Case Report

Enteroinvasive *Escherichia coli* infection in a noncompliant HIV patient

Abstract

Poorly controlled HIV infection increases the risk of opportunistic infections. We are presenting here a case of an HIV patient who was non-compliant with highly active antiretroviral therapy (HAART) regimen and who developed a diarrheal illness secondary to enteroinvasive *Escherichia coli* (EIEC) infection. The patient presented with severe gastrointestinal symptoms including frank bloody diarrhea, and febrile illness. He was eventually diagnosed with EIEC infection. We discuss the challenges faced in managing this patient and the potential consequences of medication noncompliance in the context of HIV.

Keywords: HIV, AIDS, non-compliant to HIV medication, opportunistic infection, enteroinvasive *E. coli*, HAART

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Abbreviations: HIV, human immunodeficiency virus; AIDS, acquired immune deficiency syndrome; EIEC, enteroinvasive *E. coli;* HAART, highly active antiretroviral therapy; ETEC, enterotoxigenic *Escherichia coli;* IDSA, infectious diseases society of America; ISTM, International society of travel medicine

Introduction

Infectious gastroenteritis is a universally major cause of morbidity and mortality. It is important to identify the causative pathogen of diarrhea in acutely ill patients to determine the targeted therapy for their treatment. *Escherichia coli* constitutes a main cause of diarrhea outbreaks and may be very invasive such as the case of enteroinvasive *E. coli* (EIEC) that can cause tissue destruction and inflammation like shigellosis.[1] Strict adherence to antiretroviral therapy is crucial for effective management of HIV infection ensuring viral suppression and healthy immune function. Noncompliance may lead to immunosuppression and increased susceptibility to opportunistic infections and contribute to higher mortality.[2,3] In this case report, we present an HIV patient who developed EIEC infection due to non-compliance with antiretroviral medication. Enteroinvasive *Escherichia coli* (EIEC) is a potentially fatal bacterial infection that can be very severe in immunocompromised HIV patients who are not receiving HAART.

Case presentation

A 40-year-old male patient with human immunodeficiency virus (HIV) infection who has been noncompliant with his HAART regimen over the past 2 years presents to the emergency department with abdominal pain, bloody diarrhea, nausea, and vomiting that have been ongoing for the last 7-8 days. He was also having fever and back pain. On examination, the patient was ill, with poor dentition and mild to moderate tenderness in the lower abdomen without rebound, guarding or rigidity. On blood work up, White Blood Cell count was 8900 (normal, 3.5-10.5 K/uL), with severely depressed Helper T- Lymphocyte CD4 count of 59 (normal, 490-1740 cells/uL). Gastrointestinal panel with BioFire was able to detect Enteroinvasive *E coli* (EIEC). Blood cultures were negative. The patient was admitted and was initiated on Intravenous ceftriaxone 2 grams every 24 hours. Furthermore, the patient received supportive care including intravenous fluids and electrolyte replacement to manage his dehydration. During the hospital stay, the diarrhea improved within 48 hours, and he started feeling better. He received a 5-day treatment course for the infection and was educated on the importance of adhering to antiretroviral therapy and the risk of opportunistic infection due to compromised immune system. The patient was discharged with a referral to HIV care clinic for ongoing management with highly active antiretroviral therapy (HAART).

Discussion

Escherichia coli are a regular part of the normal flora of the large intestine and constitute the predominant aerobic organism of normal fecal flora. *E. coli* strains usually constitute no harm to the host if they do not have genetic elements encoding for virulence.[1] Once they receive a bacteriophage or plasmid DNA that encodes for invasion, they become pathogenic and cause an array of diseases from a simple watery diarrhea to a severe inflammatory dysentery. Enterohemorrhagic *E. coli* (EHEC) such as *E. coli* O157:H7 can cause bloody diarrhea and Hemolytic uremic syndrome. Enterotoxigenic *Escherichia coli* (ETEC) strains produce enterotoxins that may be cytotoxic or cytotonic, and as such, enhancing the loss of water and electrolytes. It is the most common cause of traveler's diarrhea. Enteropathogenic *E. coli* (EPEC) causes diarrhea but produces no toxins or invasion factors. *E. coli* strains that have invasion factors causing inflammation similarly to *Shigella* are known as Enteroinvasive *E. coli* (EIEC). The invasive capacity of EIEC is related to a plasmid that is very significantly similar to the invasion plasmid in *Shigella*.[4,5] It can pass into the intestinal wall to cause severe diarrhea.

