hemithorax. It is important that the patient has unequivocal preoperative evidence of compression of relatively normal lung parenchyma. In patients with underlying emphysema in the remaining lung tissue, bullectomy may not be helpful in relieving dyspnea and other pulmonary symptoms and thus, some authors believe that it is not indicated. It has also been stated that severe respiratory failure is a contraindication to bullectomy surgery due to poor outcome. Other authors believe that patients are at greater risk of a poor outcome if their FEV₁ is not greater than 40% of the predicted value.

The current case involves a young man with severe bullous emphysema. Initially, surgical resection of the bullae was not considered due to the underlying emphysematous changes in his compressed lung, an FEV₁ of only 14% of predicted, and respiratory failure. However, as his hypoxemia worsened, surgical intervention was believed to be the only viable option. This appears to be the first case of successful surgical resection of giant bullous lesions in a patient with severe respiratory failure receiving mechanical ventilatory assistance. This case demonstrates that bullectomy can be a lifesaving operation in carefully selected patients. The goal of bullectomy—resection of nonfunctional space-occupying bullous lesions to allow reexpansion of compressed, but presumable functional lung tissue—was clearly achieved in this patient. Successful surgery allowed him to resume an active life.

REFERENCES


Influenza A Pneumonitis Following Treatment of Acute Cardiac Allograft Rejection with Murine Monoclonal Anti-CD3 Antibody (OKT3)*

Richard P. Embrey, MD; and Lois J. Geist, MD

A 51-year-old man developed fever, cough, and dyspnea 5 days after completing murine monoclonal anti-CD3 antibody (OKT3) treatment for acute cardiac allograft rejection. Samples of BAL fluid grew influenza A virus. Progressive pulmonary infiltrates, respiratory compromise, and hypoxia developed, and the patient ultimately required 5 days of mechanical ventilation. Treatment with amantadine hydrochloride and ribavirin was prescribed, and the patient was discharged after 19 days. Influenza A virus has not been an important pathogen in cardiac transplant recipients. However, this is the first reported case of influenza A pneumonitis complicating anti-T lymphocyte therapy for cardiac allograft rejection. In comparison with our patient, two previously reported cases of influenza A infection in cardiac transplant patients have been less severe. The virulence of our patient’s, life-threatening infection appears to be secondary to impairment of T lymphocyte-mediated immunity by OKT3. The role of therapeutic and even prophylactic amantadine therapy in this clinical setting has yet to be determined.

(CHEST 1995; 108:1456-59)

Key words: cardiac transplantation; influenza A; immunosuppression; OKT3

Influenza A is a common viral pathogen that typically causes a low-grade febrile illness and mild respiratory symptoms. This rather innocuous pathogen may be life-threatening in elderly, debilitated or immunocompromised patients, however. Solid-organ transplant recipients are particularly susceptible to viral infections, and this risk is increased by anti-T lymphocyte therapy for graft rejection. This report documents a case of severe influenza A pneumonitis, which occurred in a heart transplant patient following treatment.

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with murine monoclonal anti-CD3 antibody (OKT3) (Ortho Pharmaceutical; Baritan, NJ).

CASE REPORT

In December 1992, a 51-year-old man underwent orthotopic heart transplantation for ischemic cardiomyopathy. Both donor and recipient were cytomegalovirus antigen-positive, and a standard triple-drug immunosuppression protocol was employed. The immediate postoperative course was uneventful until grade II rejection was discovered on the 5th weekly posttransplant biopsy. Treatment was begun with intravenously administered methylprednisolone, 500 mg once daily for 3 days. Maintenance therapy consisted of 20 mg of prednisone and 150 mg azathioprine per day as well as cyclosporin 275 mg given twice daily with levels of 217 to 321 ng/mL (liquid chromatographic method on whole blood). Subsequent endomyocardial biopsies in the 7th and 9th postoperative weeks were interpreted as grade I b rejection.

A routine surveillance catheterization in the 12th postoperative week found normal hemodynamics in the right side of the heart, but biopsy showed grade II-IIa rejection. The patient was hospitalized and received a 10-day course of OKT3, 5 mg/day. Five days after completing treatment, the patient was readmitted to the hospital. He had a fever (temperature of 38.3°C, oral), a cough, mild dyspnea, nasal congestion, and myalgia. Physical examination disclosed aphthous ulcers on the soft palate and lower lip, clear eye grounds, and fine crackles on auscultation of the lung bases. The WBC count was 28,600/mm^3 (institutional normal values, 3,700 to 10,400) with an increased neutrophil count (26,312/mm^3; normal, 1,750 to 6,359/mm^3) but no increase in immature forms; monocytosis (2,002/mm^3; normal, 0 to 709/mm^3), and relative lymphopenia (286/mm^3; normal, 590 to 3,199 mm^3). Lactate dehydrogenase was mildly elevated (360 IU/L; normal, 100 to 210 IU/L). Arterial blood gas levels with the patient breathing room air revealed a pH of 7.53 (normal, 7.35 to 7.45); Paco2 of 27 mm Hg (normal, 35 to 45 mm Hg); and a Paco2 of 57 mm Hg (normal, 80 to 90 mm Hg). A radiograph of the chest (Fig 1) showed no changes when compared with one taken postoperatively, showing left lower lobe atelectasis secondary to an elevated left hemidiaphragm. No infiltrates were noted.

