Case Report

Empiric treatment of diarrhea in patient with HIV infection: a case report

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ABSTRACT

Diarrhea is common opportunistic infection in patient with Human immunodeficiency virus (HIV) infection. Diarrhea in patient with HIV infection that contributes the negatively to quality of life. The etiology of diarrhea in patient with HIV infection is multifactorial include infectious, non-infectious, ART-association diarrhea. In addition, this diarrhea can be associated with empiric therapy. This article a 31 years old male patient with 3 days fatigue and diarrhea. Physical examination dry mucous membranes, abdominal pain especially in in the upper abdomen and increase small bowel peristalsis. Stool examination test doesn't have blood, parasites, and fungi. Stool cultures for Salmonella, Shigella, Campylobacter organisms no presence. The treatment metronidazole oral 500 mg every 8 hours was again performed. Metronidazole is available for the management of diarrhea in patient with HIV that can't be treated with other antibiotics.

Keywords: Diarrhea, HIV, Metronidazole

INTRODUCTION

Infection with human immunodeficiency virus (HIV) imposes monumental suffering on affected individual and in the developing world in particular it places a great burden on the medical system. For Indonesia as a developing country with the population of 240 million spread across 514 cities and districts, faces specific challenge in its response to HIV. One of the most health problems among HIV destroys the immune system and renders patients susceptible to opportunistic infection.[1,2]

Diarrhea is described as three or more loose or watery stools with the contain of water more than 200 gram or 200 ml/24 hours. The classification of diarrhea is acute diarrheal are due to infectious etiology and chronic diarrhea is commonly categorized in three groups; watery (secretory and osmotic), fatty (malabsorption), or inflammation. Patient are usually diagnosed with chronic diarrhea when this pattern is abnormal passage of three or more loose or liquid stools per day for more than 4 weeks

and/or daily stool weight greater than 200g/day.[3] Chronic diarrhea is one such very common clinical condition in AIDS-defining, according to World Health Organization (WHO) criteria.[1]

The etiology of diarrhea in patients with HIV is opportunistic infectious agents that cause protozoa, fungi, viruses and bacteria; and noninfectious diarrhea includes ART-associated diarrhea and gastrointestinal damage related to HIV infection (enteropathy).[4] In addition, infectious diarrhea can be caused by pathogens that are unique to the HIV population depend on standard of living among developed versus developing countries and differences in availability of care for patients with HIV, the incidence and type of various diarrhea-associated infections in immunocompromised patients may vary substantially by region.[5-7]

In other hand the site of origin of the diarrhea small bowel ("enteritis") or colon ("colitis"). Enteritis is classically manifested as large volume (often > 2L/d) watery stools,

often associated with dehydration, electrolyte disturbances, malabsorption and weight loss. In contrast colitis is characterized by frequent, small volume stools, which may contain mucus, pus and/or blood, tenesmus, frequency, urgency, dyschezia and proctalgia.[8]

With the previous background, this study discuss the empiric therapy in HIV/AIDS cases with diarrhea. This study was to understand the microbial etiologies of diarrhea, specific therapy for this patient.

CASE REPORT

A 31 years old male patient came to the emergency department with three days fatigue and diarrhea. Diarrhea with watery stool, frequency of defecation of four times in a day, no bloody, mucoid, fatty, pus stools accompanied by nausea and vomiting, lack of appetite and drink. Patients also complain of abdominal pain or crampy in all part of abdomen, bloating, flatulence dan fever. Patients had history about HIV and toxoplasmosis with the routine treatment use ARV (tenofovir + lamivudine + efavirenz) and in one month patient doesn't consume of toxoplasmosis drug.

Physical examination showed a blood pressure of 120/80 mmHg, heart rate of 88 beats per minute, respiratory rate of 18 times per minute, body temperature of 37,8 C, dry mucous membranes. The abdominal pain especially in the upper abdomen and increase small bowel peristalsis.