Traditional testing methods are slow, labor intensive, and sometimes fail to reveal the etiology of a patient's gastrointestinal symptoms. While Shiga toxin-producing *E. coli* strains (STEC) can be diagnosed by detecting Shiga toxins via molecular or immunoassays, enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), enteroinvasive *E. coli* (EIEC), and enteroaggregative *E. coli* (EAEC) need other diagnostic modalities. In 1 study, while the majority of the *E. coli* isolates were lysine decarboxylase positive, all EIEC isolates were lysine decarboxylase negative.[6] BioFire and BD have FDA approved multiplex molecular GI panels for the detection of different pathogenic *E. coli* strains. The organisms can be detected using nucleic acid tests, including multiplex panels. The use of BioFire® FilmArray® Gastrointestinal (GI) Panel (BioFire Diagnostics, LLC, Salt Lake City, UT) eliminates limitations from conventional methods by providing faster, more accurate, and comprehensive results.[7]

EIEC is rare in the U.S. but may cause outbreaks. EIEC is related to *Shigella* species, and both can cause similar gastrointestinal diseases. EIEC does not produce enterotoxins. EIEC may be differentiated from *Shigella* principally by the fact that EIEC strains ferment glucose and xylose. It causes diarrhea by invading the epithelial cells of the colon. Acute inflammatory response and direct tissue invasion of the intestinal epithelial cells are characteristic of this highly virulent *Shigella*-like *E. coli*. EIEC invades the intestinal cell, multiplies intracellularly, and extends into the adjacent intestinal cells. The same genes facilitate pathogenesis of both EIEC and *Shigella*.[8] Patients may experience fever, abdominal cramps, and sometimes tenesmus with scanty stool containing blood and mucus. Dysentery or bloody diarrhea may happen although uncommonly. Clinical guidelines are not clear about the role of antimicrobial treatment for gastroenteritis due to this infection.

Most of the time, diarrheal illnesses are self-limited. Host defense plays a major role in the pathogenesis of enteroinvasive E coli. This defense is usually deficient in the young and the elderly, reflecting the epidemiology of this diarrheal illness and its severity in this age group. Infection with this pathogen produces an inflammatory cell response that is responsible for the diarrhea symptoms. The immune response mechanisms that contribute to the control of diarrheal disease are important. Cytokines play an important role in controlling the homoeostasis of the immune system. In one study,[9] increased levels of TNF-α and IL-6 were associated with decreased durations of EPEC infection and increased ETEC durations. Increased IL-4 and IFN-γ levels were associated with decreased and increased durations of both EPEC and ETEC infections respectively. Increased IL-10 levels were related to increased and decreased durations of asymptomatic and symptomatic EPEC infections, respectively, and increased durations of ETEC infections.

HIV infected patients commonly suffer from diarrhea. In patients with AIDS, recurrence of infection is common, and may cause chronic diarrhea.[10,11] A case of enteroinvasive *E. coli* bacteremia has been described in an AIDS patient who was having diarrhea, fever, and who was improving each time he received antibacterial therapy. However, he developed symptoms of septicemia prior to the diagnosis of bacteremia with EIEC.[12] In HIV infection, there is dysregulation of cytokines, and this abnormal cytokine production contributes to the impairment of cell-mediated immunity. For instance, in HIV-1 infection, the production of T-helper type 1 cytokines, like interleukin (IL)-2, and antiviral interferon (IFN)-gamma, is decreased, whereas production of T helper type 2 cytokines, IL-4, IL-10, proinflammatory cytokines (IL-1, IL-6, IL-8) and tumor necrosis factor (TNF)-alpha, is increased. Cytokines such as TNF-alpha, TNF-beta, IL-1 and IL-6 are considered HIV inductive because they stimulate HIV-1 replication in T cells and monocyte-derived macrophages, IL-2, IL-7 and IL-15 upregulate HIV-1 in T cells, and macrophage-colony stimulating factor. HIV-suppressive cytokines include IFN-alpha, IFN-beta and IL-16, which inhibit HIV-1 replication in T cells and monocyte-derived macrophages and IL-10 and IL-13, which inhibit HIV-1 in monocyte-derived macrophages.[13] Thus the important role of highly active antiretroviral therapy in regulating cytokine production and as such controlling the severity of diarrheal illness.

Treatment of Enteroinvasive *E. coli* is usually supportive care with fluid, electrolyte, and nutritional management. Antibiotics are only reserved for those who have severe illness that lasts greater than 7 days and who continues to have fever and bloody diarrhea. HIV patients, and namely those who are not on HAART, may qualify for antibiotic therapy because they may have more severe or persistent infection, viewing their immunocompromised status. Rifaximin, azithromycin, and ciprofloxacin are currently recommended by the Infectious Diseases Society of America (IDSA) and the International Society of Travel Medicine (ISTM) to treat E. coli diarrheal illness.[13]

This case highlights the complex correlations between HIV infection, non-adherence to antiretroviral therapy and opportunistic infection such as enteroinvasive *Escherichia coli*. Individuals with compromised immune system are at risk of severe infectious disease and non-compliance to medication exacerbates this risk. To effectively manage such cases, it is imperative to provide comprehensive patient education and support services to ensure continued adherence to antiretroviral therapy which is critical for restoring immune function along with suppressing HIV replication.

Conclusion

This report presents the case of enteroinvasive *E. coli* diarrheal illness in an immunocompromised patient with AIDS, who did not have the capacity to clear the pathogen on his own, viewing his noncompliance to HAART. It also emphasizes the difficulties encountered in managing enteroinvasive *E.coli* infection in HIV patients compounded by non-adherence to HIV medication. Effective management requires prompt intervention, suitable antimicrobial treatment and comprehensive approach that addresses the medical factors.

Acknowledgments

None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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