Melioidosis – Case Reports and Review of Cases Recorded Among Bangladeshi Population from 1988-2014

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Abstract

Melioidosis, caused by *Burkholderia pseudomallei,* is a potentially fatal infectious disease. Early and correct diagnosis is important, as mortality in untreated melioidosis is high. The first case of melioidosis from Bangladesh was reported in 1988. Since then a few cases have been reported from Bangladesh. We report here four culture confirmed cases of melioidosis diagnosed in BIRDEM Genaral Hospital during May 2009 to April 2010.The detail demographic data, clinical features and outcome are discussed. We have also reviewed all the melioidosis cases among Bangladeshi population recorded from 1988 to 2014.

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Introduction

Melioidosis is an emerging infection in Bangladesh. It is a disease caused by *Burkholderia pseudomallei*, a Gram-negative bacterium, found in wet soil, mud and pooled surface water in the tropics and subtropics. It is endemic in many countries of the world.[1] Documented reports of melioidosis from Bangladesh have been few and sporadic. The first culture proven case was reported from Bangladesh in 1988.[2] Later on, in 2001 another case of melioidosis in an adult with diabetes mellitus was reported from BIRDEM hospital.[3]

With the existing geographical and climatic conditions and a susceptible population, Bangladesh seems to have ideal conditions for endemicity of this disease. Its true prevalence in Bangladesh is not known, due to misdiagnosis and under reporting. Moreover, many laboratories are not well equipped for the identification of *B. pseudomallei*. The organism may simply be labeled as *Pseudomonas* species or even discarded as contaminants.

Mortality associated with this infection is high and early diagnosis and specific antimicrobial therapy can minimize the fatal outcome.[4-6] Therefore, awareness regarding the disease and correct identification of the offending organism is important.

We report here four culture confirmed cases of melioidosis diagnosed in BIRDEM Genaral Hospital during May 2009 to April 2010. The detail demographic data, clinical features and outcome are discussed. We have also reviewed all melioidosis cases among Bangladeshi population recorded from 1988 to 2014.

Case 1 (2009)

A 60-year-old diabetic (Type 2) male from Tangail district presented with persistent high-grade fever and burning sensation during micturation for two months. He was initially treated for these complains in the local district hospital with intravenous ceftriaxone for 12 days, but fever did not subside. So, he was admitted in BIRDEM Genaral Hospital on 3rd November 2009 for better management. He had a history of successfully treated pulmonary tuberculosis ten years ago. Physical examination revealed low-grade fever. Spleen, liver and lymph nodes were not palpable. There was no documentation of per rectal examination of prostate

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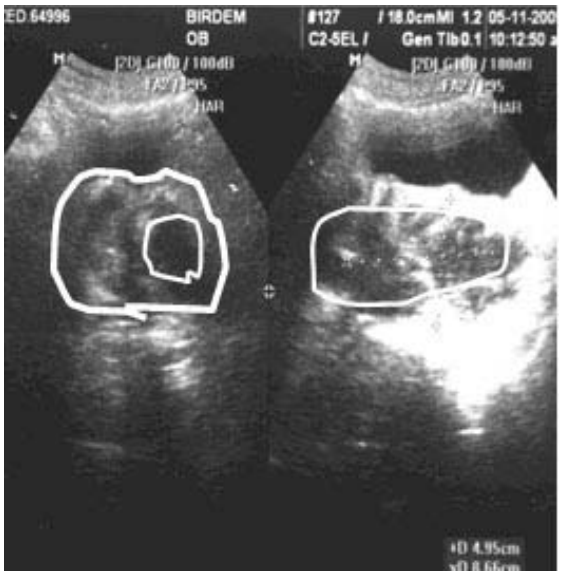

