.2% and a DLCO of 42.8% predicted. The patient then underwent five FOB lavages on the third, fifth, ninth, 11th, and 15th day of hospital admission, respectively, for the right lower lobe, the left lower lobe, the right lower lobe, the left lower lobe, and the right lower lobe.
lobe. The average volume of instilled saline solution was 1,920 mL, and that of the returning fluid was 500 mL. The patient’s $P_{aO_2}$ while breathing room air increased to 80.3 mm Hg 2 days after undergoing the final lavage. Polycythemia and LDH level declined. However, cough and dyspnea on exertion persisted, and radiographic opacities and the results of pulmonary function tests did not improve. He then received four cycles of whole-lung lavage (two for each lung). Symptoms improved, and radiographic infiltrates partially cleared after four whole-lung lavages (follow-up time, 6 months).

**Discussion**

Whole-lung lavage is now considered to be the most effective treatment for PAP. The major adverse effect of whole-lung lavage is hypoxemia, especially during the emptying phase, which decreases airway pressure and increases the perfusion of the lavaged lung.**11,12** Hemodynamic instability may develop during a whole-lung lavage,**11,13** which may necessitate invasive BP monitoring and may further complicate the course of treatment. Noninvasive hemodynamic monitoring by bioimpedance has been found to be useful.**21** The technology, however, is complex and not widely available. Whole-lung lavage requires general anesthesia and an anesthesiologist who is experienced in placing the double-lumen endotracheal tube and is capable of frequently checking and adjusting the tube during the lavage procedure. Leakage of the lavage fluid into the contralateral ventilated lung must be avoided. An experienced team will be required to work for at least 4 h in an operating theater. A postoperative care facility is also needed. The repeated placement of a double-lumen endotracheal tube (PAP patients need an average of four to six cycles of pulmonary lavage) may lead to endotracheal granuloma and stenosis. Other reported complications include pleural collections, hydro-pneumothoraces, and surgical emphysema.**8,10**

Studies in mice that are deficient in GM-CSF or the GM-CSF receptor gene have suggested that defects in GM-CSF signaling may lead to PAP by the impairment of surfactant clearing.**23,24** Recombinant GM-CSF has been shown to have therapeutic effects in 43% of patients with PAP,**15** a potential alternative to whole-lung lavage. However, there are patients who do not show response to GM-CSF and may still need to undergo whole-lung lavage. The time needed to improve the alveolar-arterial oxygen pressure difference in responders (ie, 4 to 6 weeks) may be too long for patients with severe cases of PAP. The long-term safety of this hematopoietic growth factor and its benefits vs its costs have not been established.

Segmental or lobar lavage has been reported as a possible alternative. Harris and colleagues**16** used a cuffed bronchoscopic catheter to perform lobar lavage under fluoroscopic guidance. Brach et al**17** used a modified bronchoscope with an inflated tracheostomy cuff and a Venturi mask to perform the lavage procedure. Heymach et al**18** used general anesthesia to perform a bronchoscopic lavage. Nagasaka et al**20** used trypsin as the lavage fluid. These studies involved either complicated procedures or trypsin, which carries the potential danger of an allergic reaction and proteolytic damage.

Our study, using local anesthesia, ordinary FOB equipment, and normal saline solution, showed that multiple lobar lavage could be an alternative to whole-lung lavage in patients with mild cases of PAP. Two to four cycles of lobar lavage resulted in satisfactory clinical and physiologic improvement. The two patients showing positive responses had no limitation in their daily activity and were able to work for up to 14 months after treatment. In case 3, however, FOB lobar lavage failed to achieve clinical or pulmonary function improvement, despite improved oxygenation. The causes of failure included the following: advanced disease status, as evidenced by the severe hypoxemia; diffusion block and diffuse radiographic infiltrates, including a honeycomb pattern suggestive of interstitial fibrosis; and the poor return of the lavage fluid. The latter probably resulted from widespread atelectasis. The entire procedure was safe. Hypoxemia occurred during lavage, especially when the patient experienced a severe cough. But patients remained hemodynamically stable, and, due to the smaller volume of lavage fluid, there was less risk of its overspilling. FOB lobar lavage did not require endotracheal intubation, double-lumen tubes,
general anesthesia, or a postoperative care facility. Disadvantages included severe cough, which may lead to the termination of the procedure. The volume of the lavage fluid thus was limited to about 2 L, roughly one tenth of the volume that would be used in a whole-lung lavage. Therefore, FOB lobar lavage was not effective for patients with advanced cases of PAP (eg, the patient in case 3). The small volume of lavage fluid also calls for multiple cycles of lavage, which prolongs the discomfort of the patients. Another possible disadvantage is that while whole-lung lavage has been shown to improve alveolar macrophage migration25 and to decrease the incidence of opportunistic infection,26 such effects have not been proven with FOB lobar lavage.

Hammon and colleagues27 reported that during a whole-lung lavage, manual chest percussion is superior to mechanical percussion and no percussion in clearing proteinaceous material and radiographic infiltrates in patients with PAP. We used a pair of ultrasonic vibrators to apply continuous vibration during the performance of FOB lavage. We found the vibrators to be useful in decreasing the severity of cough during the procedure. More studies are required to establish their therapeutic effects.

