Case Report

An uncommon cause of fever in a patient with hyperthyroidism

Krishna P. Gautam[1], Kanakkankotil U. Lijesh[1], John Jude[2], Riddhi D. Gupta[1], Thomas V. Paul[1]

[1]Departments of Endocrinology and [2]Clinical Microbiology, Christian Medical College and Hospital, Vellore, Tamil Nadu, India

Abstract

Fever as an indicator of disease has always been and remains a clinical symptom of great importance. It may be a manifestation of any inflammatory process of the thyroid and also may be presenting feature of thyroid storm. Melioidosis, is an infection caused by the gram negative bacterium Burkholderia pseudomallei and the commonest co-morbidity observed in India is diabetes mellitus. Here we present a case of Graves disease (hyperthyroidism) who was referred by primary care physician with history of prolonged fever of more than one month duration and later diagnosed to have melioidosis. It is important in primary care setting as family physicians need to be aware of this infection as it can affect many organs and early diagnosis and treatment will result in cure of this condition.

Keywords: Burkholderia pseudomallei, fever, hyperthyroidism, melioidosis

Introduction

Melioidosis is an emerging infection in India, especially in males from rural areas, with diabetes and alcoholism being the commonest risk factors. Both sepsis with bacteremia and localized disease involving joints and focal abscesses are common. Melioidosis is more prevalent in immunosuppressed populations with diabetes mellitus or malignancy.[1] The commonest co-morbid condition observed was diabetes mellitus (80%) in a case series of 114 of whom 25 had liver abscesses who succumbed to their illness.[2] Prolonged febrile illness may be the presenting symptom in Melioidosis. Primary care and family physician needs to be aware of this infection as early diagnosis and treatment will reduce the morbidity associated with this condition.

A 32-year-old woman referred by a primary care physician presented with a history of prolonged fever of 40 days duration. She was a homemaker with no known contact to animals, farming, or gardening. She had two to three spikes of fever with chills per day with temperatures recorded up to 38°C. She had a history of receiving quinolones and penicillin group of drugs for febrile illness. She was earlier diagnosed to have hyperthyroidism and was on medical treatment with carbimazole. System symptom review was unremarkable. On examination, she was malnourished with BMI of 19.5 kg/m^2. She was febrile with a temperature of 38.2°C, had tachycardia of 120 beats per minute with regular rhythm. She had a grade-2 diffuse goiter and there was no ophthalmopathy or dermopathy. Rest of the examination was essentially normal.

Investigations revealed normocytic anemia with a hemoglobin 10.2 gm/dL and rest of the cell lines were normal. She had an elevated C- reactive protein of 114 ng/L (N <3) and ESR of 70 mm/hour (N 0–15). Her blood smear examination was negative for a malarial parasite. Her liver function was normal except for low albumin of 2.5 gm/dL (N 3.5–4.4) and an albumin-globulin ratio reversal (total protein 8 gm/dL). Her TSH was <0.008 mIU/L (N 0.4–4.2) with free T4 of

Address for correspondence: Dr. Riddhi D. Gupta, Department of Endocrinology, Diabetes and Metabolism, Christian Medical College, Vellore - 632 004, Tamil Nadu, India.
E-mail: riddhi_dg@rediffmail.com

Received: 22-10-2019 **Revised:** 28-11-2019
Accepted: 13-12-2019 **Published:** 28-01-2020

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_933_19

How to cite this article: Gautam KP, Lijesh KU, Jude J, Gupta RD, Paul TV. An uncommon cause of fever in a patient with hyperthyroidism. J Family Med Prim Care 2020;9:432-4.

