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CASE REPORT

Esophageal Actinomycosis in a Patient with AIDS

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Actinomycosis has been rarely reported in patients with HIV/AIDS in contrast to other opportunistic and common pathogens. We report a case of esophageal ulcer disease, secondary to actinomycosis occurring in a patient with recurrent odynophagia. The diagnosis was made histologically only after repeated upper endoscopy with biopsies.

INTRODUCTION

HIV-infected persons are at increased risk of developing a wide array of infections due to opportunistic and routine pathogens. Despite this, actinomycosis has been rarely described in this population. We report a case of esophageal actinomycosis occurring in an HIV-infected patient, whose clinical course was complicated by recurrent esophageal ulcers.

CASE REPORT

A 41-year-old African-American male with late stage HIV infection (absolute CD4+ lymphocyte count 14 cells/mm^3 and plasma HIV RNA 95,000 copies/ml) presented in October 1997 for evaluation of severe odynophagia. Physical examination was unremarkable except for poor dentition. There was no history of heavy alcohol use. He was empirically treated with fluconazole (100 mg per day) for one week without resolution of symptoms. An esophagogastroduodenoscopy (EGD)[d] was then performed, which showed a 5-cm distal esophageal ulcer. Histology of esophageal biopsies revealed no evidence of malignancy or viral inclusions, and special stains were negative for cytomegalovirus (CMV), herpes simplex virus (HSV), and fungi. Viral cultures were also negative. Omeprazole was prescribed to help promote healing of the ulcer. The patient clinically improved, suggesting an initial non-infectious etiology of the ulcer. He was discharged with follow-up scheduled to

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[d] *Abbreviations*: CMV, cytomegalovirus; EGD, esophagogastroduodenoscopy; HSV, herpes simplex virus.

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reassess symptoms and discuss initiation of antiretroviral therapy.

The patient was lost to follow-up until two months later, when he presented with recurrent odynophagia and decreased oral intake. Oral examination showed moderate thrush. The patient was treated with fluconazole (100 mg per day) for seven days without improvement, at which time a second EGD was performed, which showed the previously visualized distal esophageal ulcer, although now overlain with yellow exudate. Esophageal brushings were positive for budding yeast, consistent with *Candida* species. Mycology culture was not performed. Viral cultures were again negative. The patient was continued on fluconazole; he clinically improved and was discharged to complete a two-week course of therapy as an outpatient with close clinical follow-up planned.

The patient was again lost to follow-up and presented two months later complaining of progressively worsening odynophagia. Oral examination was negative. A third EGD was performed, which now showed two deep hemi-circumferential ulcers, one corresponding to the previously visualized lesion, and a new, more distal ulcer measuring 3-cm. Histology of biopsy specimens revealed rare budding yeast and numerous sulfur granules containing abundant fine elongate hyphal forms consistent with *Actinomyces* species (Figure 1). Fungal culture grew 3+ *Candida glabrata*. Bacterial cultures were not performed. Viral studies were again negative.

The patient was treated with intravenous penicillin G (20 million units per day in divided doses) and amphotericin B suspension. Within four days, he showed marked clinical improvement. He was discharged to home where he completed six weeks of intravenous penicillin therapy, at which time his symptoms had fully resolved. A six-month course of penicillin VK (500 mg QID) was prescribed and discussions regarding antiretroviral therapy were planned. Unfortunately, the patient was again lost to follow-up.

DISCUSSION

Actinomyces comprise part of the normal oral flora, and may colonize the gastrointestinal tract, bronchial tree, and female genital tract. As human commensals, these organisms have a low degree of pathogenicity and generally only cause infection following disruption of normal barriers, such as after local trauma [1]. Infection often occurs in association with other pathogenic organisms [2]. All age groups can be affected, although actinomycosis is seen less frequently in persons less than 10 or greater than 60 years of age. There appears to be a male predominance [3, 4]. Most affected individuals have underlying co-morbid conditions, such as odontogenic disease, recent surgery, cardiovascular disease, or malignancy [2]. Actinomycosis is not usually considered an HIV-related opportunistic infection, and it appears to be a rare event in HIV-infected persons. This may be in part due to the frequent use of antibiotics in this population, many of which have activity against *Actinomyces*. However, it remains unclear which components of the immune response are most important in controlling actinomycosis and the specific impact of HIV/AIDS in these infections.

Actinomyces species most commonly cause disease of the oral-cervicofacial regions, less commonly the thorax, abdomen, or pelvis and rarely the central nervous system. Infection of nearly every anatomic site in the alimentary tract, from the oropharynx to rectum, has been reported. However, there are only four cases in the literature of esophageal actinomycosis, three occurring in HIV-infected individuals, and the fourth in a patient with pancreatic adenocarcinoma [5].

