



CASE REPORT

REVISED 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 2; peer review: 1 approved]

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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 paragonimus 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



This article is included in the [Mahidol Oxford Tropical Medicine Research Unit \(MORU\)](#) gateway.

Open Peer Review

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1

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[view](#)

1. **Cherry Lim**, Mahidol University, Bangkok, Thailand

Any reports and responses or comments on the article can be found at the end of the article.

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REVISED Amendments from Version 1

Here are the summary of changes made in previous version according to the reviewer's suggestion.

In the Case presentation Past medical history paragraph,

- The SMRU (Shoklo Malaria Research Unit) is being spelled out as well as mentioned in the list of abbreviation section.
- We have stated "During admission at TB clinic" to be more specific about the timing of COVID vaccination.

In the [Figure 1](#)

- We have spelled out FBS "Fasting Blood Sugar"
- Day 0 point was added

In the laboratory investigation session,

- We have elaborated the COVID-19 investigation timing "The patient was firstly screened by PCR at outpatient isolation department for Covid-19 and was negative before admitting to inpatient ward".
- We have added the time (days) to *B. pseudomallei* culture positive result "5 days after sample collection"

Any further responses from the reviewers can be found at the end of the article

Abbreviations

ALP	Alkaline Phosphatase
AFB	Acid-Fast Bacilli
bpm	beat per minute
CBC	Complete Blood Count
CRP	C reactive protein
CXR	Chest X-Ray
g/dl	gram/deciliter
Hb	Haemoglobin
Kg	Kilogram
Mg	Milligram
mg/dl	milligram/deciliter
mmHg	millimeter of mercury
SMRU	Shoklo Malaria Research Unit
ULN	Upper limit of normal
H	Isoniazid
R	Rifampicin
Z	Pyrazinamide
E	Ethambutol

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 Shoklo Malaria Research Unit (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 contact dermatitis lesions on the fingertips off and on for two years and fungal nail infection for more than five years. During admission at TB clinic, 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 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.

Laboratory investigation

The patient was firstly screened by PCR at outpatient isolation department for Covid-19 and was negative before admitting to inpatient ward before admitting to inpatient ward. 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 leukocyte count ($9.3 \times 10^3/\mu\text{L}$) with neutrophilia, lymphocytopenia, increased monocytes, and normal eosinophil percent (83.2, 6.2, 10, and 0.1% respectively); platelet count was normal ($189 \times 10^3/\mu\text{L}$). Hemoglobin typing performed by high pressure liquid chromatography (HPLC) provided a diagnosis of beta-thalassemia trait ($\text{HbA}_2=5.9\%$). C-reactive protein by Nycocard (Abbott) was elevated ($>200\text{mg/dL}$). 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. *Mycobacterium 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 5 days after sample collection. 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