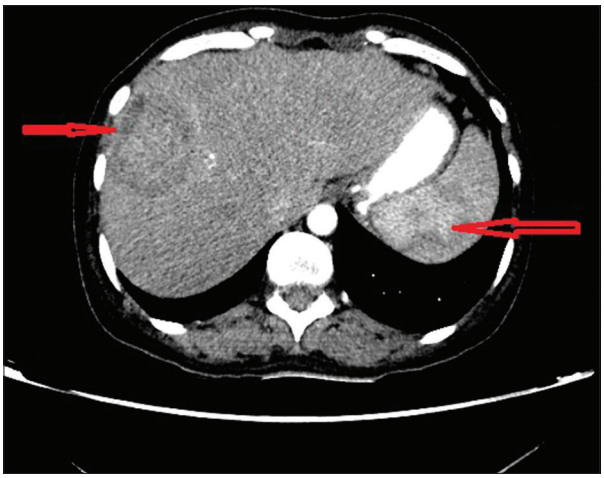

Figure 1: CT scan showing heterogeneously enhancing liver lesion with honeycombing filling defect

3.4 (N 0.8–2 ng/dL). Her urine examination, chest radiograph, and electrocardiogram were non-contributory. Serial blood cultures were also collected. She was started on carbimazole 30 mg/day and also on a beta-blocker.

Her ultrasound abdomen and pelvis showed a heterogenous hypoechoic lesion in the right lobe of liver (3.7 cm × 6.5 cm × 6.3 cm) seen as multicystic with thick internal septae with demonstrable internal vascularity along the septae in the right lobe of liver. Her contrast-enhanced computerized tomogram [Figure 1] displayed heterogeneously enhancing liver lesion with honeycombing filling defect. A similar hypodense lesion was evident in the spleen. The honeycomb lesions in liver and spleen prompted the possibility of melioidosis. An ultrasound-guided aspirate from the liver lesion and blood culture [Figure 2] revealed the presence of gram-negative bacterium *Burkholderia pseudomallei*. A diagnosis of melioidosis on the background of hyperthyroidism was made.

She was started on parenteral ceftzadime and doxycycline. She made a dramatic improvement with resolution of fever within a week and on discharge, she was advised to continue the antibiotics (ceftazidime and co-trimaxazole) and antithyroid medication under the supervision of her primary care physician. She was scheduled for a review after one month.

The melioidosis was named from the Greek "melis"(distemper of asses) and "eidos"(resemblance) by Stanton and Fletcher in 1932.[3] It is a potentially fatal illness caused by the soil saprophyte gram-negative bacterium *Burkholderia pseudomallei* and is found in contaminated water and soil and spreads to humans through inhalation and inoculation. A high index of suspicion to detect melioidosis in the early stages and administer appropriate antibiotics is needed.[4] It is probably underreported from Indian continent and most cases have been reported from southwestern coastal Karnataka and northeastern Tamil Nadu.[2]

As elsewhere, the majority of cases have type-2 diabetes mellitus and occupational exposure to the environment.[5] Most present

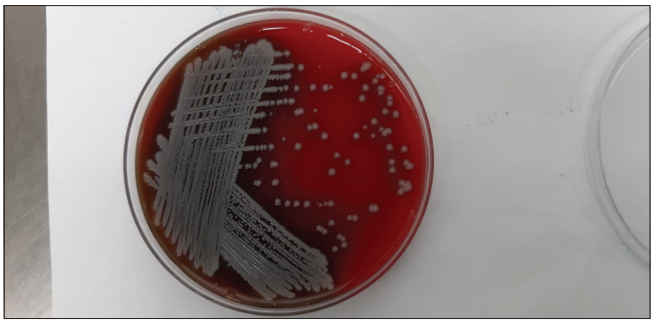

Figure 2: *B. pseudomallei* colonies in MacConkey agar

with community-acquired pneumonia and/or bacteremia, especially during heavy rainfall. The high seropositivity rate (29%) in Karnataka and isolation of B. pseudomallei from the environment in Tamil Nadu and Kerala confirm India as melioidosis-endemic although the full extent of the distribution of the organism across the country is unknown.[6]

