Indian J Gastroenterol (March–April 2017) 36(2):141–144
DOI 10.1007/s12664-017-0741-9

CASE SERIES

Gastrointestinal manifestations of melioidosis: A single center experience

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Received: 30 November 2016 / Accepted: 9 March 2017 / Published online: 29 March 2017

Abstract Melioidosis, being increasing, is reported from India. Gastrointestinal manifestations are typically reported as unusual cause of liver and/or splenic abscess. We aimed to describe various gastrointestinal manifestation of melioidosis in the present study. We retrospectively collected data of culture positive melioidosis cases from hospital database during August 2014–October 2016 at Asian Institute of Gastroenterology, Hyderabad. A total of nine culture positive cases (8 male) of melioidosis with median age of 40 years (range 23–66) were analyzed. Median duration of symptoms was 45 days. Two patients were being treated as tuberculosis. Three patients presented with liver abscess with two of them having simultaneous splenic abscess, and one had prostatic abscess. Three patients (43%) with history of acute pancreatitis had infected pancreatic collection, and one patient had left empyema with splenic abscess. One patient had wound infection with left lower limb cellulitis, presented as acute in chronic liver failure and another as spontaneous bacterial peritonitis (SBP). Diabetes and/or alcoholism was present in all patients. Seven patients had disseminated organ involvement. Seven patients underwent percutaneous intervention for drainage of abscess. Induction therapy as ceftazidime (n=4) or meropenem (n=5) followed by continuation therapy as oral cotrimoxazole (n=6) and doxycycline (n=1) was given. Six patients completed therapy and asymptomatic at end of follow up. Two patients died in the study period. One patient died due to acute-on-chronic liver failure (ACLF) with acute kidney injury and the other due to cardiac failure. One patient with SBP had lost to follow up. Apart from being unusual cause of liver/splenic abscess, melioidosis can present with infection of pancreatic collection, SBP, and infection in a compensated cirrhosis which can precipitate ACLF. Early recognition and specific therapy can improve prognosis.

Keywords Acute-on-chronic liver failure · Melioidosis · Pancreatitis · Spontaneous bacterial peritonitis

Introduction

Melioidosis is caused by the gram-negative soil-dwelling bacillus *Burkholderia pseudomallei*, which mainly present as pneumonia and multiple abscesses [1]. Melioidosis is endemic in North Australia and Southeast Asia with annual incidence rates of up to 50 cases per lakh people. In India, increasing number of cases of melioidosis are being diagnosed and reported mainly from South India; however, there is substantial under-reporting [2]. Recent study reported four *B. pseudomallei* isolates in the soil of the coastal areas in the South India, which can give insight into epidemiology of melioidosis in India [3]. It carries mortality as high as 40% in Thailand, exceeded by only human immunodeficiency virus (HIV) and tuberculosis. Various risk factors such as diabetes mellitus, excessive alcohol consumption, chronic renal disease, and rural residence are associated with melioidosis. *B pseudomallei* infection has varied clinical manifestations, and severity varies from an acute fulminant septic illness to a chronic infection which may mimic malignancy or tuberculosis [1].

Melioidosis is considered as unusual cause of the multiple splenic and/or liver abscesses. Pancreatic involvement in melioidosis has been scarcely reported and typically manifests as multifocal micro-abscesses which is associated with

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pancreatic abnormalities [4]. In this series, we described culture positive patients with melioidosis presenting with gastrointestinal (GI) manifestations at a single super speciality tertiary health care center in South India.

Methods

After approval from institutional review board, we retrospectively collected data of nine culture positive melioidosis cases during August 2014–October 2016. We collected data from hospital database using standardized format which included baseline demographic, risk factors (occupation, alcohol abuse, diabetes mellitus, history of corticosteroid or other immunosuppressant medications, and other concurrent diseases), clinical feature, laboratory, imaging, and microbiological data. Radiological interventions, antimicrobial therapy, and clinical outcome in the hospital and during follow up were collected. Microbiologically, the growth of *B. pseudomallei* was identified by typical appearance of 1–2 mm silver white "oil paint" like glistening colonies with central umbonation after 72 h of incubation (Fig. 1).

