Opportunistic Lung Infections in Renal Transplanted Patients

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Summary

Opportunistic lung infection occurs soon after rejection episodes in immunosuppressed renal transplant patients. Rapid identification of the causal organism is essential if acute respiratory failure is to be avoided and open lung biopsy may be necessary at an early stage.

Introduction

The renal transplant patient who is receiving immunosuppressive drugs is particularly vulnerable to invasion of the respiratory system by organisms which take advantage of the weakened defence mechanisms. Viruses, fungi, yeasts, protozoa as well as bacterial invaders lay siege to the unfortunate recipient of a transplant organ. The survival of the subject is made hazardous by two factors:

1. difficulty in identifying the causal organism(s) and hence administration of specific treatment
2. the rapidity with which the lungs fail in conditions where excess fluid gathers in the lungs (Crosbie et al, 1972).

This paper describes some of the factors present in eleven renal transplant subjects who developed serious chest infections in which ‘opportunistic’ organisms played a major role.
FINDINGS

The eleven patients included seven males and four females aged between 23 and 54 years (mean 39). They were all in chronic renal failure and had been treated by haemodialysis for a mean of 1.9 years (range 0 to 5 years). Eight had received cadaveric grafts, and three had grafts from living related donors.

Three points emerge from this investigation.

(a) eight of the patients had developed significant rejection episodes within one week of transplantation. All the subjects were receiving prednisone and azathioprine at the time, but additional treatment in the form of intravenous boli of methyl prednisolone or deep x-ray therapy to the transplanted organ was necessary. In three subjects the rejection episode occurred later, but still within 12 weeks of transplantation (Figure 1).

- C - CMV, M - MONILIA, T - TOXOPLASMOSIS, TB - TUBERCULOSIS,
- PC - PNEUMOCYSTIS CARINII, S - STRONGYLOIDES.

Figure 1. Time scale of rejection (●) and respiratory infection (○) in 11 renal transplant subjects.
(b) All of our patients developed significant antibody titres to the cytomegalic virus following their transplant rejection (Figure 2). Some had detectable titres beforehand, but these had increased in the post operative stage.

![Graph showing antibody titres](image)

Figure 2. Cytomegalic virus titres in 11 renal transplant patients.

(c) The resultant respiratory illness was a serious condition characterised by breathlessness, with a normal chest x-ray and absence of abnormal physical signs in the chest in the early stages. Later the chest x-ray showed an alveolar infiltrate pattern but this was complicated by renal and cardiac secondary effects. Identification of the major causal organism could be difficult and open lung biopsy was necessary on three occasions. The causal organism was cytomegalic virus in five, pneumocystis carinii in two and one case each of pneumonia due to monilia, tuberculosis, toxoplasmosis and strongyloides. There was a high mortality (six of eleven died) because of respiratory failure despite intensive therapy.

**DISCUSSION**

Infection is the main cause of death following renal transplantation (Gurland et al, 1973) and pulmonary infections form a significant proportion of the total. The lungs appear to be particularly vulnerable to unusual or opportunist organisms which produce a serious complication in debilitated subjects. The analysis of our 11 subjects confirms that this type of infection commonly follows an acute rejection episode usually within one to two weeks. All had received additional immunosuppressive measures before they developed respiratory symptoms. The combination of reduced lung defences, a general anaesthetic during their transplant operation and a hospital environment leads to invasion of the lungs by these organisms.
We also confirmed that cytomegalovirus infection is common in the post transplant phase. This could be a first infection or a reactivation of a latent state produced by suppression of the immunological mechanism. This has been reported before (Rifkind et al, 1966; Anderson & Spencer, 1969), but the significance may not have been recognised. Five of our subjects seem to have limited their lung infection to this organism, but in the other six there was a dual invasion with other organisms. The respiratory illness produced by these infections poses a serious threat to the survival of the renal transplanted patient. Often the individual is already in poor physical condition after years of haemodialysis and has little cardio-pulmonary reserve to meet the demands of respiratory failure. Time can be short in which to make a diagnosis and institute specific treatment. Identification of the causal organism can be difficult since examination of the sputum, serological tests and bronchoscopy are diagnostically unhelpful. Open lung biopsy was necessary in three of our subjects to obtain the organism. Blind antibiotic cover is fraught with danger since the possible spectrum of infection can cover all known pathogenic invaders. In addition, some drugs which could be used may cause deterioration in kidney or liver function. Six of our subjects died of respiratory infection. The causal organism had been identified before death in all the subjects, but specific treatment had only been started a few days before their death and several weeks after they developed respiratory symptoms.

References

Rifkind, D, Goodman, M, and Hill, R B Jr. (1966) Annals of Internal Medicine, 66, 1116

Open Discussion

CANTALUPI (Milan) What is your anti-rejection scheme? We have observed a higher incidence of lung infections after four or more pulses of methyl prednisolone compared to that observed after three pulses or less.

CROSBBIE It varied over the group of 11 so I cannot say there was one common policy, but the major line of treatment would be bolus of high dosage of steroids for one or possibly two days. In four of the patients, I think I mentioned already, we applied deep X-ray therapy to the transplanted organ.

BRUNNER (Basle) Many transplanted patients develop cytomegalovirus infection as far as rising antibody titres would indicate, or exhibit CMV excretion in the urine. This does not mean that CMV infection causes disease. How did you
diagnose that it was this virus that was causing the lung disease?

CROSBBIE The five patients I designated as suffering from a CMV pneumonia all developed X-ray changes that were consistent with established thought in this field. They were all breathless, they all developed a serious respiratory condition associated with the development of high titres of CMV.

CHANTLER (London) What percentage of all your patients develop a rise in CMV titres?

CROSBBIE That is something we are trying to find out, but it is very hard.

VERBECKMOES (Louvain) We have seen at least four or five times, acute respiratory distress occurring during or after a rejection episode. This distress was resistant to all therapy except that it responded dramatically to transplantectomy within a couple of hours, so my question is whether indeed, in some of your cases it was what has been called a transplant lung with a totally non-specific infection; viral infection occurring at the same moment?

CROSBBIE I think you are saying that there is a combination of rejection effects on the lungs, with an infection, and it is difficult to sort out how much of each is responsible.

VERBECKMOES The combination between rejection and cytomegalovirus has been repeatedly found but nothing is certain about which is the cause of the other.

CROSBBIE The patients who died had, at autopsy of their lungs, the characteristics of an infection. That was the dominant finding in the histology of the lungs at autopsy.

WATT (Preston) This is a question asked out of pure ignorance. If we believe that effective immunosuppression is a major component of the opportunistic infection, why do we get such very striking elevations in antibody titres to both CMV and toxoplasma in these conditions?

CROSBBIE I think this is a relative state in that we would be worse off if we did not have these titres.