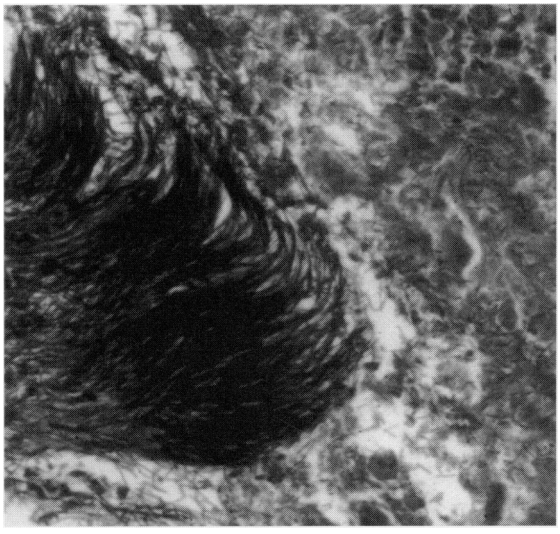

Figure 1. Esophageal biopsy showing squamous mucosa with ulcer and numerous sulfur granules containing abundant fine elongate hyphal forms consistent with *Actinomyces*. Immunostains were negative for CMV and HSV.

In the two cases of esophageal actinomycosis described by Poles et al. [6], both patients had advanced HIV infection and CMV esophagitis. Following initial improvement from systemically administered antivirals, each patient presented with fever and recurrent odynophagia, at which time repeat upper endoscopy was performed, which revealed *Actinomyces* by histologic analysis. The patients evidenced symptomatic as well as endoscopic resolution of their infections following prolonged treatment with IV and/or oral penicillin (Table 1). Spencer et al. [7] reported the third case of esophageal actinomycosis. The patient was a 47-year-old HIV-infected male, who presented with odynophagia, accompanied by thrush on oral examination. Endoscopy showed white esophageal plaques, and histology revealed sulfur granules and Gram-positive branching bacteria consistent with actinomycosis. Unfortunately, treatment data were not provided. In this report, the patient had concurrent candidal infection and possibly also aphthous ulcer disease of the esophagus. It is presumed that the mucosal disruption of the esophagus caused by these events allowed *Actinomyces* to establish infection at this site.

There are 13 additional cases of actinomycosis occurring in HIV-infected persons reported in the literature (Table 1). Of these, 10 cases were male, one female, and two were not specified. The mean age was 35 years (range, 23 to 51 years). As occurred with our patient, the majority of cases were diagnosed by histology (seven), as opposed to culture (six), the latter not performed due to either lack of clinical suspicion and/or the known fastidious nature of the organism. Sites of infection were cervicofacial (seven), thoracic (three), gastrointestinal (two) and cutaneous (one). This distribution by anatomic site of disease is similar to that reported in non-AIDS case series. CD4+ lymphocyte counts were noted in only five cases, and ranged from 2 cells/mm^3 to 499 cells/mm^3. Thus, actinomycosis may occur in patients with relatively early as

Table 1. Cases of actinomycosis and HIV Infection in the literature.

Case	Age/ Sex	Additional Conditions	Location	Diagnosis	Treatment	Outcome	Comments
Yeager 1986	23/M		Cervico-facial, S/p dental extraction	Cx, *A. israeli*	IV PCN x 6 wk PO PCN x 3 mo	Recovered but had persistent adenopathy	Had marked R sided adenopathy the neck and axilla, with involvement of R mandible
Gresser 1988	29/F		Cutaneous lower extremity	Cx, *A. israeli*	Cefotaxime, metronida-zole, ofloxacin, debridement	Recovered	Disseminated skin abscesses (German)
Klapholz 1989	42/M	IVDU alcoholism, poor dentition	Pulmonary	Histology (trans-bronchial bx)	IV PCN	Recovered	Other cultures negative
Fry 1991	42/M	H/o UGI bleed due to gastric ulcer, h/o perirectal abscess	Perianal fistula	Cx, *A. naelundii*	Incision & drainage, PO PCN x 6 wk	Recovered	*Enterococcus* and *E. coli* also isolated
Watkins 1991	29/M	IVDU, h/o *pneumocystis* pneumonia, poor dentition	Oral	Cx, *A. naelundii*	Debridement IV PCN	Recovered	Nonhealing dental extraction site
Molina 1991	28/M	IVDU	Cervical	Histology (surgical specimens)	Debridement PCN	Recovered	(Spanish)
Smith 1992	28/M		Anorectal with sinus	Cx, *A. israeli*	PCN	Recovered	Presented with diarrhea; initial diagnosis was Crohn's disease
Spencer 1993	47/M	Oral thrush, oral hairy leukoplakia	Esophageal	Histology (EGD)	NS	NS	No details of treatment or outcome provided
Cendan 1993	47/M		Endo-bronchial lesion	Histology (bronchial washings)	IV PCN	Died from cryptococcal meningitis	Sputum Cx grew *H. influenzae*, Bx showed only necrotic material

Table 1. Cases of actinomycosis and HIV Infection in the literature (continued).