Fig.1: *Ultrasonography of prostate showing enlarged prostate with multiple hypoechoic areas suggestive of abscess. Left seminal vesicle was enlarged and loculated (Case -1)*

of this patient. His total leucocyte count was 10x10^9/L with a shift to left, ESR 150 mm in 1st hour, HbA1c 10.0%, fasting blood glucose 15.3 mmol/L. Other biochemical parameters were within normal limits. Ultrasound showed enlarged prostate with prostatic abscess involving left seminal vesicle and cystitis (Figure-1). Routine urine investigations revealed pyuria. Culture of the midstream urine grew oxidase positive, lactose fermenting gram-negative bacilli, which were identified as *Burkholderia pseudomallei* by standard biochemical test. The strain was resistant to gentamicin, netilmicin, aztreonam, cefotaxime, colistin and sensitive to ceftazidime, ceftriaxone, ciprofloxacine, cotrimoxazole, piperacillin and imipenem. Subsequently, transurethral resection of prostate (TURP) with endoscopic drainage of prostatic abscess was done. Pus and tissue were sent for further evaluation. Histopathology report revealed acute and chronic prostatitis with abscess. Pus from abscess yielded growth of *B. pseudomallei*. The antibiotic sensitivity pattern was same as the strain isolated previously from urine. He was treated with intravenous ceftazidime 1gm 8 hourly for four weeks and oral co-trimoxazole (800/160mg) twice daily. He was discharged after remission of fever and improvement of overall condition with advice to continue cotrimoxazole twice daily for a period of six months. On follow up after one month and six months after discharge, he was asymptomatic and his urine culture showed no growth.

Case 2 (2009)

In 2nd November 2009, a 65 years old diabetic man from Bhaluka, Mymensingh district presented with four months history of fever and abdominal pain. On admission, the patient was toxic with high-grade fever (103^0 F), tachypnoeic and slightly icteric, with pulse 122/min, BP 110/70 mmHg. Liver and spleen could not be palpated due to severe tender abdomen. Lymph nodes were not palpable. Her total leucocyte count was 17.2x10^9/L with a shift to the left with ESR-140 mm in 1st hour, fasting blood glucose 11.1 mmol/L, HbA1c 10.7%, SGPT 44 IU/L, SGOT 132 IU/L, serum bilirubin 1.2 mg/dl. Ultrasound showed hepatomegaly

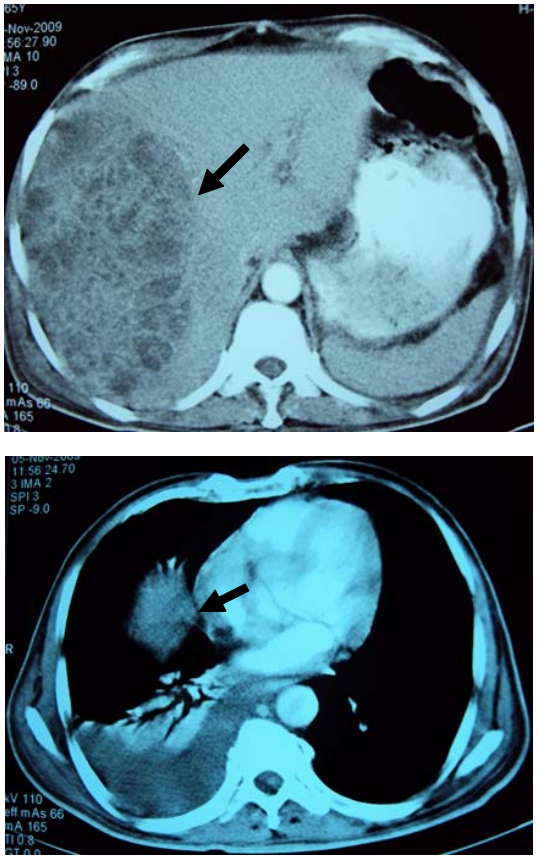

Fig.2: *CT scan of upper abdomen showing large multiloculated (reticular appearance) hypodense area in right lobe suggestive of abscess (Case 2)*