Results

Summary of the eight culture-proven of melioidosis cases are shown in Tables 1 and 2. Eight patients were male. Median age was 40 years (range 23–66 years). All except one patient presented during rainy season (June to October). Median duration of symptom was 45 days (range 2 days to 6 months). All patients had fever at presentation, six patients had abdominal pain, and one patient each had dyspnoea and left lower limb cellulitis. Three patients presented with liver abscess with two of them having simultaneous splenic abscess, and one patient had prostatic abscess. Three patients (43%) with history of acute pancreatitis had infected pancreatic collection, and one patient had left sided empyema with splenic abscess. One patient had wound infection with left lower limb cellulitis, who was known case of compensated cirrhosis due to nonalcoholic steatohepatitis (NASH), presented as acute-on-chronic liver failure (ACLF). Another patient with decompensated chronic liver disease–NASH related presented with spontaneous bacterial peritonitis. Two patients were being treated as tuberculosis with anti-tubercular therapy by primary care physician before melioidosis was diagnosed. Diabetes mellitus and alcoholism were the risk factors with each patient suffering from either of them. Mean hemoglobin and TLC were 8.9 (±1.8) gm/dL and 13,633 (±3593) cells/mm^3, respectively. Mean albumin was 2.4 (±0.5) gm/dL. Five (55.5%) patients had both pus and blood positive for *B. pseudomallei*. All patients had positive pus cultures. One patient each had positive urine, pleural, and ascites fluid culture.

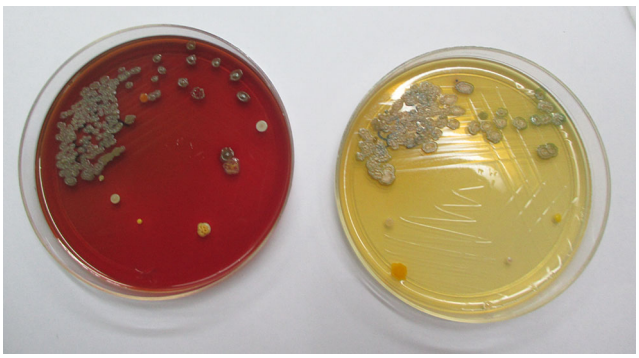

Fig. 1 Blood and chromogenic agar showing white glistening "oil paint" like colonies with central umbonation

Two weeks induction therapy either with injectable ceftazidime (50 mg/kg up to 2 g of IV every 6 hours in total four patients) or meropenem (25 mg/kg up to 1 g of IV every 8 hours in total four patients) followed by oral cotrimoxazole (240/1200 mg twice daily in six patients), or oral doxycycline (100 mg twice daily in one patient) for 6 months as continuation therapy. Two patients (25%) underwent percutaneous drainage of liver abscess, two patients (25%) underwent percutaneous drainage of infected pancreatic collection, and one patient each required transrectal drainage of prostatic abscess and intercostal drainage of empyema. Drainage catheters placed were removed successfully in all patients during follow up. Two (25%) patients were being treated as tuberculosis by primary care physicians before final diagnosis of melioidosis was made. Total of two patients (22.2%) died in the study period. One patient with ACLF died during hospitalization due to sepsis and acute renal failure, and another patient died within 1 month of diagnosis due to cardiac failure. One patient with SBP had lost to follow up after completion of 2 weeks of induction therapy. The remaining six patients were asymptomatic at the end of the treatment. Median duration of follow up was 9 months (range 11 days to 14 months).

Discussion

Burkholderia pseudomallei have been classified by the Center for Disease Control and Prevention as a category B bioterrorism agent [1]. Melioidosis is an infectious disease caused by small, motile gram negative, oxidase positive bacilli *Burkholderia pseudomallei* [1]. It was previously classified as part of the pseudomonas genus; it is phylogenetically related to Burkholderia *mallei* which causes glanders. It grows on standard bacteriologic media, forming colonies that vary from mucoid and smooth to rough and wrinkled and in color from cream to orange [3].

Human infection probably originates from soil, fresh water, and rice paddies by contamination of skin abrasions and possibly by ingestion or inhalation. Melioidosis may manifest

Table 1 Case wise demographic and clinical presentation

Case	Age (years)	Sex	Presentation month	Duration of symptoms (days)	Symptoms	Risk factors and underlying disease
1	39	M	September	60	Fever, abdominal pain	DM
2	40	M	September	45	Fever, abdominal pain	Ethanol, AP
3	30	M	June	120	Fever, weight loss	Ethanol
4	37	M	July	30	Abdominal pain, fever	Ethanol, AP
5	55	M	October	90	Dyspnoea, fever, and abdominal pain	DM
6	42	M	May	90	Fever, abdominal pain	DM
7	23	F	August	30	Abdominal pain, fever, dyspnoea	DM
8	66	F	October	2	Fever, left lower limb cellulitis	DM, CLD
9	56	M	October	15	Fever, abdominal pain	DM, CLD

DM diabetes mellitus, *AP* acute pancreatitis, *CLD* chronic liver disease

itself as acute, subacute, or chronic infection. In a large prospective study of 540 patients from Australia, most common presentation was pneumonia (51%), followed by genitourinary infection (14%), skin infection (13%), bacteremia without evident focus (11%), septic arthritis or osteomyelitis (4%), and neurologic involvement (3%) [5]. It was first reported from India in 1991 and since then various case reports and case series [6] have been published. According to Indian studies, clinical presentation of melioidosis is similar to published literature worldwide; however, there is relatively higher proportion of musculoskeletal, dental, and lymph node involvement as compared to endemic areas [5, 7]. Being a single super speciality center, all of the cases in this study were having predominant GI manifestation which could lead to selection bias.

