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## Odynophagia in a 29-Year-Old Male Prisoner with HIV

### Introduction

We discuss a case of odynophagia in an HIV patient as the second published case in the monthly Clinicopathological Conference conducted by the University of Illinois at Urbana-Champaign. A clinical faculty member is presented with a case of which he/she has no prior knowledge and then proceeds to describe the clinical reasoning involved in reaching a final diagnosis. This case was discussed in September 2007.

### Discussants

Infectious Diseases: Janet Jokela, MD, MPH  
Pathology: Ikechukwu Uzoaru, MD  
Gastroenterology: Thomas Huber, MD

### Case Presentation

*A 29-year-old African-American male HIV patient complained of odynophagia of six to eight weeks duration. Pain had worsened significantly over the last two weeks and was associated with dysphagia to both solids and liquids. The pain was described as 8/10 in intensity, midsternal, burning in nature, radiating to the back, and caused the patient to refrain from eating. This resulted in an unintentional 20 lb weight loss. The patient denied experiencing fever, chills, nausea, vomiting, diarrhea or abdominal pain. The patient had not been on antiretroviral therapy for 21 months prior to presentation.*

*Past medical history is significant for HIV infection diagnosed seven years ago; T-cell count was 240 in 2002. The patient was incarcerated and denied alcohol or tobacco use. Family history was non-contributory.*

*The patient's vital signs were unremarkable. Conjunctivae and pupils were normal. Extraocular movements were intact. Nasopharynx was normal. Oropharynx was moist without erythema or exudates. Heart, lungs and abdomen examinations were unremarkable. No pedal edema or rashes were observed.*

### Discussion

Esophageal diseases are important complications in patients with acquired immunodeficiency syndrome (AIDS), with at least 30% of patients having esophageal symptoms at some point in the course of their disease. The incidence increases with worsening immunodeficiency. Infections are the most common cause of esophagitis, with *Candida* species (45%) the most prevalent organisms, followed by cytomegalovirus (CMV) (24%) and herpes simplex virus (HSV) (5%). The majority of noninfectious causes are idiopathic (Idiopathic Esophageal Ulcer, IEU) (21%) or GERD-related (5%).<sup>1,2</sup>

### Differential diagnosis

Dysphagia and odynophagia are common problems with significant morbidity in acquired immunodeficiency syndrome (AIDS) patients. Esophageal Candidiasis is the most common cause of dysphagia in AIDS patients. The presence of oral thrush in combination with symptoms of dysphagia almost certainly indicates the presence of esophageal candidiasis in AIDS patients. Patients with severe odynophagia without dysphagia or thrush are more likely to have ulcerative esophagitis, with a viral or idiopathic etiology. Opportunistic infections of the esophagus with HSV, cytomegalovirus, histoplasmosis, cryptosporidiosis or, rarely, mycobacterium species are other causes of swallowing disorders in AIDS. Additional etiologies include pill-induced esophagitis (PIE), reflux ulcers, and malignancies (Kaposi's sarcoma, Non-Hodgkins Lymphoma). Because of the high incidence of esophageal candidiasis causing dysphagia in AIDS, it is suggested that in most cases a therapeutic trial with an antifungal agent, such as fluconazole, may be appropriate before radiologic or endoscopic examination. Further investigation can be reserved for patients who have severe symptoms, do not respond to empiric antifungal therapy, or have clinical evidence suggesting another esophageal disorder.<sup>1-5</sup>

Esophagogastroduodenoscopy (EGD) with biopsy is the best diagnostic procedure for evaluation of esophageal disorders in AIDS. Endoscopic finding of esophageal diseases can be divided into ulcerative and non-ulcerative lesions. (Table 1) Esophageal candidiasis usually manifests with plaque-like lesions presenting predominantly with dysphagia. This may also be seen with other fungi. Esophageal Tuberculosis presents with either fistulas or mass-like lesions. Esophageal neoplasms in AIDS are uncommon and Kaposi's sarcoma is the most common neoplasm involving the esophagus, and is usually asymptomatic. Viral esophagitis manifests as one or more ulcerations. HSV esophagitis typically presents with multiple shallow ulcers typically small in size, some of which may have a volcano appearance. A CMV esophagitis can present with one or more ulcers which are typically deep and large in contrast to HSV. The appearance of CMV ulcers parallels that of IEU and is indistinguishable. When ulcers are noted, biopsy of the ulcer edge is important to exclude herpes virus esophagitis. Cytomegalovirus viral cytopathic effects reside in the granulation tissue in the ulcer base. Culture of esophageal biopsies for fungi and viruses are less useful than histology as they do not distinguish from secondary colonizers. Brushings are less sensitive than biopsies. Barium studies can aid in identifying esophageal ulcers but cannot distinguish the etiology. Endoscopy with biopsy is necessary for definitive diagnosis.<sup>1-9</sup>

