Diagnosis and Management of Blastocystis Hominis Infection in Patient with HIV/AIDS

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ABSTRACT

The incidence of AIDS/HIV infection has been increasing worldwide. Patients with AIDS/HIV infection is at high risk to get opportunistic infection which is often become life-threatening. Common infections associated with AIDS/HIV are tuberculosis (TB) infection and viral hepatitis. Commensal organism found in human body is actually not pathogenic. Blastocystis hominis is generally considered as commensal organism of intestinal tract and might cause opportunistic infection in patients with AIDS. We reported a case of young male patient with AIDS/HIV infection and evidence of opportunistic infection of Blastocystis hominis found in ascitic fluid along with concomitant lung TB and viral hepatitis. Patient was well-responded to treatment of B. Hominis.

***Keywords**: AIDS/HIV infection, opportunistic infection, Blastocystis hominis*

INTRODUCTION

AIDS (acquired immunodeficiency syndrome) was first reported in the United States in 1981 and has since become a major worldwide epidemic. AIDS is caused by HIV (human immunodeficiency virus). By killing or damaging cells of the body's immune system, HIV progressively destroys the body's ability to fight infections and certain cancers. People diagnosed with AIDS may get life-threatening diseases called opportunistic infections, which are caused by commensally microbes such as viruses or bacteria that usually do not make healthy people sick.[1]

More than 900,000 cases of AIDS have been reported in the United States since 1981. As many as 950,000 Americans may be infected with HIV, one-quarter of who are unaware of their infection. The epidemic is growing most rapidly among minority populations and is a leading killer of African-American males ages 25 to 44. According to the Centers for Disease Control and Prevention (CDC), AIDS affects nearly seven times more African Americans and three times more Hispanics than whites. In recent years, an increasing number of African-American women and children are being affected by HIV/AIDS. In 2003, two-thirds of U.S. AIDS cases in both women and children were among African-Americans.[1]

CDC's definition of AIDS includes all HIV-infected people who have less than 200 CD4+ T cells per cubic millimeter of blood (healthy adults usually have CD4+ T-cell counts of 1,000 or more). In addition, the definition includes 26 clinical conditions that affect people with advanced HIV disease. Most of these conditions are opportunistic infections. In people with

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AIDS, these infections are often severe and sometimes fatal because the immune system is so ravaged by HIV that the body cannot fight off certain bacteria, viruses, fungi, parasites, and other microbes.[1,2] One of the opportunistic infection is an infection of *Blastocystis hominis*.[1-3]

The taxonomic classification of *Blastocystis hominis* is mired in controversy. It has been previously considered as yeasts, fungi, or amoeboid, flagellated, or sporozoan protozoa. Recently, however, based on molecular studies, especially dealing with the sequence information on the complete SSUrRNA gene, *B. hominis* has been placed within an informal group, the stramenopiles.[4] Stramenopiles are defined, based on molecular phylogenies, as a heterogeneous evolutionary assemblage of unicellular and multicellular protists including brown algae, diatoms, chrysophytes, water molds, slime nets, etc.[11]

B. hominis has been recognized as a common inhabitant of the human intestinal tract for many years, although its taxonomic position remains uncertain. Recent evidences, however, indicates that *B. hominis* is potentially pathogenic, a) if it is found in stool in remarkable quantity, i.e. five or more cell per x 40 microscopic field, b) the absence of other pathogenic organisms in the sample and c) response to treatment with iodoquinol or metronidazole. The presence or the absence of clinical symptoms depends on the interaction between the host and parasite. Although it is less clear, commensally organisms may become pathogenic opportunistically.[3,5-6]

B. hominis has three morphological forms (vacuolar, granular and amoeboid), but recent studies have revealed several additional forms; cyst, avacuolar, and multivacuolar. The mode of transmission is uncertain, but probably with fecal-oral route. The disease is characterized by acute or chronic and recurrent diarrhea, sometimes self-limited, accompanied by abdominal pain, tenesmus, anorexia, nausea and/or vomiting, cramps, fatigue and fever. In immunosuppressed patients, the outcome is generally severe.[5]

The prevalence of *B. hominis* has been found to be similar in asymptomatic and symptomatic patients by Udkow and Markell.[9,13] Its prevalence varies from place to place and according to the studied population. The prevalence of *B. hominis* in healthy persons was reported between 0.5% and 20.3%. On the other hand, its prevalence was detected as 43% in homosexual persons and between 25% and 46% in AIDS patients. Its prevalence, in Turkey varies from 1.15% to 13.16% in healthy persons but there is no information about the immunocompromised persons. The prevalence of *B. hominis* (7.7%) was found to be similar to that reported in healthy persons. Even though the prevalence (10.9%) was highest in the samples obtained from patients with malignancy, it was not different from that reported in healthy persons.[3,8-9]