The laboratory examination results were: white blood cells $3.23 \times 10^3/ \mu L$; Hemoglobin level 8.4 g/dl; hematocrit 23.4%; platelet count $179 \times 10^3/ \mu L$; SGPT 113 U/L; SGOT 171 U/L; BUN 292 mg/dl; SC 9.3 mg/dl; Na 121 mmol/L; K 3.3 mmol/L; Cl 98 mmol/L. Stool examination (macroscopic and microscopic) doesn't have blood, parasites, and fungi. Stool culture for *Salmonella, Shigella, Campylobacter, Staphylococcus, E. coli* organisms no presence. No abnormalities were found on chest x-ray.

The diagnosis of HIV AIDS, toxoplasmosis and chronic diarrhea was made at the end evaluation. In the hospitalization, patient was treated with esomeprazole injection 40 mg BID, cefoperazone injection 1 gram BID, attalpugite 2 tablets TID, azitromisin tablet 500 mg, metronidazole tablet 500 mg TID.

DISCUSSION

Diarrhea is described as three or more loose or watery stools with the contain of water more than 200 gram or 200 ml/24 hours.[3] Diarrhea disease is a common complication of HIV infection among adults seen in more than 50% of all patients with AIDS. HIV has an impact on intestinal infection at all stages, but the effects of HIV on the mucosal immune system are most apparent in acute infection period. Data from patients with HIV show that within weeks of infection, the mucosal lamina propria CD4+ lymphocytes are depleted. This depletion occurs

well before any decrease in CD4+ T cells is seen in the periphery and likely reflects the greater expression of the CC chemokine receptor type 5 (CCR5), which functions as the primary coreceptor for the majority of infective HIV strains, on mucosal CD4+ cells.[9] The expression of the chemokine receptor on these cells supports the entry of the virus, but their state of physiologic activation is responsible for enhanced HIV replication in the mucosal compartment and subsequent mucosal CD4+ T cell depletion. HIV persist within Gut-associated lymphoid tissue (GALT) lymphocytes, even after repletion of CD4+ T cells in the periphery.10 The etiology of diarrhea in HIV-infected patients is multifactorial such as infectious and noninfectious.

The infectious causes of diarrhea in AIDS are bacteria and mycobacteria, parasites, virus and fungi and the most important etiologic agents will be briefly discussed individually focusing on geographic differences in prevalence. In the world population, the most common causes of diarrhea in HIV-infected patients are enteric bacteria including *Shigella flexneri, Salmonella enteriditis* and *Campylobacter jejuni*. In contrast to the normal host, these bacteria have been identified in stool from patients with chronic diarrhea.[11-13] *Clostridium difficile* is a prevalent pathogen in developed countries, whereas tuberculosis is a common complication of AIDS in developing countries.[14,15] *Cryptosporidia* is the most frequently identified parasitic cause of diarrhea throughout the world.[11-13]

In other hand the etiology agents of origin diarrhea in HIV infection in the intestine. Small intestine ("enteritis"): *Cryptosporidia, Microspiridia, Isospora belli, Mycobacterium avium complex, Salmonella species, Campylobacter species, Giardia lamblia.* Large intestine ("colitis"): *Cytomegalovirus, Crytosporidia, Mycobacterium avium complex, Shigella sonnei, Clostridium difficile, Campylobacter jejuni, Histoplasma capsulatum, Adenovirus, Herpessimplex, Pneumocystis carinii*.[8,16]

HIV enteropathy is a non-infection form of diarrhea in patients with HIV. It occurs in 50% of patients and is characterized by rather watery diarrhea and worsen with the consumption of food but improves with defecation because the mechanism are unclear.[17] Several studies have established crypt epithelial proliferation in response to HIV infection, malabsorption, decreased transepithelial electrical resistance, decreased sodium-dependent glucose absorption, and increased intercellular permeability in HIV-infected cells.[18-20] On the other hand diarrhea has also been described as a side effect of ARV, Rufo and colleagues demonstrated that protease inhibitors in general and nelfinavir in particular potentiate signaling through muscarinic and calcium-dependent receptors of intestinal cells, resulting in increased chloride secretion into the lumen. This study also showed that sodium and chloride concentrations in stool samples from patients with HIV

taking nelfinavir were elevated, consistent with secretory diarrhea.[21,22]

