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Melioidosis an Imported Infection in Qatar: Case Series and Literature Review

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Abstract

Introduction: Melioidosis is a tropical infectious disease caused by Gramnegative bacteria Burkholderia pseudomallei (B. pseudomallei). This soil-borne disease is endemic in Southeast Asia and Northern Australia. In our country it was reported once before in 2000 in a patient who presented with subdural empyema. Case Series Report: We are reporting six cases of Melioidosis presented to our hospital in very close time with different clinical presentations. All patients were from Indian subcontinent. In 3 cases we treated with Meropenem plus Trimethoprim-Sulfamethoxazole (TMP-SMX) followed by oral TMP-SMX and Doxycycline for around 6 months with good clinical and radiological response, while the fourth case was treated with oral TMP-SMX and Doxycycline for 1 month but he lost to follow up, the Fifth cases were treated with IV Ceftazidime followed by TMP-SMX and Doxycycline for 9 weeks, the Sixth cases were treated with IV Ceftazidime followed by TMP-SMX and Amoxicillin/Clavulanic acid for 20 days, there was no mortality reported in our case series for both types Bactraemic and Abactraemic Melioidosis. **Conclusions:** This case series highlights the importance of early identification of B. pseudomallei which requires a high index of clinical suspicion as well as good understanding of demographical and travel history. Microbiological identification of B. pseudomallei is essential and requires notification of the microbiologist for suspicion of that infection. Prolonged antimicrobial therapy is required for a better clinical outcome.

Keywords

Melioidosis, Bactraemic, Abactraemic Melioidosis, *Burkholderia* pseudomallei, Infection

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1. Introduction

Melioidosis is a tropical infectious disease caused by Gram-negative bacteria *B. pseudomallei*; it is widely distributed in the soil and water within endemic areas.

B. pseudomallei (the agent of Melioidosis) are related to the genus Burkholderia which includes another four species: B. cepacia, B. gladioli, B. pickettii and B. mallei [1] [2].

It is endemic in certain parts of the world including Southeast Asia and northern Australia [3].

Recent data indicate that it is now endemic to most of the Indian subcontinent, southern Chinese Mainland, Hong Kong (China), Chinese Taipei, Papua New Guinea, and other regions [4].

Qatar is a peninsula in Arabian Gulf with estimated population of 2,881,060 million till March 2022, the number of economically active population doubled three times in 14 years (from 444.133 in 2004 to 2.097 million in 2018). This unprecedented growth resulted primarily from the recruitment of large numbers of foreign workers needed for the country's ambitious development plans. Most of this workforce is from Southeast Asia and Indian subcontinent [5].

Most cases reported in other regions were acquired during residence in or travel to disease-endemic regions. In our country it was reported once before [6].

We think that there is no local transmission of the disease, and all cases are imported cases.

Melioidosis has different presentations including latent infection, local cutaneous lesions, sub-acute pneumonia, focal organ abscess, Musculo-skeletal infection, and lethal fulminant pneumonia [3] [4] [7] [8] [9] [10].

The disease can cause up to 20% of all community-acquired sepsis in the tropics, including 40% of sepsis-related mortality in Northern Thailand and up to ~20% in the higher-technology setting of Northern Australia [1] [3] [7] [9] [10].

2. First Case

47-year-old Nepalese male, diabetic not on treatment working in Qatar for 2 years as Gardner with no recent travel history presented to our Accident and Emergency in Hamad Hospital on 23/9/2011 with 10 days history of fever and burning micturition with no other complain.

On examination patient looks dehydrated, drowsy, and pale temp. 39.7°C, Bp: 90/60, pulse: 120/min. RR 24 Systemic examination was unremarkable.

He was started on I.V Piperacillin-Tazobactam 4.5 grams IV every 8 Hours. His initial investigations showed leukocytosis 13.4×10^3 /uL, hemoglobin (Hb) 6.5 g/dl (required blood transfusion) with normal coagulation profile, normal renal function test, his liver enzymes where elevated (AST 56 U/L, ALT 49 U/L, ALP 626 U/L).

Blood cultures were requested, and initial results was showing gram negative bacilli reported later as *B. pseudomallei*, Antibiotics were changed to IV Meropenem 1-gram Q8 Hrs.; repeated blood culture on 28/9 was persistently positive

for *B. pseudomallei*.

Ultrasound abdomen was requested which showed multiple hepatic and splenic lesions? Abscess (**Figure 1**), ultrasound guided drainage was done on 4/10 draining 70 ml of pus and pig tail catheter was inserted for three days. Repeated blood culture became negative.

Patient received 15 days of I.V. Meropenem and discharged on 12/10 on oral Trimethoprim-Sulfamethoxazole (TMP-SMX) double strength (DS) 960 mg BID PLUS Doxycycline100 mg PO BID.

Followed in infectious disease outpatient clinic, repeated ultrasound abdomen on 26/12 showed no collection with complete resolution of the previously describe abscesses (**Figure 2**). Antibiotics were stopped a total of 100 days were received; follow up to one year doesn't show any evidence or recurrence.

3. Second Case

51-year-old Indian male fisherman living in Qatar for the last 2 years with no recent travel history, known case of chronic carrier of hepatitis B virus with no regular follow up, occasional alcohol consumer, admitted on the 19/12/12 with 10 days history of fever and neck pain, he sought medical attention given oral antibiotics with no improvement.

On admission he was agitated, confused, febrile temperature was 38.2°C, blood pressure was 100/60, and his systemic examination apart from neck stiffness was unremarkable.

