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IMMUNOSUPPRESSED PATIENTS

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# Pulmonary surgery in immunosuppressed patients

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After organ transplantation under immunosuppression, there has been a high incidence of serious or lethal lung complications. The most common cause of the pulmonary lesions has been infection,<sup>1</sup> and the second most common has been pulmonary embolization.<sup>1, 2</sup> For both conditions, the preferred methods of treatment are usually nonoperative. However, there may be occasional circumstances in which the only hope for survival lies in aggressive surgical intervention with consideration of pulmonary resection. The present report will recount our observations with cases of this type. To our knowledge, there have been no other reports of a similar experience.

## Case reports

CASE 1. A 34-year-old man received a renal homograft from his brother. Postoperatively, he was treated with azathioprine, prednisone, and horse antihuman-lymphocyte-globulin (ALG). Acceptable renal function was obtained and maintained. During the tenth post-transplantation week, he developed pleuritic pain and hemoptysis. A chest x-ray film revealed an infiltrate in the middle lobe of the right lung. Systemic heparin therapy was instituted after a diagnosis of pulmonary embolization was made.

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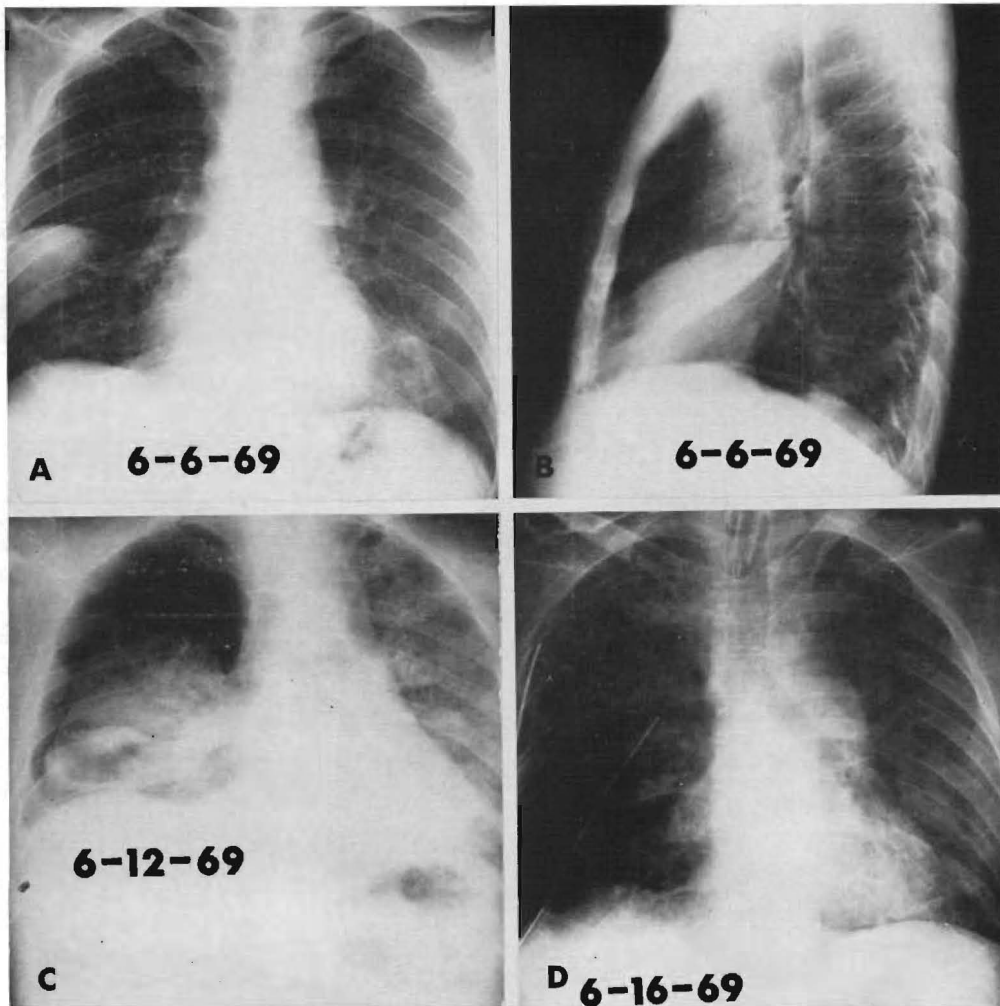
During the subsequent weeks, he had intermittent low grade fever coincident with an infiltrate in the right middle lobe (Fig. 1, A and B). On the one hundred and sixth post-transplantation day, the pulmonary lesion rapidly cavitated, and 2 days later it ruptured into the pleural space (Fig. 1, C).