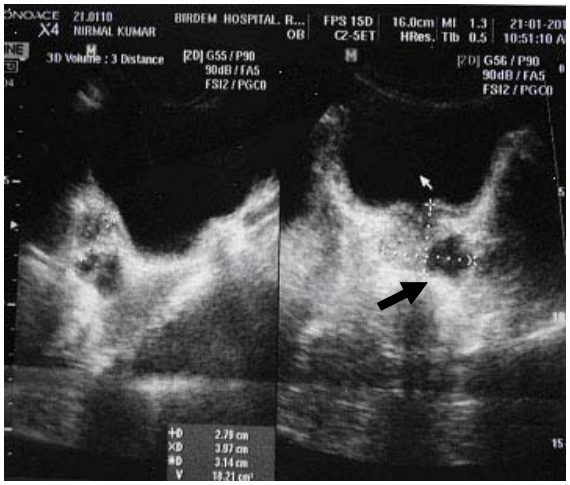

Fig.3: *Ultrasonography of prostate showing multiple hypoechoic areas suggestive of abscess (Case 3)*

with multiloculated cyst in liver. There was pleural effusion and cyst in the left kidney. Computerized tomography (CT) scan of upper abdomen revealed multiloculated liver abscess (Figure-2). He underwent ultrasonography (USG) guided aspiration of the suspected liver abscess. But, he went into septicemic shock following liver aspiration and expired on the 7th day of his admission. Pus culture from liver abscess grew gram-negative bacterium, which was subsequently identified as *B. pseudomallei*.

Case 3 (2010)

On 16th January 2010, a 41 years old diabetic man from Gazipur district presented to BIRDEM General Hospital with painful right ankle joint, three months history of low grade fever, weight loss and burning micturation for 4 days. He had been admitted in our hospital one month ago for similar pain in right ankle joint and was then diagnosed as a case of reactive arthritis with hyponatraemia and treated accordingly. At that time culture of urine was yielded no growth though pyuria was noted in routine microscopy of urine. Physical examination revealed low grade fever with tender and swollen right ankle joint. Liver and spleen was normal. There was no documentation of per rectal examination of prostate. Investigation revealed total leucocyte count $7.5x10^9$/L with a shift to left, ESR 130 mm in 1st hour, HbA1c 7.1%, fasting blood glucose 14.1 mmol/L and serum uric acid 2.9 mg/dl. The plain x-rays of right ankle joint were normal but USG of whole abdomen showed prostatic abscess (11x23mm; Figure-3)) and cholelithiasis. Urine microscopy showed pyuria and on culture *B. pseudomallei* grew, which was sensitive to ceftazidime, augmentin, cotrimoxazole, imipenem and resistant to amikacin, netilmicin, gentamicin, ciprofloxacin, polymixin B. He was treated for 45 days with intravenous ceftazidime 2 gm 8 hourly, followed by oral cotrimoxazole (800/160mg) twice daily for 20 weeks. The prostate abscess was not drained. He made a good recovery, remained well six months after discharge.

Case 4 (2010)

In 23rd January 2010, a 41 years old diabetic female from Savar, (about 27 km north of Dhaka city) presented with 20 days history of fever, cough, and breathlessness. Prior to admission in BIRDEM hospital on 23rd January'15, she was diagnosed as a case of diabetes mellitus with ketoacidosis and lung abscess in another hospital and was treated with intravenous ceftriaxone and levofloxacine. After recieving antibiotics for twelve days she continued to remain febrile, hence she was referred to our hospital. Physical examination was unremarkable. X-ray chest (P/A view) revealed a large lung abscess in right upper lobe (Figure-4). Sputum examination was negative for AFB. Blood analysis yielded haemoglobin 8.9 g/dl, total leucocyte count $8.23x10^9$/L with neutrophil 77%, ESR-120 mm in 1st hour, HbA1c 15%, blood glucose

