CASE REPORT

Case Report: A case report of multiple co-infections (melioidosis, paragonimiasis, Covid-19 and tuberculosis) in a patient with diabetes mellitus and thalassemia-trait in Myanmar [version 1; peer review: awaiting peer review]

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Abstract
Burkholderia pseudomallei is a soil-dwelling aerobic bacterium prevalent in tropical and subtropical regions, particularly in Southeast Asia and Northern Australia. It is the causal organism of melioidosis, a severe infection that can manifest as chronic debilitating pneumonia resembling pulmonary tuberculosis. Here, we report a case of melioidosis, pulmonary tuberculosis, covid-19, and paragonimiasis co-infection in a 50-year-old male with poorly controlled diabetes mellitus and β-thalassemia trait. The patient recovered with intravenous antibiotics and standard anti-tuberculosis treatment.

Keywords
Pulmonary TB, Paragonimiasis, Melioidosis, Diabetes, Covid-19

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**Case presentation**

**Past medical history**

The patient was a 50-year-old male carpenter who lives nearby the paddy field and presented in March 2021, to SMRU TB clinic, located in Shwe Kokko village close to the Myanmar-Thailand border. He complained of lower leg pain due to a closed fracture of the right tibia, as well as a productive cough for one and half months, intermittent high fever and constitutional symptoms for a month, and chest pain for two weeks. He was a chronic smoker, alcoholic, and a known diabetic which had been diagnosed during the surgical treatment of a gluteal abscess a year before. He was taking oral hypoglycemic drugs on an irregular basis. The patient also had intermittent dermatitis lesions on the fingers and on for two years and fungal nail infection for more than five years. He received two doses of CoviShield (ChAdOx1 nCoV- 19) in Myanmar four weeks apart in March and April 2021.

**Clinical assessment**

On physical examination, the patient’s body weight was 45 kilograms; he was fully conscious, slightly pale with a tympanic temperature of 39.0°C, pulse rate 107 bpm, respiratory rate 24/min, blood pressure 90/70 mmHg, and oxygen saturation 98% on air. Finger clubbing, lymphadenopathy, or organomegaly were absent. Air entry was reduced on the middle and lower zones of the right lung. Clinical findings and management timelines are summarized in Figure 1. Chest X-ray

![Figure 1](image_url)

*Figure 1. The clinical and management timeline of the patient (Temperature: Red solid line, CRP: Purple dotted line, FBS: Black solid line).*
Laboratory investigation
Malaria rapid diagnostic (SD Bioline) and HIV antibody tests (Determine) were negative. The random blood sugar level was 436 milligram/deciliters on admission. Complete Blood Count showed hypochromic microcytic anemia (hemoglobin 8.4 gram/dL) with increased RBC count, normal leucocyte count (9.3 × 10^3/μL) with neutrophilia, lymphocytopenia, increased monocytes, and normal eosinophil percent (83.2, 6.2, 10, and 0.1% respectively); platelet count was normal (189 × 10^3/μL). Hemoglobin typing performed by high pressure liquid chromatography (HPLC) provided a diagnosis of beta-thalassemia trait (HbA_2=5.9%). C-reactive protein by NycoCard (Abbott) was elevated (>200mg/dL). Renal function tests and liver function tests were within normal limits except for an elevated ALP (192 U/L). Acid-Fast Bacilli (AFB) were not seen in either early morning and spot sputum specimens by microscopy. *Myco-bacterium tuberculosis* (MTB) DNA was detected by GeneXpert MTB/Rif assay without Rifampicin resistance. A week after admission, a blood culture was collected because of persisting fever and *B. pseudomallei* was isolated. The identification was given by colony morphology on Ashdown’s agar (Figure 3), latex agglutination test¹ and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF)².

Management
Ceftriaxone two grams intravenously once a day was given while awaiting the laboratory results, as well as metformin 500mg twice a day. The standard regime of anti-TB drugs (2HRZE/4HR) following WHO guideline³ was initiated. The blood glucose level was well under control within a week by metformin. After seven days of Ceftriaxone, intermittent high fever and cough still presented with chest, back, and leg pain. Profuse sweating was also present and the hydric loss was compensated with intravenous normal saline infusion. Melioidosis treatment consisted of intravenous Ceftazidime two grams every eight hours and oral Co-trimoxazole (sulfamethoxazole + trimethoprim) 480mg four tablets every 12 hours for two weeks, followed by maintenance therapy with Co-trimoxazole for 14 weeks as per recommended protocol⁴.