Emergency middle lobectomy was carried out within 6 hours. After the induction of anesthesia, a Carlen's endotracheal catheter was inserted to prevent contamination of the left lung from the abscess. Exploration of the chest by means of a posterolateral incision revealed that the abscess was in the lateral segment of the middle lobe; its wall was necrotic. At the site of perforation there was little inflammatory reaction. The liquid residual content of the abscess had a chocolate color and contained *Pseudomonas aeruginosa* in pure culture. The lobectomy was not difficult, and there was no subsequent air leak (Fig. 1, D).

The resected specimen contained an abscess cavity with a bronchopleural communication. Histologically, recent and organizing thrombi were seen in the medium-sized arteries. There were also small collections of *Pneumocystis carinii*.

Postoperatively, ventilator support was maintained for the first 10 postoperative days and then discontinued. Antibiotic therapy was with carbenicillin, cephalothin, and gentamicin. The patient was also treated with pentamidine isothionate for the *Pneumocystis carinii*. The pre-existing immunosuppressive therapy with azathioprine and prednisone was drastically reduced, and ALG was continued as before. The transplanted kidney failed, and the patient required hemodialysis thereafter.

The patient developed a stroke after the middle lobectomy and died 16 days postoperatively. Postmortem examination of the brain showed one



**Fig. 1.** Case 1. *A* and *B*, Frontal (*A*) and lateral (*B*) chest roentgenograms made 10 weeks after renal homotransplantation demonstrate an infiltrate in the right middle lobe. *C*, Chest film now shows the ruptured abscess involving the right lung. *D*, Postoperative film following resection of the right middle lobe containing the ruptured lung abscess.

large and several small areas of hemorrhagic necrosis, probably secondary to arterial emboli. Cultures of these areas produced a few colonies of *Aspergillus fumigatus*. The lungs had widespread congestion and parenchymal consolidation. Histologically, there were many focal areas of inflammation, one of which contained fungi. A few colonies of *Aspergillus* were cultured from the postmortem lung tissue, but no bacteria could be isolated.

**CASE 2.** A 29-year-old man had bilateral nephrectomy, splenectomy, and renal homotransplantation; the new kidney was donated by his brother. In addition to chronic glomerulonephritis, the patient's past history was significant be-

cause of a left pneumonitis and empyema 1 year previously that had required thoracotomy and decortication.

Three days after the kidney transplant, the patient aspirated and developed signs of bronchopneumonia and an infiltrate in the lower lobe of the right lung. Subsequently, a moderately severe homograft rejection developed despite immunosuppressive treatment with azathioprine, prednisone, and ALG. This was reversed, but in the meanwhile the right lower lobar infiltrate increased in size, evolved into an abscess, and ruptured into the right pleural space. The complication was treated for a day with tube thoracostomy, but the air leak was very large and

showed no signs of diminishing. Consequently, right lower lobectomy was carried out.

The operative findings were similar to those in Case 1 except that the abscess in the lower lobe contained streptococcus and *Aerobacter-Klebsiella*. There was a temporary small air leak which ceased after 6 days. However, other infiltrates developed in both lungs, and he died 49 days after transplantation and 13 days after pulmonary resection.

In the pulmonary artery branches of the resected right lower lobe, there were many small clots. At autopsy, there were also multiple emboli

in the left lung as well as necrotizing pneumonitis. The source of the emboli could not be determined in spite of a diligent search. There was minimal fibrin deposition at the renal vein anastomosis but no large thrombi.

CASE 3. A 38-year-old man received a renal homograft from his sister. Subsequently, there was a moderately severe and protracted but ultimately controllable rejection while he was on therapy with azathioprine, prednisone, and ALG. Five months after the transplantation, an infiltrate was detected in the superior segment of the right lower lobe (Fig. 2, A). This increased

