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Case Series

Radiology Section

Melioidosis: A Rare But Emerging Infectious Disease in India and Role of Radiologist in Diagnosis

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ABSTRACT

Melioidosis is an endemic disease in South East Asia and in North Australian countries caused by gram-negative bacterium *Burkholderia pseudomallei*. It was sporadic in India, but recent trend shows increase in number of the cases in the last few years making it as an emerging infectious disease. It presents with great clinical diversity, from skin ulcers to pneumonia, fulminant septic shock or abscesses in multiple organs including liver, spleen, kidney, brain and in musculoskeletal system with diabetes mellitus being the important predisposing factor. Radiologically it presents as consolidation, nodules, cavitatory lesions and abscesses in lung, multiple abscesses in abdominal visceral organs, with multiple discrete abscess in liver and spleen, which are highly suggestive of melioidosis. In CNS it presents as parenchymal abscess or as calvareal osteomyelitis, in musculoskeletal system as osteomyelitis, septic arthritis and as abscess in muscle. Melioidosis is called "great mimicker" as it mimics tuberculosis and malignancy radiologically. Even though radiological findings are not specific and confirmation is by culture of blood, sputum, abscess or other body fluids, radiologist have a definite role to play in suspecting melioidosis with clinical background in endemic areas and in countries like India, where it is an emerging infectious disease.

Keywords: *Burkholderia pseudomallei*, CT/MRI, Infection

INTRODUCTION

Melioidosis is an infectious disease, which is caused by gram-negative bacterium *Burkholderia pseudomallei*, which was first described by Whitemore and Krishnaswami in Burma in 1912 [1]. The bacillus spreads through inhalation, ingestion or through skin lesions and found in tropics with South East Asia and North Australia being the endemic zones [2,3]. Sporadic cases have been reported from India, Taiwan, Sri Lanka, Korea, China, the Middle East and the America [3-7] with it being increasingly recognized across India [8-10].

Melioidosis has varied presentations ranging from asymptomatic, subclinical to acute localized and septicemia to chronic forms. Most infections are asymptomatic, severe infection occurs with underlying risk factors like diabetes mellitus, chronic renal disease, alcoholism, malignancy and in immuno-compromised status [6,11-14]. Melioidosis can occur in any organ but is most common in lung, spleen and liver [6,14-18] with mortality of more than 80% in acute septicemia form if not treated with appropriate antibiotics [2].

The definitive diagnosis requires positive blood culture of the organism or culture from the abscess of involved organs, throat swabs, body fluid, and skin ulcer or from the biopsy of the infected organs [19]. Advanced imaging like ultrasonography, CT-scan and MRI will help in suggesting the diagnosis of melioidosis, especially with multiple abscesses in liver and spleen which is highly suggestive of melioidosis. Since, the clinical findings are nonspecific, the diagnosis of this infection should be suspected in the clinical setting in endemic areas and in countries like India, where it is an emerging infectious disease. The radiological findings are supportive of the diagnosis in endemic areas.

CASE REPORT

CASE 1

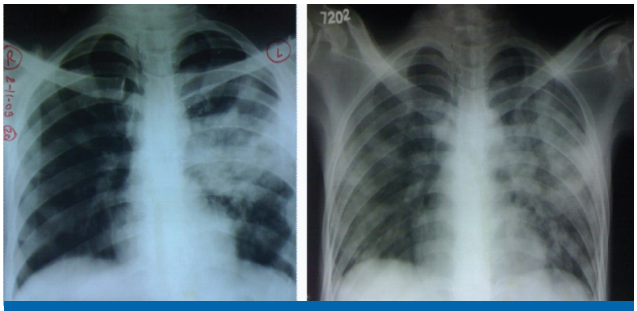
A 20-year-old male labourer from rural background presented to Emergency Department with fever, cough and breathlessness. The chest radiography showed in homogenous air space opacities suggestive of consolidation in left lung with multiple nodular opacities in lower zone

[Table/Fig-1a, 1b] and sputum culture done was negative for gram staining. Patient was treated with empirical antibiotics on outpatient basis. He again presented to the ED, with worsening of his symptoms, pain abdomen and hypotension. Patient was a known case of type I Diabetes mellitus for the last 2 years and on insulin with controlled blood glucose level.

