Recurrent varicella pneumonia complicating an endogenous reactivation of chickenpox in an HIV-infected adult patient


ABSTRACT: We report the case of an adult patient with acquired immune deficiency syndrome (AIDS) presenting with acute dyspnoea and cutaneous disseminated lesions suggestive of an atypical varicella. The chest radiograph and the computed tomography (CT)-scan revealed a miliary pneumonia. On a previous serum sample varicella-zoster (VZV)-specific serum immunoglobulin (Ig)G titre was 1/200. A high dose acyclovir treatment was effective, but recurrences occurred twice when the treatment was discontinued. During the first recurrence the polymerase chain reaction (PCR) detected the presence of VZV in the bronchoalveolar lavage (BAL) sample. These findings confirmed the diagnosis of secondary varicella with pulmonary involvement.

Secondary varicella pneumonia has not been reported in a human immunodeficiency virus (HIV)-infected adult until now. The use of PCR on a BAL sample was very useful in this case because viral culture remained negative. Recurrences of the varicella pneumonia suggested that a maintenance treatment was required in this deeply immunocompromised patient.


Varicella pneumonia in human immunodeficiency virus (HIV)-infected individuals is uncommon [1, 2]. Most of the few reported cases involve HIV-infected children [3] or adults [2] with primary varicella. The diagnosis of varicella pneumonia is usually based on clinical and radiological features. However, the virological final diagnosis, potentially useful in immunocompromised patients, is quite difficult to confirm, because of the lack of sensitivity of the viral culture.

We report the first case, to our knowledge, of varicella pneumonia in an HIV-infected adult, due to an endogenous reactivation of chickenpox. The presence of the pulmonary infection was detected by the polymerase chain reaction (PCR) on a bronchoalveolar lavage (BAL) sample, while the viral culture remained negative.

Case report

A 31 yr old i.v. drug user was diagnosed HIV-positive in 1986. A disseminated tuberculosis occurred in 1993. Since January 1995 his CD4 lymphocyte count has been below 10 cells·mm⁻³. In 1996 he developed chronic oropharyngeal and recurrent oesophageal candidiasis. He was treated with zidovudine 500 mg·day⁻¹, lamivudine 300 mg·day⁻¹, fluconazole 200 mg·day⁻¹, and cotrimoxazole 1 strength tablet·day⁻¹. His family did not remember any varicella history in his childhood. He was in no contact with a child with varicella in the weeks prior to admission.

He was admitted to our hospital on March 24, 1996. He complained of acute dyspnoea, with a few days his-tory of fever. On admission, he was cachectic (48 kg, 185 cm); physical examination revealed a body temperature of 39°C, scarce cutaneous vesicular and necrotic lesions all over the body (scalp, face, trunk, arms, legs), and he suffered from painful ulcerative pharyngeal lesions in addition to his known oropharyngeal candidiasis. Each cutaneous lesion had a diameter of approximately 1 cm. Chest examination was unremarkable. The chest radiograph revealed a miliary pattern (fig. 1), which was also seen on a computed tomography (CT)-scan of the lungs (fig. 2). Arterial blood gas values were as follows: arterial oxygen tension (PₐO₂) 8.25 kPa (62 mmHg), arterial carbon dioxide tension (PₐCO₂) 3.99 kPa (30 mmHg), pH 7.35. He had no specific varicella-zoster virus (VZV) immunoglobulin (Ig)M antibody, and the serum titre of the VZV IgG antibody on admission was 200. We retrospectively performed a VZV serology on a frozen serum sample taken on August 11, 1995, which also revealed a 1/200 IgG titre. The CD4 lymphocyte count was 4 cells·mm⁻³. HIV viral load was 134,492 ribonucleic acid (RNA) copies·mL⁻¹ of plasma. Bronchoscopy revealed ulcerative and necrotic lesions scattered throughout the bronchi. The BAL did not detect any herpes virus in culture, and no other significant micro-organism was found. There were 400 red blood cells·mm⁻³ and 520 nucleated cells·mm⁻³ (macrophages 91.6%, lymphocytes 7.2%, polymorphonuclear cells 1.2%). No viral-like inclusion was seen. The patient was treated with high doses of i.v. acyclovir (500

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mg every 8 h) for 15 days, and subsequently with oral acyclovir (800 mg every 8 h) for 1 month. The cutaneous and mucous lesions progressively healed, leaving only scars. The chest radiograph as well as the arterial blood gas values were normal on May 10, 1996 and he was discharged from hospital. No maintenance treatment was prescribed.

The patient was again hospitalized on June 6, 1996 because of dyspnoea and oesophageal candidiasis. New painful vesicular and necrotic disseminated cutaneous lesions had developed. The chest radiograph again revealed an increase of the micronodular shadows, and a lobar pneumonia. Arterial blood gas measurements were: $P_{a,O_2} = 7.18$ kPa (54 mmHg), $P_{a,CO_2} = 5.72$ kPa (43 mmHg), pH 7.36. Blood cultures grew *Streptococcus pneumoniae*. Culture of a cutaneous lesion did not grow any herpes virus (PCR was not done). After 1 month of treatment with amoxicillin (6 g·day$^{-1}$) and i.v. acyclovir (400 mg every 8 h), the cutaneous lesions had crusted, and arterial blood gas measurements as well as the radiographic appearance markedly improved. A maintenance treatment with oral acyclovir was started. However, the clinical status of the patient gradually deteriorated, and he died of acquired immune deficiency syndrome (AIDS)-associated wasting syndrome on November 7, 1996.

