CASE REPORT

Idiopathic Oropharyngeal and Esophageal Ulcers Related to HIV Infection Successfully Treated with Antiretroviral Therapy Alone

Yohei Hamada¹, Naoyoshi Nagata², Haruhide Honda¹, Katsuji Teruya¹, Hiroyuki Gatanaga¹, Yoshimi Kikuchi¹ and Shinichi Oka¹

Abstract

We herein report the case of an HIV-positive man who was diagnosed with idiopathic esophageal and oropharyngeal ulceration. The esophageal and oropharyngeal ulcers were considered to be idiopathic and related to HIV infection after excluding the possibility of infection with known pathogens. Both the esophageal and oropharyngeal ulcers showed significant improvements following antiretroviral therapy alone. Idiopathic esophageal ulcers are a well-known complication of late-stage HIV infection. However, involvement of both the esophagus and pharynx is rare. Furthermore, antiretroviral therapy without concomitant steroids is effective against idiopathic esophageal and oropharyngeal ulcers related to HIV infection.

Key words: HIV infection, idiopathic esophageal ulcer, pharyngeal ulcer, antiretroviral therapy, gastrointestinal diseases

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Introduction

Esophageal ulceration is a common complication in patients with human immunodeficiency virus-1 (HIV) infection, especially in the late stage. Although esophageal ulcerations can be caused by various infectious agents, such as Candida species, cytomegalovirus (CMV) and herpes simplex virus (HSV), a large proportion of patients are diagnosed with idiopathic esophageal ulcerations (1, 2) with no detectable etiology. Oropharyngeal ulcers are also an important comorbidity that can become progressive in HIV-infected patients (3, 4). The common infectious agents of esophageal ulcerations are known to also cause oropharyngeal ulcerations, although some cases are considered idiopathic with no identifiable etiology (5, 6). However, simultaneous involvement of the esophagus and oropharynx is uncommon outside of HSV esophagitis (5). We herein report a case of unusual discrete ulcers of the oropharynx and esophagus in a patient with HIV infection that showed a rapid improvement following treatment with antiretroviral therapy alone.

Case Report

A previously healthy 60-year-old Japanese homosexual man presented with severe odynophagia. He was diagnosed with oral candidiasis and HIV infection and therefore had been referred to our hospital (day-1). Laboratory tests showed a low CD4+ cell count (49/μL), a high HIV-RNA titer (1.0×10⁶ copies/mL) and a low serum albumin level (Alb 2.9 g/dL). Whole-blood polymerase chain reaction (PCR) was negative for both CMV and HSV. The patient was treated with fluconazole for seven days for suspected esophageal candidiasis. Despite this treatment, the odynophagia did not improve. Since oral ulcers were noticed, treatment with oral valaciclovir at a dose of 1,000 mg/day was initiated based on a presumptive diagnosis of HSV infection. However, the odynophagia persisted, and the oral ulcers did not show any improvement despite a 3-week...
course of anti-HSV therapy; thus, upper gastrointestinal endoscopy was performed. Endoscopy showed large, discrete and well-circumscribed esophageal and pharyngeal ulcers (Figure a, b). Because a diagnosis of CMV esophagitis was suspected based on the endoscopic appearance of the ulcers, treatment with intravenous ganciclovir at a dose of 5 mg/kg every 12 hours was initiated and the valaciclovir was discontinued. However, a histopathological examination of the biopsy specimen obtained from the base and edge of an ulcer before the initiation of ganciclovir therapy revealed lymphocytic infiltration without intranuclear or intracytoplasmic inclusion bodies. Immunohistochemical staining for CMV and HSV was negative. PCR assays of both pharyngeal and esophageal biopsies were negative for CMV-DNA and HSV-DNA (<40 copies/μg DNA). Furthermore, repeat endoscopy performed after two weeks of ganciclovir therapy showed exacerbation of the ulcers. Based on these findings, we administered antiretroviral therapy consisting of ritonavir-boosted darunavir with abacavir/lamivudine. The ganciclovir therapy was discontinued after the completion of a 3-week course of treatment. The odynophagia gradually improved and ultimately disappeared two weeks later, while the CD4 count increased to 91/μL and the HIV-RNA titer decreased to 4×10^4 copies/mL. Endoscopy performed on day 22 of antiretroviral therapy demonstrated significant reductions in the size and depth of the pharyngeal and esophageal ulcers (Figure c, d). Additionally, resolution of the oral ulcers was noticed.

**Discussion**

To our knowledge, this is the first report of idiopathic esophageal and oropharyngeal ulcers successfully treated with antiretroviral therapy alone in a patient with late-stage HIV infection. Steroids are commonly used as the standard treatment for idiopathic esophageal ulcers (2, 7). However, steroids can lead to serious opportunistic infections due to their immunosuppressive effects. The efficacy of steroids is mostly based on reports from the pre-highly active antiretroviral therapy era, and the efficacy of antiretroviral therapy has not been examined. As described above, steroid therapy may not be necessary when a potent combination of antiretroviral therapy is administered. The etiology of idiopathic esophageal ulcers is still not fully understood. Although such ulcers are considered to be associated with HIV infection, they have been referred to as idiopathic when no identifiable etiologic agent other than HIV infection is present (8, 9). The potential pathogenesis of these ulcers includes apoptosis of the esophageal mucosa induced by HIV infection (10). Based on this probable pathogenesis, it is therefore considered to be rational to administer antiretroviral therapy to treat idiopathic esophageal ulcers.
The diagnosis of idiopathic oropharyngeal and esophageal ulcers is established by excluding other infectious agents known to cause esophageal ulceration, including CMV, HSV and Candida sp, by performing histopathological and immunological examinations of biopsy specimens (1, 2, 5, 6). In our case, the histopathological findings showed no evidence of any infectious pathogens, and CMV and HSV infection were also excluded by PCR assays, which have a high sensitivity (11, 12). Furthermore, the oropharyngeal and esophageal ulcers were refractory to anti-CMV and anti-HSV therapy. In addition, the ulcers showed significant improvement following the administration of antiretroviral therapy alone. Therefore, the final diagnosis was idiopathic oropharyngeal and esophageal ulcers related to HIV infection.

Involvement of both the oropharynx and esophagus in HSV-related ulcers is not uncommon (5). However, in our patient, the esophageal and oropharyngeal ulcers were considered idiopathic, which is extremely rare. In this case, the ulcers in both regions were examined endoscopically. Therefore, performing careful endoscopic examinations of not only the esophagus, but also the pharynx, is considered to be important for establishing the cause of odynophagia in HIV-infected patients.

In conclusion, a pharyngeal and esophageal biopsy obtained using upper gastrointestinal endoscopy was useful for establishing the diagnosis in this case. Furthermore, antiretroviral therapy alone resulted in a significant improvement of the idiopathic ulcers in our HIV-infected patient. The initiation of antiretroviral therapy without steroids is therefore a reasonable option for treating idiopathic oropharyngeal and esophageal ulcers in HIV-infected patients.

The authors state that they have no Conflict of Interest (COI).

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References