He was diagnosed as Meningoencephalitis managed initially with I.V fluids, intravenous Ceftriaxone, Vancomycin and Acyclovir admitted to intensive care unit. Laboratory results where within normal except for elevated liver enzymes ALT 90 U/L AST 194 U/L, high INR of 1.7 and high procalcitonin level 25.14 ng/ml, C-reactive protein 293 mg/l, ESR 58 mm/1hr, lumbar puncture was ordered but could not be done initially due to high INR, but it was done three days later and shows WBC 30 cells, mainly lymphocytes with high protein 5.12 g/l, glucose 3.5 mmol/l.

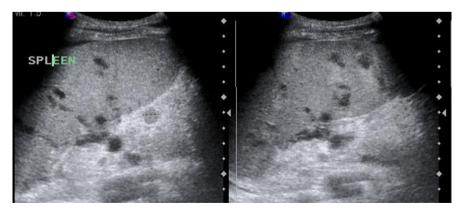


Figure 1. Ultrasound examination of the abdomen shows multiple hypo-echoic lesions in the spleen suggestive of multiple splenic abscesses.

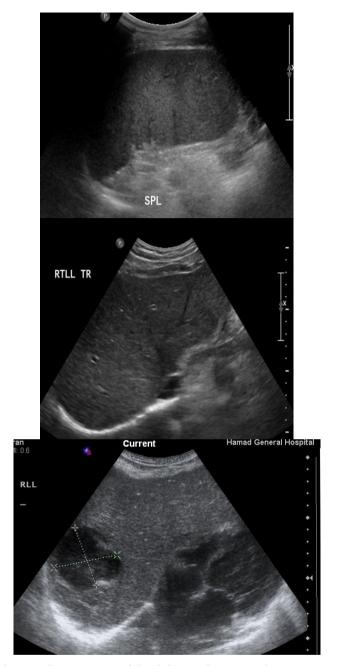


Figure 2. Ultrasound examination of the abdomen show normal appearance of the right lobe of the liver and spleen with no collection or abscess formation. Ultrasound examination of the abdomen show complex well-defined area in the right lobe of the liver measuring 9×409 c.

Blood cultures were requested on admission and reported as $\it B. pseudomallei$; antibiotics changed to Meropenem 1 gram IV Q 8 Hrs. PLUS TMP-SMX 250 mg of trimethoprim component IV Q6 Hrs. according to patient weight.

Repeated blood cultured were negative, patient improved clinically, but unfortunately while he is on antibiotics, he developed difficulty in walking, with signs of spinal card compression on clinical examination, urgent MRI lumbar spine was requested and showed Para vertebral collection 1.5 cm by 0.75 cm

(Figure 3). CT guided aspiration was done, pus was aspirated culture was negative for bacteria and tuberculosis. Meropenem PLUS TMP-SMX were continued, patient was transferred to rehabilitation unit, he showed good recovery where he was able to walk again without support, repeated MRI showed regression of the Para vertebral collection (Figure 4).

IV antibiotics were changed to PO Doxycycline plus TMP-SMX. He was treated for total six months. With no recurrence six months after completion of medical treatment.

4. Third Case

36-year-old Indian male patient living in Qatar for the past 4 year, he was working as fisherman. Newly discovered chronic carrier of hepatitis B virus He presented on 27/1/13 to our hospital with history of fever and right knee pain for the last 15 days, no history of trauma, raw milk ingestion, sexual contact, urinary symptoms, or urethral discharge.

On examination the right knee was tender, swollen, hot with limitation of movement, no other joint involvement, admitted to surgical floor as right knee septic arthritis, started on IV Ceftriaxone 2 grams IV once daily.



Figure 3. MRI lumbar spine shows Para vertebral collection 1.5 cm by 0.75 cm.

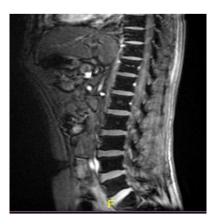


Figure 4. Follow up MRI lumbar spine showed regression of the Para vertebral collection.

His blood count and chemistry profile within normal, blood and urine culture where negative, fluid aspirate from the knee shows WBC-11300, mainly neutrophils.

Patient continued to have fever, MRI of left knee showed early osteomyelitis of lower one third of femur surrounded by tissue swelling and effusion (**Figure 5**), underwent incision and drainage of the knee joint multiple times, Synovial fluid and bone tissue culture showed *B. pseudomallei*.

Antibiotics were changed to Meropenem 1 gram IV Q 8 Hrs. and TMP-SMX 200 mg of trimethoprim component IV Q12 Hrs. according to patient weight which was given for 9 weeks which was changed to oral TMP-SMX plus Doxycycline upon discharge.

He was treated for total 5 months with good clinical improvement and no evidence of recurrence on 1 year follow up.

5. Fourth Case

20-year-old Nepalese male, working in Qatar for 18 months as carpenter, He presented to our hospital on 10/6/12 with history of pus discharge from the right groin for 20 days (**Figure 6**), no history of fever, abdominal symptoms, trauma, or sexual contact.

His complete blood count, chemistry, and liver function within normal and urine, blood cultures where negative, but the swab culture shows *B. pseudomal-lei*. Ultrasound groin shows multiple lymph nodes with collection at subcutaneous tissue 7.7 ml of right groin area (**Figure 7**).

He refused hospital admission, so he was given oral Doxycycline plus TMP-SMX. Follow up Ultrasound showed decrease of the size of the collection to 1 ml (Figure 8).

Patient lost follow up later.

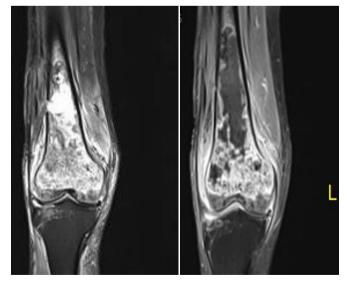


Figure 5. MRI of left knee shows early osteomyelitis of lower one third of femur surrounded by tissue swelling and effusion with intra medullary abscess formation.



Figure 6. Right groin discharging sinus.

