A CASE REPORT: MULTIDRUG-RESISTANT TUBERCULOSIS IN A 53-YEAR-OLD PATIENT

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Abstract : A Case Report: Multidrug-Resistant Tuberculosis In A 53-Year-Old **Patient.** A 53-year-old man with multidrug-resistant tuberculosis (MDR-TB) presented with clinical symptoms such as cough with yellow-white sputum for a month, shortness of breath, fever, night sweats, and weight loss. After completing six months of TB treatment in 2010, he developed MDR-TB, proven by resistance to rifampicin. Initial diagnosis by chest X-ray showed signs of pulmonary TB and right pleural effusion, while the sputum test confirmed Mycobacterium tuberculosis with moderate bacterial load. Laboratory results showed anemia, leukocytosis, and hypoalbuminemia. The patient's therapy included a combination of bedaquiline, levofloxacin, linezolid, clofazimine, cycloserine, and vitamin B6, along with additional treatments such as antibiotics, symptomatic therapy, and nutritional support. The medical team conducted regular monitoring and consultation with pulmonary, psychiatry, and nutrition specialists to ensure treatment compliance. This case highlights the challenges in managing MDR-TB, especially in patients with a history of TB. Early detection of drug resistance and prompt implementation of appropriate therapy are essential to improve treatment outcomes and prevent further spread. This report emphasizes the need for a multidisciplinary approach and close monitoring in the management of MDR-TB.

Keywords: Drug Resistant Tuberculosis, Long-term Regiment, Tuberculosis

Abstract: Laporan Kasus: Tuberkulosis Multidrug Resistant Pada Pasien 53 **Tahun.** Seorang pria 53 tahun dengan tuberkulosis multi resisten obat (MDR-TB) menunjukkan gejala klinis seperti batuk berdahak kuning putih selama sebulan, sesak napas, demam, keringat malam, dan penurunan berat badan. Setelah menyelesaikan pengobatan TB enam bulan pada 2010, ia mengalami MDR-TB, terbukti dengan resistensi terhadap rifampicin. Diagnosis awal melalui rontgen dada menunjukkan tanda TB paru dan efusi pleura kanan, sementara tes dahak mengonfirmasi Mycobacterium tuberculosis dengan beban bakteri moderat. Hasil laboratorium menunjukkan anemia, leukositosis, dan hipoalbuminemia. pasien mencakup kombinasi bedaquiline, levofloxacin, linezolid, clofazimine, cycloserine, dan vitamin B6, disertai perawatan tambahan seperti antibiotik, terapi gejala, dan dukungan nutrisi. Tim medis melakukan pemantauan rutin serta konsultasi dengan spesialis paru, psikiatri, dan gizi untuk memastikan kepatuhan pengobatan. Kasus ini menyoroti tantangan dalam menangani MDR-TB, terutama pada pasien dengan riwayat TB sebelumnya. Deteksi dini resistensi obat dan penerapan segera terapi yang tepat sangat penting untuk meningkatkan hasil pengobatan serta mencegah penyebaran lebih lanjut. Laporan ini menegaskan perlunya pendekatan multidisiplin dan pemantauan ketat dalam penanganan MDR-TB.

Kata Kunci: Regiment jangka panjang, Tuberculosis, Tuberkulosis resisten obat

INTRODUCTION

Tuberculosis (TB) is a substantial worldwide health obstacle. Approximately 10 million individuals contract the illness annually, resulting in 1.4 million documented fatalities in 2019 alone. Mycobacterium tuberculosis, the primary pathogen, mostly targets the lungs but can potentially disseminate to other organs. Although there are effective treatment regimens available, the rise of multidrug-resistant TB (MDR-TB) has made TB control efforts more challenging. Multi-drug resistant tuberculosis (MDR-TB) is characterized by its resistance to both isoniazid and rifampicin, which are the two most potent drugs employed in the treatment of tuberculosis. Consequently, MDR-TB necessitates a more extended and intricate treatment regimen (Nahid., et al. 2019). Tuberculosis is a respiratory disease that affects many people around the world, and it is found in many developing countries because of one of the facts that affected them from a poor socio-economic point of Identification of activities that can be done on the ground can be one of the major milestones in the eradication of tuberculosis outbreaks. Identification can start with management, prevention, and enforcement (Mustofa et al., 2023).

This case report provides a comprehensive account of the clinical manifestation, diagnostic procedure, and treatment of a 53-year-old male patient identified as Tn. A who was diagnosed with MDR-TB (multi-drugresistant tuberculosis). The patient had previously had effective treatment for tuberculosis (TB) in 2010. However, the patient currently exhibits classic signs of TB, such as a chronic cough, fever, night sweats, and substantial weight loss.

Rifampicin-resistant tuberculosis worsened patient's situation, the necessitating а thorough and interdisciplinary treatment strategy (Zignol m., et al. 2016). In the studies that have been carried out, there are complications in the outbreak of chronic tuberculosis, such as the occurrence of pneumothorax or the accumulation of radiation that occurs spontaneously between the lungs and the chest wall. complication is usually characterized by symptoms of chest discomfort and dyspnea (Mustofa & Antoni, 2023).

