^{99m}Tc-MDP whole body bone scan in a case of acute disseminated melioidosis

Case Report

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ABSTRACT

Melioidosis is a potentially fatal infectious disease occurring predominantly in the tropics, caused by a Gram-negative, motile, rod shaped obligatory aerobic non-spore forming bacillus, Burkholderia pseudomallei. It can produce localised or disseminated disease largely affecting immunocompromised patients. It is a challenge to identify melioidosis early as this disease can manipulate host's cellular immune response to escape detection. Although musculoskeletal involvement in melioidosis is said to be the predominant manifestation, reports have shown widespread involvement in the form of abscesses in lung, liver and spleen etc. It predominantly occurs in patients with diabetes mellitus or those suffering from chronic alcohol abuse, cirrhosis, smoking, chronic lung disease or patients on longstanding corticosteroid use. We present a 43-year-old diabetic male with fever and headache of 5 months duration, abdominal and left sided hip pain with difficulty in walking for 3 weeks. ^{99m}Tc-MDP three phase bone scan revealed increased tracer uptake in left femur leading to a diagnosis of focal osteomyelitis. In view of dull aching, intermittent abdominal pain, further investigation was carried out. Contrast enhanced CT abdomen showed hepatosplenomegaly with rim enhancing tiny lesions scattered in liver and spleen suggesting possibility of micro abscesses. Serial blood cultures grew Gram-negative bacilli, which was later identified as B.pseudomallei. Patient was subsequently started on meropenem, doxycycline and cotrimoxazole. Bone scan was the first investigation to identify the pathology and mooted further investigation to identify visceral involvement guiding appropriate management. He was followed up for a period of 6 months and had an uneventful recovery.

Key words: Nuclear medicine imaging; Bone scan; Melioidosis; Osteomyelitis; Diabetes

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INTRODUCTION

Tropical climates and immunocompromised conditions of patients can encourage many infections to set in, like tuberculosis, sarcoidosis, melioidosis etc. Reports show that South Asia has a high burden of Melioidosis (44% of all cases) [1]. Sri Lanka and Bangladesh are known to be melioidosis endemic. There is a paucity of case detection from Indian subcontinent with an additional high incidence of diabetes [2]. The true melioidosis burden in India remains unknown and may be attributed to factors like limited awareness, laboratory constraints and socioeconomic conditions etc. Melioidosis is caused by Burkholderia pseudomallei, a soil saprophyte that is usually found in stagnant water and paddy fields. Human transmission occurs through skin abrasions and inhalation especially in paddy field workers [3]. Susceptibility increases in the patients with pre-existing co morbidities like diabetes mellitus, chronic renal failure, alcoholism, cirrhosis, and other immune compromised status [4, 5]. The commonest risk factor is thought to be diabetes mellitus, found in more than 50% of all patients infected with melioidosis worldwide. There is a100-fold higher risk of melioidosis after adjusting for age, sex, and other risk factors [6]. The organism can also infects humans through oral route [7]. Disease usually manifests after a recent exposure. However the signs and symptoms for melioidosis are nonspecific compounded by neuropathy in diabetics, therefore it is also nicknamed *"the great mimicker*". The usual presentation is febrile illness ranging from septicaemia, pneumonia to abscess formation which may involve almost every organ in the body. The lung is the most affected organ presenting as pneumonia along with abscesses in the abdominal organs like spleen and liver. Osteomyelitis caused by B pseudomallei infection is uncommon with few reported cases in literature [8-11]. We report a case of disseminated skeletal melioidosis (femoral involvement) with visceral micro abscesses (liver and spleen) in a diabetic Indian male patient.