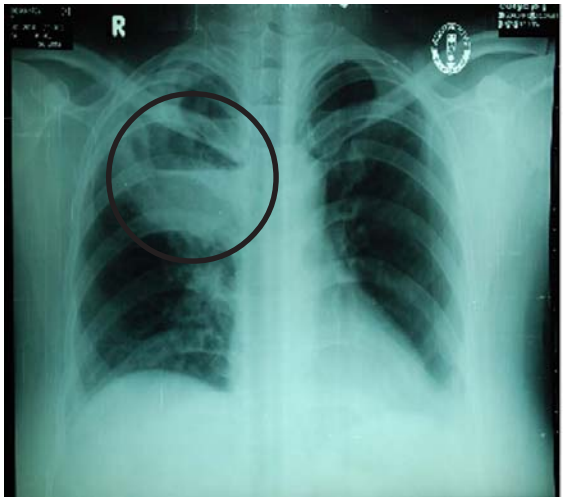

Fig-4: *X-ray chest (P/A view) showing large lung abscess in right upper lobe (Case 4)*

Table-1: *Summary of four cases of melioidosis described above*

Case	Age (yrs)	Geographical location	Occupation	underlying medical illness	Clinical features & findings	Organ involvement	B. *pseudomallei* isolated from	Outcome
1	60	Tangail	Business	DM	Fever, symptoms of UTI & prostate abscess	Prostate and UT	Urine and Pus from prostate	Cured
2	65	Mymensing Bhaluka	Farmer	DM	Fever, abdominal pain & tenderness liver abscess	Liver	Pus from liver	Died
3	41	Gazipur Kapasia	Teacher	DM	Fever,symptoms of UTI, joint tenderness prostate abscess	Prostate UT & joint	Urine	Cured
4	41	Dhaka Savar	Housewife	DM	Fever, cough, breathlessness lung abscess	Lung	Sputum	Cured

Note: DM: diabetes mellitus, HTN: hypertension, PTB: pulmonary tuberculosis, UT: urinary tract

2 hours after breakfast 9.2 mmol/L, serum cholesterol 202 mg/dl, triglyceride 144 mg/dl. Blood and urine culture were negative, but sputum culture yielded growth of *B. pseudomallei* which was sensitive to ceftazidime, tetracycline, augmentin, cefotaxime, imipenem but resistant to ciprofloxacin, cotrimoxazole, aminoglycosides and polymyxin B. She was treated with intravenous ceftazidime (120 mg/kg/day) and oral doxycycline 200 mg twice daily for initial one month. The patient showed marked clinical, microbiological and radiological improvement in one month. She was discharged with oral doxycycline 200 mg twice daily for six months.

Fig.5: *Culture shows the growth of B. pseudomallei in Blood (left) and MacConkey (Right) agar plates. Note the shiny metallic texture of the colonies.*

All four cases were culture confirmed (Figure-5) chronic suppurative form of melioidosis involving different organs of the body. The demographic data, clinical feature and outcome of the four cases described above are summarized in Table-1.

Discussion

Melioidosis, caused by *B. pseudomallei*, was first reported from our neighboring Rangoon in 1912. Since then, many cases of melioidosis have been reported in India, Srilanka, Thailand, Malaysia and many other countries of the world. Though Bangladesh has similar environmental and climatic conditions, only two cases of culture confirmed melioidosis have so far been reported during the period from 1988 to 2009.[2-3] Other six cases of melioidosis were reported among immigrant Bangladeshi population in UK between 1991 to 1999 (Table-2).[7-9] In 2007, a 90 years old Belgium traveler developed melioidosis after visiting Rangpur district of Bangladesh several times particularly in rainy months of the year.[10]

In the present report, we have described a cluster of four cases of chronic suppurative form of melioidosis diagnosed in our hospital during a period of 12 months from May 2009 to April 2010. All of the four patients presented

with fever and abscess in different organs of the body. Two out of the four patients had prostate abscess while one patient had liver and another had lung abscesses.

