Clinical-pathologic conference in general thoracic surgery: Bilateral lung transplantation for sarcoidosis with aspergilloma

G. Alexander Patterson, MD

From the Washington University
School of Medicine, Barnes-Jewish
Hospital, St Louis, Mo.

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Participants

From the Washington University
School of Medicine, Barnes-Jewish
Hospital, St Louis, Missouri

Thoracic Surgery

Dr G. Alexander Patterson
Dr Anna Maria Ciccone

Radiology

Dr Harvey Glazer

Pulmonary Medicine

Dr Elbert Trulock

Surgical Pathology

Dr Jon Ritter

Case Presentation

Dr Ciccone: The patient is a 47-year-old man who was hospitalized 16 years ago for "asthma." He had a less than complete response to initial therapy, and his treating physician's inclination at that time was that he had tuberculosis. That same year, a diagnosis of sarcoidosis was established after a lung biopsy. He had a history of systemic hypertension, osteoporosis, and gout. His condition remained stable until 3 years ago, at which time his symptoms of dyspnea worsened. He required increasing supplemental oxygen. Two years ago he was seen, evaluated, and eventually listed for bilateral lung transplantation. By spirometry, the forced expiratory volume in 1 second was only 0.55 L, 16% of predicted, and the forced vital capacity was 1.81 L, or 44% of predicted.

Six months ago he was hospitalized for an exacerbation of his respiratory symptoms. He was treated and enrolled in our pulmonary rehabilitation program.

On physical examination, the patient had poor chest excursion and coarse breath sounds bilaterally. The remainder of his physical examination was unremarkable.

Perhaps we could review the relevant radiographic findings.

Dr Glazer: Chest radiograph and computed tomographic images demonstrate findings consistent with the clinical diagnosis of end-stage sarcoidosis. The chest radiograph (Figure 1) shows extensive bullous formation and scarring, predominantly in the mid and upper lungs, with compensatory hyperinflation in the lower lungs. Superior retraction of the hila is seen. An opacity is seen within the dependent portion of a large cystic space in the left upper hemithorax, likely representing a fungus ball.

Similar findings are seen on the computed tomographic scan (Figure 2). Large cystic spaces are noted with central bronchial distortion and angulation. A dependent opacity, likely a fungus ball, is seen within a large cystic space in the left lung.

Dr Patterson: Dr Glazer, we typically think of sarcoidosis as being an inflammatory fibrotic lung disease. This certainly is not the picture of classic pulmonary fibrosis with decreased lung volumes. Would you describe the radiographic findings as being typical of a diagnosis of sarcoidosis?

Dr Glazer: End-stage sarcoidosis is characterized by a variety of findings, including bronchial distortion, linear opacities, peripheral honeycombing, and in

From the Washington University School of Medicine, Barnes-Jewish Hospital, St Louis, Mo.

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Address for reprints: G. Alexander Patterson, MD, Washington University School of Medicine, Department of Cardiothoracic Surgery, One Barnes Hospital Plaza, Suite 3108 Queeny Tower, St Louis, MO 63110 (E-mail: pattersona@msnotes.wustl.edu).

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Figure 1. Chest radiograph demonstrates extensive bullous formation and associated hyperinflation. Upper lobe scarring with hilar retraction is seen. An opacity (arrow), likely a fungus ball, is seen within a large cystic space in the left upper hemithorax.

Figure 2. Computed tomographic image confirms dependent opacity (arrows), likely a fungus ball, in a large cystic space in the left hemithorax. Bronchial distortion (arrowheads) is also noted.

some patients, large cystic/bullous spaces. As in this patient, the findings usually predominate in the upper lung zones with compensatory hyperinflation in the lower lungs. In some cases, conglomerate masses of fibrosis may be seen. The combination of upper lobe fibrosis, central bronchial distortion, and cystic spaces is a known manifestation of severe end-stage pulmonary sarcoidosis. Associated fungus ball formation is a widely described complication.

Dr Ciccone: How does the diagnosis of sarcoidosis influence evaluation for lung transplantation, and does the

presence of aspergilloma affect eligibility for subsequent transplantation?

Dr Trulock: This patient underwent the standard evaluation protocol that has been used in our institution for a number of years. He had no contraindication to transplantation, such as coexisting malignant disease or other major medical problems. Transplantation was appropriate because his disease had progressed to severe pulmonary impairment despite medical treatment.

Sarcoidosis is one of the diseases that is known to recur in the allograft. In most cases the recurrence has been an incidental discovery on transbronchial biopsy specimens that were obtained to monitor for rejection, and recurrence has not been associated with an adverse outcome. Hence, sarcoidosis itself is not a contraindication to transplantation.

