



Multidrug-resistant Tuberculosis and COVID-19 Coinfection with Diabetes Mellitus in Medan, Indonesia: A Case Report

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Abstract

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BACKGROUND: Coronavirus disease 2019 (COVID-19) has distracted the global health system due to significant morbidity and mortality. There are increasing mortality rates related to the existence of comorbidities. Due to immunologic conditions, other infectious diseases, such as multidrug-resistant tuberculosis (MDR-TB), might coinfect with COVID-19. We describe a case of MDR-TB with diabetes mellitus and critical COVID-19 patient with fatal outcome.

CASE REPORT: A 60-year-old man was admitted to our hospital with shortness of breath for 2 days. A history of recurrent shortness of breath has developed for about 7 months. Room air oxygen saturation was at 66%. RT-PCR SARS-CoV-2 nasopharynx swab result was positive. The chest X-ray series result showed destroyed left lung with increasing infiltrate in the lower right lung. The patient was diagnosed with pulmonary MDR-TB based on GeneXpert and LPA (Line Probe Assay) test 6 months prior and also has had history of diabetes mellitus for 7 years. Then, the patient was diagnosed with COVID-19, pulmonary MDR-TB, and diabetes mellitus. MDR-TB regimen, anti-diabetic medication, and management of COVID-19 were carried out. On the 6th day, the patient's condition worsened to the point, where he needed intubation. The patient eventually passed away.

CONCLUSION: The treatment outcome was highly related to the severity of COVID-19 symptoms and complications of comorbidities when patients are admitted to the hospital. The early screening and treatment of COVID-19 are important to prevent deteriorating clinical conditions caused by comorbidities.

Introduction

The global number of cases of coronavirus disease (COVID)-19 is reaching more than 263 million and above 5 million deaths since found the outbreak in December 2019 then followed by declaration as a global pandemic on the March 11, 2020 by the World Health Organization (WHO) [1]. The new emerging coronavirus (COVID-19) has distracted with global structure of health, social and economic since 2020. This condition makes the double burden with increasing of number people diagnosed with tuberculosis (TB) drug resistant [2], [3]. In 2019, the WHO estimated global incidence about 465,000 diagnosed with TB drug resistant from 9.96 million TB cases [4], [5].

In 2021, Indonesia is fighting to reduce TB drug resistant about 24,695 cases or 8.8 / 100,000 people, and likewise with province North Sumatera, health ministry revealed 1838 cases of TB drug resistant [5], [6]. They are calamitous potential impact of COVID-19 pandemic. The patients who suffered pulmonary TB (PTB) have derivation of ability cellular immunity and are vulnerable to viral infections [7]. In

addition, we should considered another comorbid that worsened both of COVID-19 and TB, such as diabetes mellitus, hypertension, cardiovascular diseases, cancer, and other chronic disease [8]. Here, we report a case of multidrug-resistant TB (MDR-TB) and COVID-19 coinfection with diabetes mellitus, while he admitted into Haji Adam Malik General Hospital and how the course of his disease was complicated.

Case Report

On August 20, 2021, a 60-year-old male adult presented with a shortness of breath in the past 7 months worsened in 2 days, history of cough for 6 months and deteriorated in 3 days, with difficulties to expectorate sputum, felt myalgia, and headache in 1 week before admitted to the hospital. It was associated with a history of 15 kg involuntary weight loss in the past 7 months. The patient has taken regularly anti-diabetic medicine in the past 7 years. He diagnosed and treated as MDR-TB in the past 6 months based on GeneXpert and LPA (Line

Probe Assay) test 6 months prior before presented. On physical examination, findings at admission revealed conscious, afebrile, oxygen saturation 66% room air, and 94% with 15 L/min non-rebreathing-mask (NRM), and chest finding with bronchial and crackles at the lower right lung and diminished on auscultation at the left chest. The result of real-time reverse transcription-polymerase chain reaction (RT-PCR) SARS-CoV-2 test specimens was positive.