CASE PRESENTATION

A 43-year-old male who was a known case of Type 2 diabetes mellitus, came with complaints of fever and headache of 5 months duration. Patient also had left sided hip pain with difficulty in walking for 3 weeks. He was apparently normal 5 months back when he developed high grade fever which was continuous in nature and was not associated with chills, rigors or delirium. He had frontal headache during the febrile episodes, occasional vomiting and abdominal pain (dull aching, intermittent in nature). Bowel and bladder habits were normal. Patient was treated locally with broad spectrum antibiotics, but fever recurred after subsiding for few days. Patient had weight loss of 5 kilograms over 5 months along with loss of appetite. Therefore, patient was brought to our tertiary care institute for further evaluation and management. His C reactive protein on admission was very high (334 mg/l, normal range 0.0-1.0 mg/l) along with serum procalcitonin levels (4.43ng/ml, normal range 0 - 0.15 ng/ml). His HbA1c was 8.8 % (range 4.5- 6 % in non-diabetics). Renal function tests were also found to be within normal limits. Serum alkaline phosphatase was high (386.0 IU/ml, normal range 0.0-130 IU/ ml). In view of left hip pain, patient was referred to our department for whole body skeletal scintigraphy. Technetium-99m methylene diphosphonate (^{99m}Tc-MDP) three-phase regional and whole-body bone scan was performed using 20 mCi (740 MBq) of ^{99m}Tc-MDP injected intravenously. Vascular and soft tissue phase images of pelvis and femurs were acquired. Three hours later whole body anterior and posterior images were acquired using GE Optima NM 640 dual head gamma camera. Imaging was performed using the following parameters; feet first supine position in 256 x 256 matrix. Anterior, posterior images whole body sweep images were acquired in continuous scan mode at 13cm/min scan velocity. Skeletal phase images showed diffuse heterogeneously increased tracer uptake along the full thickness cortex of middle and lower 1/3rd shaft of left femur (Figure 1). No other hot spots were detected in the rest of whole body survey. Single Photon Emission Computed Tomography – computed tomography (SPECT CT) of the bilateral femurs was also acquired. The CT parameters used consisted of 120 kilovolt, with tube current of 30 mill-amperes. Each CT slice had a thickness of 2.5mm, and matrix of 512 x 512. Ordered subset expectation maximisation with 2 iterations, 10 subsets. Filter used for reconstruction was vendor specified Butterworth filter, Critical Frequency of 0.48 and power 10. There was the presence of cortical thickening corresponding to increased ^{99m}Tc-MDP uptake on SPECT-CT images, which could represent osteomyelitis (Figure 2). Blood and urine cultures detected the growth of gram negative bacilli which was identified as Burkholderia pseudomallei. Contrast enhanced multi detector computed tomography of abdomen showed hepatosplenomegaly with multiple hypoenhancing tiny lesions scattered in liver and spleen suggestive of granulomas/microabscesses (Figure 3). A rapid method for determination of microbial sensitivity to antibiotics was used (i.e Mibg sensitivity). It revealed the bacterium to be sensitive to cotrimoxazole, ceftazidime, meropenem and doxycycline. Patient was started on IV Meropenem 1gm twice daily along with cotrimoxazole 960 mg twice a day. Patient showed improvement in the symptoms, became afebrile and was able to walk without support after 3 days of treatment. He was discharged on maintenance regime of oral cotrimoxazole 960 mg twice a day and oral doxycycline 100 mg twice a day for 20 weeks.

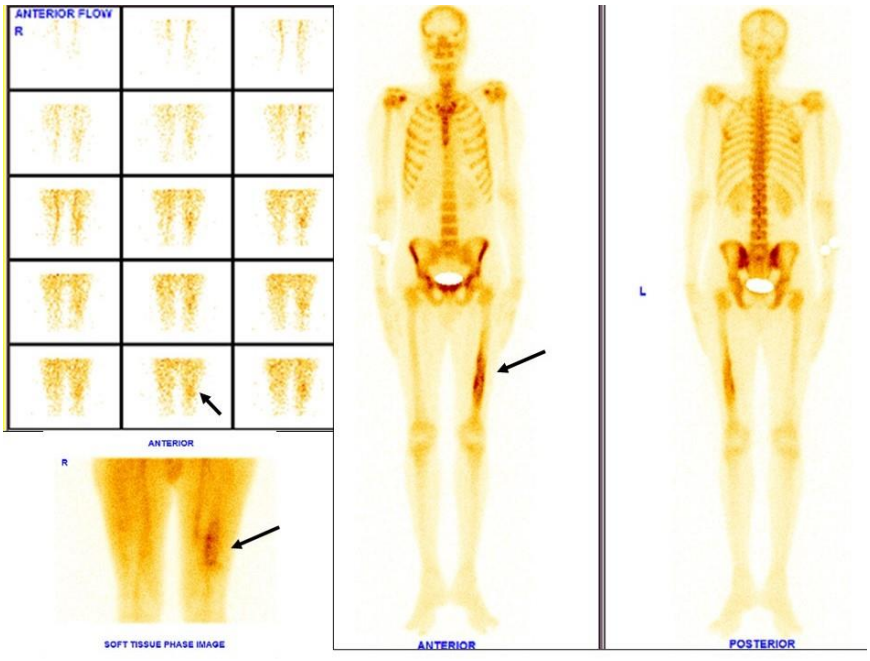

Fig 1. ^{99m}Tc-MDP three phase and whole-body bone scan images show increased vascularity, soft tissue tracer uptake along with diffuse heterogeneously increased tracer uptake in full thickness cortex of middle and lower 1/3rd shaft of left femur (arrow) with central interspersed photopenia.

Patient had an uneventful recovery and remained asymptomatic after 6 months of follow up. Subsequent ultrasound abdomen showed resolution of the liver and splenic lesions.

