our patient. Constrictive pericarditis has been reported rarely,\textsuperscript{1,4} and epicardial fibrosis has not been described previously, to our knowledge. The occurrence of severe pleural, pericardial, and epicardial fibrosis in our patient was remarkable and suggests an underlying immunologic disorder, although we were unable to define a specific immunologic defect.

This patient demonstrates that excessive fibrosis from \textit{H capsulatum} infection can occur not only in the mediastinum, pericardium, and pleura, but also in the epicardium. Recurrent massive pleural effusions may occur. Histoplasmosis is not currently listed as a possible etiology for pleural effusions,\textsuperscript{14} but it should be included in the differential diagnosis in view of our findings. Congestive heart failure refractory to medical or surgical therapy can occur as a result of epicardial fibrosis.

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Combined Laser Phototherpy and Growth Factor Treatment of Bronchial Obstruction after Lung Transplantation*


Lung transplantation has resulted in dramatic functional improvement in patients with end-stage pulmonary disease. Among the complications of lung transplantation are dehiscence and stenosis at the site of the bronchial or tracheal anastomosis. In this case report, we describe a single lung transplant recipient in whom partial bronchial dehiscence, followed by exuberant growth of granulation tissue, resulted in obstruction of the bronchial lumen. After mechanical dilation failed to produce lasting relief of bronchial obstruction, a novel approach to this problem was successfully employed: YAG laser phototherpy was used to remove obstructing granulation tissue, followed by application of a preparation derived from autologous blood platelets to promote epithelialization of the bronchial anastomosis. The bronchus remains patent and fully epithelialized six months after therapy. (Chest 1991; 100:1717-19)

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CASE REPORT

The patient is a 35-year-old woman who developed exertional dyspnea associated with interstitial infiltrates on chest roentgenogram. An open lung biopsy specimen demonstrated pulmonary lymphangioleiomysomatosis. Medical treatment consisted of medroxyprogesterone acetate (Depo-Provera) monthly for 3½ years, and tamoxifen for 1½ years. Her course was complicated by recurrent bilateral pneumothoraces and deteriorating respiratory function, and she was referred to the University of Minnesota, Minneapolis, for consideration of lung transplantation.

Pretransplant examination included pulmonary function tests that showed an FEV₁ of 0.7 L and an FVC of 1.5 L. The arterial Po₂ was 49 mm Hg on room air. Cardiac catheterization was performed: the pulmonary artery pressure was 28/14 mm Hg, the pulmonary artery occlusion pressure was 10 mm Hg, and the cardiac output was 5.5 L/min.

In June 1989, the patient underwent right single lung transplantation. The bronchial anastomosis was wrapped with the recipient's omentum, which had been brought up through the right hemidiaphragm. The posttransplant immunosuppressive regimen included cyclosporine A and azathioprine. Fourteen days after transplantation, oral prednisone therapy 30 mg daily was begun with a tapering schedule to attain a dose of 7.5 mg daily at six months after transplantation.

A productive cough began six days after transplantation. Bronchoscopy demonstrated an avascular area 1 cm in greatest dimension involving the medial aspect of the anastomosis and extending 1 cm distally along the medial wall of the donor bronchus. The remainder of the anastomosis appeared well vascularized. Ten weeks after transplantation, repeated bronchoscopy demonstrated loosening of the sutures at the bronchial anastomosis. During the ensuing four weeks, increasing dyspnea developed associated with a reduction in FEV₁/FVC (percent) from 73 percent to 40 percent. A loud wheeze was heard over the right anterior chest. Bronchoscopy revealed 90 percent obstruction of the right bronchus just distal to the bronchial anastomosis by an exophytic mass of granulation tissue arising from the medial aspect of the right main bronchus (Fig 1). Plain tomography and computed tomographic (CT) scan confirmed the presence of a polyoid excrescence in the bronchial lumen, but did not demonstrate any anatomic disruption of the bronchus or air outside of the bronchus.

Bronchial dilation with a 6-mm Reicker rigid bronchoscope was performed. Postoperatively, the patient reported reduced dyspnea, and repeated flexible bronchoscopy demonstrated reestablishment of a bronchial lumen that was approximately 50 percent of the normal bronchial caliber. The patient remained well for two weeks but then developed recurrent dyspnea associated with increasing obstruction of the right main bronchus. Dilation with the rigid bronchoscope was carried out on two subsequent occasions, and was followed both times by initial relief with rapid recurrence of symptoms and bronchial obstruction.

In an effort to afford more durable symptom relief, the patient underwent YAG laser phototherapy and 1100 J of laser energy were applied to photocogulate the granulation tissue occluding the bronchus. Repeated bronchoscopy revealed that the caliber of the right bronchial lumen was 70 percent that of the left, and the patient reported marked relief of her dyspnea. Increasing cough developed seven weeks after the first laser procedure and a second laser procedure was performed to remove residual granulation tissue. Following the second laser procedure, a preparation derived from the patient's blood platelets was applied to the site of injury in an attempt to promote epithelialization and retard the formation of granulation tissue. This preparation, designated platelet-derived wound healing formula (PDWHF) was applied via a bronchoscopically directed catheter in a dose of 5 ml daily for five consecutive days following laser therapy.

