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CASE REPORT

Pneumonia failing to respond to treatment☆

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Summary
Herpes simplex virus type 1 (HSV-1) is frequently isolated from the respiratory tract of critically ill patients. However, diagnosis of clinically significant HSV-1 pneumonia is difficult as the presentation is non-specific and there is no diagnostic reference standard to differentiate from non-infectious contamination.

We present a case of HSV-1 pneumonia in a young asthmatic patient who was potentially immunocompromised through long-term corticosteroid usage. The quantitative PCR titre from bronchoalveolar lavage fluid was high (9×10^3 copies/ml) and the patient made a dramatic clinical and radiographic recovery upon treatment with acyclovir. We suggest that similar PCR levels in the appropriate clinical setting should prompt consideration of anti-viral therapy.

Case report

A 39 year old female presented to the emergency department with a 3-week history of dyspnoea and cough productive of green sputum. She had a history of asthma since childhood, complicated by ongoing cigarette smoking, poor compliance with medication, obesity and recurrent lower respiratory tract infections. During the six months prior to her admission she had been treated with numerous courses of antibiotics and received oral corticosteroids on an almost continuous basis.

On physical examination she was cyanosed and tachypnoeic but afebrile and haemodynamically stable. Chest auscultation revealed bilateral inspiratory and expiratory wheeze with poor breath sounds. Blood tests showed a normal white cell count but slightly reduced lymphocyte count at 0.5×10^9/L. Arterial blood gas analysis demonstrated hypoxia. The C-reactive protein was elevated at 292 mg/L. Coagulation and biochemistry studies were otherwise normal. Subsequent sputum and blood cultures and atypical pneumonia screen were clear. Chest X-Ray demonstrated diffuse fine bilateral pulmonary infiltrates (Fig. 1). Computed tomography (CT) of thorax demonstrated bilateral diffuse ground glass infiltrates,

☆ This work was performed in St. James's Hospital, Dublin, Ireland.

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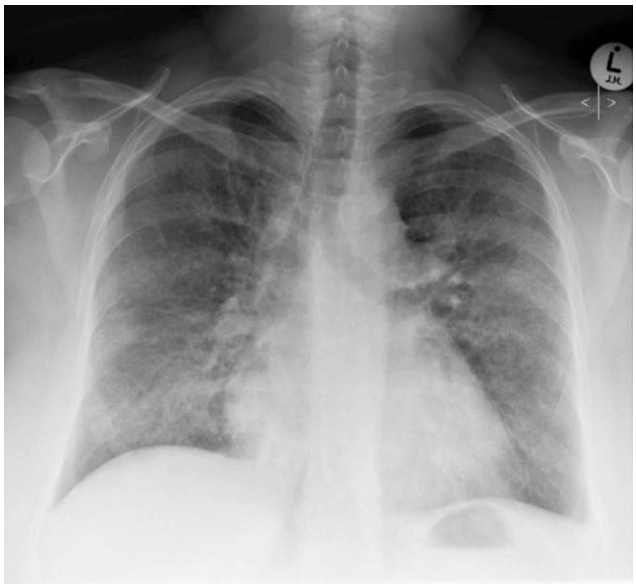

Figure 1 Chest X-Ray on initial presentation.

predominantly in the upper lobes without evidence of interstitial fibrosis (Fig. 2a and b).

She was admitted to the intensive therapy unit (ITU) and treated with broad spectrum antibiotics, antifungal therapy and corticosteroids. However, she continued to deteriorate and required intubation, ventilation and inotropic support. Bronchoscopy was normal and bronchoalveolar lavage (BAL) fluid was sent for viral, fungal and bacterial culture. In addition, a video-assisted thoracoscopic lung biopsy was performed, histological examination of which revealed non-specific diffuse alveolar damage only. However, quantitative PCR of BAL fluid revealed a HSV-1 PCR titre of 9×10^3 copies/ml. In addition, a serum sample collected at the same time was positive for HSV-1 by realtime PCR at 1×10^3 copies/ml. HSV-1 was isolated eventually from BAL. No other micro-organism was identified. A diagnosis of HSV-1 pneumonia was suspected and therapy was commenced with intravenous Acyclovir. Within 24 h there was a marked clinical improvement and several days later she was weaned from mechanical ventilation and discharged to the ward. A repeat CT scan prior to her discharge showed clearing of her bilateral infiltrates (Fig. 3).