The presentation of melioidosis ranges from localized to systemic infection. Infection by the causative agent *B. pseudomallei* causes abscess formation in different organs of the body, which includes lung, liver prostate and soft tissues.[11-13] It presents as a febrile illness, ranging from acute fulminent septicemia to a chronic, debilitating localized infection. About 18% of adult males with melioidosis in North Australia had prostate abscess compared with fewer than 2% in Thailand.[14] The lung is another most commonly affected organ in melioidosis, which can present as acute or chronic pneumonia to abscess formation.[15] In our fourth case, cavitary lesion with large lung abscess in right upper lobe was seen in chest X-ray. Cavitary lesions may sometimes mimic the lesion seen in pulmonary tuberculosis, but diagnosis of melioidosis was demonstrated by isolation of *B. pseudomallei* from the sputum culture.

B. pseudomallei has been considered as a potential cause of liver abscess in India, Thailand and Malaysia.[4] The second case in our report highlights that this organism can be a potential cause of liver abscess in Bangladesh.

Melioidosis is most commonly associated with underlying diseases like diabetes mellitus, renal disease

Table-2: *Cases of melioidosis recorded among local and immigrant Bangladeshi population from 1988 to 2014 (Total cases - 15)*

Source & Year	No cases & Underlying disease	Anatomical Site (Specimen)	Geographical location of case in Bangladesh (District)
BIRDEM Hospital Record[a]			
Year 2013	Four cases; All 4 had DM	C1. Septicemia (Blood) C2. Facial cellulites (Pus) C3. Supraclavicular abscess (Pus) C4.Septicemia (Blood)	Gazipur Gazipur Gazipur Narayangang
Year 2014	Two cases; Both had DM	C1. Soft tissue (Pus) C2. Knee joint (Synovial fluid)	Khagrachari (CHT) Mymensingh
Published Case Reports			
Struelens et al,[2] 1988	Infant	Septicemia	Not mentioned
Kibbler et al,[3] 1991	DM	Pulmonary, Blood, BAL	Not mentioned (Immigrant in UK from Bangladesh)
Hoque et al,[8] 1999 (3 cases)	Three cases All 3 had DM	C1. Septic arthritis Rt elbow C2. Septic arthritis Rt knee C3. Septic arthritis, Multiple joints and prostate (Pus in all 3 cases)	Sylhet Sylhet Sylhet (All 3 were Immigrant in UK from Bangladesh)
Dance et al,[10] 1999	PTB	Not mentioned	Immigrant in UK
Nazimuddin et al,[3] 2001	DM	Abscess left shoulder, Pus	Sherpur
Ezzedine et al, 2007[10]	DM	Cutaneous (Pus) Belgian Traveler	Rangpur
Majumder et al,[17] 2013	DM	Multiple abscess (Seropositive, Culture not done)	Not mentioned

Note: Four cases described in Table-1 are not included in this Table. [a]All cases mentioned from BIRDEM Hospital record were culture positive. C=Case

and immunodeficiency disorders.[4-6] Of these, diabetes is the most common risk factor,[7,8] as was seen in our all four patients (Table-1). The estimated relative risk of melioidosis for diabetic patients was 13.1% in Australia.[4] Table-1 summarizes the presentation and organ involvement in four cases of melioidosis.

Mortality rate remains high, even with aggressive antibiotic therapy. In endemic areas mortality rate ranged from 19% to 68%.[4,6,12] One of our cases died before the diagnosis of melioidosis was made. It stresses the need for quick diagnosis and early initiation of appropriate treatment. The antibiotic of choice for melioidosis is ceftazidime. Imepenem is safe and effective and considered as alternatives to ceftazidime. Since relapse rates are high, initial parenteral treatment followed by maintenance therapy with cotrimoxazole (8-12 & 40-62 mg/kg/day) or doxycycline (4 mg/kg/day) or co-amoxyclav (20/5 mg/kg 8 hourly) for 12 to 20 weeks are recommended.[11,15,16]