The aspergilloma in the left upper lobe presented a significant dilemma. The aspergilloma was asymptomatic at the time of evaluation, and it did not cause any clinical problems during the waiting period. At the time of his evaluation, itraconazole treatment was begun as a cautionary measure to limit the likelihood of complications while awaiting transplantation and to provide antifungal coverage for the transplant operation.

Airway contamination by *Aspergillus* is not unusual among potential transplant recipients with bronchiectasis, such as those with cystic fibrosis. Our approach is the same in these patients. Itraconazole therapy is begun during the waiting period and continued for 3 months after transplantation and until posttransplantation bronchoscopic cultures are negative for *Aspergillus*.

Dr Patterson: I think we could be criticized for doing a transplant operation in a patient with an active aspergilloma. We actually spent considerable time considering this patient's management in advance of this transplant. We thought that one option was to drain the aspergilloma cavity by cavernostomy. However, we concluded that the morbidity of this procedure and the unknown date of transplant might cause some complications. We therefore elected to make an effort to deal with the aspergilloma cavity at the time of transplant. The operation was specifically tailored to deal with the aspergilloma cavity in the safest possible way at the time of lung extraction.

Dr Ciccone: A suitable donor was identified in Duluth, Minnesota. Donor PaO_2 at an FiO_2 of 100% was 448 mm Hg. Examination with a flexible bronchoscope demonstrated purulent secretions in the left lower lobe. In addition, the donor chest x-ray film demonstrated some volume loss in the hemithorax and a double density behind the left side of the heart, suggestive of left lower lobe atelectasis. Nonetheless, at the time of direct inspection, the lungs including the left lower lobe appeared to be of suitable quality for transplantation. The lungs were preserved by means of standard preservation techniques. The lungs were harvested en bloc

Figure 3. The initial postoperative chest radiograph (A) demonstrates moderate left perihilar and left basilar opacity, likely representing edema and atelectasis. Pneumonia could have a similar radiographic appearance. Improvement was noted by the third postoperative day (B).

and separated into separate lung grafts on arrival at Barnes-Jewish Hospital.

Recipient quantitative ventilation/perfusion imaging demonstrated 75% and 25% perfusion to the right and left lungs, respectively. The operation was commenced via a left posterolateral thoracotomy. After donor lung arrival, the left lung was extracted. The resection over the area of the fungus ball was conducted in an extrapleural plane. During ex vivo examination, the donor left lower lobe was somewhat atelectatic. There was a significant amount of purulent secretion in the donor left lower lobe. Nonetheless, we proceeded with implantation. The anterior cartilaginous airway was closed with interrupted figure-of-8 sutures of 4-0 polydioxanone (PDS; Ethicon, Inc, Somerville, NJ). Peribronchial soft tissue was approximated anteriorly to cover the bronchial anastomosis. The pulmonary artery and left atrial anastomoses were performed in standard fashion. After the lung had been deaired, clamps were removed, the

Figure 4. Sections of the hilar lymph nodes showing marked elastosis and sclerosis.

lung was reflected anteriorly, and the membranous airway was closed with a continuous suture. The donor left lower lobe did not inflate as easily as the upper lobe. However, gas exchange was satisfactory. After chest closure, the patient was turned supine and, via a right anterolateral thoracotomy, the recipient right lung was extracted and the donor right lung implanted via a standard technique.

Immediate postoperative gas exchange was excellent, with a P_{aO_2} on 100% F_{iO_2} of 508 mm Hg. The patient was extubated on the third postoperative day. On the seventh postoperative day he was reintubated after an episode of atrial fibrillation and hypoxia. He was extubated on the ninth postoperative day and discharged from the hospital on the fourteenth postoperative day.

Perhaps we could ask Dr Glazer to comment on the early postoperative chest x-ray films.

Dr Glazer: The initial postoperative chest radiograph demonstrates moderate left perihilar and left basilar opacity likely representing edema and atelectasis, although pneumonia could have a similar radiographic appearance (Figure 3, A). Improvement is seen by the third postoperative day (Figure 3, B).

Dr Ciccone: Dr Patterson, could you give us some insight as to the operative approach in this particular patient and the impact of the marginal lung on that selection?

Dr Patterson: Our usual practice is to conduct bilateral sequential single lung transplants through an anterolateral approach. Historically, these procedures were performed through bilateral anterolateral thoracotomies with a transverse sternotomy (clamshell incision). However, for 5 years we have been routinely avoiding sternal division. Currently we conduct the vast majority of these bilateral procedures through separate anterolateral thoracotomies, irrespective of the recipient diagnosis.

