CASE REPORT

Shortness of breath in a patient with inflammatory bowel disease

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SUMMARY

Cytomegalovirus (CMV) is an important cause of morbidity and mortality in immunocompromised patients. Although immunosuppressive therapy is the mainstay of medical treatment for patients with inflammatory bowel disease, the importance of CMV as a cause of pneumonia in this group is less well recognised. This case report presents a case of shortness of breath, dyspnoea and fever in a 51-year-old man with Crohn's disease on azathioprine and highlights the importance of considering CMV as a cause of pneumonia in this group.

BACKGROUND

Cytomegalovirus (CMV) is an important cause of morbidity and mortality in immunocompromised patients. Although immunosuppressive therapy is the mainstay of medical treatment for patients with inflammatory bowel disease (IBD), the importance of CMV as a cause of pneumonia in this group is less well recognised. This case report presents a case of shortness of breath, dyspnoea and fever in a 51-year-old man with Crohn's disease on azathioprine and highlights the importance of considering CMV as a cause of pneumonia in this group.

CASE PRESENTATION

The patient was admitted under the medical team following general practitioner referral with a 1-week history of temperatures over 38°C, dry cough, dyspnoea and general malaise. Ten days prior to the onset of symptoms he had been on a cruise to Israel and Turkey. His medical history included Crohn's disease, diagnosed 8 years previously. He had been on azathioprine for more than 5 years and in clinical remission for the past 3 years. He also had mild pancreatic insufficiency and bile salt malabsorption.

On examination, he was feverish with a temperature of 40°C, tachycardic at 116 bpm, normotensive and had saturations of 90% on room air. Respiratory examination was recorded as significant for bibasal crepitations. Other systems were normal.

INVESTIGATIONS

Blood investigations showed a white cell count of 3.59×10^9 , hyponatraemia (124 mmol/L), raised inflammatory markers (ferritin 8157 µg/L, C reactive protein 241 mg/L) and slightly abnormal liver function tests (aminotransferase 54 U/L, alkaline phosphatase 251 U/L, bilirubin 0.9 mg/dL). Urea was 10.7 mmol/L and creatinine was 99 µmol/L. A chest radiograph at this stage revealed clear lung fields (figure 1). An abdominal ultrasound was

Figure 1 A chest radiograph showing clear lung fields.

carried out and showed mild hepatomegaly, likely secondary to fatty change, as well as a single simple cyst in the right lobe of the liver and splenomegaly at 15.2 cm.

An initial diagnosis of lower respiratory tract infection was made and he was started on intravenous coamoxiclav and clarithromycin. Over the next 48 h he continued to have swinging fever and increasing oxygen requirements with respiratory distress and increasing wheeze. He was admitted to critical care for continuous positive airway pressure support via a hood device and haemodynamic support with vasopressors. Repeat bloods were significant for neutropenia (1.49×10^9 /L) and lymphopenia (0.35×10^9 /L), and a chest radiograph showed bilateral infiltrates in middle and lower zones. CT of the chest showed small bilateral pleural effusions and bilateral basal lung consolidation (figure 2). Owing to the clinical presentation and recent travel history, an atypical cause of pneumonia was suspected and the patient's treatment was switched to intravenous piperacillin with tazobactam (Tazocin). Clarithromycin was continued. Multiple blood cultures, urinary legionella antigen, respiratory cultures (including bacterial pathogens, respiratory syncytial virus, parainfluenza, adenovirus, rhinovirus, human metapneumovirus, CMV, influenza A, influenza B), hepatitis screen, brucella and HIV testing were all negative.

Further serology revealed CMV IgM and Epstein-Barr virus (EBV) IgG were positive, suggesting previous EBV infection and possible acute CMV infection. Viral PCR was requested and 5 days into critical care admission CMV viral titre was returned at 437, 122 copies/mL. CMV

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Figure 2 A CT thorax slice showing bilateral posterior basal lung consolidation.

viraemia was confirmed and at this point a diagnosis of CMV pneumonia was made. Repeat respiratory culture was also positive for CMV.