The full blood count, electrolyte, liver function test, renal function test, lipid profile, D-dimer, and hemostasis test were normal at presented. The result of fasting blood glucose at 1st day was 143 mg/dL with HbA1c which was 7.4%. Blood gas analysis showed metabolic acidosis with partial compensated. Lactate dehydrogenase test was 2.5 times of the upper normal limit. HIV test was negative. Based on e-TB Manager (TB National Data System) 6 months ago, Sputum GeneXpert result was rifampicin resistant, then Line Probe Assay (LPA) second-line indicated MTB detected (D), and resistance not detected (RND) for second-line medication. The patient admitted with MDR TB regimen; levofloxacin, cycloserine, and clofazimine (Figure 1).

The patient received antiviral (remdesivir), azithromycin, dexamethasone, vitamin C, zinc sulfate, insulin, enoxaparin, and continue MDR-TB regimen. On the 6th day, full blood count result was leukocytosis (18,600/ μ L), neutrophilia (92.5%), lymphopenia (2.8%), D-dimer (1,000 ng/dL), and blood glucose, which was increasing up to 402 mg/dL. Peripheral blood morphology showed normochromic normocytes, toxic granule, and big thrombocyte. Unfortunately, we did not do procedure blood culture or sputum culture. Chest X-ray figured worsened with increasing infiltrate in the right lung. At the 6th day, the patient condition developed unconscious, hypotension, and oxygen saturation, which was 65% with high flow nasal cannula. We decided to intubate the patient, but the patient eventually passed away.

Discussion

As an endemic country with TB, we should concern about community perception of MDR-TB with long treatment, additional cost, as well as being unemployed. Other barriers are the difficulties of accessing health services and perception of the side effect on MDR-TB regimen. These might raise the level of fear and anxiety of patients to visit health care in pandemic situation, though they have known that MDR-TB and COVID-19 coinfection was a deathly condition. They avoid to visit healthcare, and the hope of symptoms will resolve on their own in due course of time [9], [10]. This patient admitted as suspect of having COVID-19 with insidious acute respiratory signs and symptoms, but we found typical chronic symptoms (cough, shortness of breath, and weight loss) of TB. Fortunately, relatives informed the ongoing MDR-TB treatment, it simplified the screening and assessment processes. The patient did not have history of contact with suspicious or confirmed COVID-19. The research reported how household transmission and infection risk of COVID-19. It estimated overall transmission risk of 17.1%, although there was wide variation across studies. Households become the most possible environments for transmission. They are what are known as 3Cs environments, as they are closed spaces, where family members may crowd and be in close contact with conversation. Lack of personal protection on gathering time would be high risk condition [11], [12].

Destroyed lung is defined as the total destruction of the lung parenchyma secondary to recurrent or chronic inflammation/infection, tumors, or vascular abnormalities. PTB is associated with many pulmonary and extrapulmonary complications including destruction of the lungs; however, complete destruction of an entire lung is uncommon [13]. In this report, the patient was diagnosed with MDR-TB 6 months before presented and had received MDR-TB treatment. In



Figure 1: (a) Chest X-ray at outpatient department on August 2, 2021, showed destroyed left lung and minimal infiltrate in the right paracardial. (b) Chest X-ray on August 20, 2021 at Adam Malik Hospital Emergency Room showed increasing infiltrate appear in the lower lobe right lung. (c) Chest X-ray, at COVID-19 isolation room on August 26, 2021 showed increasing infiltrate in the right lung compared to the first and second chest X-ray

serial chest showed, there are steady increasing infiltrate in the right lung with permanent left lung destroyed. Rapidly appearance of infiltrate in the lower lobe right lung was typically chest X-ray of COVID-19. The destroyed lung may cause severe complications such as massive hemoptysis, septicemia, and left-right shunt requiring urgent medical attention. The shunt can produce pulmonary hypertension and respiratory failure despite having a normal contralateral lung [14].

Diabetes mellitus (DM) in patients with COVID-19 is associated with a two-fold increase in mortality as well as severity of COVID-19, as compared to non-diabetics. It is necessary to understand how significant effects of comorbidities on TB include diabetes mellitus [15]. DM increases the risk of TB as 1.5–7.8 times compared to people without DM. PTB patients with DM that have the risk of developing to MDR-TB as much as 2.1–8.8 times compared to TB patients without DM [16]. Diabetics were at higher risk of severe pneumonia, uncontrolled inflammatory response, higher levels of tissue injury-related enzymes, and higher hypercoagulable state. The potential mechanisms that increase the susceptibility for COVID-19 in patients with DM include: (1) Higher affinity cellular binding and efficient virus entry, (2) decreased viral clearance, (3) diminished T-cell function, (4) increased susceptibility to hyperinflammation and cytokine storm syndrome, and (5) presence of cardiovascular disease [17].