**Table 1. Relative Frequency of Esophageal Ulceration in HIV Infection**

	Percent
Cytomegalovirus	45
Idiopathic Esophageal Ulcer	40
Herpes Simplex Virus	5
GERD	4
HSV/CMV	4
Other	2

CMV = cytomegalovirus; GERD = gastroesophageal reflux disease; HSV = herpes simplex virus; IEU = idiopathic esophageal ulcer

*Diagnostic testing was notable for a WBC count of  $1.79 \times 10^3/\mu\text{L}$ , absolute neutrophil count of 800, and CD4 count of 5. The CMV IgG was positive. EGD revealed a large, proximal,  $6 \times 3$  cm esophageal ulcer with rolled edges and a clean base.*

*Biopsy and histopathology revealed non-specific ulceration associated with acute and chronic inflammation and*

*granulation tissue. Immuno-histopathology revealed no evidence of infectious or malignant etiology. The patient was started on a course of oral prednisone, as well as antiretroviral therapy for treatment of his HIV. By three-month follow-up, the odynophagia had resolved and he had regained most of the weight he had previously lost.*

**Final diagnosis:** Idiopathic Esophageal Ulceration

### Conclusion

Idiopathic esophageal ulcerations (IEU) are a known non-infectious complication of AIDS. High-titer viremia, inflammatory cytokines, and altered gastrointestinal immuno-pathophysiology are potential etiological factors contributing to the development of these ulcers. However, the pathogenesis of these ulcers remains unclear. Idiopathic esophageal ulcer is seen in the later stages of immunodeficiency when the CD4 lymphocyte count is less than  $100/\mu\text{L}$ . Odynophagia is the typical presenting symptom; however, other features such as dysphagia and burning substernal chest pain are also reported. Esophagoscopy with biopsy is the best procedure to diagnose IEUs. They manifest as giant ulcers (greater than 1 cm in diameter), typically in the mid-to-distal esophagus, and are often quite deep. Ulcers are commonly surrounded by erythema and edema with overhanging edges. The histopathological diagnosis of IEU is a diagnosis of exclusion. There is evidence of tissue necrosis and inflammation consistent with ulceration but final diagnosis is made when there is a failure to identify pathogens that can produce similar endoscopic findings (ie, cytomegalovirus, HSV).<sup>10-15</sup>

Corticosteroids have been demonstrated to be effective in healing IEUs of AIDS. However, caution needs to be exercised before initiating steroid therapy due to AIDS-induced immunosuppression, and frequent follow-up visits are warranted. Therapy with prednisone results in rapid clinical and endoscopic improvement. Comparison of a 4-week prednisone regimen to a 2-week regimen demonstrated that the longer course of treatment resulted in a better clinical response and significantly lower ulcer relapse rate. Thalidomide is also effective in healing IEUs and markedly improves odynophagia and dysphagia. The development of esophageal stricture from IEUs is uncommon. Wilcox examined 160 HIV patients with esophageal ulcer over a 7.5 year period and found only 16 developed esophageal strictures. Only four strictures (2.5% of all ulcer cases) were due to idiopathic ulcers.<sup>12-15</sup>

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## CME Questions 5a-d

Please select the best answer for the following:

- 5a. What is the most common cause of dysphagia in AIDS patients?
- Candida species
  - Idiopathic esophageal ulcers
  - Herpes virus infection
  - Mycobacterial species
- 5b. You are asked to evaluate an AIDS patient with progressive odynophagia that developed over the past two weeks. Physical exam is unremarkable. Which of the following is the best diagnostic test?
- Barium studies
  - Contrast-enhanced computed tomography of the chest
  - Upper GI endoscopy with biopsy
  - Viral serologies
- 5c. A 43-year-old African American male is seen in your office for evaluation of difficulty swallowing over the past four weeks. Dysphagia is mostly for solids. He is able to tolerate a pureed diet. He denies weight loss. He has been diagnosed with HIV and is compliant with anti-retroviral therapy. His last CD4 count was 407. Physical exam is remarkable only for oral thrush. What is the most appropriate next step in management?
- Viral serologies
  - Fluconazole
  - Acyclovir
  - Upper endoscopy with biopsy
- 5d. During an evaluation for odynophagia, a 24-year-old male recently diagnosed with AIDS was found to have an idiopathic esophageal ulcer. In addition to starting anti-retroviral therapy, what is the next step in management?
- Fluconazole
  - Prednisone
  - Acyclovir
  - Fungal serologies