The basic algorithm for the diagnosis and evaluation of diarrhea in patients with HIV to the examination of diarrhea in the immunocompetent host and starts with a through medical history, a careful review of medications, travel history, contact with ill individuals, recent ingestions, family history, surgical history, and social history is in evaluating acute and chronic diarrhea in the patient infected with HIV. Physical examination and medical history of a patient with HIV such as basic vital signs, orthostatic vital sign, bitemporal wasting, weight changes, skin turgor, mucosal dehydration, gastrointestinal examination is to evaluate the severity and causes of diarrhea. Laboratorium test should include complete blood count with cell differential, blood cultures, HIV viral load, and CD4+ T cell count to measure the level of immune suppression. Fecal examination to evaluation causes diarrhea from bacteria, parasites, fungi. If non pathogen is identified, workup needed with an endoscopic examination.[23]

The case at hand had diagnosis HIV AIDS and chronic diarrhea, this case can be diagnosed as chronic diarrhea because diarrhea during three days and watery stool, frequency of defecation of four times in a day. Etiology diarrhea in this case can't not defined specific because in day II evaluation with fecal examination and cultures examination doesn't have result use empiric therapy and in day V fecal and cultures examination no presence. Anamnesa and physical examination diarrhea with watery stool, no mucoid, bloody, fatty, pus, fever and have crampy in all part of abdomen etiology agents origin diarrhea in small intestine ("enteritis").

HIV patients with diarrhea therapy consider to treat HIV infection and diarrhea. Treatment of diarrhea in patients with HIV is essential connected with a state of decreased immunity, opportunistic infection. General therapy for treatment of noninfectious diarrhea in patients with HIV are primarily supportive. Hydration via intravenous and oral routes, repletion of electrolytes and treating the underlying cause, if possible, are important therapies for any patient with diarrhea.[24] Antidiarrheal medications used in noninfectious diarrhea can be divided into several classes: adsorbents, antimotility, antisecretory agents.[24-33] Adsorbent drugs bind bacterial toxins, fluids, and other compound in the intestines to improve stool consistency include attalpugite, bismuth subsalicylate, kaolin, pectin. Antimotility agents include loperamide, diphenoxylate/atropine, tincture of opium.[27] In addition to supportive, antimicrobials are widely used to treat infectious diarrhea in patient with HIV AIDS depend on etiology bacterial infection for example: management of *Campylobacter* infection is based on ciprofloxacin recommended for 14 days, mycobacterium avium complex with oral 500 mg clarithromycin every 12 hours, *clostridium difficle* with oral 500 mg metronidazole every 8 hours for 10 to 14 days or oral of 125-250 mg vancomycin every 6 hours for 10 to 14 days.[34-36] Etiology of parasitic infection therapeutic option in Isospora belli are trimetropim/sulfamethoxazole (160 mg/800mg) every 6 hours for 10 days or 500 mg of ciprofloxacin every 12 hours for 7 days.[37]

In this case the patient was first treated for diarrhea with cefoperazone injection 1 g BID and azitromisin oral 500 mg every 24 hours without clinical improvement or reduction of diarrhea until fecal and cultures examination no presence. The patient was treated empiric therapy of metronidazole oral 500 mg every 8 hours, diarrhea was stopped. The second treatment with metronidazole was more continuous in 7 days and efficient. Metronidazole is drug treatment of broad range of infection of anaerobic bacteria, protozoa infection.[38]

CONCLUSION

Diarrhea is a common opportunistic infection in HIV that has substantial clinical ramification. The major cause of diarrhea in this patient with HIV is infectious agent but can other cause such as noninfectious and use ARV therapy. Medications use for infectious agent include adsorbent drug and antibiotic therapy which has been shown reduce diarrhea patient with HIV.

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