CASE ILLUSTRATION

Mr J 29 years old, single, lived in Jakarta, came to hospital with chief complaint in abdominal pain since two weeks before admission. Since two months before admission the patient felt abdominal pain and discomfort in his stomach. He often felt nausea and vomiting, lost of appetite, decreased of body weight, diarrhea and mild fever. Since two weeks before admission his abdominal pain worsened, his abdomen was very painful. The pain was localized. The patient had constipation but he could flatus. Urination was normal.

Beside those problems, he also had cough with white sputum without blood streak. There was no history of shortness of breath or night sweat. When the patient came to the hospital, he was on treatment of tuberculosis for 8 months from public medical services (primary health care). Before that the patient came to other hospital, under went chest X-ray and was given anti TB drug for one month but he stopped the medication by himself because he felt better. He under went a test for HIV in hospital and the result was positive.

There was no history of illness, no history of family illness. He was an intravenous drug abuser for 10 years. He used needle together with his friends. He also used marijuana and other illegal drugs. He was jobless. He had been smoking for 15 years, minimum 1 pack a day. He was a last son of 4 children in the family.

A physical examination, patient looked seriously ill, fully alert. Blood pressure was about 100/70 mmHg, heart pulse about 100 x/minute, respiratory rate about 28x/minute and temperature about 37.8^{o}C. Body weight 165 cm and body height 50 kg. The conjunctiva of the eye was pale, sclera was icteric. Ears, nose and throat was normal. Jugular vein pressure was 5-2 cm H_2O. There was oral thrush. Lymph node was palpable in left neck (½ cm x ½ cm x 1 cm). On chest examination, it was symmetrical on static and dynamic condition; breath sound was sonor, vesicular, there was rales in all hemisphere, no wheezing. Heart sound was normal, regular, there was no murmur and no gallop. Abdomen was not really distended, turgor was good, and there was a lamp in left upper region. The lamp size was 5 x 4 x 3 cm with unclear border and tenderness and undulation positive. Chessboard phenomenon was not found. Liver and spleen size was difficult to be evaluated because the patient felt very painful. Shifting dullness was found. The bowel sound was decreased.

Laboratory examination found microcytic

hypochromic anemia (hemoglobin level was 8.5/dl with MCV 76.9 fl, MCH 22 pg, and MCHC 25.1 g/dL). Leukocyte count was in normal range (leukocyte count 8,200/mm^3), but there was thrombocytopenia (thrombocyte count 128.000/mm^3). There was increase in erythrocyte sedimentation rate (ESR 110 mm). Ureum, creatinin and electrolytes were normal. Transaminase enzyme was increased (AST 82 U/l ALT 27 U/l). Urinalysis was normal. The albumin level was 1.9 g/dl and the globulin level was normal (6.1 g/dL). And the total bilirubin level was 10.3 mg/dl with increased direct bilirubin 7.8 mg/dl. Chest X-ray showed infiltrate in apex and basal, and there was pleural effusion. ECG was unremarkable.

The problems at admission were abdominal pain due to suspected intra abdominal mass with differential diagnosis peritoneal abscess or partial obstruction with impending perforation and tuberculosis (TB) peritonitis. The other problems are pulmonary TB with secondary infection, bisitopenia, HIV reactive, oral candidiasis, liver function disorder and hypoalbuminemia. It was planned to perform is feces analysis, ascites fluid analysis, USG abdomen, acid fast bacilli, gram, MOR, liver function test, seromarker for viral hepatitis, echocardiography, throat swap, diff count, ELISA, CD4, viral load and consultation to surgery department and psychiatry department. The patient was given O_2 2 liter/minute, IVFD of dextrose and normal saline, sistenol 500 mg three times daily, ceftriaxone 2 g once daily, intravenous metronidazole 500 mg three times daily, rifampisin 450 mg once daily, INH 300 mg once daily, and pirazinamid 500 mg twice daily and supplementation of vitamin B_6 10 mg, mycostatine 3 x 1 cc drop, and packed red cell transfusion until the hemoglobin level more than 10 g/dL.

Abdominal pain due to suspected intra abdominal mass with differential diagnosis peritoneal abscess or partial obstruction with impending perforation and tuberculosis peritonitis based on abdominal pain in whish the abdomen was not really distended, turgor was good, and there was a lump in left upper region. The size of the lump was 5 x 4 x 3 cm with unclear border, tenderness and undulation positive. Chessboard phenomenon was not found. Liver and spleen enlargement could not be evaluated because the patient felt very painful. Shifting dullness was found. The bowel sound was decrease.