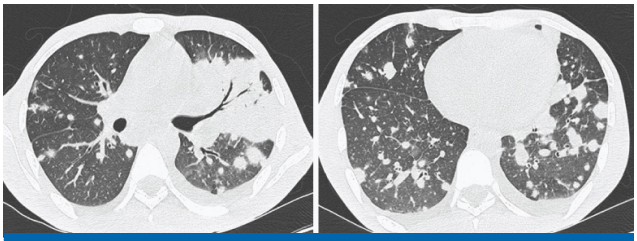
His routine blood investigation revealed elevated TLC (15,000/cumm), elevated FBS (150mg/dl) and PPBS (310mg/dl), with normal electrolytes, renal and liver function tests. His blood culture showed growth of gram-negative bacterium *Burkholderia pseudomallei*. Sputum was negative for AFB for three consecutive day samples and showed no growth on culture.

The repeat chest radiograph revealed increase in number of opacities in bilateral lung compared to previous radiograph in addition to consolidation in the left mid zone [Table/Fig-1]. Ultrasound abdomen revealed mild hepato-spleenomegaly with multiple ill-defined hypoechoic lesions in liver and spleen with suggestion of abscess/granulomatous lesion.

CECT chest and abdomen revealed multiple nodular opacities of various sizes distributed diffusely in bilateral lung fields and consolidation with air bronchogram in the left mid lobe [Table/Fig-2] with mild pleural effusion with underlying atelectasis. The nodular lesions and consolidation were showing heterogenous enhancement with necrotic areas



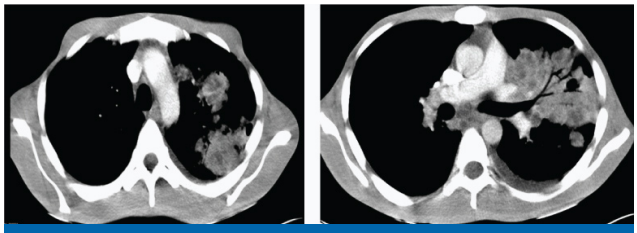
[Table/Fig-1a]: Chest radiograph at first visit shows inhomogeneous air space opacities suggestive of consolidation in left mid zone with multiple nodular opacities in lower zone.
[Table/Fig-1b]: Chest radiograph after 7 days of presentation showed increased alveolar nodular opacities in both lung fields.



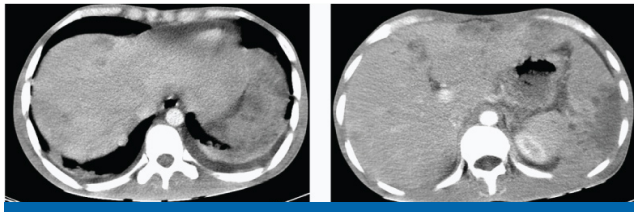
[Table/Fig-2]: CECT chest in lung window shows multiple nodular opacities of varying sizes distributed diffusely in bilateral lung fields and consolidation with air bronchogram in the left lingular lobe with mild pleural effusion.

in consolidation [Table/Fig-3]. Multiple mediastinal and left hilar lymphnodes were seen. Abdomen CECT shows mild hepatosplenomegaly with multiple peripheral ring enhancing ill-defined lesions suggestive of abscess [Table/Fig-4]. Splenic abscess aspiration was done under ultrasound guidance and sent for culture. Culture came positive for gram-negative bacterium *Burkholderia pseudomallei*.

Patient was diagnosed as a case of melioidosis with the back ground of blood culture and splenic abscess culture and supportive radiological findings. He was treated with supportive therapy and antibiotic therapy with Imipenem 1 gram 6 hourly for 2 weeks and Cotrimoxazole (trimethoprim 180mg + sulfamethazole 360 mg) was initiated as eradication therapy and continued for 3 months. Patient responded well for the antibiotics with clinical improvement and resolving lung lesions. Clinically patient became asymptomatic in 2 weeks and he was kept on follow-up every 3 weeks. At the end of the treatment schedule he was completely asymptomatic.



[Table/Fig-3]: CECT chest in mediastinal window shows, consolidation with air bronchogram in the left lingular lobe with mild pleural effusion, multiple nodular opacities in left lung and mediastinal necrotic nodes.