Both of COVID-19 and MDR-TB deteriorated with diabetes mellitus. The patient received short and long-acting insulin as effort to control the blood glucose, but it was still high until at 6th day, that indicated the failure of treatment. The using of corticosteroid become consideration of persistency of high blood sugar. A meta-analysis found that corticosteroids therapy may reduce mortality for patients with COVID-19 and ARDS, but adult patients with non-severe COVID-19 pneumonia, early, low-dose, and short-term corticosteroids were associated with worse clinical outcomes [18]. A number of glucocorticoid side effects are a result of glucocorticoid-mediated inhibition of glucose uptake and other metabolic alterations of basic cellular metabolism, which typically occur in most cells and tissues [19].

In this case report, the patient was diagnosed with MDR-TB for 6 months before admission. Some similar symptoms of MDR-TB and COVID-19 have warranted a close monitoring laboratory with RT-PCR SARS-CoV-2, especially in COVID-19 pandemic. However, high-cost test or difficult procedure in the primary healthcare may cause of delayed detection. In addition, this condition has complicated by coincidences of diabetes mellitus that become disadvantages for immunity course of diseases. Knowledge about the symptoms of COVID-19 and the worsening of symptoms in MDR-TB patients must also be known by MDR-TB patients and their families, to be able to detect early the possibility of COVID-19 infection in MDR-TB patients.

Conclusion

The treatment outcome was highly related to the severity of COVID-19 symptoms and complications of comorbidities when patients admitted to the hospital. The early screening and treatment of COVID-19 are important to prevent comorbidities deteriorate the clinical conditions. We need to consider for probability coinfection of COVID-19 infection in TB endemic areas during this pandemic. Mimicry of signs and symptom between COVID-19 and TB could cover worsening condition.

Authors' Contributions

BYMS described and designed the article. BYMS, JPS, and PS were involved in treating the patient. BYMS, JPS, and PS participated in editing the manuscript critically. All authors declared that they contributed to this article and that they have read and approved the final manuscript.

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References

1. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. Geneva: World Health Organization; 2021. Available from: <https://covid19.who.int>. [Last accessed on 2021 Nov 12].
2. Chakaya J, Khan M, Ntoumi F, Aklillu E, Fatima R, Mwaba P, et al. Global tuberculosis report 2020 reflections on the global TB burden, treatment and prevention efforts. *Int J Infect Dis.* 2021;113(Suppl 1):S7-12. <https://doi.org/10.1016/j.ijid.2021.02.107>
PMid:33716195
3. Fekadu G, Bekele F, Tolossa T, Fetensa G, Turi E, Getachew M, et al. Impact of COVID-19 pandemic on chronic diseases care follow-up and current perspectives in low resource settings: A narrative review. *Int J Physiol Pathophysiol Pharmacol.* 2021;13(3):86-93.
PMid:34336132
4. World Health Organization. COVID-19 and TB. Global Tuberculosis Report. Geneva: World Health Organization; 2021. Available from: <https://www.who.int/publications/digital/global-tuberculosis-report-2021/covid-19>