Following the second laser procedure and application of PDWHF, the patient has remained free of cough and has required no further therapy. Bronchoscopy six months after therapy demonstrates a well-epithelialized bronchial wall (Fig 2). The patient continues to

**FIGURE 1A (upper).** Bronchoscopic appearance of right main bronchus prior to laser therapy. The lumen (arrow) is nearly completely occluded by an exophytic soft tissue mass arising from the medial aspect just distal to the anastomosis, preventing visualization of the lobar bronchi. **B (lower).** Microscopic appearance of the endobronchial biopsy specimen demonstrates typical granulation tissue with no evidence of omental fat (× 150).

**FIGURE 2.** Bronchoscopic appearance of right main bronchus after YAG laser phototherapy and application of PDWHF. The entire bronchial wall is epithelialized. The right upper lobe bronchus and bronchus intermedius can now be seen. Sutures in the foreground mark the site of the bronchial anastomosis.
have stenosis of the right main bronchus, the bronchial lumen being approximately 60 percent of the caliber of the normal left main bronchus.

**DISCUSSION**

Bronchial dehiscence and stenosis are among the most serious problems confronting clinicians caring for lung transplant patients. After combined heart and lung transplantation, blood flow to the tracheal anastomosis occurs via collateral vessels arising from the coronary arteries. During single or double lung transplantation, these collaterals are disrupted, predisposing to inadequate vascularization of the tracheal or bronchial anastomosis. Steroid-sparing cyclosporine-based immunosuppressive strategies, coupled with the development of omental wrapping to promote revascularization of the anastomosis, have resulted in a marked reduction in the incidence of these complications. Other approaches to this problem include wrapping the anastomosis with donor pericardium and the use of a "telescoping" bronchial anastomosis (Trinkle, personal communication). Despite these innovations, airway complications still occur in a significant minority of lung transplant recipients. The pathologic events leading to airway occlusion in our patient were complex. The initial step was partial dehiscence of the bronchial anastomosis, most likely due to inadequate vascularization despite omental wrapping at the time of transplantation. Prior to the introduction of omental wrapping, bronchial dehiscence would likely have proven catastrophic. In this case, however, complete bronchial separation was prevented by the omental buttress. Following dehiscence, the bronchial "wound" underwent a healing process which, although successful at filling the defect in the bronchial wall, resulted in exuberant growth of granulation tissue that obstructed the bronchial lumen.

The relief afforded by this mechanical dilation of the bronchus with the rigid bronchoscope was very short-lived on three occasions. In view of the absence of a true bronchial wall, we were initially reluctant to employ laser phototherapy in this patient because of the risk of creating a bronchomedial fistula. However, a biopsy specimen of the endobronchial tissue showed granulation tissue rather than herniation of omental fat through an anastomotic rent. These data convinced us that perforation was unlikely. Indeed, complete debridement without complications was achieved using YAG laser phototherapy.

Regrowth of granulation tissue occurred seven weeks after the initial laser treatment. This exuberant granulation tissue most likely originated from the omental wrap around the bronchial anastomosis. We hypothesized that continued irritation of the nonepithelialized granulation tissue resulted in unrestric ted growth. This has been seen clinically in patients with chronic nonhealing wounds where epithelialization is impaired by recurrent trauma. One of us (D.R.K.) has extensive experience with the topical application of PDWHF to induce repair of chronically nonhealing wounds. PDWHF is an α-granule releasate from autologous platelets. It contains locally acting growth factors such as platelet-derived growth factor, epidermal growth factor, and transforming growth factor-β. In clinical trials with various chronically nonhealing wounds, topically applied PDWHF stimulated rapid epithelialization of a capillary dense granulation tissue resulting in accelerated repair. Therefore, following debridement of granulation tissue with the YAG laser, PDWHF was applied bronchoscopically. We have now used PDWHF in two patients with nonhealing bronchial anastomoses after single lung transplantation and in both patients airway healing has occurred. Although we have remedied the problem of granulation tissue growth in the bronchial lumen, this patient's pulmonary function remains impaired because of bronchial stenosis in the area of the previous dehiscence. This lesion represents the final result of the wound healing process after bronchial disruption. Approaches to bronchial stenosis have included mechanical dilation, laser phototherap y, and placement of wire or Silastic stents. At the present time, our patient's condition is clinically stable and her exercise tolerance is adequate to allow an active life-style, but further therapy may be required if progressive airway stenosis occurs in the future.

Based on our experience, we believe that YAG laser phototherapy is an attractive alternative to bronchial dilatation when intraluminal granulation tissue causes obstruction of the bronchial lumen after lung transplantation. In addition, PDWHF appears to have contributed to the healing of the bronchial anastomosis by promoting epithelialization of the wound. Confirmation of the efficacy of this preparation will await more extensive and controlled experience.

**REFERENCES**