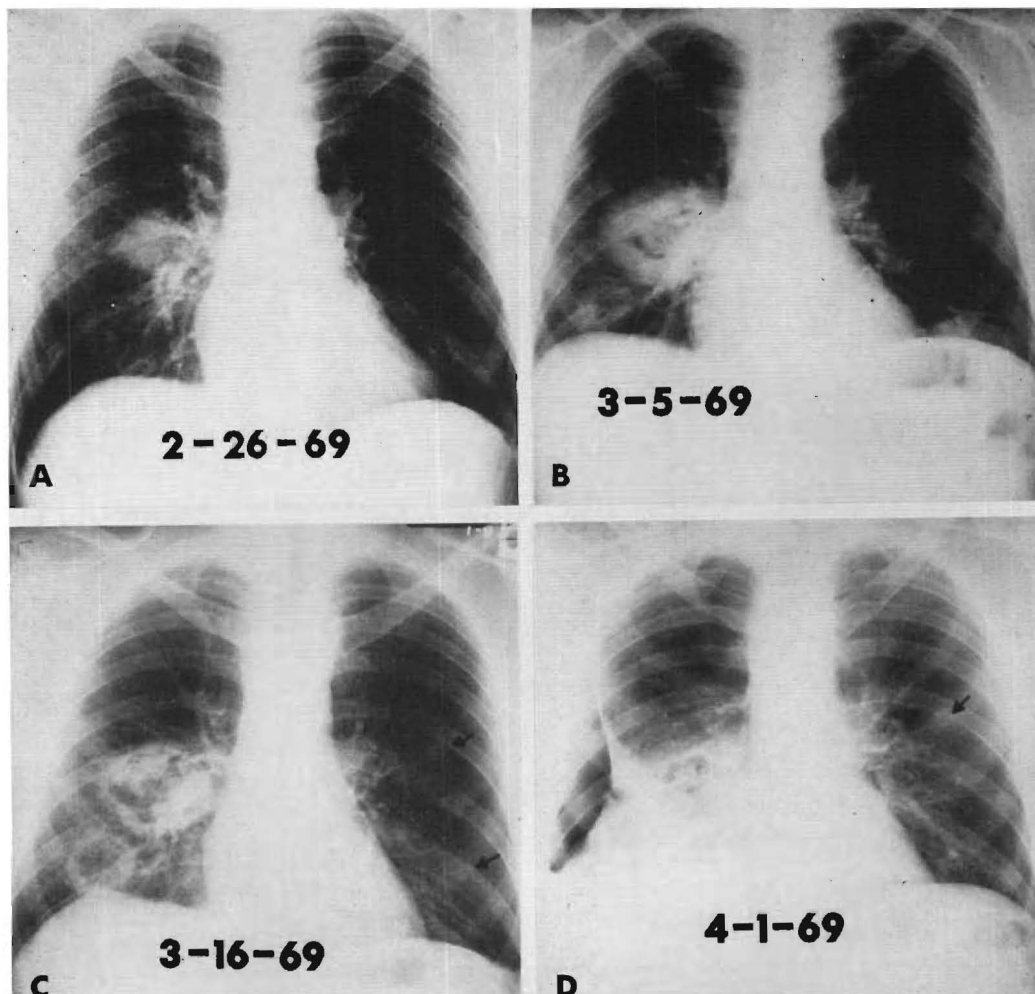


Fig. 2. Case 3. A, Chest x-ray film shows an infiltrate in the superior segment of the right lower lobe 5 months following renal homotransplantation. B, The lesion in the right lung has rapidly enlarged and cavitated. C, Chest film shows multiple cavities in the right lung in addition to lesions in the opposite lung (arrows). D, Abscess cavity (*Aspergillus fumigatus*) has ruptured 6½ months following transplantation. A lesion in the left lung is still present (arrow).