Pulmonary tuberculosis with secondary infection based on chronic cough with sputum, fever, body weight loss, night sweat, history of tuberculosis treatment, moist rales in the lungs, palpable lymph nodes and no leukocytosis. Chest X-ray showed specific process.

Bisitopenia based on fatigue, lost of appetite, diarrhea, no bloody stool, tachypneu, tachycardia. Laboratory examination showed microcytic hypochrome anemia and thrombocytopenia. Microcytic hypochrome anemia was suspected due to iron deficiency with differential diagnosis anemia chronic disease and anemia of chronic bleeding.

The patient was HIV positive based on test the laboratory finding from UKI hospital. The patient was a drug abuser. He used needle together with his friends. He also used marijuana and other illegal drug. Oral candidiasis based on history of intravenous drug abuser for 10 years, oral thrush positive. Oral candidiasis was suggested due to HIV infection.

Liver function disorder based on elevated transaminase serum, thrombocytopenia, and hypo-albuminemia. This condition was suggested due to viral hepatitis B and C infection with differential diagnosis drug induced hepatitis. Hypoalbuminemia based on lost of appetite, diarrhea, and low level of albumin. Hypoalbuminemia was suggested due to malnutrition with differential diagnosis of malabsorption and liver function disorder.

In the next day, the patient condition worsened. His abdominal pain worsens, and the patient wanted to discharge. Digestive surgery department suspected an impending perforation with intra abdominal mass and suspected partial obstruction with differential diagnosis was suspected tuberculosis. The patient was consult to the department of psychiatry and the diagnosis from department of psychiatry was psychotic because of physical condition and withdrawal syndrome was very possible. It was planned to perform three position of abdominal X-ray. The patient was given nasogastric tube to decompress, but the tube was always pulled by the patient. The patient was not cooperative and really difficult to handle.

The result of USG showed hepatosplenomegali and ascites with a lot of fibrin. CD4 result was 67, seromarker of hepatitis C and HbsAg were positive. Patient and the family refused to do anything related to the surgery include three position of abdominal X-ray, but the patient was given hepatoprotector and cotrimoxasole.

In the 16th day after admission, the ascites fluid was taken with USG guidance. In USG there was a lot of fibrin. The clinical pathology analysis was failed because the fluid could not be analyzed. Analysis of parasitology from ascites fluid stated there were full of *Blastocystis hominis*, and the patient was suggested to receive intravenous Metronidazole 750 three times daily and ciprofloxacine 500 mg twice daily.

The patient escaped from hospital, but he came back to admission. The condition in his second admission was worse than the previous one. In the 20th day of hospitalization, the patient died due to sepsis.

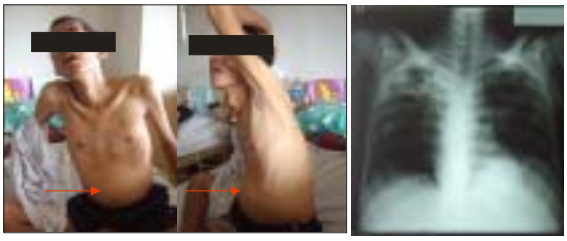

Figure 1. Patient condition with asymmetrical abdomen and his chest X-ray

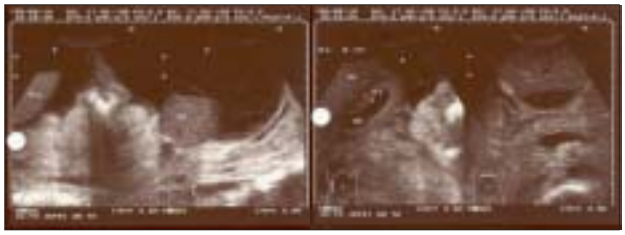

Figure 2. USG showed ascites, hepatomegaly and a lot of fibrin

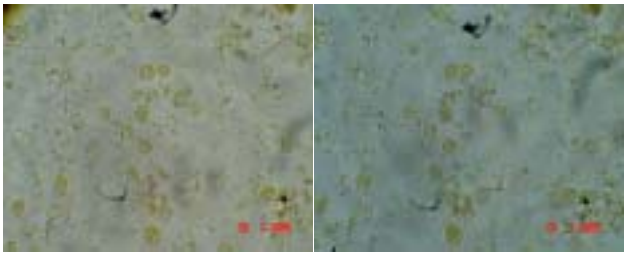

Figure 3. Full of *Blastocystis hominis* in the ascites fluid

DISCUSSION

This case is presented due to the increasing incidence of HIV infection. The incidence of *B hominis* would be increased is concordance with the increasing of HIV case. Beside that the patient has other opportunistic infection like lung TB and oral candidosis. This case can be a good sample of HIV case with the infection of commensal microorganism in human body. The case is more interesting because *B. hominis* was found in ascites fluid.