[Table/Fig-4]: Abdomen CECT shows mild hepato-splenomegaly with multiple peripheral ring enhancing ill-defined lesions suggestive of abscess.

CASE 2

A 47-year-old male, farmer presented with history of fever for one month with chills and rigors, not responding to regular antibiotics. He had history of anorexia and had lost about 8 kg weight over the past 45 days. Patient is known case of diabetes since one year and is on oral hypoglycemic drugs, with controlled blood sugars. His chest roentgenogram was reported elsewhere shows cavitating lesion with thin walls in upper lobe of left lung.

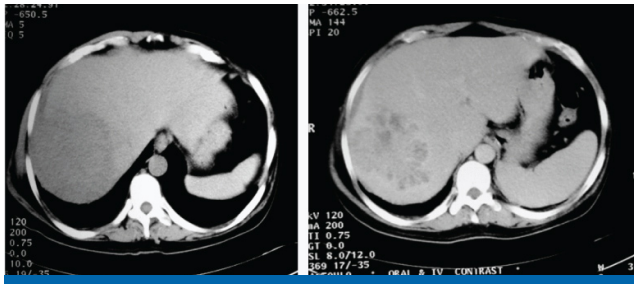
Three months back, he had fever, breathlessness, sore throat, loose stools and also history suggestive of cutaneous pustules and abscesses on head, trunk and extremities. For

which he took treatment in the local hospital which gradually subsided.

His blood investigation revealed elevated serum alkaline phosphatase (562 U/L), elevated TLC of 14,500/cumm and ESR of 68mm. Sputum was negative for acid fast bacilli.

Patient underwent USG abdomen and pelvis, which revealed heterogenous lesion in the right lobe of liver, which could not be characterized further but a possibility of abscess was given. CT of abdomen [Table/Fig-5] was done which shows ill-defined hypodense lesion in segment VII and VIII. On contrast the lesion shows predominantly heterogeneous peripheral enhancement, which favors the diagnosis of abscess.

FNAC from the liver lesion was done under USG guidance.



[Table/Fig-5]: CT of abdomen was done; pre-contrast study shows ill-defined hypodense lesion in segment VII and VIII. On contrast the lesion shows heterogeneous peripheral enhancement.

Pus was aspirated and sent for culture, which was positive for gram-negative bacterium *Burkholderia pseudomallei*. Patient was started on with Imipenam and Bacterim. Pig tail insertion was done for liver abscess under USG guidance and left for 7 days till complete drainage of the abscess. Patient was discharged after 10 days with no clinical symptoms and was followed-up on regular OPD basis.

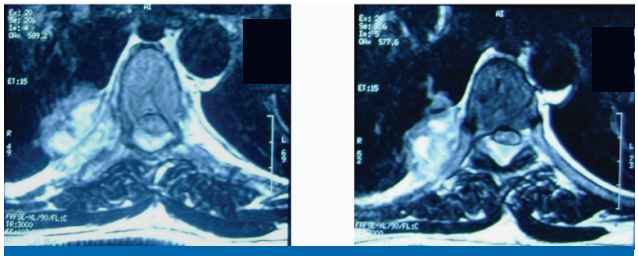
CASE 3

A 40-year-old male, carpenter by occupation was a known diabetic and alcoholic. He presented with sudden onset of backache for 20 days with high grade fever with chills and rigors for 1 week, severe abdominal pain for 1 week and sudden onset of weakness in lower limbs, urinary and fecal incontinence since 2 days.

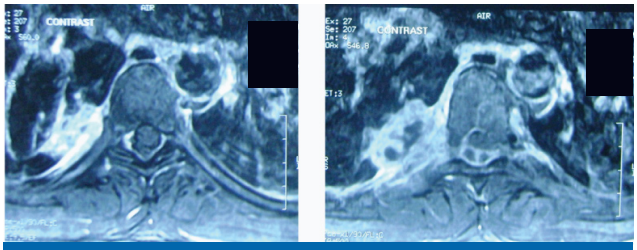
He had a history of recent visit to Malaysia 10 months ago. No past history of trauma or tuberculosis contact. On clinical examination, he had tenderness over the back from T6 -10 level with normal motor system examination in upper limbs, flaccid lower limbs with power of 0 / 5 in all muscle groups and DTR absent in lower limbs. On sensory system examination there was decreased sensations from T7 level with tenderness over the back from T6-10 level. With these findings, clinical diagnosis of acute paraplegia due to infection (pyogenic or tuberculosis) was made.