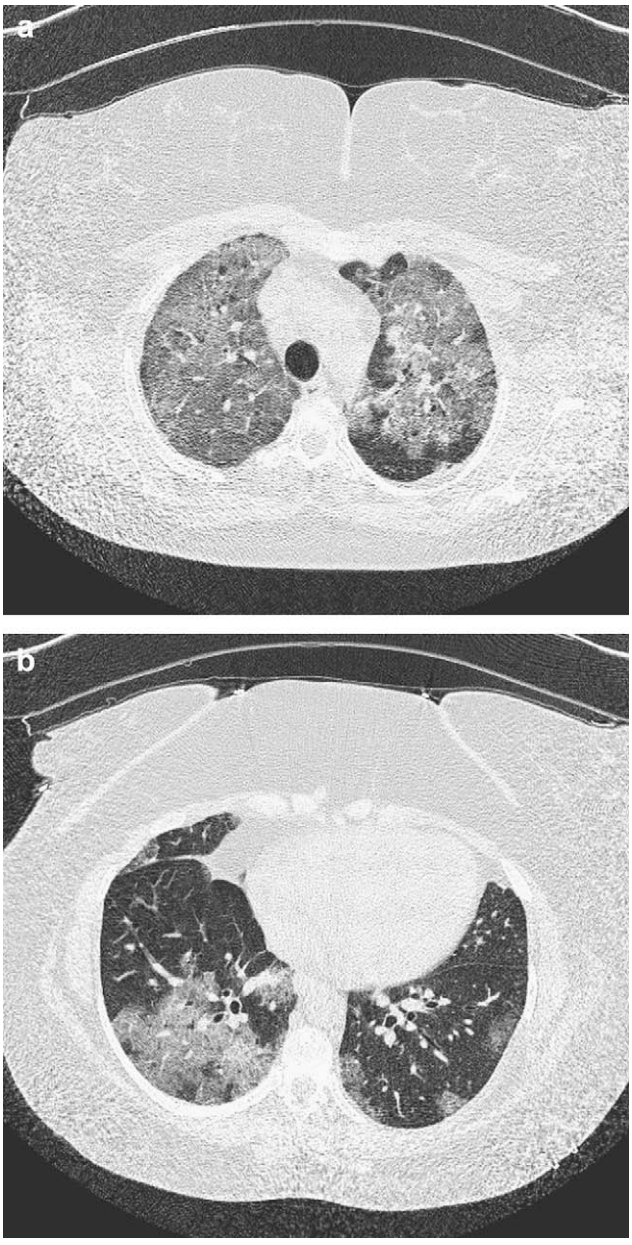

Figure 2 Computed tomography of thorax; sections from (a) upper and (b) lower lobes.

Discussion

HSV-1 pneumonia is well documented in immunocompromised patients. Burns, solid organ and haemopoietic stem cell transplant, malignancy, pregnancy, HIV infection, and immunosuppressive drug therapy have all been associated.[1–5] However, in the immunocompetent, confirmed pulmonary infection is rare[6] and the clinical relevance and pathogenicity of the virus, although frequently isolated from the lungs of critically ill ventilated patients,[7] is uncertain. HSV-1 contamination of the lower respiratory tract may occur by spread or aspiration from oropharyngeal lesions that may be facilitated by endotracheal intubation. It is often unclear, therefore, whether HSV-1 isolation represents infection or is merely a side manifestation of severe lung disease and/or immunocompromise with contamination by reactivated virus. Although some investigators have demonstrated that HSV-1 isolation from the lungs of such patients is associated with a poorer outcome and increased mortality,[8–10] others have not.[11]

Clinical differentiation between HSV-1 infection and other cause of pneumonia is unreliable; the symptoms are non-specific, as are the typical radiographic findings that include scattered multi-focal segmental and subsegmental ground glass opacities, focal areas of consolidation and pleural effusions.[12]

In the laboratory a diagnostic reference standard to differentiate clinically relevant HSV lung infection from non-infectious contamination is lacking.[6] Detection of HSV-1, in bronchial lavage or biopsy samples, may be achieved by viral culture, serology, PCR or demonstration of HSV-specific

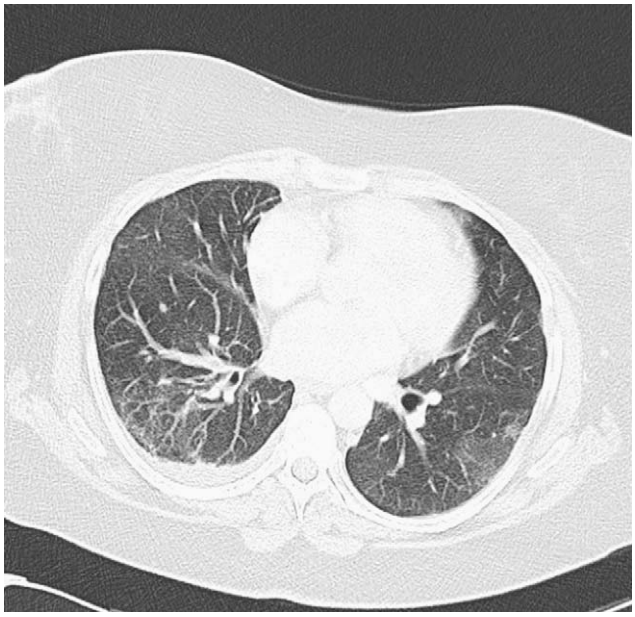

Figure 3 Computed tomography of thorax after treatment with acyclovir.

cellular nuclear inclusions. Lung biopsy has been shown to be unreliable and has failed to demonstrate evidence of viral infection despite isolation of the virus from lung tissue at autopsy.[13] More recently, quantitative PCR has shown promise by demonstrating an association between viral load and mortality that may guide treatment.[14]

In our patient a diagnosis of HSV-1 pneumonitis was made based on a quantitative BAL PCR finding of 9×10^3 copies/ml, with clinical and radiological evidence of pneumonia on a background of potential immunocompromise due to long-term steroid use. Treatment with intravenous acyclovir, when multiple other therapies had failed, was associated with a dramatic clinical and radiological improvement. We suggest that a similar HSV-1 PCR titre in the appropriate clinical setting should prompt consideration of anti-viral therapy at least until future studies better define a reference range.

Conflict of interest statement

None of the authors listed in this manuscript have any financial or other conflicts of interest to disclose.

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