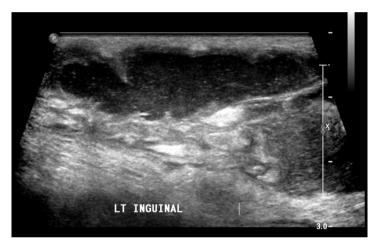


Figure 7. Ultrasound groin shows multiple lymph nodes with collection at subcutaneous tissue 7.7 ml of right groin area.

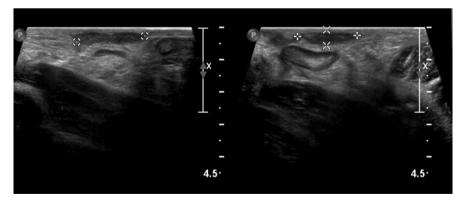


Figure 8. Follow up ultrasound showed significant reduction in the size of abscess to 1 ml with multiple reactional Lymph nodes.

6. Fifth Case

49 year old Nepalese male patient not known to have any chronic illness before

admitted on 19/06/2013 with 10 days history of fever, left hip dull pain. Fever was associated with chills, rigors and fatigue. He had no other complain, no contact with sick patients, no contact with birds or animals Working as Masson in construction, living in Qatar for 5 years with no recent travel history.

On admission examination was remarkable for fever T 38°C and palpable spleen 4 cm below costal margin.

He was started on Piperacillin-Tazobactam and blood cultures were sent. His initial labs showed WBC 4×10^3 /uL, Hb 11.4 g/dl, Platelets 147×10^3 /uL ALT 35 U/L AST 23 U/L, Na 122 mmol/L creatinine 231 umol/L with high blood sugar 31.4 mmol/l.

He underwent US abdomen which showed Splenomegaly 14.7 cm. With two heterogeneous to hypoechoic lesions are noted in the spleen with tiny punctate calcifications. The hypoechoic lesions measure 43×30 mm and 38×30 mm. Punctate calcifications noted throughout the spleen (Figure 9).

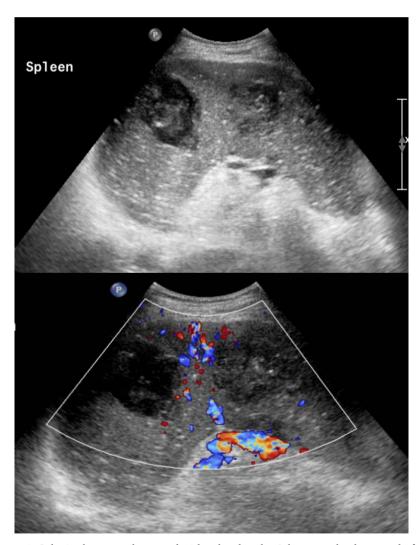


Figure 9. Splenic abscesses ultrasound with color doppler & b gray scale ultrasound of the spleen: 2 Well defined hypoechoic heterogenous lesions with no vascularity in an enlarged spleen with coarse echotexture.

CT abdomen was done and showed enlarged spleen with multiple hypo dense minimal peripherally enhancing lobulated lesions of variable size are noted in the spleen largest measuring 3.5×6.8 cm in the posterior aspect of spleen. There is of rupture of the two of the splenic lesions with mild peri splenic fluid.

Liver in enlarged in size with two well-defined hypo dense peripherally enhancing lesion measuring 20×19 mm and 9×8 mm in segment VIII and V respectively. Mild fluid was noted in the right iliac fossa.

2 days after admission patient deteriorated requiring oxygen transferred to MICU with worsening laboratory results WBC 2.6×10^3 /uL, Hb 10.4 g/dl, platelets 77×10^3 /uL with evidence of DIC.

At that time blood culture cam as gram negative bacilli so antibiotics was escalated to Meropenem, general surgery were consulted advised for CT guided aspiration which was done under complete aseptic technique 2 drainage catheters were inserted into the two largest hypodense lesions noted in the spleen. Thick yellowish-greenish pus was aspirated and sent for analysis.

Patient condition continues to deteriorate intubated and underwent splenectomy.

Later, blood culture reported as *B. pseudomallei* sensitive to Meropenem, Ceftazidime and TMP-SMX so patient was changed to Ceftazidime IV after 4 days of Meropenem, the same organism was isolated also from splenic aspirate.

Patient was investigated further for possibility of disseminated abscesses, so he underwent CT THORAX WITH CONTRAST which showed widespread variable-sized patchy areas of pulmonary consolidation are seen predominantly distributed at the upper lobe. Speculated mass lesion measuring 1.4×1 cm is seen at the right middle lobe surrounded by fibrotic changes. Adjacent pulmonary nodules are seen the largest measures 7 mm. Evidence of right sided sub-pulmonic pleural effusion is seen.

Bilateral mild pleural effusion is seen. Multiple small mediastinal lymph nodes are seen the largest at the right paratracheal region measuring 8 mm in short axis dimension. Subpleural blebs are noted at the apical segment of the right upper lung lobe. In the visualized part of the upper abdomen: focal hypodense lesions are seen in segment VIII and V respectively showing peripheral enhancement representing small liver abscesses.

Residual free fluid and fat stranding are seen at the surgical bed at the site of splenectomy and adjacent to the posterior stomach wall.

Left sided perinephric free fluid is noted. Also, small loculated fluid collection at the site of splenectomy measuring approximately 5×1 cm.

He underwent MRI for both thigh with contrast on 03.07.2013: which showed heterogeneous signal intensity in the stairs sequences and T2-weighted images with fat saturation which involving the intramedullary, subcortical area of the head, neck and proximal part of the left femur and adjacent surrounding muscles extending posteriorly involving the posterior lateral part of the left gluteus maximus muscle associated with presence of the none drainable abscess collection intramedullary and within the soft tissue as mentioned above.