However, in this patient we believed there was a specific indication for a posterolateral approach on the left. In view of the extensive pleural fibrosis associated with the aspergilloma and the absolute requirement to conduct the left lung

Figure 5. Photomicrograph of larger airways with intramural sclerosis.

Figure 7. Terminal bronchiole surrounded by sclerosis with adjacent parenchymal emphysema.

Figure 6. Sclerosis surrounding a small airway.

Figure 8. Section of a bulla wall.

explant without opening the aspergilloma, I thought that a posterolateral thoracotomy was the only suitable option. The bilateral transplant procedure can be easily initiated through this posterolateral approach. Indeed, we have used this approach in a number of other circumstances, typically in the situation of significant mediastinal shift associated with such lateral displacement of the heart that an anterior approach would provide unsafe exposure to the hilum. I really do not think there is any problem conducting the posterolateral thoracotomy first, implanting the first lung, then turning the patient supine for conduct of the second lung transplant. The only disadvantage is the inevitable delay of separate wound closure, dressing, and patient repositioning.

The marginal donor did present some difficulties. I had underestimated the degree of left lower lobe pneumonitis. Nonetheless, the immediate intraoperative and early postoperative allograft function was very satisfactory. Over a 2- to 3-week follow-up period, the left lower lobe pneumonitis cleared quite nicely, ultimately providing the patient with a satisfactory result.

Dr Ciccone: Perhaps at this point we could have the pathologist present the findings on this patient.

Dr Ritter: This patient had a history of a right upper lobe transbronchial biopsy in 1985, which showed noncaseating granulomas. Furthermore, a bone marrow biopsy in 1993 showed multiple noncaseating epithelioid granulomas throughout the bone marrow compartment. No microorganisms were identified in either specimen.

Sections of the hilar lymph nodes show marked elastosis and sclerosis (Figure 4). There is scant remaining lymphoid tissue. The contour of the sclerosis suggests “burnt-out” granulomas; however, there is no active granulomatous inflammation in the lymph nodes. Sections of the large airways show marked peribronchiolar sclerosis with deposition of elastotic material (Figure 5). This sclerosis extends into the smaller airways (Figures 6 and 7). The sclerosis has a similar quality to that seen in the lymph nodes. We speculate that this may also represent “burnt-out” granulomatous disease. However, multiple sections do not reveal any active granulomatous inflammation. The surrounding

Figure 9. Sections of the wall of the aspergillus cavity showing mixed inflammatory infiltrate.

Figure 10. Low-magnification view of bulla contents showing inflammatory debris and hyphae.

lung parenchyma (Figure 7) shows emphysema. Multiple bullae are present (Figure 8). One of the bullae became the site of a noninvasive aspergilloma. Sections of the wall of this cavity show a mixed inflammatory infiltrate consisting primarily of plasma cells and scattered neutrophils (Figure 9). At low power, the hyphal nature of the contents of this bulla can be appreciated (Figure 10). At high power, it can be seen that these hyphae are branching at 45° angles, a characteristic of *Aspergillus* (Figure 11). Sections through one of the larger pulmonary arteries (Figure 12) show intimal thickening, suggesting pulmonary hypertension.

In summary, the findings include peculiar sclerosis in lymph nodes and along airways. There were pulmonary artery hypertensive changes. Distal bullous disease was also seen. These features are compatible with a diagnosis of advanced sarcoidosis.

Dr Patterson: In view of these pathologic findings, perhaps Dr Trulock might wish to comment regarding the

Figure 11. High-magnification view of branching hyphae.

Figure 12. Sections through one of the larger pulmonary arteries showing intimal thickening.

security of the original diagnosis. In the absence of granulomatous inflammation, is there any reason to doubt the diagnosis of sarcoidosis?

Dr Trulock: The diagnosis of sarcoidosis is quite secure. A prior lung biopsy demonstrated noncaseating granuloma. Furthermore, the clinical course and radiographic features are consistent with the diagnosis of sarcoidosis.

Dr Ciccone: At present the patient is doing well 4 months after lung transplant. At the most recent follow-up examination, spirometry showed a forced vital capacity of 3.13 L or 76% predicted and a forced expiratory volume in 1 second of 2.60 L or 78% predicted. Resting room air pulse oximetry was 98%. During a 6-minute walk test, he covered a distance of 1200 feet and maintained an arterial oxygen saturation of 96% without supplemental oxygen. He continues to have ongoing subjective improvement in his level of exertional tolerance. He walks three times weekly for 1 hour on a flat surface covering approximately 2 miles. He is free of pulmonary symptoms.