5. KEMENKES. Petunjuk Teknis Penatalaksanaan Tuberkulosis Resisten obat di Indonesia [Technical Guidelines for the Management of Drug-resistant Tuberculosis in Indonesia]. Dirjen P2PKementerian Kesehatan Republik Indonesia. Jakarta: Kementerian Kesehatan RI; 2020. Available from: <https://tbindonesia.or.id/pustaka/pedoman/tbro/petunjuk-teknis-penatalaksanaan-tuberkulosis-resistan-obat-di-indonesia>. [Last accessed on 2021 Jan 10].
6. Subdit TB Kemenkes RI. Mobile Dashboard Laporan TB [TB Report Mobile Dashboard]. Jakarta: Subdit TB Kemenkes RI; 2021. Available from: <https://play.google.com/store/apps/details?id=id.or.tbindonesia.dashboard>. [Last accessed on 2021 Jan 20].
7. Marwah V, Peter DK, Ajai Kumar T, Bhati G, Kumar A. Multidrug-resistant tuberculosis in COVID-19: Double trouble. *Med J Armed Forces India*. 2021;77(Suppl 2):S479-82. <https://doi.org/10.1016/j.mjafi.2021.05.002>
8. PDPI, PAPDI, PERKI, PERDATIN, IDAI. Pedoman Tatalaksana COVID-19 [COVID19 Management Guidelines]. 3rd ed. PDPI PAPDI PERKI PERDATIN IDAI, editor. Jakarta: PDPI PAPDI PERKI PERDATIN IDAI; 2020.
9. dos Santos FL, Souza LL, Bruce AT, de Crispim JA, Arroyo LH, Ramos AC, *et al*. Patients' perceptions regarding multidrug-resistant tuberculosis and barriers to seeking care in a priority city in Brazil during COVID-19 pandemic: A qualitative study. *PLoS One*. 2021;16(4):e0249822. <https://doi.org/10.1371/journal.pone.0249822>
PMid:33836024
10. Hogan AB, Jewell BL, Sherrard-Smith E, Vesga JF, Watson OJ, Whittaker C, *et al*. Potential impact of the COVID-19 pandemic on HIV, tuberculosis, and malaria in low-income and middle-income countries: A modelling study. *Lancet Glob Health* 2020;8(9):e1132-2. [https://doi.org/10.1016/S2214-109X\(20\)30288-6](https://doi.org/10.1016/S2214-109X(20)30288-6)
11. Metlay JP, Haas JS, Soltoff AE, Armstrong KA. Household transmission of SARS-CoV-2. *JAMA Netw Open*. 2021;4(2):e210304. <https://doi.org/10.1001/jamanetworkopen.2021.0304>
PMid:33635324
12. Madewell ZJ, Yang Y, Longini IM, Halloran ME, Dean NE. Household transmission of SARS-CoV-2. *JAMA Netw Open*. 2020;3(12):e2031756. <https://doi.org/10.1001/jamanetworkopen.2020.31756>
PMid:33315116
13. Ibrahim HU, Kabir H, Jahun MG. Right destroyed lung due to tuberculosis in a Nigerian child: Case report and review of the literature. *Pyramid J Med*. 2021;4(1):46. <https://doi.org/10.4081/pjm.2021.46>
14. Hossain AZ, Rahman MH. CT evaluation of unilateral destroyed lung among Bangladeshi population. *TAJ J Teach Assoc*. 2021;34(1):75-9. <https://doi.org/10.3329/taj.v34i1.54909>
15. Kumar A, Arora A, Sharma P, Anikhindi SA, Bansal N, Singla V, *et al*. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. *Diabetes Metab Syndr*. 2020;14(4):535-45. <https://doi.org/10.1016/j.dsx.2020.04.044>
PMid:32408118
16. Tegegne BS, Mengesha MM, Teferra AA, Awoke MA, Habtewold TD. Association between diabetes mellitus and multi-drug-resistant tuberculosis: Evidence from a systematic review and meta-analysis. *Syst Rev*. 2018;7(1):161. <https://doi.org/10.1186/s13643-018-0828-0>
PMid:30322409
17. Muniyappa R, Gubbi S. COVID-19 pandemic, coronaviruses, and diabetes mellitus. *Am J Physiol Metab* 2020;318(5):E736-41. <https://doi.org/10.1152/ajpendo.00124.2020>
PMid:32228322
18. Li Q, Li W, Jin Y, Xu W, Huang C, Li L, *et al*. Efficacy evaluation of early, low-dose, short-term corticosteroids in adults hospitalized with non-severe COVID-19 pneumonia: A retrospective cohort study. *Infect Dis Ther*. 2020;9(4):823-36. <https://doi.org/10.1007/s40121-020-00332-3>
PMid:32880102
19. Alexaki VI, Henneicke H. The role of glucocorticoids in the management of COVID19. *Horm Metab Res*. 2021;53(1):9-15. <https://doi.org/10.1055/a-1300-2550>
PMid:33207372