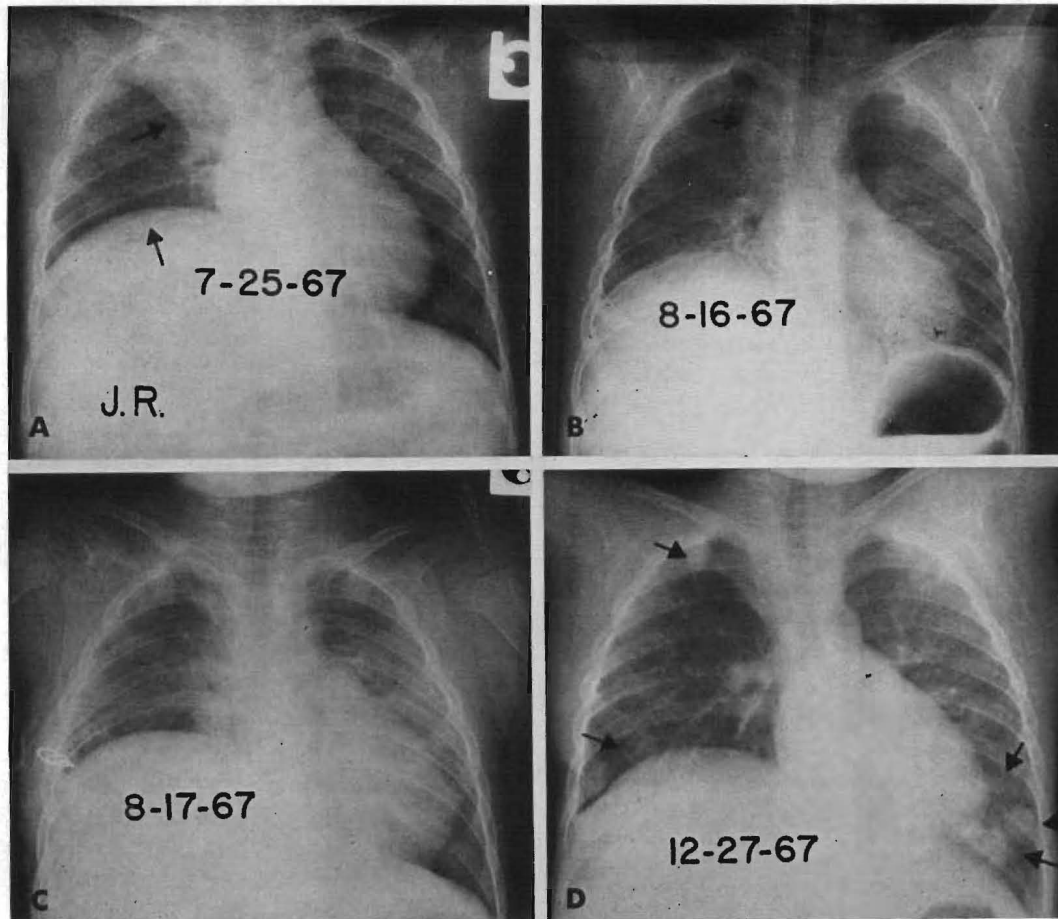
in size and eventually cavitated (Fig. 2, B) 9 days later at about the same time as other discrete lesions appeared in the contralateral lung (Fig. 2, C). Sputum cultures contained  $\beta$ -hemolytic streptococcus, *Gaffkya tetragena*, and a few colonies of *Aspergillus fumigatus*; blood cultures intermittently grew *G. tetragena*.

Right lower lobectomy was considered but decided against because of the infiltrates in the other lung. Six and one half months after transplantation, the abscess ruptured into the pleural space (Fig. 2, D) and was treated with closed thoracostomy drainage. *Aspergillus fumigatus* was cultured from the thick pus in the pleural space. Despite continued closed drainage and therapy

with amphotericin B, the patient died 21 days later. The bronchopleural fistula never showed signs of diminishing. The patient terminally became profoundly leukopenic and developed *Pseudomonas* septicemia even though all immunosuppression except prednisone had been discontinued many days earlier.

At autopsy a 5 cm., ruptured, thin-walled, lung abscess was demonstrated in the lower lobe of the right lung. Solid granulomatous lesions were demonstrated in the left lower lobe. Microscopically, both lungs were involved with a severe necrotizing bronchopneumonia and multiple abscesses.

CASE 4. A 46-year-old man with glomeru-



**Fig. 3.** Case 5. A, Right upper lobe collapse secondary to temporary paralysis of the phrenic nerve created during orthotopic transplantation of the liver. B, Continued partial atelectasis of the right upper lobe in spite of efforts of re-expansion. C, Postoperative chest film following resection of the right upper lobe 25 days after liver transplantation. D, Bilateral pulmonary metastases (arrows) are seen 5 months after transplantation. The patient died of carcinomatosis 400 days following transplantation.

lonephritis received both kidneys from a baboon donor.<sup>2</sup> Concomitant bilateral nephrectomy and splenectomy were carried out. Immunosuppression was with azathioprine and prednisone. Initial heterograft function was adequate.

Ten days after transplantation, the patient developed an acute left pyopneumothorax. After a few hours of closed thoracostomy drainage, it was obvious that the air leak was very large and unremitting. Consequently, a left lower lobectomy and lingulectomy were performed. The air leak came from a necrotic area which had broken into the free pleural space and which contained *Escherichia coli*. In the remaining days of life, there was a small and slowly diminishing parenchymal air leak. After the thoracotomy, the kidney heterografts began to fail, and the patient died 35 days post-transplantation.

The resected specimen contained several septic infarcts. Many of the small pulmonary arteries were packed with emboli. At autopsy, more emboli were found bilaterally in the lungs.

CASE 5. A 19-month-old female received an orthotopic liver homograft for the treatment of a hepatoma. Temporary paralysis of the right diaphragm was apparently caused by the crushing of the right phrenic nerve during the operation. Subsequently, the right upper pulmonary lobe collapsed and could not be re-expanded (Fig. 3, A and B). Sputum cultures contained *E. coli*. Because she was being treated with the 3 immunosuppressive agents, azathioprine, prednisone and ALG, it was thought that the complication might cause lethal sepsis.