In the present study, all patients presented with high grade fever of varying duration (median duration 45 days; range 2 days to 6 months). Predisposing factors either diabetes or alcoholism were present in all patients. Majority patients presented between June and October which indicate its association with rainy season, as described in previous studies [8]. Three patients presented liver abscesses out of which two had splenic involvement and one had prostatic abscess. One patient had empyema with splenic abscess and one had left lower

Table 2 Case wise laboratory, imaging, and therapeutic interventions

Case	Hb	TLC	Alb	Organ involved	Culture		Intervention	Antibiotics	Outcome
					Blood	Pus			
1	9.8	18,700	3.5	Liver, prostate	−	+Urine	PCD, transrectal drainage	Ceftazidime + Cotrimoxazole	Improved
2	10.1	14,400	2.5	Pancreatic fluid collection	+	+	STA	Ceftazidime + Cotrimoxazole	Improved
3	5.7	9500	2.6	Liver, spleen	+	+	PCD	Ceftazidime + Cotrimoxazole	Improved
4	9.2	8200	2.0	Pancreatic fluid collection	−	+	PCD	Meropenem + Cotrimoxazole	Improved
5	12.2	18,400	2.3	Spleen, lung	−	+Pleural fluid	ICD	Meropenem + Doxycycline	Died–Cardiac failure <1 month
6	8.4	14,300	2.1	Liver, spleen	−	+	Not done	Meropenem + Cotrimoxazole	Improved
7	9.5	15,000	2.0	Pancreatic fluid collection	+	+	PCD	Ceftazidime + Cotrimoxazole	Improved
8	7.9	11,500	2.0	Lower limb cellulitis	+	+	Incision and drainage	Meropenem	Died–ACLF with MODS index admission
9	7.4	12,700	2.8	SBP	+	+Ascites	Not done	Meropenem	Lost to follow up

Hb hemoglobin, *TLC* total leukocyte count, *Alb* albumin, *SBP* spontaneous bacterial peritonitis, *PCD* percutaneous drainage, *STA* single time aspiration, *ICD* intercostal drainage, *ACLF* acute-on-chronic liver failure, *MODS* multiorgan dysfunction syndrome

limb cellulitis. The remaining three patients had infected pancreatic collections. Disseminated involvement was seen in 7/9 (77.8%) patients, and localized involvement is 2 (22.2%) patients who had infected pancreatic fluid collections. Patients with disseminated disease had either more than one organ involvement (4 patients) or blood cultures were positives (3 patients). Drug sensitivity pattern in this study was similar to previously published reports [9]. We used 2 weeks of induction therapy either with injectable ceftazidime or meropenem followed by oral cotrimoxazole (240/1200 mg twice daily) or oral doxycycline (100 mg twice daily) for 6 months as continuation therapy. Six patients who completed therapy were asymptomatic at the end of the treatment.

Uniquely in this study, three patients presented as infected pancreatic collections, out of which one had bacteremia. We consider infected pancreatic collections due to bacterial translocation from intestine. *B. pseudomallei* could have been acquired by ingestion. Pancreatic involvement in melioidosis can range from multifocal microabscesses to focal large collection [4]. Extrahepatic infection can commonly precipitate ACLF. One patient had ACLF precipitated by left lower limb cellulitis due to melioidosis which to our knowledge is the first case being reported. One patient presented as SBP. *B. pseudomallei* and other Burkholderia species have been reported as causes of SBP in few case reports [10]. Two patients were initially misdiagnosed as tuberculosis which delayed correct diagnosis and treatment initiation.

Melioidosis is being increasingly reported worldwide. Misdiagnosis as tuberculosis in subacute and chronic melioidosis can delay diagnosis with dismal outcomes. Melioidosis can present not only as unusual cause of liver/splenic abscess but also with pancreatic involvement and SBP and can precipitate ACLF. Increasing awareness among health care workers, high index of suspicion, improved microbiological methods, and prompt initiation of treatment can give better outcome in melioidosis. Further research in developing serological test for diagnosis, treatment strategies to reduce duration of treatment, and vaccine development is required.

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