The patient was intravenous drug abuser for more than 10 years. He used needle together with his friends. Some of his friend was death because of HIV/AIDS. He also used marijuana and other illegal drugs. His HIV test was reactive with CD4 only 67. In the journal, during the course of HIV infection, most people experience a gradual decline in the number of CD4+ T cells, although some may have abrupt and dramatic drops in their CD4+ T-cell counts. A person with CD4+ T cells above 200 may experience some of the early symptoms of HIV disease. Others may have no symptoms even though their CD4+ T-cell count is below 200.[1,2] Lymph node of the patient was palpable in left neck (½ cm x ½ cm x 1 cm). As the immune system worsens, a variety of complications start to take over. For many people, the first signs of infection are large lymph nodes or "swollen glands" that may be enlarged for more than 3 months. Other symptoms often experienced months to years before the onset of AIDS include lack of energy, weight loss, frequent fevers and sweats, persistent or frequent yeast infections (oral or vaginal), persistent skin rashes or flaky skin, pelvic inflammatory disease in women that does not respond to treatment, short-term memory loss. Some people develop frequent and severe Herpes infections that cause mouth, genital, or anal sores, or a painful nerve disease called shingles.[1]

The patient was jobless. Many people are so debilitated by the symptoms of AIDS that they cannot hold a steady job nor do household chores. Other people with AIDS may experience phases of intense life-threatening illness followed by phases in which they function normally.[1]

The patient may, however, have a flu-like illness within a month or two after exposure to the virus. This illness may include fever, headache, tiredness enlarged lymph nodes (glands of the immune system easily felt in the neck and groin) these symptoms usually disappear within a week to a month and are often mistaken for those of another viral infection. During this period, people are very infectious, and HIV is present in large quantities in genital fluids. More persistent or severe symptoms may not appear for 10 years or more after HIV first enters the body in adults, or within 2 years in children born with HIV infection. This period of "asymptomatic" infection varies greatly in each individual. Some people may begin to have symptoms within a few months, while others may be symptom-free for more than 10 years.[1]

Even during the asymptomatic period, the virus is actively multiplying, infecting, and killing cells of the immune system. The virus can also hide within infected cells and lay dormant. The most devastating effect of HIV infection is a decline in the number of CD4 positive T (CD4+) cells found in the blood-the immune system's key infection fighters. The virus slowly disables or destroys these cells without causing symptoms.[1]

Since two months before admission the patient felt abdominal pain and discomfort in his stomach. He often felt nausea and vomiting, lost of appetite, decrease of body weight, diarrhea and mild fever. Since two weeks before admission his abdominal pain worsen, his abdomen was very painful, with no spread of pain. The patient has no defecation but he could flatus. Urination was normal. Symptoms of opportunistic infections common in people with AIDS include coughing and shortness of breath, seizures and lack of coordination, difficult or painful swallowing, mental symptoms such as confusion and forgetfulness, severe and persistent diarrhea, fever, vision loss, nausea, abdominal cramps, and vomiting, weight loss and

extreme fatigue, severe headaches, coma. One of the opportunistic infection is caused by *Blastocystis hominis*.[2,4-6]

Whether *Blastocystis hominis* can cause symptomatic infection in humans is a point of active debate. This is because of the common occurrence of the organism in both asymptomatic and symptomatic persons. Those who presume symptoms could be related to infection with this parasite have described a spectrum of illness including watery diarrhea, abdominal pain, perianal pruritus, and excessive flatulence.[5,7-9]

Diagnosis is based on finding the cyst-like stage in feces. Permanently stained smears are preferred over wet mount preparations because fecal debris may be mistaken for the organisms in the latter. Do not wash specimens in water (e.g. during concentration procedures) as this will lyses the organisms, resulting in false negatives.[7-9] In abdominal USG there was a lot of fibrin. The clinical pathology analysis was failed because the fluid was lyses. Analysis of parasitology from ascites fluid stated there were full of *Blastocystis hominis*, and the patient was suggested to receive intravenous metronidazole 750 mg three times and ciprofloxacine 500 mg twice daily. The next step should be analysis of the feces, but the patient and the family was not really cooperative at the time and the patient discharged without doctor's permission from hospital. When we would check it the patient became worse and finally he died before we analyzed his feces. How *B. hominis* could be found in ascitic fluid might be due to perforation of the gut.

