Penicillium Marneffei Mesenteric Lymphadenitis in Human Immunodeficiency Virus -infected Children

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Abstract

Disseminated *P. marneffei* infection is one of the common opportunistic infections seen in HIV-infected patients in Southeast Asia. We report 3 cases of HIV-infected children with mesenteric lymphadenitis presented with prolonged fever and abdominal pain. The first two patients were diagnosed as peritonitis and acute appendicitis prior to exploratory laparotomy. Operative findings revealed multiple enlarged mesenteric lymph nodes. Histopathologic findings of mesenteric lymph nodes biopsy were characteristic for *P. marneffei* infection. Mesenteric lymphadenitis in the last patient was diagnosed by abdominal ultrasound. All three cases had positive blood and bone marrow cultures for *P. marneffei*. These patients were treated with amphotericin B. Fever declined in 3-6 days. The first two patients survived but the last one subsequently died from underlying hemophilia A (GI bleeding).

Conclusion: Acute mesenteric lymphadenitis can be one of the unusual manifestations caused by *P. marneffei*. Southeast Asia is an endemic area for *P. marneffei* and is severely affected by acquired immunodeficiency syndrome epidemic. Therefore, mesenteric lymphadenitis should be considered in HIV-infected persons who present with prolonged fever and abdominal pain.

Penicillium marneffei is a fungus which can cause systemic mycosis in both healthy and immunocompromised hosts[1-4]. Since the current epidemic of HIV infection in Thailand, there are an increasing number of cases of *P. marneffei* infection among HIV-infected persons[3,4]. Here we report three cases of *P. marneffei* mesenteric lymphadenitis in HIV-infected children.

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CASE 1

A 3 year old girl presented with abdominal pain and fever for 2 weeks. No history of vomiting, constipation and diarrhea was noted. She had been treated as viral gastroenteritis and dyspepsia at a private clinic without improvement. Physical examination revealed multiple cervical and inguinal lymph nodes enlargement, generalized abdominal guarding and tenderness, positive rebound tenderness and decreased bowel sound. No hepatosplenomegaly were detected. Initially, the patient was suspected to have a ruptured acute appendicitis. Subsequent exploratory laparotomy was performed. The operative findings were multiple and matted mesenteric and para-aortic lymph nodes enlargement with chylous ascites. Mesenteric lymph node biopsy was carried out and revealed *Penicillium marneffei* infection. Anti HIV-antibody was checked and found to be positive. Other investigations are shown in Table 1.

CASE 2

A 7 year old boy with a 3 weeks' history of fever and abdominal pain was admitted to the Pediatric Surgery ward. The initial diagnosis was acute appendicitis. He underwent exploratory laparotomy which revealed generalized mesenteric lymphadenitis and a normal appendix. The meseteric lymph nodes were biopsied. Post-operatively, the fever and abdominal pain appeared to be subsiding. The patient was therefore discharged. Two weeks later, he was readmitted with abdominal distension and vomiting. Physical examination revealed body temperature of 40°C, distended abdomen, hepatosplenomegaly and generalized lymphadenopathy. He also had papular skin lesions with central umbilicated necrosis on his face and extremitries. Anti-HIV antibody test was positive. The skin and bone marrow smear revealed organisms characteristic of *P. marneffei*. The rechecked histopathology of the mesenteric lymph nodes revealed *P. marneffei* organism. The skin, bone marrow, mesenteric lymph nodes and blood cultures were positive for *P. marneffei*. He was treated with amphotericin B and gradually responded. Other investigations are shown in Table 1.

CASE 3

A 6 year old hemophiliac boy had acquired HIV infection through blood transfusion several years ago. Two weeks before admission, he had abdominal pain, diarrhea and fever. Physical examination revealed hepatosplenomegaly, mild tenderness and generalized abdominal guarding. Ceftriazone was given with the initial impression of recurrent salmonella bacteremia. He deteriolated and his hemocultures for bacteria were negative. Abdominal signs of peritonitis were clearly present at this time. Abdominal ultrasound demonstrated intra-abdominal lymphadenopathy with ascites (Fig. 1). His initial two hemocultures were later reported as growing *P. marneffei*. Bone mar-

Table 1. Laboratory investigations.

	case 1	case 2	case 3
Hematologic findings			
Hemoglobin (mg/dl)	9.7	7.1	9.4
Hematocrit (%)	29.8	23	30
White blood cell count (/mm^3)	3,150	7,400	4,400
Platelet (/mm^3)	140,000	73,000	219,000
Abdominal ultrasound	not done	multiple small (<1 cm) round hypoechoic lesions at porta hepatis (lymphadenopathy)	Matted enlarged multiple lymph nodes around celiac artery and mesenteric vessels
Microbiological findings			
Mesenteric lymph node biopsy	*P. marneffei*	*P. marneffei*	not done
Bone marrow smear	*P. marneffei*	*P. marneffei*	*P. marneffei*
Skin lesion smear	not done	*P. marneffei*	not done
Bone marrow culture	*P. marneffei*	*P. marneffei*	not done
Hemoculture	*P. marneffei*	*P. marneffei*	*P. marneffei*

Fig. 1. The abdominal ultrasound shows round multiple hypoechoic lesions representing intra-abdominal lymphadenopathy.

row aspiration performed due to bicytopenia demonstrated the presence of *P. marneffei*. Amphotericin B was therefore started with clinical improvement noted on the 4th day. Unfortunately, later in the course of treatment he died from severe gastrointestinal hemorrhage.