**Discussion**

The findings in the present case confirmed the diagnosis of secondary and recurrent varicella, presenting with cutaneous and pulmonary involvement, in a patient with a deep immunosuppression due to HIV.

Primary VZV infection, or varicella, occurs almost exclusively during childhood [4], and is a self-limited, benign disease. In otherwise healthy children, pneumonia is an infrequent complication (7–16% of the varicella cases) [5], although in immunocompromised children it may increase to 40% [3]. Only 1–5% of all varicella reported cases occur in adults. In this setting, 5–50% of the varicella cases may complicate with pneumonia [6, 7]. Some immunosuppressive conditions including leukaemia, malignant lymphoma, corticosteroid therapy or pregnancy predispose to varicella pneumonia. However, perhaps due to the scarcity of varicella in HIV-infected adults, it is unclear whether the incidence of varicella pneumonia is increased in this condition. We found only nine cases of primary varicella pneumonia in HIV-infected adults in the literature [1, 2], and no case report of a pneumonia complicating an endogenous reactivation.

The diagnosis of varicella pneumonia is usually based on the association of typical cutaneous lesions of chickenpox with radiologically compatible pulmonary opacities. In an immunocompromised patient, such a presumptive diagnosis may not be sufficient. However, virological diagnosis is quite difficult to establish, because the viral culture of BAL specimens lacks sensitivity. Therefore, PCR is thought to be the best method, and is in fact, very
sensitive to finding the VZV [8] in some subsets of cells or biopsy specimens in immunocompromised patients [9, 10]. In this case of clinically suspected pulmonary involvement of varicella, PCR was the only diagnostic tool to confirm this assumption. However, due to contamination of the bronchoscope during procedure, it should be stressed that in patients with pharyngeal VZV-lesions, the result of VZV-PCR on the BAL could lack specificity, just reflecting the presence of VZV in the upper airways. We did not find any previous report of VZV detection by PCR in the BAL fluid in the literature.

Our patient had an endogenous reactivation of a previous clinically unrecognized varicella. In fact, his family was not able to remember any past episode of chickenpox. However, varicella may pass unnoticed: in two out of three cases of chickenpox reactivation in adults with AIDS, no previous history of varicella was found [1]. In another study, 89% of HIV-infected adults without a previous history of chickenpox did have a positive VZV serology [11]. In our patient, the demonstration of IgG antibodies in a previous serum sample, confirmed at the beginning of his illness, and the absence of any known contact with a child with chickenpox, are diagnostic of secondary varicella. In otherwise healthy adults as well as in immunocompromised individuals, endogenous reactivation of the VZV usually appears as zoster. Likewise, varicella-like reactivation does not exist in healthy adults or children. Conversely, in HIV-infected children, some atypical, persistent, chronic or recurrent cases of both primary and secondary varicella have been reported [12, 13]. Recurrent illnesses do not involve any extracutaneous organ; persistent/chronic varicella may involve the lungs, especially in children who are deeply immunocompromised. In HIV-infected adults, some cutaneous atypical recurrences may occur, as in our patient (scarce necrotic lesions); these atypical presentations may alternate with recurrent zoster [1]. Although few cases of varicella pneumonia have been reported during primary VZV-infection in HIV-infected adults [2], we did not find any report of pulmonary involvement during an endogenous reactivation of varicella, furthermore in a recurrent form, in a such setting. However, it must be borne in mind that this patient had been deeply immunocompromised for a very long time.

Pneumonia is considered to be the most common cause of death in adults with varicella [3] as it is an adverse complication of chickenpox in children [13] and adults [5, 6]. Although there are no controlled trials proving the efficacy of acyclovir in varicella pneumonia, this therapy has been used with some success in most reported cases occurring in immunocompromised patients [2, 14]. In our patient, the treatment with acyclovir was very effective, with a healing of all cutaneous lesions. However, two recurrences occurred when the maintenance treatment was discontinued. This should underline the usefulness of a maintenance treatment following the early high-dose acyclovir therapy of varicella in deeply immunocompromised patients, and the importance of compliance to treatment, in order to prevent recurrences. This secondary prophylaxis could also decrease HIV replication promotion by herpes virus infection. Few cases of acyclovir-resistant varicella have been reported in AIDS patients; in some instances, foscarnet has proved to be effective [15, 16].

In conclusion, this is the first report of a case of an endogenous reactivation of varicella with pulmonary involvement, in a human immunodeficiency virus-infected adult. In this case, polymerase chain reaction analysis of the bronchoalveolar lavage sample was a useful tool to make the definite diagnosis of the varicella-zoster virus. Secondary prophylaxis after an early high dose acyclovir treatment may be indicated to prevent recurrences in deeply immunocompromised patients.

References