Patient started to improve, and he became afebrile at day 10 of admission, continued IV Ceftazidime for total 6 weeks, then shifted to oral TMP-SMX + amoxicillin/clavulanic acid for another 2 weeks. Discharged home but he lost follow up later.

7. Sixth Case

53 yrs. Old Bangladeshi male patient known case of DM, HTN, coronary artery disease (CAD), chronic kidney disease (CKD) he was admitted on 18/06/2013 to Heart Hospital with 5 days history of dry cough, bilateral chest pain increased with coughing and intermittent fever. He is in Qatar for 20 years, last travel history to Bangladesh was 3 months back, working as Mosque Imam (religious position).

His initial examination was unremarkable with normal vital signs. Initial investigations showed leukocytosis 15.1×10^3 /uL with normocytic, normochromic anemia with Hb 9.6 g/dl, creatinine 227 umol/L (same as baseline).

Chest X ray showed Mild increased prominence of the vascular markings noted within both lung zone, blood cultures were sent, and he was started on Ceftriaxone + Azithromycin as case of Community Acquired Pneumonia + Atypical chest pain, blood cultures sent.

Later, blood cultures came back as *B. pseudomallei* sensitive to Meropenem, Ceftazidime, TMP-SMX and ciprofloxacin following that he was transferred to medical floor after cardiology clearance and shifted to IV Ceftazidime.

CT chest showed few areas of fibrotic strands with early bronchiectatic changes noted at the posterior segment of the right upper lobe.

Patient developed right thigh pain so he was evaluated by US THIGH RT which showed Small well defined hypodense oblong area measuring 1.8×0.3 mm is noted in the subcutaneous tissue of the right mid-thigh (at the sight of complain), no evidence of vascularity, likely representing a small subcutaneous collection (Figure 10).

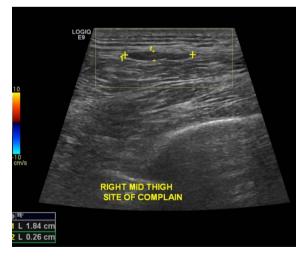


Figure 10. Ultrasound of the right thigh: well defined hypoechoic subcutaneous small collection in the mid-thigh.

Seen by general surgery with no intervention needed.

Continued ceftazidime for total 10 days then shifted to Doxycycline + TMP-SMX PO for another 10 days.

Follow up blood cultures were negative, no follow up thigh Ultrasound.

Patient was seen in the clinic 1 month after discharge and he was doing well with no further complains.

Summary of Melioidosis cases reported in Qatar is shown in Table 1.

8. Microbiology Identification

Laboratory identification of *B. Pseudomallei* can be difficult in our cases all identified by Vitek Compact (bioMérieux, Marcy l'Etoile, France) and Phoenix (Becton Dickinson, New Jersy and USA). Re-evaluation of the Gram stain and susceptibility pattern was done. The safety pin appearance of the GNB and resistance to Colistin and Gentamycin raised the possibility of *B. pseudomallei* or *B. mallei*. The strain was sent to the Mayo Clinic Medical Laboratories (Rochester,

Table 1. Summary of Melioidosis cases reported in Qatar.

	Age	Nationality	Occupation	Length of stay in Qatar and travel history	Risk factors	Site of infection	Treatment	Duration	Outcome
1	47 yrs.	Nepal	Gardner	2 years with no recent travel history	Diabetes Mellitus (DM)	Bacteremia + liver and splenic abscesses	Iv Meropenem	3 months and 10 days	Cured
2	51 yrs.	India	Fisherman	2 years with no recent travel history	Chronic hepatitis B + alcohol consumption + DM	Bacteremia + vertebral osteomyelitis + paraspinal abscess	Iv Meropenem + TMP-SMX Followed by Doxycycline + TMP-SMX	6 months	Cured
3	36 yrs.	India	Fisherman	4 year with no recent travel history	Chronic hepatitis B, No History of Diabetes Mellitus	Knee septic arthritis + osteomyelitis	Iv Meropenem + TMP-SMX Followed by Doxycycline + TMP-SMX	6 months	Cured
4	20 yrs.	Nepal	Carpenter	18 months with no recent travel history	No risk factors	Groin sinus	Doxycycline + TMP-SMX PO	1 month	Lost follow up
5	49 yrs.	Nepal	Masson	5 years with no recent travel history	DM	Bacteremia + liver and splenic abscesses + thigh abscess	Iv Meropenem then Ceftazidime Followed by Amoxi/ clav +TMP-SMX	9 weeks	Lost follow up
6	53 yrs.	Bangladeshi	Mosque Imam	20 years with recent travel history 3 months prior to presentation	DM, HTN, CAD, CKD	Bacteremia + thigh abscess	Iv Ceftazidime Followed by Doxycycline + TMP-SMX	20 days	Cured
7 (Faraj S. <i>et al.</i>)	45 yrs.	Unknown	Unknown	Returned from India few days prior to presentation	DM	bacteremia + Disse- minated infection	Ceftazidime + TMP-SMX followed by cefuroxime + TMP-SMX	6 months	Cured

USA) which identified the organism as *B. pseudomallei* 16S RNA sequencing. 2 strains genetic sequencing shows that they are different strains.

9. Discussion

B. pseudomallei and its role in human disease were first described by Whitmore and Krishnaswami in 1912 [11]. Transmission of infection can occur through skin, lungs (inhalation, aspiration) and occasionally by ingestion. Inhalation thought to be the most common route of acquisition of *B. pseudomallei* by different case reported in the literature [12] [13].

But now percutaneous inoculation during exposure to wet season soils or contaminated water is considered the predominant mode of transmission [14] [15] [16]. Cases of pneumonia following skin injuries are well documented, suggesting that the organism can reach the lungs via the hematogenous route [15].