DISCUSSION

Opportunistic infections are increasing among HIV-infected patients. *Penicillium marneffei* infection is one of the common opportunistic infections seen in South East Asia[1-4]. Common clinical and laboratory features of disseminated *P. marneffei* infection include high fever, generalized lymphadenopathy, hepatosplenomegaly, papular skin lesions with central umbilication, severe anemia and thrombocytopenia[3,4]. Gastrointestinal diseases in HIV-infected patients have been reported to be caused by various etiologies, such as cytomegalovirus, Cryptosporidium, *Mycobacterium* species, *Histoplasma* species, *Microsporidium* and malignancies[5,6]. Our report added another etiology to the gastrointestinal diseases in HIV-infected patients. It presents another manifestation of disseminated *P. marnefferi* infection which has clinical features of abdominal pain and signs of peritonitis on physical examination. Surgical conditions were difficult to exclude, which led to unnecessary exploratory laparotomy in the first two patients. The last patient also had diarrhea which might be the presentation of *P. marneffei* colitis as was reported in an adult patient[7]. Although our patients did not have intestinal perforation, the delay in diagnosis and treatment might have led to this complication as has been reported with another fungal infection, *Histoplasma capsulatum*[6].

Amphotericin B is an effective drug for the treatment of disseminated *P. marneffei* infection. In this report, fever declined from 3 to 6 days after initiation of amphotericin B. Long term prophylaxis may be necessary[8]. Despite regular oral ketoconazole prophylaxis, the second patient had a recurrent disseminated *P. marneffei* infection 12 months following the first episode.

Avoiding unnecessary abdominal surgery in HIV-infected patients who present with acute abdomen is difficult. In this report, these patients may have other clues of disseminated *P. marneffei* infection, such as, characteristic skin lesion smear and/or bone marrow aspiration smear[4]. The abdominal ultrasound which showed multiple enlarged mesenteric lymph nodes was also very helpful.

SUMMARY

Acute mesenteric lymphadenitis can be one of unusual manifestations caused by *P. marneffei* infection. Southeast Asia is an endemic area for *P. marneffei* and is severely affected by an acquired immunodeficiency syndrome epidemic. Therefore, mesenteric lymphadenitis should be considered in HIV-infected persons who present with prolonged fever and abdominal pain.

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การติดเชื้อเพนิซิลเลียม มาร์เนฟฟีไอ ที่ต่อมน้ำเหลืองในท้อง ของผู้ป่วยเด็กที่ติดเชื้อเอดส์

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โรคติดเชื้อทุติยภูมิที่พบได้บ่อยในผู้ป่วยเด็กเอดส์ โดยเฉพาะแถบเอเชียตะวันออกเฉียงใต้คือ การติดเชื้อ *P. marneffei* รายงานนี้รายงานผู้ป่วยเด็ก 3 รายที่วินิจฉัยเป็น mesenteric lymphadenitis จากเชื้อ *P. marneffei* โดยมีอาการไข้สูงเป็นเวลานานร่วมกับอาการปวดท้อง ผู้ป่วย 2 รายแรกได้รับการวินิจฉัยเป็น peritonitis และ acute appendicitis ก่อนถูกนำไปผ่าตัด ผลการผ่าตัดพบเพียง multiple enlarged mesenteric lymph nodes และจากผลชิ้นเนื้อพบเชื้อ *P. marneffei* สำหรับผู้ป่วยรายสุดท้ายได้รับการวินิจฉัยโดยการทำ ultrasound ประกอบกับผู้ป่วยทั้ง 3 ราย มีการเพาะเชื้อในเลือดและในไขกระดูกให้ผลบวกต่อเชื้อ *P. marneffei* ผู้ป่วยได้รับการรักษาด้วย Amphotericin B ไข้ลงใน 3-6 วัน ผู้ป่วยรายสุดท้ายเสียชีวิตจากเลือดออกในทางเดินอาหาร

สรุป ภาวะ acute mesenteric lymphadenitis จากเชื้อ *P. marneffei* เป็นภาวะที่พบได้ในผู้ป่วยที่ติดเชื้อเอดส์ และมีอาการไข้สูงเป็นเวลานานร่วมกับอาการปวดท้องโดยเฉพาะอย่างยิ่งถ้าอาศัยอยู่แถบเอเชียตะวันออกเฉียงใต้ ซึ่งเป็น endemic area ของ *P. marneffei*

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