18-Fluorine-Fluorodeoxyglucose Positron Emission Tomography–Computed Tomography in the Evaluation of the Great Masquerader Melioidosis: A Case Series

Abstract

Melioidosis is an emerging infectious disease in India. The disease has a crippling effect on the patient owing to its widespread dissemination and complications post bacteremia. The role of 18-fluorine-fluorodeoxyglucose (FDG) positron emission tomography–computed tomography (PET-CT) is becoming increasingly important in terms of documenting the extent of disease and response to treatment. Herein, we present cases of two patients who were referred for a whole-body 18F-FDG PET-CT scan with a history of long-standing fever that went undiagnosed. 18F-FDG PET-CT scan was performed to evaluate pyrexia of unknown origin. A conclusion was reached after blood culture which showed the growth of *Burkholderia pseudomallei* – which is considered to be the cause of this rare but debilitating disease.

Keywords: *Burkholderia pseudomallei, emerging infection and 18-fluorine-fluorodeoxyglucose positron emission tomography–computed tomography, melioidosis*

Pramukh Kulkarni, Simon Shelley, Indirani M Elangoven, A. Jaykanth, Asra Patel Ejaz, Nikita Sampathi Rao

Department of Nuclear Medicine and PET-CT, Apollo Hospitals, Chennai, Tamil Nadu, India

Introduction

The first description of melioidosis, glanders-like disease, was by Alfred Whitmore and his colleague Krishnaswami who described it among drug addicts in Rangoon, Burma, in 1911.[1]

The disease was called melioidosis – the word originates from the Greek word "melis" meaning distemper disease of donkeys and "eidos" (resemblance) by Stanton and Fletcher in 1932.[2] The Gram-negative organism is now known by various names such as *Bacillus pseudomallei*, *Bacillus whitmorii* (or Bacille de Whitmore), and *Burkholderia pseudomallei*.

The geo-distribution of the pathogen is mostly confined to South East Asia and Northern Australia and has off late gained importance as an emerging pathogen in India. Infection is thought to be acquired after bacterial inoculation, ingestion, or inhalation.[3] The extent of the disease consists of a wide spectrum with localized infection at one end to widespread bacteremia leading to fulminant sepsis at the other end. It is capable of causing various clinical manifestations such as pneumonia, septicemia, arthritis, and abscess and is associated with high morbidity and mortality.

The largest case series of melioidosis from India by Gopalakrishnan *et al*.[4] reported 32 culture-proven cases of melioidosis.

They noted that the incidence of infection was more common among males with a median age of 42.5 years, with most of the cases presenting with fever and weight loss.

In India, most of the cases diagnosed have been reported from the southern states such as Kerala[5] and Tamil Nadu.[6] A few cases have also been reported from the eastern and northeastern parts of India. Early and correct diagnosis and institution of a proper antimicrobial therapy are important to reduce morbidity and mortality and have a favorable outcome.

Case Reports

Case 1

A 39-year-old male from the state of Assam, India, presented with intermittent fever for 3 months associated with generalized weakness due to which he was bedbound for

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Address for correspondence:
Dr. Pramukh Kulkarni, Department of Nuclear Medicine and PET-CT, Apollo Hospitals, Chennai, Tamil Nadu, India.
E-mail: pkmedhub@gmail.com

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2 months with a history of passing high colored urine. He was on regular medications for diabetes mellitus for 6 years. He was treated as a case of septic arthritis elsewhere.

On examination, he was febrile (body temperature = 102° F), icteric, dehydrated, hypotensive (blood pressure: 90/70 mmHg), tachypneic (respiratory rate: 50 cycles/min), and had tachycardia (heart rate: 128/min). On auscultation, crackles were heard on both sides. The spleen was mildly enlarged (4 cm below the costal margin) with no evidence of free fluid in the abdomen. No neurological abnormality was noted. On local examination, he had multiple skin lesions over the right forearm [Figure 1] and a Grade 3 bedsore in the left gluteal region.