Person-to-person transmission is extremely unusual, despite the large bacterial load in severely ill patients with Septicemic pulmonary Melioidosis [17] [18]. Transmission from Mother to infant can happen during breastfeeding especially in the setting of *B. pseudomallei* mastitis [10] [19]. Laboratory-acquired infections and iatrogenic infections from contaminated hospital or surgical equipment occasionally occur [17] [20] [21].

Transmission related to animal exposure is very rare; three possible cases have been described in Australia [22] [23]. Ingestion of water also postulated as uncommon routes of transmission. However, a study from Thailand raised the possibility that ingestion of water contaminated with *B. pseudomallei* may be a more common source of infection than previously thought, especially in endemic regions with unchlorinated water supplies [15] [17] [24] [25] [26]. Sexual transmission is uncommon [27] [28].

The most important risk factors for Melioidosis are diabetes, hazardous alcohol use, and chronic renal disease [16] [29] [30] [31] [32]. Other risk factors include chronic lung disease (present in 27 percent of cases in the Northern Territory Study) [33], thalassemia [31], and kava consumption [15] (The roots of the plant are used to produce a drink with sedative and anesthetic properties. Kava is consumed throughout the Pacific Ocean cultures of Polynesia, including Hawaii, Vanuatu, Melanesia, and some parts of Micronesia). Malignancy, steroid and other immunosuppressive therapy, rheumatic heart disease and/or congestive cardiac failure [30]. Pulmonary hemosiderosis [34], chronic granulomatous disease [35], and tuberculosis are probable risk factors, but are not yet confirmed to be independent risk factors [31].

In our case series risk factors, which could be found Diabetes in 4 patients and chronic Hepatitis b infection in 2 patient one of them was also diabetic and alcohol consumer, one patient was healthy with no risk factors. Hepatitis B as a risk factor for Melioidosis was not previously described in the literature and presence of that relations need to be subjected to further studies.

Melioidosis can be classify to Acute disease is defined as symptoms lasting

for less than two months. Chronic disease is defined as symptoms persisting for longer than two months [36]. The incubation period following inoculating injury ranges from 1 to 21 days (mean nine days) [36] [37] and it can be as long as 26 years [38], depending on the inoculating dose, virulence properties of the isolate, mode of transmission, and host risk factors [39] [40]. Melioidosis is not endemic disease in Qatar, all our cases are expatriates but since they had no recent travel history except for the last case we think that they were incubating the disease prior to arrival to Qatar with relatively long incubation period.

Clinical presentation of Melioidosis can be variable but the most common manifestations are pneumonitis, lung abscess, soft-tissue infection, osteomyelitis, lymphadenitis, splenic abscess, liver abscess, and septicemia. As shown in our case series that bactraemic type with deep abscess formation is the most common presentation 75% of cases reported from Qatar (Table 1).

Treatment of Melioidosis, even mild disease, should be with initial intensive therapy (at least 2 weeks of intravenous therapy) followed by eradication therapy orally for a minimum of three months. Initial intensive therapy with one of the following regimens Ceftazidime, Meropenem, Imipenem [41]. Trimethoprim-Sulfamethoxazole (TMP-SMX) may be added to other antibiotics aiming to decrease antibiotics resistance in specific clinical presentations such as neurologic, prostatic, bone, joint, cutaneous, and soft tissue Melioidosis [42] [43]. Further studies fail to show benefit from addition of trimethoprim-sulfamethoxazole in form of decreasing mortality or culture-confirmed recurrent Melioidosis [44] [45].

In eradication therapy Trimethoprim-Sulfamethoxazole is the drug of choice, combination of Doxycycline plus TMP-SMX was evaluated and studies does not show difference in the rates of recurrence of Melioidosis but, a higher rate of adverse drug reactions were noticed when Doxycycline was added to regimen [46].

Other drugs were evaluated for treatment of Melioidosis like Amoxicillin-Clavulanate alone and oral Quinolones alone or in combination with Azithromycin and found to be less effective in preventing relapse than eradication therapy with TMP-SMX and Doxycycline with or without Chloramphenicol [47]-[53].

All our patients were treated initially with either Ceftazidime or Meropenem followed by oral antibiotics including Doxycycline/TMP-SMX for 3 - 6 months except for one patient who lost his follow up.

3 of our patients who were treated with combination therapy 1 treated with monotherapy and 2 treated with monotherapy followed by combination therapy showed good clinical response and drugs were well tolerated which may suggest that patients may get benefit from combination therapy but of course our number of patients was small and bigger studies are needed to evaluate this issue. Relapse after apparent cure of has been reported and may reach up to 15% per year of follow-up [41]. In our cases no relapse was documented with follow up 6 - 12 months.

10. Conclusions

Melioidosis, although rare in this geographic region, should be considered in the differential diagnosis for ill residents or travelers from areas of endemicity. Confirmed human sporadic cases in the Middle East have been reported in Iran, and suspected cases in Egypt, the United Arab Emirates and Saudi Arabia has been reported but not confirmed [54] and one confirmed case in Qatar, Cases in animals have also been reported from Iran, Saudi Arabia and Oman [55] [56].