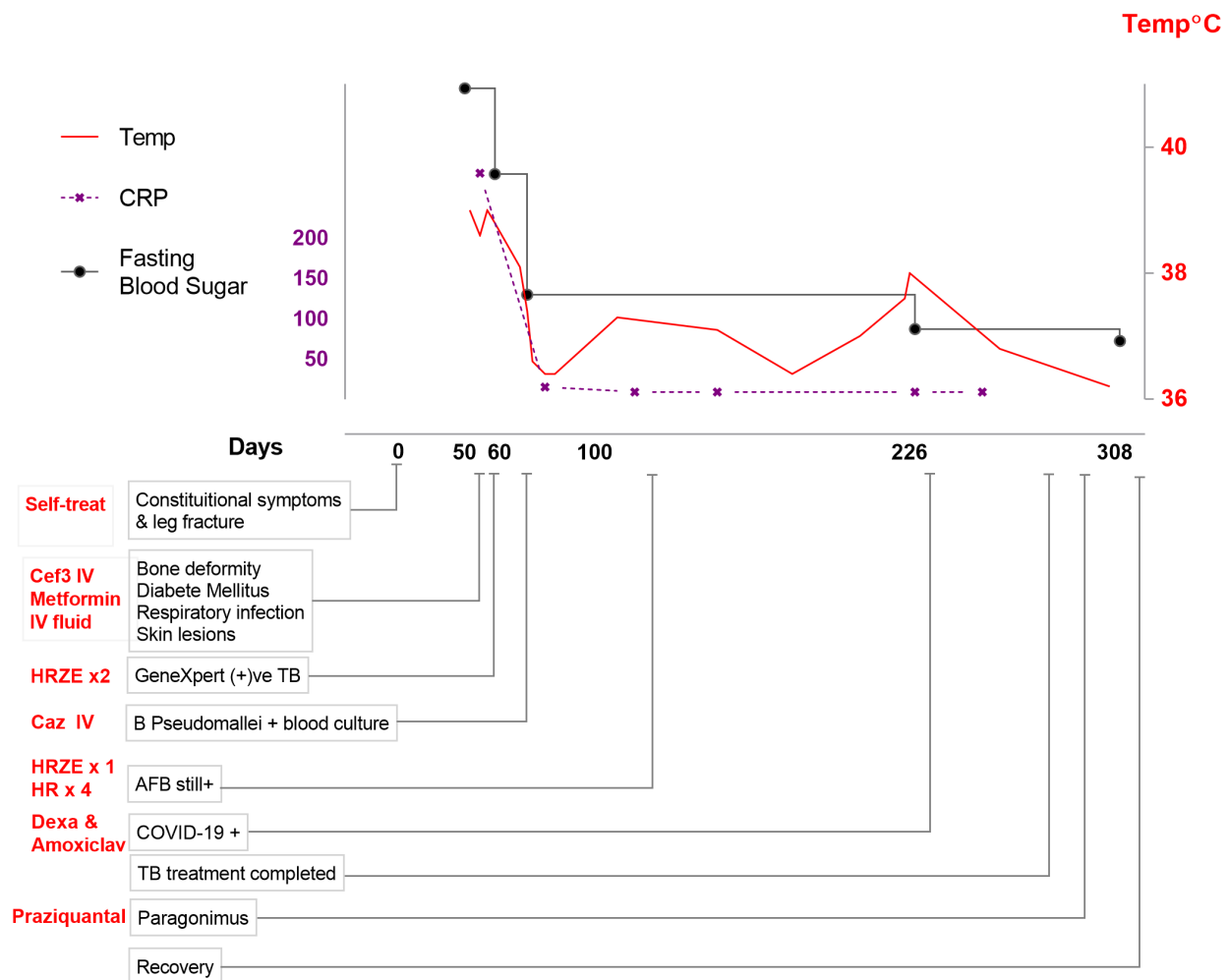


Figure 1. The clinical and management timeline of the patient (Temperature: Red solid line, CRP: Purple dotted line, Fasting Blood Sugar: Black solid line).

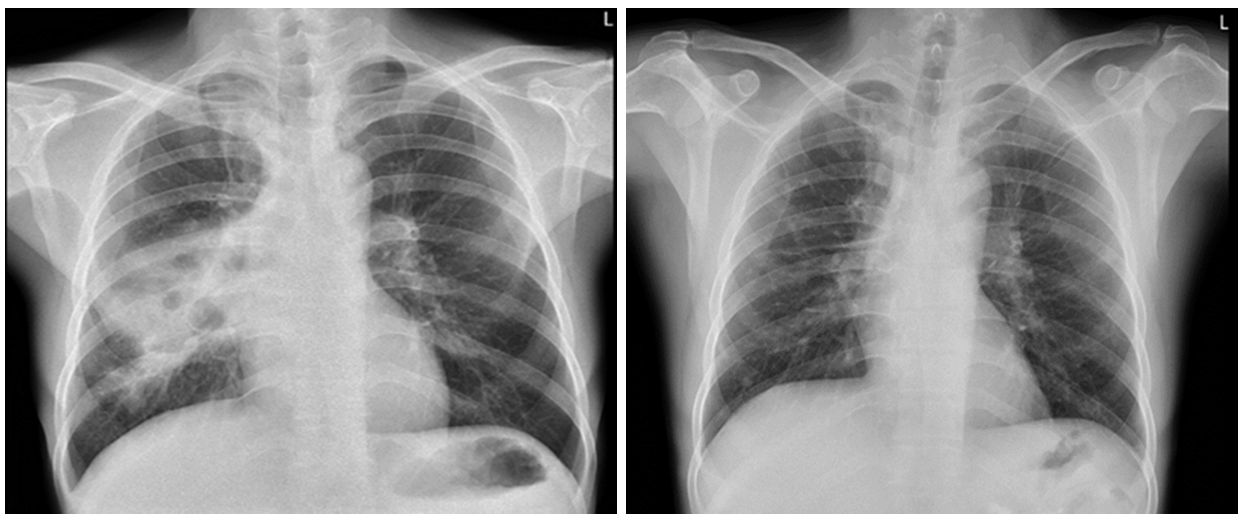


Figure 2. Chest X-ray before (left) and after (right) anti-TB treatment.