Blood investigations showed pancytopenia and elevated C-reactive protein levels. Diagnostic workup for vasculitis was negative. Ultrasound study of the abdomen showed mild ascites with bilateral pleural effusion and splenomegaly. Laboratory investigations are listed in Table 1. Chest X-ray [Figure 2] showed multiple lobulated pleural-based opacities along the left lateral pleura projecting into lung parenchyma, i.e., into left hemithorax and a similar smaller lesion along the right lateral pleura.

Whole-body 18-fluorine-fluorodeoxyglucose positron emission tomography–computed tomography (18F-FDG PET-CT) scan was performed, which showed 18F-FDG-avid multiple destructive lytic lesions with soft-tissue component and necrosis involving the entire axial and appendicular skeleton, bilateral pulmonary nodules, and hepatosplenomegaly with no focal FDG uptake [Figures 3-5].

Blood culture and sensitivity workup showed the growth of *B. pseudomallei* [Figure 6].

Case 2

A 46-year-old male from the Andaman and Nicobar Islands, India, presented with high-grade fever for 4 months associated with burning micturition and increased frequency of urination. The patient had a history of diabetes for 14 years.

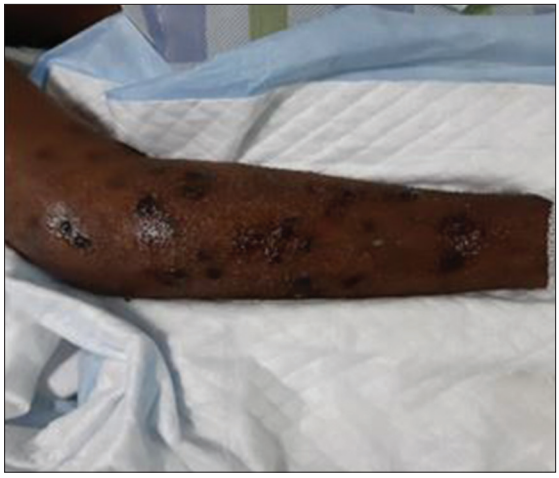

Figure 1: Multiple skin lesions over the right forearm

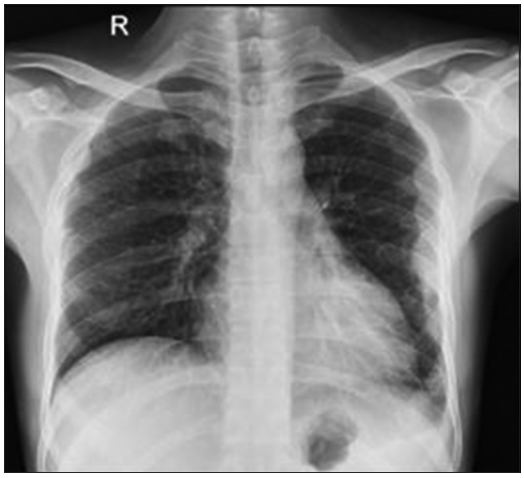

Figure 2: Chest X-ray showing multiple lobulated pleural-based opacities

Table 1: Laboratory findings

Parameter	Result	Reference value
Hemoglobin	6.4	13-18 g/dL
Packed cell volume	19	40-54%
White blood cell count	3.0	4-11×10^3 mm
Platelet count	120	150-450×10^3 mm
Neutrophils	85	40-80%
Lymphocytes	11	20-40%
Monocytes	4	2-10%
ESR	140	0-15 mm/h
Reticulocyte count	3.0	0.2-2%
Lactate dehydrogenase	336	125-220 U/L
Serum creatinine	0.6	0.9-1.3 mg/dl
Total bilirubin	2.0	0.0-1.3 mg/dl
Conjugated bilirubin	1.4	0.0-0.5 mg/dl
Alkaline phosphatase	368	<128 U/L
CRP	160	<5.0 mg/L