Routine blood investigation showed elevated TLC with neutrophilic predominance, elevated ESR 64mm in first hour.

MRI of D-L spine [Table/Fig-6] with contrast was done. Mild altered signal intensity was seen in D8 and D9 vertebra with T1 heterogenous but hypointense and T2 hyperintense soft tissue lesion in the right para-vertibral region at D8-D9 vertebral level with epidural collection extending from D7 to D9 vertebra, compressing and displacing the cord anteriorly. Post contrast image [Table/Fig-7] shows, heterogenous peripheral enhancement of the lesion suggesting abscess in para-vertibral space and in epidural space which was compressing over the cord. Considering typical clinical presentation and its imaging findings, diagnosis of Pott's spine was made on imaging. Patient underwent an emergency T6-T10 laminectomy and drainage of the abscess. About 15ml of frank pus with extensive granulation tissue over the dura was noted. Gram stain showed plenty of pus cells, no organisms were seen. AFB staining was negative. Pus and Blood in subcultures showed growth of *Burkholderia pseudomallei*, the causative agent for melioidosis. Post surgery patient was put on antibiotics. He recovered well with no residual neurological deficits. No recurrent lesions seen in 6 months follow-up.



[Table/Fig-6]: T2 axial section shows hyperintense lesion in the right paravertebral region at D8-D9 with Epidural collection compressing and displacing the cord anteriorly.



[Table/Fig-7]: Post contrast images shows heterogeneous peripheral enhancement of para-vertibral abscess and enhancing epidural collection compressing the cord.

CASE 4

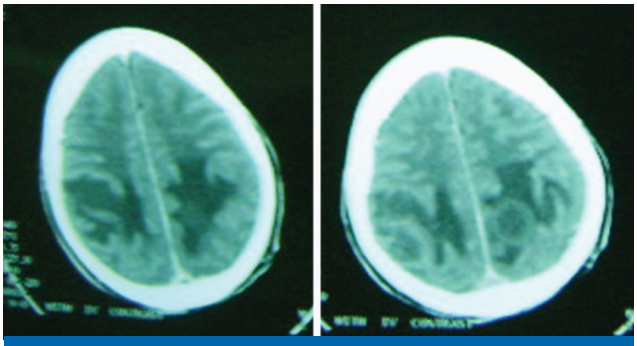
53-year-male, paddy farmer by occupation presented with chief complains of high grade fever and abdominal pain for 20 days. He developed icterus and progressively increasing

pain in the right hypochondrium since 15 days. 10 days back he had two episodes of generalized tonic-clonic seizures with dull headache.

On examination patient was disoriented and febrile. Abdomen examination revealed tenderness in the right hypochondrium. He had a soft fluctuant swelling of 3 x 4 cm over the scalp, which was tender, warm and fluctuant suggestive of an abscess.

Blood investigation elevated TLC (14,000/cumm), raised ESR of 56mm in the first hour, HIV and HBsAg – Negative.