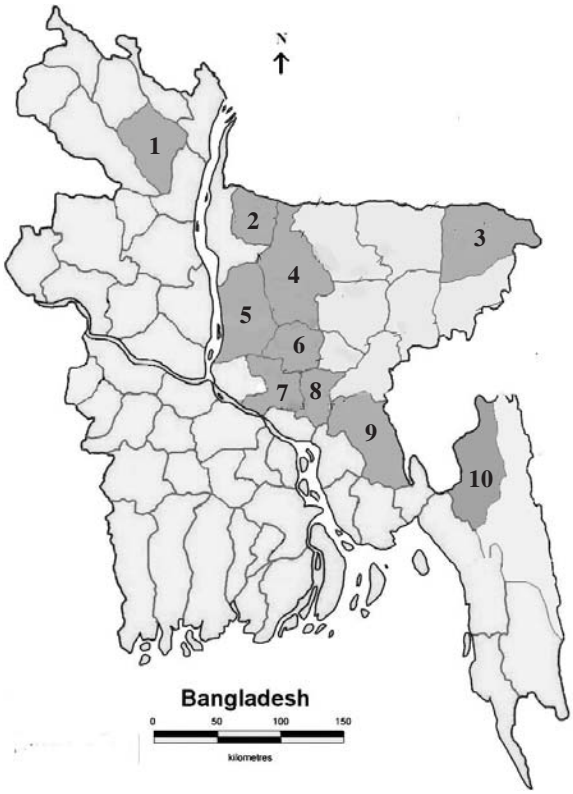

Fig.6: *Map showing geographical distribution of all recorded melioidosis cases in Bangladesh from 1988 to 2014. Note: 1-Rangpur, 2-Sherpur, 3-Sylhet, 4-Mymensingh, 5-Tangail, 6-Gazipur, 7-Dhaka, 8- Narayangang, 9-Comilla, 10-Khagrachari (CHT); Endemic districts shaded deep ash colour*

We have reviewed all known or reported cases of melioidosis detected in Bangladesh from 1988 to 2014. Altogether nineteen melioidosis cases (4 in Table 1 and 15 in Table 2) have so far been recorded either amongst the local or migrated Bangladeshi population. Out of nineteen cases, five cases of melioidosis were detected and reported from UK among Bangladeshi immigrant as 'imported cases'[7-9] while one was a 90 years-old Belgium traveler who stayed in northern district of Bangladesh (Rangpur) for sometime on several occasions.[10] Table-2 summarizes the clinical features and other epidemiological data of all those cases. Apart from the four cases described above, we have detected six more cases in BIRDEM General Hospital within the period from 2010 to 2014 (Table-2). Out of nineteen cases, majority had abscess in different parts or organs of the body while some developed septicemia. Even though the presentation of those cases varied but majority had diabetes mellitus as an underlying disease and risk factor. Out of nineteen recorded cases, few died which indicate that the outcome is favourable with correct and timely diagnosis of the condition.

The analysis of the geographical distribution shows that the melioidosis cases belonged to ten districts of the country of which seven were located in the north and northeast of capital Dhaka (Figure-6). The remaining three districts were located south of Dhaka, Narayangang, Comilla and Khagrachari (Chittagong Hill Tracts). Most of the recorded cases (16 out of 19) came from districts that are located north and northeast of Dhaka city. Majority cases came from Mymensingh, Gazipur, Sylhet and Sherpur districts of the country. Therefore, we consider those districts as the major endemic areas for melioidosis in Bangladesh.

The cases described and reviewed above indicate that melioidosis is endemic in Bangladesh particularly in north and northeastern districts of the country. Physicians and medical microbiologists should investigate for this important infection when diabetic patients, especially from endemic zone, present with characteristics clinical features. The prevalence of melioidosis is probably underestimated due to the lack of awareness among the microbiologists and doctors of the country about the disease. The true incidence of the disease in Bangladesh may actually be much higher than is currently believed. Therefore, systematic study is needed to determine the actual extent of the disease.

Rererences

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