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein

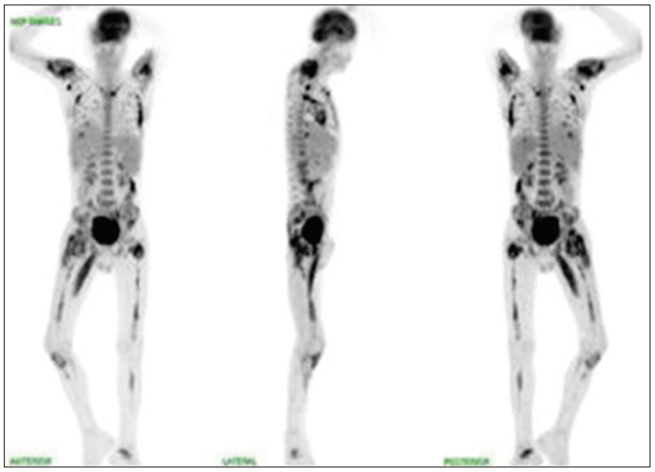

Figure 3: Maximum intensity projection of the whole body 18-fluorine-fluorodeoxyglucose positron emission tomography–computed tomography image showing tracer uptake in the entire axial and appendicular skeleton, bilateral pulmonary nodules, and multiple lymph node levels

On examination, he was febrile (body temperature: 104° F), normotensive, and had tachycardia (heart rate: 132/min). Normal vesicular breath sounds were heard. Per abdomen examination was normal. No cardiovascular or neurological abnormality was noted.

Fusion PET/CT imaging was performed, which showed bulky left kidney with ill-defined collections [Figure 7] and para-aortic, interaortocaval, and retrocaval nodes.

Following the 18F-FDG PET-CT, ultrasound-guided renal abscess aspiration was performed that was sent for culture and sensitivity. VITEK 2 method revealed *B. pseudomallei* on culture.

Discussion

B. pseudomallei is an inhabitant of the wet and temperate environment and is widely disseminated in soil, water, paddy fields, etc., Human infection occurs through inhalation or direct inoculation on damaged skin.

Active infection has been predisposed to occur in patients with many underlying conditions such as diabetes mellitus, renal disease, and HIV. Diabetes mellitus has been found to be one of the most frequent predisposing factors. Vidyalakshmi *et al*.[7] found a correlation of 76% of diabetes with melioidosis. Melioidosis is a systemic manifestation with pulmonary involvement as the most common manifestation.

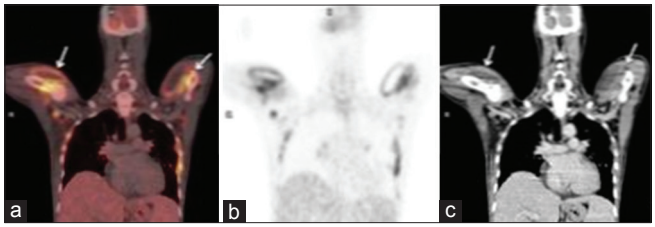

Figure 4: (a-c) Axial images (fused positron emission tomography–computed tomography, positron emission tomography, and computed tomography images, respectively) showing increased 18-fluorine-fluorodeoxyglucose uptake in multiple destructive lytic lesions with soft-tissue component and necrosis involving the right humerus

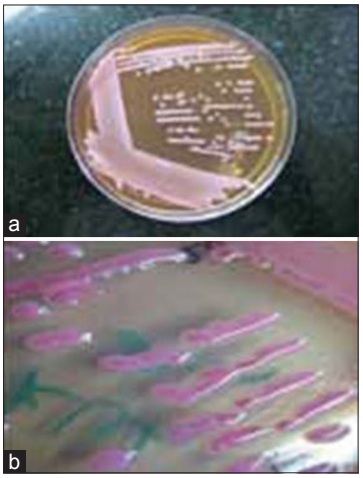

Figure 6: (a) Culture plate and (b) colonies of *Burkholderia pseudomallei*

18F-FDG PET-CT plays an integral part in the workup of a patient with pyrexia of unknown origin (PUO).

Subran *et al*.[8] in their case report described a patient who had a history of travel to Cambodia and presented with fever and bony pain. PET-CT was performed for the initial evaluation of melioidosis. Surgical bone biopsy of the right humerus revealed granuloma with necrosis. Bone marrow culture led to the isolation of *B. pseudomallei*. Pre- and postantibiotic treatment PET-CT scans revealed the disappearance of 18F-FDG uptake in the humerus lesion. They concluded that PET-CT showed complete healing more accurately than magnetic resonance imaging, which displayed chronic abnormalities related to bone marrow remodeling after osteomyelitis. Hence, PET-CT was useful to look for skeletal lesions and asymptomatic lesions and to plan length of antibiotic therapy.