DIFFERENTIAL DIAGNOSIS

- ▶ Bacterial pneumonia, including atypical causes
- ▶ Viral pneumonia
- ▶ Fungal pneumonia
- ▶ Pulmonary embolus

TREATMENT

The patient was started on intravenous ganciclovir, following which his clinical course gradually improved and he was discharged from critical care.

OUTCOME AND FOLLOW-UP

The patient continued on ganciclovir before being switched to oral valganciclovir. Total treatment course was 2 weeks. He left hospital 24 days after initial admission with a CMV titre of <180 copies/mL.

DISCUSSION

CMV is a member of the human Herpes virus family. In the healthy person, infection generally goes unnoticed and antibodies are present in approximately 80% of the population over 65 years.¹ Infection can, however, be life-threatening in immunocompromised groups, notably single organ transplant patients and those with HIV.^{2,3}

CMV antibodies were found in 96.8% of HIV positive patients in one study.⁴ CMV disease is most commonly seen in patients with AIDS and a CD-4 cell count of <50/mm³. Observational studies prior to the advent of highly active antiretroviral therapy estimated CMV disease occurred in 20–40% of patients with AIDS.⁵ Retinitis remains the most common manifestation. CMV pneumonia is a rarer presentation and occurs less frequently than gastrointestinal and central nervous system manifestations.⁶

CMV is the most common virus pathogen seen in solid organ transplant patients and symptomatic disease is reported in 30–50% of patients.⁷ The burden of CMV pneumonia specifically is highest in lung, heart and haematopoietic stem-cell transplantation where it confers significant mortality risks.^{7–9} The incidence of CMV pneumonia postlung transplant has been reportedly as high as 50%.^{7,9}

Although patients with IBD have also long been reported as being at increased risk of CMV infection, the risk of extracolonic manifestations are thought to be under recognised^{10–13}

Unfortunately, we found that the literature on this topic is scarce and relies heavily on single case reports. One recent systematic review of 13 case reports found that 77% of cases of CMV pneumonia in patients with IBD occurred in Crohn's disease and 85% of patients were on thiopurines.¹⁰ It was also noted that 8 cases (61.5%) required Critical Care admission and 4 (30.7%) resulted in death.

In retrospect, clear risk factors were evident in this case. However, we believe that diagnosis and treatment of CMV pneumonia were delayed by a lack of suspicion for the diagnosis. Other clinical features that could have helped point towards CMV pneumonia include prominent fever, non-productive cough and worsening dyspnoea despite normal initial chest radiograph findings. Subsequent bilateral infiltrates on chest radiograph or CT are also common and there is an association with haemophagocytic lymphohistiocytosis (HLH).

HLH is a hyperinflammatory syndrome, often associated with autoimmune conditions, which can precipitate systemic inflammatory response syndrome, acute lung injury and adult respiratory distress syndrome.^{10,11} Features consistent with HLH in this case included a ferritin >500 µg/L, splenomegaly, fever and cytopenia affecting more than two cell lineages.

Unfortunately, it was not possible for us to extrapolate evidence for the best treatment of CMV pneumonia in patients with IBD specifically. An international consensus report on the treatment for CMV disease in organ patients with transplant, however, advocates that in adults, the bioavailability of a twice daily regimen of oral valganciclovir is sufficient and suggests intravenous ganciclovir should be reserved for severe life threatening cases.¹⁴ Treatment should be continued for at least 2 weeks and until viraemia is eradicated on serum assay.¹⁴

CMV pneumonia should be considered in the differential diagnoses of patients on immunosuppression with IBD who present with fever and dyspnoea. A high index of suspicion is vital in order to prevent significant risk of mortality in these patients.

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Competing interests None.

Patient consent Obtained.

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