Managing MDR-TB entails the use of second-line medications, which are often less efficient and more harmful necessitate longer treatment periods compared to first-line therapy. identification and Timely suitable therapy are essential in order to halt the spread of the disease and improve the patient. This report emphasizes the challenges in diagnosing and treating underscores MDR-TB and importance of adherence to treatment protocols and continuous patient monitoring (Dheda, K., et al. 2017).

CASE REPORT

This case report chronicles the medical experience of Tn. A, a 53-yearold male, describes his experience with multidrug-resistant tuberculosis. After successfully completing comprehensive tuberculosis (TB) treatment in 2010, he experienced a series of symptoms that lasted one month. These symptoms included a cough that produced phlegm, difficulty breathing, occasional fever, excessive sweating at night, and a notable decrease in body weight (World Health Organization, 2020).

| Table 1. Laboratory examinations | | |
|---|--|---|
| | Clinical laboratory findings | Normal Range |
| Complete Blood Counts: Hb/Ht/WBC/ Platelets Differential count Neutrophils/Lymphocytes /Monocytes/ Eosinophils/Basophils | 9.8/29/14.730*/559. 000 94*/3*/4/0/0/3* | 13,2-17,3/40-52/3.800- 10.600/150.000-440.000 50-70/25-40/2-8/0-1/2-4/3- 5 |
| Na/K/Cl Ureum/ Creatinine Random Blood sugar test Albumin SGOT/SGPT Bilirubin T/D/I HIV | 135/4,6/8,6 24/0,83 77 2.8* 32/35 0.3/0.2/0.1 Non-reactive | 135-147/3,5-5,0/8,95-105 18-55/0,6-1,2 70-200 3.5-5.2 0-35/0-35 <0.1/<0.2/<1 |
| HbsAg/HAV/HCV <i>Rapid molecular test</i> using Xpert MTB/RIF | Non-reactive Positive Rif Resistant | Non-reactive |

Referring to table 1 results of the patient's blood analysis, there is an anomaly, that is, there is a picture of anemia seen from the blood hemoglobin levels below the standard of 9.8, there is an increase in the number of leukocytes, especially neutrophilic levels, that increased far beyond the normal

boundary, which indicates the presence of leucocytosis, and in the latter, there are abnormalities in the level of albumin; low levels of albumin below the normal level are 2.8, indicating hypoalbumin. Initial examinations revealed anemia, leukocytosis, and hypoalbuminemia.



Figure 1. The radiological examination revealed the presence of pulmonary tuberculosis and right pleural effusion.

As seen in Figure 1, a picture is displayed. The chest X-ray showed pulmonary TB with right pleural effusion. Testing of the sputum revealed Mycobacterium tuberculosis with a moderate bacterial load that was not

susceptible to rifampicin (Mustofa, et al., 2023). The diagnosis of MDR-TB led to a vigorous treatment regimen for the patient, which included bedaquiline, levofloxacin, linezolid, clofazimine, cycloserine, and vitamin B6. In addition,

the patient received supportive therapy such as antibiotics, nutritional assistance, and treatments to alleviate symptoms (Xie, Y., et al. 2017).

This example emphasizes the intricate and difficult nature of managing MDR-TB, emphasizing the significance of detecting it early, starting the right medication promptly, and using a multidisciplinary approach to provide care. Consistent surveillance and expert consultations were crucial for effectively addressing any problems and ensuring strict adherence to the treatment, with the primary objective of enhancing patient outcomes and halting the transmission of the disease (Esmail, A., et al. 2014)).

DISCUSSION

This case report demonstrates the intricacies associated with the treatment multidrua resistant tuberculosis (MDR-TB), especially in individuals who have previously received therapy for tuberculosis. Mr. A, a 53-year-old man, had typical signs of tuberculosis and experienced substantial weight loss, leading to a clinical suspicion of tuberculosis recurrence. Although he had been successfully treated for the disease in 2010, the fact that it has reappeared and he has now been diagnosed with MDR-TB underscores the ongoing difficulties in controlling and managing tuberculosis.

MDR-TB poses a significant public health concern because it is resistant to both isoniazid and rifampicin, the two effective main anti-TB most medications. Managing multidrugresistant tuberculosis (MDR-TB) is a more complex procedure since secondline medications are typically less effective, more harmful, and need longer treatment durations (Poty, et al., 2024). The treatment strategy for Tn. A included the administration bedaquiline, levofloxacin, linezolid, clofazimine, cycloserine, and vitamin B6. The choice of these pharmaceuticals determined by the was drug susceptibility profile and the need for an efficient treatment strategy to address the drug-resistant strain of tuberculosis (Lange., wt al. 2014).