All our reported cases are from expatriates namely from India and Nepal we believe that those cases are imported but further evidence for the existence of *B. pseudomallei* as epizootic or in soil is lacking in our region and further studies are needed. We are reporting series of confirmed cases diagnosed in Qatar in very close period and this is considered the first confirmed series of cases in humans diagnosed in our region, we could not find a clear link between those cases neither in demographic characteristics nor in genetic sequencing for two of those cases. Our cases had different clinical presentations ranging from mild infection to severe Septicemic type all treated medically with appropriate surgical intervention when needed with good outcome and no mortality recorded in our cases. Two of our cases were found to be chronic carriers of hepatitis B infection and we think that further studies are needed to determine if it could be a significant risk factor for the disease.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- Phillips, I., Eykyn, S. and Laker, M. (1972) Outbreak of Hospital Infection Caused by Contaminated Autoclaved Fluids. *Lancet*, 1, 1258-1260. https://doi.org/10.1016/S0140-6736(72)90981-6
- [2] Howe, C. and Miller, W.R. (1947) Human Glanders: Report of Six Cases. *Annals of Internal Medicine*, **26**, 93-115. https://doi.org/10.7326/0003-4819-26-1-93
- [3] White NJ (2003) Melioidosis. *Lancet*, **361**, 1715-1722. https://doi.org/10.1016/S0140-6736(03)13374-0
- [4] Currie, B.J., Dance, D.A. and Cheng, A.C. (2008) The Global Distribution of *Burk-holderia pseudomallei* and Melioidosis: An Update. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 102, S1-S4. https://doi.org/10.1016/S0035-9203(08)70002-6
- [5] Qatar Statistics Authority. https://www.psa.gov.qa/en/pages/default.aspx
- [6] Al Alousi, F.S., Al Soub, H. and El-Shafie, S.S. (2000) Subdural Empyema Due to Burkholderia pseudomallei. Annals of Saudi Medicine, 20, 272-273. https://doi.org/10.5144/0256-4947.2000.272
- [7] Wiersinga, W.J., van der Poll, T., White, N.J., Day, N.P. and Peacock, S.J. (2006) Melioidosis: Insights into the Pathogenicity of *Burkholderia pseudomallei*. *Nature Reviews Microbiology*, **4**, 272-282. https://doi.org/10.1038/nrmicro1385

- [8] Inglis, T.J., Rolim, D.B. and Sousa Ade, Q. (2006) Melioidosis in the Americas. *The American Journal of Tropical Medicine and Hygiene*, 75, 947-954. https://doi.org/10.4269/ajtmh.2006.75.947
- [9] Currie, B.J., Haslem, A., Pearson, T., Hornstra, H., Leadem, B., Mayo, M., Gal D., Ward, L., Godoy, D., Spratt, B.G., et al. (2009) Identification of Melioidosis Outbreak by Multi Locus Variable Number Tandem Repeat Analysis. Emerging Infectious Diseases, 15, 169-174. https://doi.org/10.3201/eid1502.081036
- [10] Cheng, A.C. and Currie, B.J. (2005) Melioidosis: Epidemiology, Pathophysiology, and Management. *Clinical Microbiology Reviews*, 18, 383-416. https://doi.org/10.1128/CMR.18.2.383-416.2005
- [11] Whitmore, A. and Krishnaswami, C.S. (1912) An Account of the Discovery of a Hitherto Undescribed Infective Disease Occurring among the Population of Rangoon. *Indian Medical Gazette*, **47**, 262-267.
- [12] Brundage, W.G., Thuss Jr., C.J. and Walden, D.C. (1968) Four Fatal Cases of Melioidosis in US Soldiers in Vietnam. Bacteriologic and Pathologic Characteristics. The American Journal of Tropical Medicine and Hygiene, 17, 183-191. https://doi.org/10.4269/ajtmh.1968.17.183
- [13] Mackowiak, P.A. and Smith, J.W. (1978) Septicemic Melioidosis Occurrence Following Acute Influenza a Six Years after Exposure in Vietnam. *JAMA*, 240, 764-766. https://doi.org/10.1001/jama.1978.03290080054027
- [14] Dance, D.B. (1990) Melioidosis. Reviews in Medical Microbiology, 1, 143-150.
- [15] Currie, B.J., Fisher, D.A., Howard, D.M., Burrow, J.N., Selvanayagam, S., Snelling, P.L., Anstey, N.M. and Mayo, M.J. (2000) The Epidemiology of Melioidosis in Australia and Papua New Guinea. *Acta Tropica*, 74, 121-127. https://doi.org/10.1016/S0001-706X(99)00060-1
- [16] Leelarasamee, A. and Bovornkitti, S. (1989) Melioidosis: Review and Update. *Reviews of Infectious Diseases*, **11**, 413-425. https://doi.org/10.1093/clinids/11.3.413
- [17] Dance, D.A. (2000) Ecology of *Burkholderia pseudomallei* and the Interactions between Environmental *Burkholderia* spp. and Human-Animal Hosts. *Acta Tropica*, 74, 159-168. https://doi.org/10.1016/S0001-706X(99)00066-2
- [18] Kunakorn, M., Jayanetra, P. and Tanphaichitra, D (1991) Man-to-Man Transmission of Melioidosis. *Lancet*, 337, 1290-1291. https://doi.org/10.1016/0140-6736(91)92962-2
- [19] Ralph, A., McBride, J. and Currie, B.J. (2004) Transmission of *Burkholderia pseudomallei* via Breast Milk in Northern Australia. *The Pediatric Infectious Disease Journal*, **23**, 1169-1171.
- [20] Green, R.N. and Tuffnell, P.G. (1968) Laboratory Acquired Melioidosis. *The American Journal of Medicine*, 44, 599-605.
 https://doi.org/10.1016/0002-9343(68)90060-0
- [21] Ashdown, L.R. (1979) Nosocomial Infection Due to Pseudomonas pseudomallei: Two Cases and an Epidemiologic Study. *Reviews of Infectious Diseases*, **1**, 891-694. https://doi.org/10.1093/clinids/1.5.891
- [22] Choy, J.L., Mayo, M., Janmaat, A. and Currie, B.J. (2000) Animal Melioidosis in Australia. Acta Tropica, 74, 153-158. https://doi.org/10.1016/S0001-706X(99)00065-0
- [23] Stanton, A.T. and Fletcher, W. (1932) Melioidosis. Vol. 21, John Bale and Danielson Ltd., London.
- [24] Cottew, G.S., Sutherland, A.K. and Meehan, J.F. (1952) Melioidosis in Sheep in