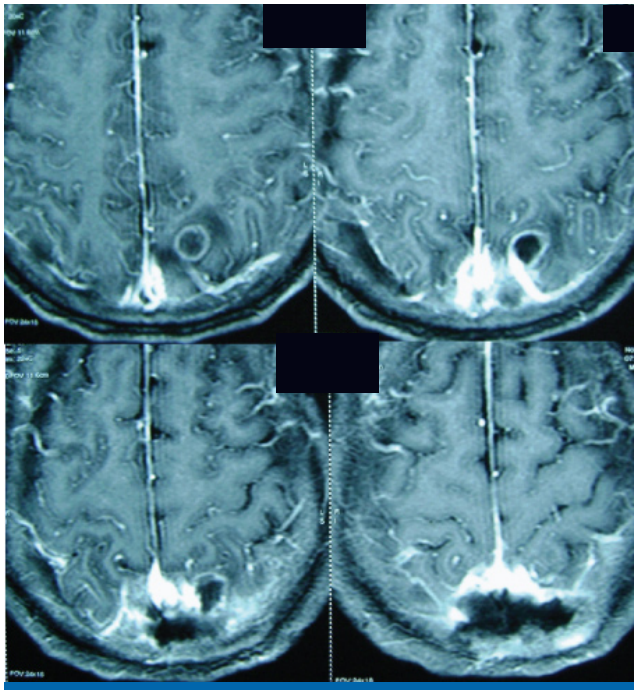
Chest radiograph was normal. Ultrasound abdomen revealed a liver abscess of 20cc. (Note: USG images not available). Further to access his scalp swelling CT brain contrast was done [Table/Fig-8], which shows peripheral ring enhancing lesion in bilateral high parietal region with significant perilesional edema suggestive of abscess. Focally thinned out calvarium with lytic and sclerotic areas were noted in the occipital bone suggestive of osteomyelitis



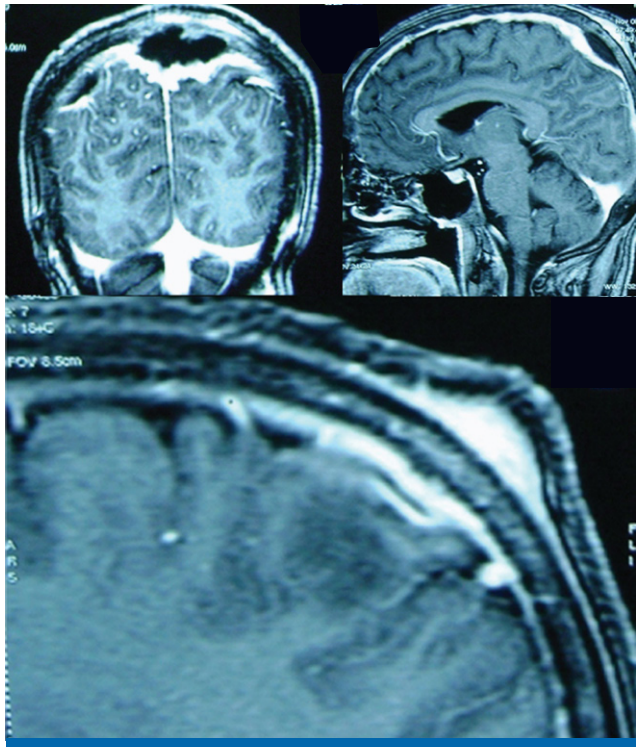
[Table/Fig-8]: Peripheral Ring enhancing lesion in bilateral high parietal region with significant edema suggestive of abscess.

MRI was done [Table/Fig-9&10] which shows, T1 hypointense, T2, FLAIR hyperintense ill defined lesion in bilateral high parietal region with obliteration of the sulcii and gyri. Hyperintense collection also noted in the adjacent subdural space and in the scalp. Post contrast study shows peripheral ring enhancing lesions in bilateral high parietal region suggestive of abscess. Non-enhancing collection suggestive of subdural abscess noted with thick enhancing meninges. Minimal enhancement of the calvaria noted suggestive of osteomyelitis with adjacent subcutaneous abscess.

Patient was operated, the osteomyelitic bone was removed, abscess collection over the dura mater drained. There was suggestion of breach of the dura with cerebritis. The intra parenchymal abscess was drained out. Blood and pus have shown growth of *Burkholderia pseudomallei*. He was started on antibiotics with good recovery. Discharged after 20 days of hospital stay. He was lost for follow-up.



[Table/Fig-9]: Axial post contrast images shows peripheral ring enhancing lesions in bilateral high parietal region suggestive of abscess, adjacent subdural abscess with thick enhancing meninges, minimal enhancment of the calvaria and involvement of superior Sagittal sinus.



[Table/Fig-10]: Coronal and Sagittal post contrast images shows subdural abscess with thick enhancing meninges and minimal enhancement of the calvaria with adjacent subcutaneous abscess.