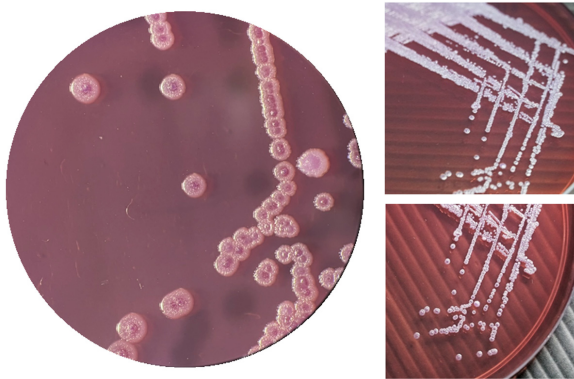


Figure 3. Colonies of *Burkholderia Pseudomallei* on Ashdowns medium.

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 Ceftriaxone 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).

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 regime (4HR) after the third month. Symptoms improved apart from 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, glycemia 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 testing showed scanty mycobacteria in 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 ($5.48 \times 10^6/\mu\text{L}$), aniso-poikilocytosis, normal leukocyte cell count ($9.4 \times 10^3/\mu\text{L}$) 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^{5,6}. However, clinical cases of melioidosis are rarely reported in the country^{7,8} where the disease was discovered⁹. 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 septicemia. 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.

Consent

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

Data availability

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

Acknowledgments

We would like to acknowledge the contribution of all SMRU staff involved in the management of this patient including the TB clinic and laboratory technicians.

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Reviewer Report 22 July 2022

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This is an interesting case report highlighting a case of multiple co-infections, including melioidosis, paragonimiasis, COVID-19 and tuberculosis. The article raises awareness about melioidosis in the Thai-Myanmar border, and highlighted the importance of early diagnosis and treatment especially in the case of co-infections.

Abstract

- The motivation and importance of this case report could be elaborated.
- The potential implication and impact in sharing the case report could be elaborated

Case Presentation

A brief introduction on melioidosis would be helpful for readers, who are not familiar with the disease, to understand the importance of the disease. A brief description on melioidosis cases that were previously reported at the Thai-Myanmar border would be useful for readers to understand the importance of this case report. A brief description on the patient population at the Thai-Myanmar border would be helpful for reader to understand general context.

Past medical history

- The authors could consider spelling out SMRU in the first sentence as it is the first time the abbreviation is used in this manuscript.
- What was the reason that the patient attended the TB clinic? Is it for COVID-19 vaccination (the text seems to suggest attending TB clinic and first dose of vaccine happened in the same month [March] however it is unclear if they happened on the same day)?

Laboratory investigation

- The authors suggested that the patient was admitted- "A week after admission...". A description on events of admission, discharge and follow-up in the main text and in the timeline in Figure 1 would be helpful in clarifying the timeline. Also, the timeline in Figure 1 and that described in the main text was slightly confusing, as the number of days between start of ceftriaxone (assuming that is also the day of admission) and "B pseudomallei + blood culture" (assuming that is the day of blood sample collection) looks like longer than 7 days in Figure 1, whereas the main text stated "A week after admission, a blood culture was collected because of persisting fever and *B. pseudomallei* was isolated.". Please clarify.
- The description on diagnosis of COVID-19: "SARS-CoV-2 was detected from the nasopharyngeal swab by real-time reverse transcriptase polymerase chain reaction (RT-PCR)." could be moved to the "Laboratory investigation" section (rather than the "Management" section).
- Was the patient tested for COVID-19 on the day of hospitalization?

Discussion

- Implication of the case report could be elaborated. Recommendations for clinicians and microbiologists who work in the setting (or similar settings) would be useful. A discussion on the epidemiology of infectious diseases and patient population within the hospital/TB clinic coverage area, where the case was observed would be helpful for readers to understand the context better.

Figure 1

- A description on what Day 0 is would be helpful in understanding the timeline.
- The authors may want to consider scaling the timeline to "Months" rather than "Days" so to be consistent with the descriptions in the main text and to help readers interpreting the timeline.
- FBS in the caption could be spelled out in full.
- Events of admission, discharge, eradication treatment, and follow-up could be added in Figure 1 to clarify the course of patient's hospitalisation.
- A footnote on definition of "recovery" could be added. Is recovery defined based on clinical presentation or repeated laboratory tests with results returned as negative?

Figure 2

- Is "after (right) anti-TB treatment" referring to after the completion of the treatment?

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: infectious disease epidemiology; antimicrobial-resistant infections; statistics

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