- Queensland. Australian Veterinary Journal, 28, 113-123.
- [25] Ketterer, P.J., Webster, W.R., Shield, J., Arthur, R.J., Blackall, P.J. and Thomas, A.D. (1986) Melioidosis in Intensive Piggeries in Southeastern Queensland. *Australian Veterinary Journal*, 63, 146-149. https://doi.org/10.1111/j.1751-0813.1986.tb02953.x
- [26] Limmathurotsakul, D., Kanoksil, M., Wuthiekanun, V., Kitphati, R., de Stavola, B., Day, N.P. and Peacock, S.J. (2013) Activities of Daily Living Associated with Acquisition of Melioidosis in Northeast Thailand: A Matched Case-Control Study. *PLoS Neglected Tropical Diseases*, 7, Article No. e2072. https://doi.org/10.1371/journal.pntd.0002072
- [27] McCormick, J.B., Sexton, D.J., McMurray, J.G., Carey, E., Hayes, P. and Feldman, R.A. (1975) Human-to-Human Transmission of *Pseudomonas pseudomallei*. Annals of Internal Medicine, 83, 512-513. https://doi.org/10.7326/0003-4819-83-4-512
- [28] Webling, D.D. (1980) Genito-Urinary Infections with *Pseudomonas pseudomallei* in Australian Aboriginals. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **74**, 138-139. https://doi.org/10.1016/0035-9203(80)90036-X
- [29] Chaowagul, W., White, N.J., Dance, D.A., Wattanagoon, Y., Naigowit, P., Davis, T.M., Looareesuwan, S. and Pitakwatchara, N. (1989) Melioidosis: A Major Cause of Community-Acquired Septicemia in Northeastern Thailand. *The Journal of Infectious Diseases*, 159, 890-899. https://doi.org/10.1093/infdis/159.5.890
- [30] Currie, B.J., Ward, L. and Cheng, A.C. (2010) The Epidemiology and Clinical Spectrum of Melioidosis: 540 Cases from the 20 Year Darwin Prospective Study. *PLoS Neglected Tropical Diseases*, 4, Article No. e900. https://doi.org/10.1371/journal.pntd.0000900
- [31] Suputtamongkol, Y., Chaowagul, W., Chetchotisakd, P., Lertpatanasuwun, N., Intaranongpai, S., Ruchutrakool, T., Budhsarawong, D., Mootsikapun, P., Wuthiekanun, V., Teerawatasook, N. and Lulitanond, A. (1999) Risk Factors for Melioidosis and Bactraemic Melioidosis. *Clinical Infectious Diseases*, 29, 408-413. https://doi.org/10.1086/520223
- [32] Currie, B.J., Jacups, S.P., Cheng, A.C., Fisher, D.A., Anstey, N.M., Huffam, S.E. and Krause, V.L. (2004) Melioidosis Epidemiology and Risk Factors from a Prospective Whole-Population Study in Northern Australia. *Tropical Medicine & International Health*, **9**, 1167-1174. https://doi.org/10.1111/j.1365-3156.2004.01328.x
- [33] Currie, B.J., Fisher, D.A., Howard, D.M., Burrow, J.N., Lo, D., Selva-Nayagam, S., Anstey, N.M., Huffam, S.E., Snelling, P.L., Marks, P.J., Stephens, D.P., Lum, G.D., Jacups, S.P. and Krause, V.L. (2000) Endemic Melioidosis in Tropical Northern Australia: A 10-Year Prospective Study and Review of the Literature. *Clinical Infectious Diseases*, 31, 981-986. https://doi.org/10.1086/318116
- [34] Ruchin, P., Robinson, J., Segasothy, M. and Morey, F. (2000) Melioidosis in a Patient with Idiopathic Pulmonary Hemosiderosis Resident in Central Australia. *Australian and New Zealand Journal of Medicine*, 30, 395-396. https://doi.org/10.1111/j.1445-5994.2000.tb00844.x
- [35] Tarlow, M.J. and Lloyd, J. (1971) Melioidosis and Chronic Granulomatous Disease. Journal of the Royal Society of Medicine, 64, 19-20. https://doi.org/10.1177/003591577106400111
- [36] Currie, B.J., Fisher, D.A., Anstey, N.M. and Jacups, S.P. (2000) Melioidosis: Acute and Chronic Disease, Relapse and Re-Activation. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, 94, 301-304. https://doi.org/10.1016/S0035-9203(00)90333-X
- [37] Sookpranee, M., Lumbiganon, P. and Boonma, P. (1989) Nosocomial Contamina-

