Oesophageal ulceration in HIV-infected patients

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Objective. To determine the aetiology of oesophageal ulceration in HIV-infected patients.

Design. A retrospective clinical, endoscopic and histopathological analysis of patients with confirmed HIV infection and an oesophageal ulcer diagnosed on endoscopy.

Setting. A tertiary referral, gastrointestinal clinic in Cape Town.

Results. Fifty-one patients with HIV infection and oesophageal ulceration were seen from January 2001 to December 2007. Median CD4 count was 26 cells/µl. Mean age was 35.5 years. Sixty per cent of patients were female. Forty-nine per cent of oesophageal ulcers were idiopathic while 23% were caused by cytomegalovirus infection. The remainder were due to miscellaneous causes.

Conclusion. A surprisingly small number of patients with HIV-associated oesophageal ulceration were seen during the study period. This may reflect local referral practices or the fact that patients with severe immunosuppression succumb before developing oesophageal ulcers. As in other series, idiopathic oesophageal ulcers and cytomegalovirus ulcers made up the majority of cases. Correct biopsy technique and appropriate histological and microbiological investigations are associated with improved diagnostic yield in these patients.

4 cases. Twenty-five patients (48%) had idiopathic oesophageal ulceration. Of the remaining ulcers, 12 were caused by CMV infection (23%), 3 by Candida (6%), 4 by TB (8%) and 1 by HSV (2%). CMV and TB were diagnosed in 1 case. In 7 cases no ulcer material was present on histological analysis, reflecting inadequate biopsy of the lesion.

Of the 4 patients with a TB oesophageal ulcer, 3 were diagnosed on direct smear whereas 1 was smear-negative but positive on TB culture.

Barium contrast studies were performed on 10 patients for suspected fistulas, and 1 was identified (Fig. 1).

Discussion

In our series, as in others, the most common oesophageal ulcers were idiopathic (Fig. 2) and those caused by CMV infection (Fig. 3). In view of the HIV epidemic, it is surprising that so few patients were seen at a tertiary referral gastrointestinal unit, which could be explained by poor referral practices. The latter seems unlikely as we have an open-access endoscopy policy for HIV-infected patients and good community networks. Our study confirms that oesophageal ulceration occurs in patients with severe immunosuppression where 81% of patients had a CD4 count ≤100 cells/µl. South African HIV-positive patients may succumb to TB and other opportunistic infections before achieving this degree of immunosuppression.

Fig. 1. Oesophago-bronchial fistula.

Fig. 2. Idiopathic oesophageal ulcer.

Fig. 3. CMV oesophageal ulcer.
Oropharyngeal lesions were seen in 21% of patients with oesophageal ulceration but this was only predictive of the aetiology of the oesophageal lesion in patients with idiopathic ulcers; however, only 16% of our idiopathic ulcer group had a simultaneous oral ulcer. Oropharyngeal ulceration was found in 11% of 124 HIV-associated oesophageal ulcer patients. We also found oral pathology an insensitive indicator of the presence and/aetiology of oesophageal ulceration.

Tuberculous oesophageal ulceration was identified in 4 (8%) cases. In Brazil, 17% of oesophageal ulcers in HIV-positive patients were due to TB. Because of the high incidence of TB in HIV-infected people in South Africa, Ziehl-Neelsen staining and TB culture should be performed on all patients.

HSV-induced ulceration of the oesophagus is common in transplant patients but less common in HIV-infected patients, with 1 case in our series. We did not include HSV immunostaining but, since the inclusions are easily recognised morphologically, this omission was probably not responsible for the low number identified.

We had no peptic oesophageal ulceration, neoplastic ulceration or pill-associated ulceration. Advanced HIV disease is associated with hypochlorhydria, and peptic ulceration is unusual in this setting.7

Candida was identified in 3 ulcers (6%), which may represent colonisation of an idiopathic ulcer since the organisms were seen in the ulcer slough rather than invading tissue.

In 7 cases, biopsy material revealed no features of ulceration reflecting inadequate biopsy of the lesion. Wilcox and colleagues employed a biopsy technique to obtain large mucosal samples in their studies of HIV-related oesophageal ulcers.7 The ‘turn-and-suction’ technique, initially devised to obtain larger samples in patients undergoing Barrett’s oesophagus surveillance, produces larger mucosal samples without complications such as bleeding or perforation.

No standardisation in terms of the number and technique of biopsies was evident in our series. The cytopathic effect of CMV is most notable in infected endothelial cells found within granulation tissue in the ulcer base. By comparison, HSV is more likely to involve squamous epithelial cells present in biopsies from the ulcer edge.4 Correct biopsy technique and sample number is important to establish an accurate diagnosis in patients with HIV-related oesophageal ulceration.

Oesophageal ulceration occurs in patients with severe immunosuppression, and antiretroviral therapy is the cornerstone of therapy. Inducing ulcer healing, preventing ulcer recurrence, analgesia and maintaining nutrition are other components of therapy.

Treatment options for idiopathic oesophageal ulceration include oral, intravenous and intraleral steroids. Systemic steroids are effective in symptomatic and endoscopic healing of idiopathic ulcers,2,10 however, relapse on withdrawal of therapy and the increased risk of opportunistic infections are limiting factors. Oral thalidomide is effective in healing idiopathic oesophageal ulcers6,11 but is associated with significant side-effects.2

We commence antiretroviral therapy in all patients with oesophageal ulceration who are not already on treatment. Identified specific opportunistic infections are treated. Nutrition is maintained with an oral puree diet or a liquid nutritional supplement. Fine-bone nasogastric tube feeding is used for patients unable to maintain nutrition orally. None in our series required percutaneous endoscopic gastrostomy tube feeding. Oral Mist Morphine is routinely used for analgesia.

Oesophageal ulceration is a debilitating manifestation of advanced HIV infection and is most often due to idiopathic ulceration or CMV. Endoscopy with adequate biopsy of the lesion is the investigation of choice. Appropriate histological and microbiological tests, including TB culture, should be performed in all cases. Contrast studies should be performed if complications such as a bronchial fistula or stricture are suspected. Pharmacological intervention should include antiretroviral therapy and treatment of the causative opportunistic infection, if identified. In addition pain management and maintenance of nutrition are important in achieving a successful outcome.

References


Accepted 30 June 2008.