Right upper lobectomy was performed 25 days after the liver transplantation (Fig. 3, C). Convalescence from the procedure was without incident, although the child developed a number of other complications related to the transplanted liver. She lived for 400 days and finally died of carcinomatosis from the malignancy for which the transplantation was initially indicated (Fig. 3, D).

The resected lung specimen was atelectatic, edematous, and hemorrhagic. The paralyzed diaphragm, which was apparently responsible for the complication, resumed movement 10 weeks after the liver replacement and 7 weeks after the pulmonary resection.

CASE 6. An 11-year-old white boy with congenital sex-linked hypogammaglobulinemia was continuously hospitalized for 2 years because of bilateral lower lobe bronchiectasis. Pulmonary resection was not thought to be feasible because of the immunologic deficiency state. It was decided to perform transplantation of his mother's spleen in an effort to provide an endogenous source of gamma globulin and with the hope of later extirpating the bronchiectatic areas. Im-

munosuppressive therapy after the spleen transplantation was with azathioprine and prednisone. There was never any concrete evidence that the new organ elaborated gamma globulin,<sup>3</sup> and the immunosuppressive therapy was discontinued after 7 months.

Even though the immunologic conditions were in no way improved by the splenic transplantation, staged pulmonary resections were carried out 5 weeks apart. First, the lower lobe of the left lung was resected and then the lower and middle lobes of the right lung. Recovery was uncomplicated on both occasions. The child is still alive, with mild respiratory insufficiency, more than 5 years later. He has lived outside the hospital for almost the entire time.

Pathologically, the resected lung tissue contained widespread purulent cylindrical bronchiectasis.

## Discussion

Patients with a naturally occurring or iatrogenically produced loss of immunologic reactivity have an increased risk from any kind of surgery. In spite of this, it has become increasingly possible to carry out transplantation procedures with prompt wound healing and with long-term survival. Moreover, reoperation upon such recipients for a variety of surgically correctable complications has proved to be feasible.

Our own experience with intra-abdominal complications after renal homotransplantation was recently reported.<sup>4</sup> In that study, observations were made that are probably applicable to certain intrathoracic problems. The most important lesson was that emergencies were best treated by prompt and often radical intervention. If there was a delay, the consequence was usually death, particularly with perforation of a viscus or with an inflammatory process. A single intraperitoneal insult could be tolerated, but if this continued the result was overwhelming sepsis.

The same lethal chain of events was observed in patients in whom the pulmonary lesions perforated into the free pleural space. Consideration had been given in 3 of the 4 patients to the prophylactic resection of the expanding cavities which it was feared might rupture. A negative decision was made, and within a short time the dreaded

complication had occurred. In all 4 patients, the pleural space was severely contaminated before corrective action was taken. Ultimately, all of the 4 recipients developed overwhelming infection from which they died. It is probable that these results will not be improved unless even earlier thoracotomy is undertaken, preferably before the onset of a bronchopleural fistula.

Despite these discouraging results, it is clear that major pulmonary resection can be successfully performed in an immunosuppressed patient. In the 2 cases in which unperforated lobes were removed, the postoperative recovery was very prompt. The surgical specimens were infected, but the microorganisms had not been spread through a bronchopleural fistula. Under these circumstances, and even in the patients with lung perforations, there was healing of the bronchial stumps.

The etiologic factors leading to a surgical intrathoracic emergency are undoubtedly highly variable. In our own experience, a particularly troublesome syndrome has apparently had its genesis in multiple pulmonary embolization with secondary infection of the resulting small infarcts. There were three examples in the 6 cases of the present series in which the resulting necrotic lung perforated. There was virtually no inflammatory walling-off of the process detectable at the time of operation. Under these circumstances, it is doubtful that healing could be expected except by excision of the dead tissue, immediate control of the bronchopleural fistula, and obliteration of the pleural space.

### Summary

Six immunosuppressed patients were subjected to thoracic surgical procedures for the treatment of pulmonary complications; 5 were receiving drugs to prevent homograft rejection, and the sixth had congenital sex-linked hypogammaglobulinemia. The indications for intervention were lung perforation (4 examples), bronchiectasis (1 example), and unyielding atelectasis (1 example). Pulmonary resection was carried out in 5 instances and closed chest thoracotomy drainage in the sixth. Two of the patients made a complete recovery. The other 4, including all those who had lung perforation and a bronchopleural fistula, died of overwhelming infections. It has been suggested that earlier operation for an expanding cavitary lesion may be one way of improving the results if it is anticipated that rupture is likely.

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