Fever, profuse sweating and bone pain subsided on the 13th day of the melioidosis treatment. Weekly liver function tests for one month were normal apart from slightly elevated ALP (between 1.5 and 2.0 times ULN).

(Figure 2) showed homogenous opacity and consolidation in the middle zone of the right lung. An underlying mass lesion could not be excluded as CT scan was not available.

![Figure 2. Chest X-ray before (left) and after (right) anti-TB treatment.](image)

![Figure 3. Colonies of Burkholderia Pseudomallei on Ashdowns medium.](image)
After two months since starting anti-TB treatment, sputum microscopy showed scanty mycobacterium (3 AFB/100 fields) and hence the intensive phase with HRZE was extended for one more month (i.e. total three months of intensive phase). However, mycobacteria were not isolated in the sputum culture. The treatment was changed to two-drug regimen (4HR) after the third month. Symptoms improved apart for the presence of occasional chest pain. Cough, chest pain and other TB symptoms were relieved, and AFB was negative in sputum microscopy after three months since starting anti-TB treatment. Haemoglobin level had risen from 8.4 to 9.8 g/dL with anemia treatment. Bodyweight increased to 54 kg from the baseline of 45kg.

The patient had a high fever again with body ache at sixth week after completion of melioidosis treatment and at six months of anti-TB therapy. SARS-CoV-2 was detected from the nasopharyngeal swab by real-time reverse transcriptase polymerase chain reaction (RT-PCR). There was no relevant finding on the chest radiograph. However, the patient was referred to the COVID-19 treatment center for appropriate management due to concerns about underlying comorbidities. Under close monitoring of vital signs, glycaemia and Co-amoxiclav treatment, the patient remained clinically stable and symptom-free within a week in the COVID-19 care facility.

At the end of TB treatment and eight months since the first presentation, sputum microscopy showing scanty mycobacteria in the spot sputum specimen (9 AFB/100 fields). MTB DNA was detected by the GeneXpert and the rifampicin status was indeterminate after repeating the GeneXpert twice. Anti-TB treatment was stopped after a total of seven months and a sputum culture for AFB was repeated where MTB was not isolated.

In the follow-up visit, a month after completion of the anti-TB regimen (after nine months since the first presentation), the blood sugar level, liver function including ALP and renal function tests were within normal limits. CBC result indicated low Hb 9.4 g/dl with normal RBC count (5.48 10^12/L), anisopoikilocytosis, normal leucocyte cell count (9.4 × 10^9/L) with normal neutrophil, lymphocyte, monocyte percent (62.3, 17.0, 1.7 respectively), but eosinophilia 18.8%, adequate platelet count and CRP <8mg/dl. Stool microscopic examination for worm infestations two times within two weeks were negative. Repeated blood culture showed no growth this time. There were no other significant findings on the CXR (Figure 2) and ultrasonography of the abdomen. *Paragonimus ovum* was found in sputum and treated by three days of oral praziquantel PO 25mg/kg every eight hours.

**Discussion**

In this report we presented the unusual case of a patient who was diagnosed with pulmonary tuberculosis but also happened to have melioidosis, another potentially severe infection. Both diseases are found in many regions of Southeast Asia and can sometimes mimic each other. Recent environmental soil surveys have revealed the prevalence of *B. pseudomallei* in the soil in different geographical regions of Myanmar\(^5\). However, clinical cases of melioidosis are rarely reported in the country\(^5\) where the disease was discovered. Clinicians and microbiologists may not consider it as a diagnosis and even less likely as a cause of co-infection in a febrile patient with a confirmed diagnosis of tuberculosis. In this patient, the source of *B. pseudomallei* could possibly be through skin lesion (via the leg fracture?) as it was associated with sepsis. He also had several known associated risk factors such as diabetes and chronic alcohol abuse. Fortunately, he was diagnosed early in the course of both infections and treated appropriately. Later, he was infected by SARS-Cov-2 but did not develop severe symptoms, most likely because he had been vaccinated against the disease. Finally, he was infected by Paragonimus, a frequent parasite (fluke) in the region, transmitted via snail and a secondary intermediate (freshwater crabs and some shrimps) that can also mimic pulmonary tuberculosis. The early detection of the ova in the sputum, triggered by the elevated eosinophilia, allowed for a prompt recovery following treatment. This case is exceptional by its number of co-infections, but it does underline the need for clinicians to suspect co-morbidities when the response to treatment is not optimal, particularly when underlying aggravating factors are present.

**Data availability**

All data underlying the results are available as part of the article and no additional source data are required.

**Consent**

Written informed consent to report these cases was obtained from the patient.

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**References**

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