- tion of Pseudomonas pseudomallei in the Patients at Srinagarind Hospital. In: Punyagupta, S., Sirisanthana, T. and Stapatayavong, B., Eds., *Melioidosis*, Bangkok Medical Publisher, Bangkok.
- [38] Mays, E.E. and Ricketts, E.A. (1975) Melioidosis: Recrudescence Associated with Bronchogenic Carcinoma Twenty-Six Years Following Initial Geographic Exposure. *Chest*, **68**, 261-263. https://doi.org/10.1378/chest.68.2.261
- [39] Howe, C., Sampath, A. and Spotnitz, M. (1971) The Pseudomallei Group: A Review. The Journal of Infectious Diseases, 124, 598-606. https://doi.org/10.1093/infdis/124.6.598
- [40] Bovornkitti, S., Leelarasamee, A. and Thamlikitkul, V. (1985) Melioidosis. *Monaldi Archives*, **40**, 203-210.
- [41] Smith, M.D., Wuthiekanun, V., Walsh, A.L. and White, N.J. (1994) Susceptibility of Pseudomonas pseudomallei to Some Newer Beta-Lactam Antibiotics and Antibiotic Combinations Using Time-Kill Studies. Journal of Antimicrobial Chemotherapy, 33, 145-149. https://doi.org/10.1093/jac/33.1.145
- [42] Cheng, A.C., McBryde, E.S., Wuthiekanun, V., Chierakul, W., Amornchai, P., Day, N.P., White, N.J. and Peacock, S.J. (2009) Dosing Regimens of Cotrimoxazole (Trimethoprim-Sulfamethoxazole) for Melioidosis. *Antimicrobial Agents and Chemotherapy*, 53, 4193-4199. https://doi.org/10.1128/AAC.01301-08
- [43] Chetchotisakd, P., Chierakul, W., Chaowagul, W., Anunnatsiri, S., Phimda, K., Mootsikapun, P., Chaisuksant, S., Pilaikul, J., Thinkhamrop, B., Phiphitaporn, S., Susaengrat, W., Toondee, C., Wongrattanacheewin, S., Wuthiekanun, V., Chantratita, N., Thaipadungpanit, J., Day, N.P., Limmathurotsakul, D. and Peacock, S.J. (2014) Trimethoprim-Sulfamethaxazole versus Trimethoprim-Sulfamethaxazole Plus Doxycycline as Oral Eradicative Treatment for Melioidosis (MERTH): A Multicenter, Double-Blind, Non-Inferiority, Randomized Controlled Trial. Lancet, 383, 807-814. https://doi.org/10.1016/S0140-6736(13)61951-0
- [44] Chierakul, W., Anunnatsiri, S., Short, J.M., Maharjan, B., Mootsikapun, P., Simpson, A.J., Limmathurotsakul, D., Cheng, A.C., Stepniewska, K., Newton, P.N., Chaowagul, W., White, N.J., Peacock, S.J., Day, N.P. and Chetchotisakd, P. (2005) Two Randomized Controlled Trials of Ceftazidime alone versus Ceftazidime in Combination with Trimethoprim-Sulfamethoxazole for the Treatment of Severe Melioidosis. Clinical Infectious Diseases, 41, 1105-1113. https://doi.org/10.1086/444456
- [45] Chierakul, W., Anunnatsiri, S., Chaowagul, W., Peacock, S.J., Chetchotisakd, P. and Day, N.P. (2007) Addition of Trimethoprim-Sulfamethoxazole to Ceftazidime during Parenteral Treatment of Melioidosis Is Not Associated with a Long-Term Outcome Benefit. Clinical Infectious Diseases, 45, 521-523. https://doi.org/10.1086/520010
- [46] Currie, B.J. (2003) Melioidosis: An Important Cause of Pneumonia in Residents of and Travelers Returned from Endemic Regions. *European Respiratory Journal*, **22**, 542. https://doi.org/10.1183/09031936.03.00006203
- [47] Chaowagul W. (2000) Recent Advances in the Treatment of Severe Melioidosis. *Acta Tropica*, **74**, 133-137. https://doi.org/10.1016/S0001-706X(99)00062-5
- [48] Rajchanuvong A, Chaowagul W, Suputtamongkol Y, Smith MD, Dance DA, White NJ. (1995) A Prospective Comparison of Co-Amoxiclav and the Combination of Chloramphenicol, Doxycycline, and Co-Trimoxazole for the Oral Maintenance Treatment of Melioidosis. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 89, 546-549. https://doi.org/10.1016/0035-9203(95)90104-3

- [49] Chaowagul, W., Suputtamongkul, Y., Smith, M.D. and White, N.J. (1997) Oral Fluoroquinolones for Maintenance Treatment of Melioidosis. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 91, 599-601. https://doi.org/10.1016/S0035-9203(97)90044-4
- [50] Chetchotisakd, P., Chaowagul, W., Mootsikapun, P., Budhsarawong, D., Thinkamrop, B. (2001) Maintenance Therapy of Melioidosis with Ciprofloxacin plus Azithromycin Compared with Cotrimoxazole plus Doxycycline. *The American Journal of Tropical Medicine and Hygiene*, 64, 24-27. https://doi.org/10.4269/ajtmh.2001.64.24
- [51] Ashdown, L.R. and Currie, B.J. (1992) Melioidosis: When in Doubt Leave the Quinolone alone! *Medical Journal of Australia*, 157, 427-428. https://doi.org/10.5694/j.1326-5377.1992.tb137276.x
- [52] Gilad, J., Harary, I., Dushnitsky, T., Schwartz, D. and Amsalem, Y. (2007, July 9) Burkholderia mallei and *Burkholderia pseudomallei* as Bioterrorism Agents: National Aspects of Emergency Preparedness. *The Israel Medical Association Journal*, 9, 499-503.
- [53] Sprague, L.D. and Elschner, M.C. (2012) Burkholderia pseudomallei: Melioidosis. In: Elschner, M.C., Cutler, S.J., Weidmann, M. and Butaye, P., Eds., BSL3 and BSL4 Agents: Epidemiology, Microbiology, and Practical Guidelines, Wiley-VCH Verlag GmbH & Co. KGaA, Hoboken, 47-56. https://doi.org/10.1002/9783527645114.ch4
- [54] Pourtaghva, M, Dodin, A, Portovi, M, Teherani, M. and Galimand, M. (1977) 1st Case of Human Pulmonary Melioidosis in Iran. *Bulletin de la Société de Pathologie Exotique*, **70**, 107-109.
- [55] Almarhabi, H., Munshi, A., Althobaiti, M., *et al.* (2022, February 3) Melioidosis Pneumonia in Saudi Arabia: A Rare Case Report and Review of the Literature. *Cureus*, **14**, Article ID: e21871. https://doi.org/10.7759/cureus.21871
- [56] Al Tamtami, N., Khamis, F. and Al-Jardani, A. (2017) Imported Case of Melioidosis in Oman: Case Report. *Oman Medical Journal*, 32, 62-65. https://doi.org/10.5001/omj.2017.11