Empirically, treatment with ganciclovir and high-dose trimethoprim-sulfamethoxazole was begun. Bronchoscopy with BAL was performed; however, stains were negative for Pneumocystis carinii and cytomegalovirus inclusions. Over the next several days, the patient became progressively more dyspneic, requiring increasing amounts of supplemental oxygen. On the 2nd hospital day, rapid screening techniques of the cultures obtained at BAL confirmed the presence of influenza A virus, and therapy with amantadine hydrochloride (100 mg twice daily, orally) was initiated. By the 4th hospital day, the radiograph of the chest began to show bilateral patchy infiltrates (Fig 2). The patient’s respiratory status continued to deteriorate despite this therapy, and on the 7th hospital day he required intubation. Bronchoscopy done a second time showed no abnormalities, and BAL fluid samples from this examination subsequently had no viral growth.

At this point, treatment with aerosolized ribavirin was started (6 g/d for a period of 18 h) and was continued for 6 days. The patient slowly improved with decreasing hypoxemia, and mechanical ventilation was discontinued on the 13th hospital day, 5 days after intubation. During his hospital course, the patient underwent three endomyocardial biopsies which were all negative for rejection. The patient was discharged on the 19th hospital day and was alive and well 24 months later. Pulmonary function, arterial blood gas values, and clinical course are summarized in Table 1.

DISCUSSION

Infectious complications continue to be the leading cause of death following cardiac transplantation, and pneumonia occurs in up to 24% of all patients within the first 18 months after transplantation.1 Typical pathogens are cytomegalovirus, P carinii and Gram-negative bacteria, with mixed infections being commonplace. Influenza A pneumonia has not been problematic in this patient population. However, two cases have been reported previously; one case was documented retrospectively by serum antibody titers, and the second infection was diagnosed concurrently by viral cultures obtained from BAL fluid specimens.2,3 All three patients presented with fever and with varying degrees of pulmonary distress, ranging from cough and chest discomfort to dyspnea and hypoxemia. One patient had a very limited febrile illness requiring 4 days of hospitalization, and only the patient described in this report required mechanical ventilator support and specific antiviral therapy. No episodes of graft rejection occurred in association with the in-

FIGURE 1. Chest radiograph taken at time of admission. The elevated left hemidiaphragm and left lower lobe atelectasis are chronic changes present since transplantation.

FIGURE 2. Chest radiograph taken on 7th hospital day showing bilateral pulmonary infiltrates.
Table 1—Arterial Blood Gas Levels, Oxygen Requirements, Temperature, WBC Count, and Therapeutic Interventions in a Heart Transplant Recipient With Influenza A Pneumonitis

<table>
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<td>101</td>
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<td>64</td>
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<td>1 L</td>
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<td>0.96</td>
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<td>38.2</td>
<td>36.8</td>
<td>37.2</td>
<td>36</td>
<td>36.3</td>
<td>37</td>
</tr>
<tr>
<td>WBC count, 1,000 cells/mm³</td>
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<td>8.2</td>
<td>10.9</td>
<td>12.4</td>
<td>8.0</td>
<td>5.7</td>
<td>6.6</td>
<td>8.9</td>
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Mechanical ventilation

Therapy

- Trimethoprim-sulfamethoxazole
- Ganciclovir
- Amantadine
- Ribavirin

Influenza A infections, and no patient died of the illness. Frequently used to treat severe lower respiratory tract infections due to respiratory syncytial virus in hospitalized children, aerosolized ribavirin has activity against a wide variety of viruses, including influenza A and B. In randomized trials, both oral and aerosolized ribavirin significantly improved signs and symptoms of influenza A infection in healthy patients vs controls; however, duration of viral shedding was not different between treated and nontreated groups. Ribavirin also has been used to treat immunocompromised patients, including bone marrow transplant recipients with respiratory syncytial virus and solid-organ transplant recipients with influenza B infections.

Unlike the previous cases of post-cardiac transplant influenza A infection, only the current patient’s illness followed treatment of acute allograft rejection with anti-T lymphocyte antibody. Similarly, this patient’s clinical course was notably severe in contrast to the upper respiratory tract illnesses of the other patients. Cell-mediated immunity plays a key role in limiting acute influenza A infections and in clearing the virus from the lungs. Thus, the impairment in cell-mediated immunity which results from administration of anti-T lymphocyte antibodies such as OKT3 or antithymocyte globulin is responsible for the virulent pneumonia which characterized this patient’s influenza A infection, a phenomenon which has been well described with other more common pathogens, such as cytomegalovirus.