Zaw *et al*.[9] described a case of melioidosis mimicking lung malignancy. Initial imaging of the chest by CT showed a right lower lobe opacity suspicious for primary pulmonary malignancy, and PET scan showed moderate FDG avidity of the lesion. Flexible bronchoscopy showed no endobronchial lesion; then, using the endobronchial radial ultrasound probe and utilizing the guide sheath technique, the lesion was localized in the posterior segment of the right lower lobe. Biopsy showed necrotic tissues, and no malignancy was detected. The culture of bronchial brushings on Ashdown's agar grew Gram-negative bacterial colonies, and bacterial colonies confirmed the organism to be *B. pseudomallei*.

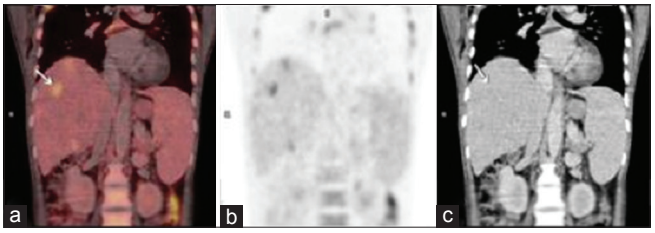

Figure 5: (a-c) Coronal images (fused positron emission tomography–computed tomography, positron emission tomography, and computed tomography images, respectively) showing focal increased 18-fluorine-fluorodeoxyglucose uptake in ill-defined hypodense lesions in the right lobe of the enlarged liver and the enlarged spleen

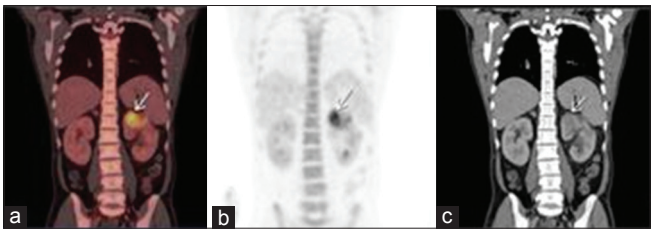

Figure 7: (a-c) Coronal images (fused positron emission tomography–computed tomography, positron emission tomography, and computed tomography images, respectively) showing bulky left kidney with multiple ill-defined collections with micro- and macro-abscess in the upper and mid-pole with the largest collection measuring 5.5 cm × 3.0 cm. Corresponding increased 18-fluorine-fluorodeoxyglucose uptake was noted with SUV_{max} of 8.1

Conrad *et al*.[10] reported a case of a 25-year-old woman with disseminated melioidosis and osteomyelitis of the femur secondary to melioidosis. The PET-CT scan acted as a tool for effective follow-up and to look for the evolution of the infection and helped in the evaluation of response to treatment.

With the advantage of the whole body, i.e., multisystem imaging, 18F-FDG PET-CT can identify symptomatic as well as asymptomatic lesions, providing the physician with a wealth of information as a baseline scan. It also helps in the evaluation of response to treatment, adequacy of treatment, and hence helps in proposing the duration of treatment during the eradication phase. The resolution of FDG uptake indicates response to therapy which is a reliable marker as compared to findings on anatomical imaging.

In this era of antibiotic resistance and increasing incidence of melioidosis infection, 18F-FDG PET-CT is a vital investigation that provides both qualitative and quantitative assessments of the extent of infection and more importantly to guide the site for biopsy in occult cases and to assess response to antibiotic therapy.

Conclusion

In our subcontinent, with the increasing use of 18F-FDG PET-CT as an important investigation for evaluating a patient with PUO, it is necessary to consider melioidosis as a differential diagnosis which closely resembles and masquerades tuberculosis and lymphoma which are considered as the most probable differentials in a patient with PUO.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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