Teaching Point
(Section Editor: A. Meyrier)

Acute respiratory infection in a renal transplant recipient

Anna Richards1, Jenny Ng Kam Chuen1, Clive Taylor2, Ralph Jackson1, Geoffrey Toms3 and David Kavanagh1

1The Freeman Hospital, Newcastle upon Tyne, NE7 7DN, 2Health Protection Agency, North East Laboratory, Newcastle upon Tyne, NE4 6BE, and 3The School of Clinical Medical Sciences, University of Newcastle, Newcastle upon Tyne, NE2 4HH, UK

Keywords: bronchoalveolar lavage; human metapneumovirus; immunocompromised; opportunistic infection; renal transplant; respiratory tract infection

Introduction

We report the case of a 43-year-old renal transplant recipient who required ventilatory support for acute respiratory tract infection. The differential diagnosis in immunocompromised individuals is extensive and requires prompt investigation.

Case report

A 43-year-old male non-smoker with end stage kidney failure due to medullary cystic kidney disease received a 1:1:1 cadaveric renal allograft in 2001. The transplant initially functioned well, but 1 month after transplantation, his renal function worsened and a renal transplant biopsy showed mild cellular rejection. He was treated with methylprednisolone (500 mg/day for 3 days) and his renal function improved to a baseline creatinine of 160 μmol/l. He subsequently had a cytomegalovirus (CMV) seroconversion illness with diarrhoea and deterioration in renal function. This was successfully treated with ganciclovir.

For the next 3 years he experienced no medical problems and his renal function remained stable on a standard immunosuppression regime of cyclosporin (125 mg twice daily), azathioprine (75 mg daily) and prednisolone (10 mg daily). He then presented acutely with fever, dyspnoea, non-productive cough and flu-like symptoms. On examination, he had a temperature of 38°C and a respiratory rate of 20/min. Auscultation revealed a right-sided pleural rub and crepitations at the right base. Investigations revealed an elevated CRP (53 mg/l; normal < 5 mg/l), lymphopenia (0.35 × 10^9/l; normal range 1.5–4 × 10^9/l) but a normal neutrophil count (4.59 × 10^9/l; normal range 2–7 × 10^9/l). Arterial blood gases on room air on admission showed a pO2 of 9 kPa (67.5 mmHg) and saturation of 91%. A chest X-ray at this time showed right lower zone consolidation. He was initially treated with amoxycillin (500 mg three times/day) and clarithromycin (500 mg twice daily) on microbiological advice. Over the course of the next 24 h his respiratory function deteriorated. His arterial blood gases on FiO2 40% showed a pO2 of 6 kPa (45 mmHg) and pCO2 of 3.3 kPa (24.7 mmHg) and his chest radiograph had progressed to bilateral consolidation (Figure 1). He was transferred to a critical care unit and was ventilated. Oral prednisolone was converted to intravenous hydrocortisone (100 mg four times/day) and azathioprine was stopped in view of his lymphopenia. His antibiotics were changed to ciprofloxacin (400 mg twice daily). He underwent bronchoalveolar lavage on the second day of admission. Bronchial washings were mucoid and blood stained. Bacterial cultures, including *Mycobacterium tuberculosis*, were negative. Bronchial washings were screened by direct immunofluorescence with fluorescein-conjugated monoclonal antibodies (Light Diagnostics, Chemicon Ltd, Hampshire, UK) to respiratory syncytial virus (RSV), influenza virus A & B, parainfluenzavirus (PIV) types 1, 2, 3 and 4, measles and adenovirus, and by indirect immunofluorescence with polyclonal antibodies to human metapneumovirus (hMPV) (a kind gift from Dr Geoffrey Toms). Immunofluorescence on bronchoalveolar lavage and nasopharyngeal secretions was strongly positive for hMPV (Figure 2) and negative for the other viruses.

When hMPV infection was proven, antibiotics were stopped and the patient received only...
supportive treatment. His renal function deteriorated during this episode of infection, necessitating continuous haemofiltration. After 5 days of ventilation, his respiratory function had sufficiently recovered to stop ventilation and his renal function had recovered to baseline. Within a further 8 days he had recovered completely and was discharged from hospital.