Laboratory diagnosis of melioidosis can be difficult. Suspect colonies on 10% sheep blood agar which are oxidase-positive and motile are subjected to agglutination using in-house B. pseudomallei anti-sera, rabbit derived which usually expedites the diagnosis.[7] The current treatment protocol of melioidosis comprises two phases. The first is the acute phase, the aim of which is to stop patients from dying of overwhelming sepsis and the second is the eradication phase, to kill any residual bacteria and to minimize the risk of infection relapsing. The combination of agents used, duration of therapy, and need for adjunct modalities depends on the type, severity, and antimicrobial susceptibility of infection.[8-10] Treatment failure has been defined in studies as fever for longer than 14 days or bacteremia for longer than 7 days. The drugs recommended in the acute phase are ceftazidime 40 mg/kg intravenous every 6 h or 8 h for 2–4 weeks plus cotrimoxazole 10/50 mg/kg (up to 320/1600 mg) every 12 h. An effective alternative is meropenem 25 mg/kg every 8 h as in case of neuromelioidosis, persistent bacteremia. The drugs recommended in the oral eradication phase are cotrimoxazole and amoxycillin-clavulanic acid and doxycycline.[9] In conclusion, primary care and family physician needs to be aware of this condition which can present as prolonged febrile illness in the presence of conditions such as diabetes mellitus or hyperthyroidism. Early detection and treatment will significantly reduce the morbidity and mortality associated with this infection.

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Nathan S, Chieng S, Kingsley PV, Mohan A, Podin Y, Ooi M-H, *et al*. Melioidosis in Malaysia: Incidence, clinical challenges, and advances in understanding pathogenesis. Trop Med Infect Dis 2018;3:pii 325. doi: 10.3390/tropicalmed3010025.
2. Koshy M, Jagannati M, Ralph R, Victor P, David T, Sathyendra S, *et al*. Clinical manifestations, antimicrobial drug susceptibility patterns, and outcomes in melioidosis cases, India. Emerging Infect Dis 2019;25:316-20.
3. Cheng AC, Currie BJ. Melioidosis: Epidemiology, pathophysiology, and management. Clin Microbiol Rev 2005;18:383-416.
4. Hoffmaster AR, AuCoin D, Baccam P, Baggett HC, Baird R, Bhengsri S, *et al*. Melioidosis diagnostic workshop, 2013. Emerging Infect Dis 2015;21. doi: 10.3201/eid2102.141045.
5. Mukhopadhyay C, Shaw T, Varghese GM, Dance DAB. Melioidosis in South Asia (India, Nepal, Pakistan, Bhutan and Afghanistan). Trop Med Infect Dis 2018;3:pii: E51. doi: 10.3390/tropicalmed3020051.
6. Saravu K, Mukhopadhyay C, Vishwanath S, Valsalan R, Docherla M, Vandana KE, *et al*. Melioidosis in southern India: Epidemiological and clinical profile. Southeast Asian J Trop Med Public Health 2010;41:401-9.
7. Dance DAB, Sihalath S, Rith K, Sengdouangphachanh A, Luangraj M, Vongsouvath M, *et al*. The cost-effectiveness of the use of selective media for the diagnosis of melioidosis in different settings. PLoS Negl Trop Dis 2019;13:e0007598.
8. Simpson AJ, Suputtamongkol Y, Smith MD, Angus BJ, Rajanuwong A, Wuthiekanun V, *et al*. Comparison of imipenem and ceftazidime as therapy for severe melioidosis. Clin Infect Dis 1999;29:381-7.
9. Inglis TJJ, Rolim DB, Rodriguez JLN. Clinical guideline for diagnosis and management of melioidosis. Rev Inst Med Trop Sao Paulo 2006;48:1-4.
10. Mohapatra PR, Behera B, Mohanty S, Bhuniya S, Mishra B. Melioidosis. Lancet Infect Dis 2019;19:1056-7.