DISCUSSION

Melioidosis is endemic in tropical countries like South East Asia and Northern Australia [2,3], with reported sporadic cases from India, Taiwan, Sri Lanka, Korea, China, the Middle East and the America [3-7] with it being increasingly recognized across India, where it is under diagnosed and under reported. Clinically and radiologically, it may imitate tuberculosis, malignancy or any other disease and hence described as "great mimicker".

The organism typically enters the host through inoculation into skin, by inhalation, or by ingestion with person-to-person transmission being rare. After entering the host, the bacillus may remain asymptomatic or cause local infection or spread to distant sites in the body via the blood. Direct inoculation into the skin can cause subcutaneous abscesses, osteomyelitis of underlying bone with discharging sinuses. Inhalation can cause pneumonia, multiple nodular opacities with cavitatory lesions and adenopathy. Through the blood, the bacillus can reach distant organs such as the liver, spleen, and brain and cause abscesses in these locations. The infection can be asymptomatic, acute or chronic. The spectrum of acute form ranges from acute localized suppurative skin infection with lymphadenitis, acute pulmonary infection, and an acute septicemic form with fulminant septicemic shock to abscesses in multiple organs including liver, spleen, brain and other organs. Chronic form presents as mild undifferentiated pneumonia, pleuritic chest pain and chronic suppurative melioidosis [20-23].

Pneumonia is one of the most common clinical presentations in pulmonary melioidosis accounting for 50% of clinical presentation [23-26]. The presentation of acute Pneumonia varies from mild variety that can be acute to sub-acute in nature to more serious fulminant septic shock, which can carry very high mortality [25, 27]. Differential diagnosis includes other bacterial infection in acute cases and tuberculosis, fungal infection in chronic cases.

Imaging plays an important role in evaluation of these cases. On chest radiograph, the presentation of Pneumonia varies from diffuse nodular opacities which can involve the entire lung, coalescent nodular pattern, cavitatory nodules or consolidation. These findings if confined to upper lobes, especially in patients from endemic areas, possibility of melioidosis has to be considered. This upper lobe predominance in endemic areas has also been reported in literature [28,29].

Chronic form of Melioidosis usually presents with fever, weight loss and cough with sputum [2,30]. Remitting and relapsing course over many years is known, however acute deterioration with septicemia can occur even though rare.

The spleen is the most common affected visceral organ, followed by the liver and kidney [13,17,18]. On ultrasound abscesses appear as multiple and small ill-defined hypoechoic lesions and multiloculated lesions. On CT, abscesses are seen as single or multiple small ill-defined hypodense discrete lesions which shows peripheral enhancement in post contrast images. Presence of hepatic and spleenic abscess together is commonly associated with melioidosis, and this finding should suggest melioidosis in endemic areas [18,31]. Generally, for most types of infection, finding a spleenic abscess is unusual. Therefore, detection of spleenic abscesses alone is suggestive of melioidosis, especially in those with co-morbid diseases or in patients living or travelling in endemic areas who present with fever of unknown origin, abdominal pain or discomfort. Concomitant liver and spleenic abscesses are also suggestive of melioidosis [13,17,18,31]. Differential diagnosis for hepatosplenic abscess includes fungal infection, tubercular abscess and rarely bacterial abscess.

CNS findings range from normal CT findings in the initial stages of cerebrities to well-defined macroabscess. MRI is more sensitive in the initial stages of the disease, with T2-weighted and FLAIR images detecting hyperintense changes in the brain parenchyma with contrast enhanced images showing irregular ring enhancing lesions. There is a predilection for infection of the frontal lobes and brainstem. Other radiological features include micro-abscesses, osteomyelitis, encephalitis, and myelitis. Differential diagnosis in CNS are mostly bacterial or tubercular infection. Other organs are rarely get affected by melioidosis. However involvement of the musculoskeletal system by melioidosis is not rare and it shows varied presentation in the form of osteomyelitis, soft tissue abscess and rarely septic arthritis.

CONCLUSION

Melioidosis, "great mimicker" is a multi-organ endemic disease in south East Asia and in northern Australian countries. It has great clinical diversity from skin ulcers to fulminant septic shock. Imaging plays an important role in disease evaluation, however knowledge of its varied presentation in imaging including consolidation, nodules, cavitatory lesions and abscesses in lung, in abdominal visceral organs which are highly suggestive of melioidosis helps in its early diagnosis.

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