Patients with PAP may have spontaneous remission without the need for lavage.28 In case 1 of our study, the hypoxemia at hospital admission was so severe that the patient was dependent on the Venturi mask. The hypoxemia dramatically improved after two cycles of FOB lavage, and the patient immediately became fully ambulatory. The clinical/physiologic response did not resemble a spontaneous resolution. In case 2, although we could not completely exclude the possibility of spontaneous remission, the fact that she became unlimited in daily activity after only 4 cycles of lavage demonstrated that lavage, rather than waiting for spontaneous remission, was indicated.22

Our experience suggests that FOB lobar lavage is a simple and safe procedure that can be carried out in most hospitals. Using only normal saline solution, it led to clinical, physiologic, and radiographic improvements in two of our three patients. In conclusion, FOB lobar lavage is useful in patients with PAP in whom whole-lung lavage with general anesthesia may be hazardous, and in patients with less advanced disease from whom proteinaceous substances can be removed with a small volume of lavage fluid.

REFERENCES

Successful Airway Stenting Using Silicone Prosthesis for Esophagobronchial Fistula*

Keisuke Miwa, MD; Masahiro Mitsuka, MD, FCCP; Kohsuke Tayama, MD; Naofumi Tomita, MD; Shinzo Takamori, MD, FCCP; Akihiro Hayashi, MD; and Kazuo Shirouzu, MD

We present the case of a 55-year-old man with advanced esophageal cancer who was successfully treated using a self-expandable metallic stent (S-EMS) for 6 months and subsequently was treated for an esophagobronchial fistula as a complication of the initial S-EMS using a silicone airway stent for an additional 4 months. This is the first report in the literature concerning penetration into the airway of an S-EMS implanted in the esophagus. The present case suggests that airway stenting using a silicone stent as treatment for an esophagobronchial fistula may represent a useful modality.

(CHEST 2002; 122:1485–1487)

Key words: bronchial fistula; esophageal fistula; self-expandable metallic stent; silicones; stent-related complication

Abbreviation: S-EMS = self-expandable metallic stent

Stent therapy using a self-expandable metallic stent (S-EMS) in patients with esophageal stenosis has resulted in improvements to the quality of life for patients with inoperable esophageal cancer.1–3 However, stent-related complications such as hemorrhage, rupture, stent migration, granulation tissue formation, and esophagotracheobronchial fistula have been reported.4 In particular, the management of esophagotracheobronchial fistulas presents difficulties. We report a case of an esophagobronchial fistula due to penetration of an S-EMS that had been implanted in the esophagus, which was successfully treated by silicone stent placement in the bronchus.

Case Report

A 55-year-old man with dysphagia due to esophageal cancer was referred to our hospital. A barium esophagogram and CT scan revealed severe stenosis in the middle esophagus and abdominal lymph node metastasis. Squamous cell carcinoma was diagnosed by endoscopic biopsy and was clinically staged as T4N3M0 stage IV on the basis of imaging by CT scan and esophagography. The patient initially received chemoradiotherapy.

Tumor-specific chemotherapy (with cisplatin and fluorouracil) and radiotherapy were undertaken. The chemotherapy regimen consisted of IV administration of 100 mg cisplatin on day 1 and 1,000 mg fluorouracil on days 1 to 4. This course of treatment was administered three times every 3 weeks. During this treatment, a 3.0-Gy dose fraction of radiation per day, 5 days per week, was administered for 4 weeks, for a total dose of 60 Gy. The radiation field included the primary tumor (with a 2.0-cm margin of healthy esophageal tissue), the infraclavicular trachea, and the left main bronchus.

As a result, although the tumor was reduced to 56% of its original size, the esophageal lumen remained stenosed and the enlarged abdominal lymph nodes displayed almost no change compared to the condition before chemoradiotherapy. Stent therapy was subsequently selected to reduce esophageal stenosis. A covered S-EMS (Covered Ultraflex Esophageal Stent System, Microinvasive; Boston Scientific Co; Boston, MA) was placed in the esophagus on the 10th day after chemoradiotherapy. The course after stent placement was initially uneventful. However, the patient complained of severe cough on oral intake in the sixth month after stent placement. Esophagography revealed an esophagobronchial fistula, and an additional stent of the same type was introduced into the previous stent in the esophagus.

Although initial improvement was observed, symptoms recurred within 1 month. Esophagography and CT scanning revealed an esophagobronchial fistula. Moreover, bronchoscopic findings revealed S-EMS penetration to left main bronchus (Fig 1). The patient subsequently received a silicone stent (Dumon Tube BD; Novatech Co; Aubagne, France) that was placed in the left main bronchus. A rigid bronchoscope was inserted under general anesthesia immediately after the second carina while slowly rotating and holding down the S-EMS, which penetrated into the left main bronchus through the vocal cords. A sheath containing the appropriate size silicone stent subsequently was inserted through the rigid bronchoscope, and the stent was released from the sheath using a pusher. The final stent position then was adjusted using forceps.

The symptoms of an esophagobronchial fistula subsequently resolved. Oral intake was resumed on the 20th day after silicone stent placement, as esophagography did not reveal an esophagobronchial fistula. Although patient recovery followed a satisfactory course, death due to cancer occurred in the fourth month after airway stent placement.