Blastocystosis is caused by *Blastocystis hominis*, a parasite that commonly resides in the caecum and large bowel of human beings. The pathogenicity of *B hominis* has been an issue of controversy. Initially, it was known as commensal organism of intestinal tract, however, recent information from retrospective studies and experimental models in animals support its pathogenicity. Blastocystosis has been characterized by symptoms including diarrhea, abdominal pain, nausea, vomiting, flatulence, anorexia, and malaise and has been implicated in patients diagnosed with irritable bowel syndrome. Data on treatment of blastocystosis are limited primarily to anecdotal studies in which metronidazole and iodoquinol, the most commonly recommended therapies, were used showing variable results.[2] A recent, single-blind, placebo-controlled study of metronidazole administered 1.5 g/day for 10 consecutive days showed improvement of diarrhea in the metronidazole-treated group and a higher rate of parasite clearance.[13-15] The patient was given intravenous metronidazole 500 mg three times daily and ciprofloxacin 500 mg twice daily but it only last for 2 days because the patient was died. In the literature the most recommended quinolone is iodoquinolone but in Indonesia it is very difficult to find the regimen.

In recent journal said that Nitazoxanide is indicated in the United States for treatment of persistent diarrhea caused by *Giardia* and *Cryptosporidium* and is being investigated for treatment of diarrhea caused by enteroviruses, *Clostridium difficile*-associated diarrhea, and Crohn's disease. It is active against a broad range of enteropathogens including protozoa, bacteria, and viruses by 3 mechanisms: interference with energy metabolism in anaerobic organisms (protozoa and bacteria), inhibition of transcription/ replication in infected cells (viruses), and inhibition of secretion of proinflammatory cytokines. Double-blind, placebo-controlled clinical studies have shown that a 3-day course of nitazoxanide is effective in treating diarrhea and enteritis caused by *Cryptosporidium* species, *Giardia intestinalis*, and *Entamoeba histolytica*, and in eliminating the organisms from the stool. The same course of treatment also has been reported to be effective in treating enteric infections caused by *B. hominis*, *Balantidium coli*, and *Cyclospora cayetanensis*.[15]

The patient has symptom of abdominal pain and chronic diarrhea. From USG we found a lot of fibrin. In physical examination there was no chest board phenomenon. He also has lung TB. The differential diagnosis of the abdominal pain was peritonitis TB. The analysis of the ascitic fluid was failed because the fluid was lyses.

When the patient comes to the hospital, he has been in tuberculosis medication for 8 months from public medical service (primary health care). Before that the patient has come to private hospital, did chest X-ray and was given tuberculosis drugs for 1 month but he stopped the medication by himself because he was getting better. Lymph node was palpable in left neck (½ cm x ½ cm x 1 cm). On chest examination, it was symmetrical on static and dynamic condition; it was sonor, vesicular, there was rales in all hemisphere, no wheezing. The patient was given rifampisin 450 mg once daily, INH 300 mg once daily and pirazinamid 500 mg twice daily and supplementation of vitamin B_6.[16-20]

It is necessary to treat patient with lung TB in HIV consider that mortality rate is higher than lung TB in HIV patient. Therapy for lung TB improvement TB symptoms but also in markers of HIV disease as CD count rise and viral loads fall independent of specific therapy for HIV. Principally the treatment not quietly different. But there are special consideration include the potential for drug interaction when antituberculosis therapy and antiretroviral co administered, timing for initiation of HIV related therapy for person diagnosed with both infections

simultaneously, the potential for prolongation of therapy in persons with advanced immunosupression due to HIV infection. Not adjustment in dosage of anti tuberculosis medication for HIV-infected person. Although the poor absorption of anti tuberculosis drugs in HIV-infected person has been theoretical concern, poor absorption leading to failure has been rarely reported and not to be clinically significant.[1-2]

Patient with HIV/AIDS and TB infection at the same time is recommended to start treatment for TB promptly. For patient who has diagnosis of TB and HIV simultaneously, treatment for TB must be initiated but the decision about when to start antiretroviral therapy is still controversial. Most of the centers suggest the administration of Anti Retroviral (ARV) after two-month treatment of TB after initial phase.[2,17-20] The patient has not given ARV yet because the transaminase enzyme was elevated due to viral hepatitis B and C infection.

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