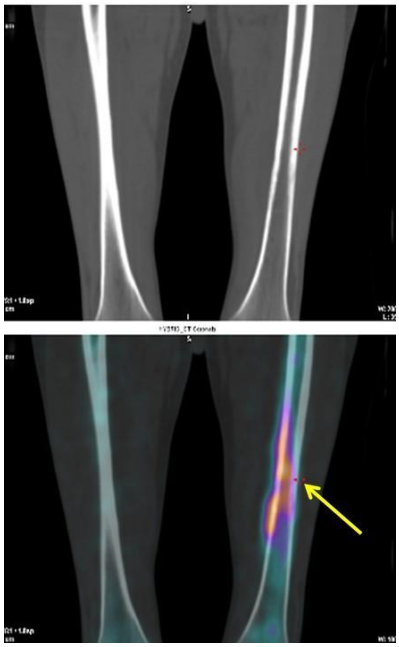

Fig 2. CT and Fused MDP SPECT CT images of femur show presence of cortical thickening (arrow) corresponding to site of increased 99mTc MDP in left femoral shaft.

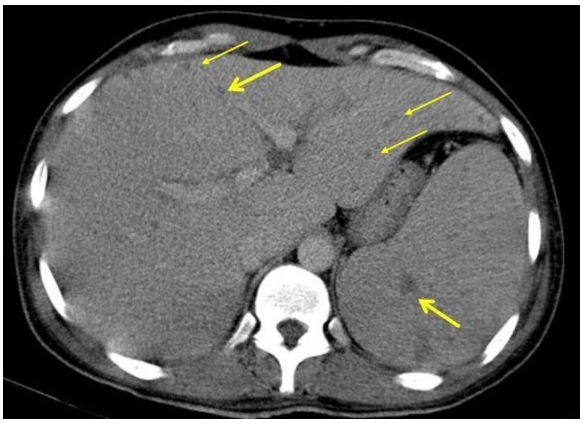

Fig 3. Transaxial sections of contrast enhanced CT abdomen showed multiple tiny hypodense lesions in liver and spleen (arrow).

DISCUSSION

Melioidosis is also known as Whitmore's disease. The bacterium was first isolated by Captain A Whitmore and the term melioidosis was coined in 1921 by Stanton and Fletcher. Human to human transmission of this bacterium is very rare. Direct inoculation through abraded skin is most common mode of transmission of this disease. The incubation period of the organism varies, due to the type of infection and severity of infection. It ranges from one day to many years [5]. Generally, symptoms will appear two to four weeks after exposure to the pathogen. Tuberculous

osteomyelitis is common in India. Osteomyelitis due to melioidosis is uncommon and only few cases are found in the literature [8-11]. In the 10-year prospective study on endemic melioidosis in northern Australia by Currie et al, among 252 cases only 4 % presented with osteomyelitis or septic arthritis [5]. Melioidosis has a potential of causing latent infection and then reactivating into an acute fulminating infection during the immunocompromised states. Although any bone can be involved in Burkholderia osteomyelitis there seems to be a predilection for long bones. In a case report by Subramanyam et al, three phase bone scan identified not only multiple sites of bone involvement but also extraskeletal renal involvement that was later proven by culture [12]. ^{99m}Tc-MDP whole body and three phase scan can prove an efficient and effective tool in detecting the skeletal involvement. Identification of early bone remodelling forms the basis of this physiological nuclear medicine technique. It identifies the site and extent of osteomyelitis during an early stage, much before the anatomic changes take place. Both X-ray and CT can identify bone changes quite late in the disease process. A typical CT can detect osteomyelitis 10 to 14 days before changes are visible on plain radiographs. Combined with blood culture, ^{99m}Tc-MDP bone scan can be instrumental in arriving at a diagnosis during the early stages of the disease. Prompt initiation of appropriate antibiotics can yield excellent results. Although common infectious etiologies such as Staphylococuus aureus and Neisseria species in acute settings and Brucella and Mycobacterium in chronic cases must be considered, the rare differential diagnosis of multifocal osteomyelitis caused by B.pseudomallei should be kept in mind. Diagnosis of Melioidosis is best achieved through the isolation of the organism from a sample taken from the blood, sputum, skin lesion, abscess, or urine. Any delay in diagnosis and initiation of appropriate therapy could prove catastrophic. Earlier the diagnosis, better is the outcome of the patient. Initially ceftazidime was considered as the treatment of choice for melioidosis but recent evidence suggests that carbapenems have a higher bone penetrating ability which makes it more efficacious. However these organisms have a capability to survive in the phagocytic cells. Carbapenems cannot act intracellularly and thus tetracyclines or fluoroquinolones must be added to prevent relapse.

CONCLUSION

Three phase bone scintigraphy is a simple, non-invasive imaging technique that can identify sites of bone infection and inflammation with high degree of sensitivity. Classical findings of osteomyelitis in three phase bone scintigraphy involves a combination of focal hyperperfusion, focal hyperemia, and focally increased bone uptake is virtually diagnostic in patients when the structure of bone is still intact. Bone scan clearly demarcates the location, extent and multifocality of lesions. Diagnosis of melioidosis can be very easily missed based on the extent, severity of disease. Based on bone scan findings, further investigations were carried out. This helped in identifying osteomyelitis and visceral microabscesses. Early diagnosis and prompt administration of IV antibiotics followed by maintenance with oral antibiotics is the key to good outcome in melioidosis.

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