Although influenza A vaccines are widely available, their efficacy in ameliorating infection in a transplant population is questionable. In renal transplant patients, Stiver et al found a fourfold antibody titer rise in only 31% of patients who received influenza A vaccination. The response to influenza vaccination in renal transplant patients receiving cyclosporin and prednisone is less than that of those patients on a regimen of azathioprine and prednisone. Furthermore, a two-dose vaccination regimen only marginally improved antibody levels in bone marrow transplant recipients. Nonetheless, because other studies have shown equivalent antibody increases in both transplant patients and controls subjects, and because vaccination has not been shown to cause graft rejection or dysfunction, yearly influenza vaccination of transplant patients is undertaken as a matter of policy in many transplant programs. Other institutions forego such routine immunizations because the safety of vaccinations has not been firmly established in this population.

Because vaccination may not be effective and influenza A pneumonitis is potentially life-threatening in cardiac transplant patients receiving antibody therapy for acute rejection, amantadine may be particularly useful in this setting. Amantadine is up to 90% effective in the prophylaxis of influenza A in a normal (ie, nonimmunosuppressed) population. Furthermore, the drug may reduce the duration and severity of symptoms if administered early during the course of influenza A illness. The side effects of amantadine are mild, and no adverse interaction with cyclosporin or azathioprine has been described in patients with normal renal function.
Although the usefulness of amantadine in the treatment of transplant patients with established influenza A infections is clear, the prophylactic use of amantadine in high-risk transplant patients has not been evaluated, despite being theoretically appealing. In cardiac transplant patients who require OKT3 or anti-thymocyte globulin for treatment of rejection during influenza A epidemics, and in patients who are not vaccinated or do not exhibit adequate antibody titers following vaccination, the prophylactic administration of amantadine may reduce the incidence and severity of influenza A infections. A regimen of amantadine, 100 mg orally twice daily, during antilymphocyte therapy and for two weeks thereafter until the patient's T lymphocyte function recovers, would seem logical. Such prophylactic treatment cannot be firmly endorsed, however, until an appropriate randomized, prospective study has been completed.

References

Myocardial Stunning Following Respiratory Arrest

Riyaz Bashir, MD, Farooq A. Padder, MD; and Farooque A. Khan, MBBS, FCCP

Myocardial stunning is defined as a prolonged myocardial dysfunction with gradual return of contractile activity after a brief episode of severe ischemia. Usually it is seen in patients with myocardial infarction following treatment with thrombolytic agents, in patients with angina, and in patients recovering from cardiopulmonary bypass surgery. We report an interesting case of myocardial stunning following respiratory arrest.

(CHEST 1995; 108:1459-60)

Key words: myocardium; respiratory arrest; resuscitation; stunning

Herein is the report of a case of myocardial stunning after respiratory arrest.

Case Report

Sudden respiratory arrest following intravenous injection of di-azepam and methohexital developed in a 24-year-old previously healthy white woman during a dental procedure. She became cyanotic and was successfully intubated within 3 to 4 min. The cardiac monitoring at that time revealed a normal sinus rhythm, and she was transferred to Nassau County Medical Center. At the time of arrival in the emergency department, findings of the physical examination were as follows: pulse, 90 beats per minute; BP, 80/50 mm Hg; temperature, 35.5°C; and spontaneous respiratory rate, 20 breaths per minute. The remainder of the physical examination disclosed no abnormalities. At the time of admission, laboratory values, including complete and differential WBC counts and renal and hepatic profiles, were normal. The arterial blood gas level with an FiO2 of 1.0 revealed a pH value of 7.52, a PaO2 value of 554 mm Hg, and a PCO2 level of 32 mm Hg. A 12-lead ECG was normal except for sinus tachycardia. For hypotension, she required temporary inotropic support. She was extubated 4 h after admission to the hospital, and the postextubation arterial blood gas values were normal.

Ten hours later, she developed precordial chest pain and shortness of breath. The pain was localized and reproducible in nature. Results of physical examination disclosed a pulse of 110 beats per minute, BP of 100/70 mm Hg, and a respiratory rate of 30 breaths per minute. She had bibasilar crackles and an S3 gallop. An ECG revealed T-wave inversions in leads 1, aVL, V3, and V6. A transthoracic two-dimensional echocardiogram revealed diffuse hypokinesia of the left ventricle with an approximate ejection fraction of 25%. Left ventricular size was normal, and there was no evidence of pericardial effusion. A chest roentgenogram showed pulmonary edema. Serial tests for creatine kinase-MB isoenzyme were negative.

The patient was treated with bed rest, analgesic agents, and diuretics, and her symptoms improved. Subsequent ECGs showed diffuse and deep T-wave inversions and QT interval prolongation. These changes were most pronounced on day 3 of hospitalization, after which they started receding gradually (Fig 1). A repeat

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