**Discussion**

Infection accounts for 15–20% of deaths following renal transplantation. Infections of organ transplant recipients by community respiratory viruses can result in significant morbidity and mortality. These viruses include RSV, PIV, influenza virus and adenovirus. As in normal hosts, infection of organ transplant recipients by these viruses can result in limited upper respiratory tract symptoms, such as rhinorrhea, cough and fever. Immunocompromised patients can also have lower respiratory tract infection, resulting in bronchiolitis, pneumonitis, respiratory failure and death.

hMPV is a novel RNA virus that has recently been discovered in the Netherlands [1]. It is a member of the paramyxoviridae, a family that contains RSV and PIV. Screening in the Netherlands has revealed that the majority of hMPV positive specimens were identified from November to May [2]. Consistent with this, our patient presented in February 2005.

hMPV infection is principally a disease of childhood with 100% seroprevalence by the age of 5 years [1]. The understanding of the illness in adults is incomplete, but surveillance in the general community found ~3% of samples from individuals attending physicians with respiratory tract infections tested positive for hMPV. Isolation of hMPV as a pathogen was historically difficult, as the virus grows poorly in cell culture.
cultures routinely used in viral diagnostic laboratories [1]. Identification of infection in the acute phase is by reverse transcriptase–polymerase chain reaction or, as employed here, indirect immunofluorescent antibody testing.

hMPV is associated with a wide spectrum of clinical symptoms [3] which are similar to those of RSV [1,4,5]. In general, community hMPV infected adults usually suffer relatively mild common cold-like respiratory symptoms such as cough, rhinorrhea, hoarseness, sore throat and sometimes fever [1,5]. Very young children, fragile elderly, people with underlying disease and the immunocompromised present with more severe disease. In a Canadian study, all of the hospitalized children under the age of five with hMPV had either pneumonia (67%) and/or bronchiolitis (58%) with 25% requiring intensive care [4]. A study among the elderly indicated that hMPV caused more severe disease in the frail elderly patients, such as nursing home residents, than in the elderly or younger adults who are fit [5].

Whilst the role of hMPV in the immunocompromised individual has yet to be fully elucidated, hMPV has been implicated as the sole pathogen in an immunocompromised child with acute lymphoblastic leukaemia (ALL) who suffered from respiratory tract infections and subsequently died [6]. There is also a report of an individual who received a haematopoietic stem cell transplant for ALL who became infected with hMPV and died from respiratory failure [7]. Data would currently suggest that mortality associated with hMPV infection is only found in individuals with co-existing medical problems. There are no previous case reports of hMPV infection in solid organ transplants. Retrospective analysis of respiratory tract samples from hospitalized patients, including renal transplant recipients, has identified hMPV but the clinical syndrome was not defined [8]. We describe, for the first time, the clinical course of a severe human metapneumovirus infection in a renal transplant recipient.

There are no agents currently licensed to prevent or treat infections caused by hMPV. Ribavirin, a compound with known broad-spectrum antiviral activity, has been shown to be effective in limiting disease and mortality in immunosuppressed individuals infected with the closely related RSV, if treatment is started early. It has also been suggested that ribavirin may be more effective in treating RSV in immunosuppressed individuals if used in combination with intravenous immunoglobulin (IVIG). Recent *in vitro* studies have suggested that ribavirin and intravenous immunoglobulin are active against hMPV [9]. This suggests that these agents, either alone or in combination, may be of some clinical benefit if treatment can be initiated early. In our case, treatment with ribavirin or IVIG was not initiated, as the hMPV was only detected once clinical recovery was underway.

This case shows the potential severity of hMPV infection in renal transplant recipients, the importance of screening for hMPV in appropriate clinical settings and highlights the need for further research into the diagnosis and treatment of hMPV, especially in immunocompromised individuals.

**Teaching points**

- Human metapneumovirus (hMPV) can be a significant pathogen in immunocompromised individuals.
- The prevalence of hMPV infection in renal transplant patients hospitalized with respiratory symptoms is unknown.
- Bronchoalveolar lavage is important in the investigation of respiratory infection in immunocompromised individuals.
- We would recommend screening for hMPV during respiratory illness in renal transplant recipients when the diagnosis is unclear.

**Acknowledgements.** We would like to thank Professor Kate Gould for helpful discussion of this case and Fiowa Ferwick for technical assistance with figure 2.

**Conflict of interest statement.** GT is a director for Viratom Ltd, who sponsored the production of the polyclonal antibody to human metapneumovirus.

**References**