Case	Age/ Sex	Additional Conditions	Location	Diagnosis	Treatment	Outcome	Comments
Poles 1994	42/M	H/o CMV gastritis, h/o micro-spordial eneritis, *S. aureus* bacteremia, CMV esophagitis	Esophageal	Histology (EGD)	IV PCN x 6 wk, PO PCN x 1 yr	Recovered	F/u EGD showed complete resolution
	29/M	CMV esophagitis, MAI duodenitis	Esophageal	Histology (EGD)	PO PCN x 6 mo	Recovered	F/u EGD and Bx showed complete resolution
Kingdom 1994	51/M	H/o IVDU, h/o pulmonary tuberculosis, h/o old facial trauma, CD4 count = 499	Nasal septum	Histology (Bx)	PO PCN Debridement	Recovered	
Manfredi 1995	25/NS	CD4 count = 9	Oro-pharyngeal	Histology (Bx)	Fluconazole ceftriaxone, netilmycin; followed by itraconazole, ceftazidime	Died from interstitial pneumonia	Had progressive disease leading to extensive bony destruction and large orononasal fistula
	36/NS	CD4 count = 2	Oro-pharyngeal	Histology (Bx)	Multiple antibiotics including IV PCN	Died from disseminated *M. Kansaii* infection and toxoplasmic encephalitis	Had progressive disease leading to extensive bony destruction and large orononasal fistula
Vazquez 1997	31/M	IVDU, hepatitis B, CD4 count = 480	Tongue (submucosal nodule)	Cx (aspiration) [species not specified]	PO amoxicillin, wide debridement	Recovered	

Table 1. Cases of actinomycosis and HIV infection in the literature (continued).

Case	Age/ Sex	Additional Conditions	Location	Diagnosis	Treatment	Outcome	Comments
Ossorio 1997	41/M	Alcoholism, poor dentition, CD4 count = 340	Pulmonary	Histology (BAL and brushings)	IV PCN x 3 wk, PO ampicillin x 6 mo	Recovered	Had bilateral nodular infiltrates on chest CT
Present 1998	41/M	*Candida* and CMV esophagitis, aphthous ulcers	Esophageal	Histology (EGD)	IV PCN x 6 wk, PO PCN x 6 wk	Recovered	

Cx, culture; Bx, biopsy; NS = not specified

well as advanced HIV disease. However, four of the cases had one or more AIDS-defining diagnoses at the time of diagnosis. Other co-morbid conditions included intravenous drug use (five), poor dentition (three), and alcoholism (two). The majority of patients (11) were treated with prolonged courses of penicillin or amoxicillin. Surgical intervention, usually debridement, was also performed in six of the 13 cases. Overall, 10 patients recovered or significantly improved and three patients died (two of progressive destructive facial actinomycosis, the third of cryptococcal meningitis).

The treatment of choice for actinomycosis remains penicillin, typically administered initially via intravenous route for two to six weeks, employing a dose in the range of 18 to 24 million units per day, followed by oral therapy with either penicillin VK or amoxicillin for six to 12 months. Less extensive infection occurring in an immunocompetent patient, particularly when limited to the cervicofacial region, may not require such a prolonged course of treatment. Minocycline, tetracycline, erythromycin, and clindamycin may be considered as alternatives. Anecdotal success has also been reported with ceftriaxone [8] and imipenem [9].

In summary, although seemingly rare, *Actinomyces* can occasionally cause invasive disease in persons with HIV infection. The rarity of this event is noteworthy, given the multiple defects in host immune function which occur during the HIV disease course. It remains unclear, how HIV/AIDS affects the frequency and progression of actinomycosis in this population. As *Actinomyces* can infect virtually any anatomic site, a high degree of clinical suspicion is required to make the diagnosis, particularly in patients who develop recurrent symptoms despite appropriate therapy for a previously identified alternate infection. Prior mucosal injury, resulting from another infectious or inflammatory process, with resultant loss of normal protective anatomical barriers, may be a necessary antecedent event for invasive disease to occur. With prolonged antibiotic therapy, and in select cases surgical debridement, *Actinomyces* infection can often be successfully managed. Whether or not addition of highly active antiretroviral therapy would allow a shorter course of antibiotic therapy than is generally recommended, and/or prevents the need for surgical intervention, is unclear from the available published literature.

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