CASE REPORT

Oesophagobronchial fistula caused by varicella zoster virus in a patient with AIDS: a unique case

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Human herpesvirus oesophagitis in human immunodeficiency virus positive patients is caused by cytomegalovirus and herpes simplex virus; no cases of oesophagitis and oesophagobronchial fistula as a result of varicella zoster virus (VZV) have been reported to date. This report describes the case of a patient with a 2–3 mm deep oesophageal ulcer whose viral culture was positive for VZV. The patient was treated with acyclovir with resolution of the symptomatology. After the end of the induction treatment, because of the onset of fever and fits of coughing during eating, the patient underwent oesophagography, which showed an ulcer with an oesophagobronchial fistula in the middle and lower third of the oesophagus. This case report stresses the role of VZV infection as a possible cause of oesophagobronchial fistula, a rare but benign condition in patients with AIDS.

Human herpesvirus oesophagitis is a well known infectious complication of patients with an impaired immune system, and has also been described as a self limiting illness in immunocompetent patients.¹ The herpes viruses so far described as being related to oesophagitis in patients with human immunodeficiency virus (HIV) infection are cytomegalovirus (CMV) and herpes simplex virus types 1 and 2 (HSV 1/2).² Reactivation of varicella zoster virus (VZV) as herpes zoster is a well recognised cause of morbidity in the HIV infected host: other described complications are ocular, neurological, and chronic atypical skin lesions.³ No cases of oesophagitis and spontaneous oesophageal perforation caused by VZV have been reported.

CASE REPORT

Here, we describe an oesophagobronchial fistula caused by VZV in a 31 year old homosexual man, with known HIV infection since 1994, who received antiretroviral treatment with zidovudine plus zalcitabine from October 1994 to December 1995, and zidovudine plus saquinavir until January 1997. He had a previous history of *Pneumocystis carinii* pneumonia. His childhood illnesses included measles, mumps, and varicella; there was no antecedent zoster rash.

In January 1996, his CD4+ cell count was less than 100/mm³ and he reported the appearance of painful dysphagia: a first upper gastrointestinal endoscopy showed the presence of a hiatus hernia without signs of candidiasis or ulcers. Two weeks later, because of a worsening of the chest pain, he underwent a second upper gastrointestinal endoscopy that showed a linear ulcer 5–6 cm long and 2 cm wide in the middle and lower third of the oesophagus. A biopsy was diagnostic for peptic ulcer. Viral isolation was negative for CMV. In spite of this negative result, and based on the high frequency of oesophageal ulcers caused by this virus in patients with AIDS, the subject was started on the induction dose of ganciclovir for 21 days. After one week he reported an improvement

in the symptomatology and began eating both solid and liquid foods. One month later, he again started complaining of dysphagia, especially for solid foods. A third upper gastrointestinal endoscopy revealed second grade oesophageal candidiasis and fluconazole treatment was begun. Because of the persistence of epigastric pain and dysphagia for both liquid and solid foods, the patient was admitted to the St Luigi Centre (St Raffaele Hospital, Milan) in April 1996 for further tests.

He underwent treatment with ganciclovir because of the suspicion of relapsing CMV infection. A fourth endoscopic examination showed the presence in the middle third of the oesophagus of an ulcer 2–3 mm deep, 35 cm from the dental arch. Serological tests for anti-HSV-1, anti-HSV-2 and anti-VZV IgM antibodies were negative. Small biopsy fragments from the endoscopically identified lesions were collected for further virological assays and long term viral cultures for herpes viruses were started. For CMV isolation, one or two vials were fixed 24 to 72 hours later and stained with a specific monoclonal antibody to p72 CMV matrix protein. For HSV and VZV isolation, cultures were maintained for two and three weeks, respectively, and checked for the appearance of specific cytopathic effects. VZV infected cultures were then fixed and stained using specific monoclonal antibody (anti-VZV IgM monoclonal antibody; fluorescein isothiocyanate conjugated; Whittaker-MD, Paris, France).⁴ Viral cultures for CMV, HSV-1, and HSV-2 were negative, but immunohistochemistry and a viral culture for VZV were positive. Therefore, the patient was started on treatment with acyclovir (650 mg three times daily, intravenously), with good resolution of the dyspeptic symptomatology. A further endoscopic examination showed a clear improvement in the previous picture, with no evidence of inflammation or parietal ulcer, but with persistence of muscle depression. At that time, viral isolation of CMV, HSV-1/2, and VZV was negative. After the resolution of the dysphasia and the improvement in the endoscopic picture, the patient continued acyclovir at a maintenance dose of 800 mg twice daily by mouth.

Two weeks after the completion of the induction treatment with acyclovir, because of the onset of fever and fits of coughing, especially during eating, the patient underwent oesophagography with hydrosoluble contrast medium, which showed hypotony in the middle and lower third of the oesophagus and an irregular parietal outline stretching sideways, where an ulcerous lesion was present. At this site, a 2 cm long fistula was evident.

After a period of total parental nutrition, in September 1996 the patient underwent percutaneous endoscopic gastrostomy to allow enteral feeding.⁵ Two subsequent radiological examinations showed a gradual improvement in the fistula and the

Abbreviations: CMV, cytomegalovirus; HIV, human immunodeficiency virus; HSV, herpes simplex virus; VZV, varicella zoster virus

closure of the pathological connection between the oesophagus and the trachea. The last oesophagoscopy performed (April 1997) showed complete resolution of the ulcer. Since then, the patient has not complained of dysphagia or retrosternal pain and is now on antiretroviral treatment with stavudine plus lamivudine and indinavir, and has a CD4+ count of more than 200 cells/mm³.

DISCUSSION

VZV can cause necrotising oesophagitis in severely immunosuppressed patients with herpes zoster. Both vesicles and confluent necrosis can be seen in the oesophagus. Oesophageal VZV may also be a harbinger of disseminated visceral VZV in the absence of skin involvement.⁶⁻⁸ To our knowledge, although oesophagobronchial fistulas are a complication of mediastinal lymph node tuberculosis and of HSV oesophageal ulceration, this is the first case of a VZV oesophageal ulcer causing fistulisation in a patient with AIDS.⁹⁻¹³

"Recognition of the spectrum of the clinical manifestation of zoster in the HIV infected host is of increasing importance in light of the changing natural history of HIV infection in the era of improved therapeutic and prophylactic regimens"

The histological finding of multinucleated giant cells, the response to antiviral treatment, the positivity of the viral culture, and the lack of evidence of another infectious aetiology support the role of VZV in this ulcer. Recognition of the spectrum of the clinical manifestation of zoster in the HIV infected host is of increasing importance in light of the changing natural history of HIV infection in the era of improved therapeutic and prophylactic regimens. To define the real aetiology of oesophageal idiopathic ulcers in patients with AIDS, we therefore recommend a complete virological investigation, including the less frequently detected (or searched for) VZV, which is responsible for a benign condition with long term remission and survival.

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Take home messages

- This report describes the case of a patient with an ulcer with an oesophagobronchial fistula in the middle and lower third of the oesophagus whose viral culture was positive for varicella zoster virus (VZV)
- The patient was treated with acyclovir with resolution of the symptomatology
- This case report stresses the role of VZV infection as a possible cause of oesophagobronchial fistula, a rare but benign condition in patients with AIDS

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