Prompt identification and prompt initiation of appropriate therapy are crucial for improving patient outcomes preventing the further dissemination of multidrug-resistant tuberculosis (MDR-TB). The prompt detection of rifampicin resistance by sputum testing facilitated the timely implementation of a treatment regimen tailored multidrug-resistant to (Singh (MDR-TB) tuberculosis Chibale, 2021). The patient's treatment regimen was augmented with supportive care, encompassing the administration of antibiotics to combat secondary provision of infections, nutritional assistance, and implementation symptomatic therapies, aimed managing the consequences of the condition and improving overall health (Brigden. 2014).

Vitamin B6 in TB treatment is highly recommended, as vitamin B6 treatment can be associated with second-line TB treatment, such as cycloserin and isoniazid use. The use of vitamin B6 has the benefit of preventing the occurrence of peripheral neuropathy. Peripheric neuropathies can occur due to the use of the drugs cycloserin and isoniazide, so prevention of the negative effects of this medication supplied by consumption of vitamin B6, so that the side effects of MDR-TB treatment in combination can be prevented (World Health Organization, 2022).

In the case of the above patient, his low hemoglobin values are characterized by anemia. The cause of anemia in the patient is the infestation of MDR TB experienced because, in the chronic MDR phase of TB, there is disruption of iron metabolism, so there is a decrease ervthropoietin, erythropoietin is low, red blood cells are difficult to form. In addition, in MDR-TB, there is cytocystic interleukin-6 (IL-6) and alpha-factor necrosis (TNF-a), which cause inhibition of the spinal cord, the production of red blood cells, and iron disorders (Weiss G, 2015). Another cause of anemia in MDR-TB patients is the presence of drug toxicity, which can malnutrition occur due to cormobidity. The drug toxicity occurs due to the inhibition of linezolid, which

has side effects of spinal cord suppression, so that the production of red blood cells decreases. Malnutrition and cormobidity factors result from a lack of iron, vitamin B12, and folic acid in red blood cell synthesis. Comorbid disorders, such as the presence of HIV, can cause fairly significant anemia (Lee et al., 2012).

In the above cases, there is an increase in leukocytes above the normal threshold due to the mechanisms of inflammatory physiological stress, response, and chronic inflammation. Of the three mechanisms, that's what causes an excessive increase in leukocytes. Pro-inflammatory cytokines such as TNF-a, IL-1, and IL-6 trigger inflammatory responses. Further, chronic inflammation in MDR TB can affect the release of cortisol, which can stimulate the production of leukocytes in the bone marrow(Syal, 2014). And in the case of TB MDR above, it was also found that hypoalbumin or body albumin levels that are below normal limits are often associated with the presence of malnutrition and an inflammatory response that occurs in MDR TB patients(Katz, 2011).

comprehensive plan for addressing MDR-TB must incorporate input from a variety of disciplines. To address potential side effects and offer comprehensive treatment, it was critical to monitor and consult with specialists in cancer, psychiatry, ophthalmology, and nutrition on a regular basis. This approach also emphasized significance of continually teaching and supporting patients in order to help them stick to the difficult and lengthy treatment regimen (Udwadia, Z., et al. 2014).

This example underscores the ongoing challenges of controlling tuberculosis (TB), particularly the critical need for effective public health policies to prevent TB from recurring and to avoid the development of treatment resistance. In order to effectively battle multidrug-resistant tuberculosis (MDR-TB), continuous monitoring, extensive rigorous patient education, and adherence to treatment regimens are essential. Future projects must focus the

development of more potent and less dangerous drugs, as well as the upgrading of patient care services, in order to successfully treat the condition and avoid transmission within communities (Pontali., et al. 2013).

CONCLUSION

The patient's medical condition's progression highlighted the importance of ongoing monitoring, professional advice, and rigorous adherence to treatment procedures in order to control possible difficulties and achieve positive outcomes. This example emphasizes the need for strong public health initiatives, patient education, and support networks to prevent tuberculosis recurrence and limit the spread of multidrug-resistant tuberculosis (MDRTB). Future efforts should concentrate on improving diagnostic procedures, finding more efficient and less harmful medicines, and providing full patient care to confront the chronic worldwide problem of tuberculosis.

REFFERENCES

Brigden, G., Hewison, C., Varaine, F., & Rich, M. L. (2014). New developments in the treatment of drug-resistant tuberculosis: clinical utility of bedaquiline and delamanid. *Infectious Diseases of Poverty*, *3*(1), 3.

Dheda, K., Gumbo, T., Maartens, G., Dooley, K. E., McNerney, R., Murray, M., et al. (2017). The epidemiology, pathogenesis, transmission, diagnosis, and management of multidrugresistant, extensively drugresistant, incurable and tuberculosis. Lancet Respiratory Medicine, 5(4), 291-360.

Dheda, K., Limberis, J., Pietersen, E., Phelan, J., Esmail, A., Lesosky, M., (2017).al. Outcomes, infectiousness, and transmission dynamics of patients with extensively drug-resistant tuberculosis and home-based care: a longitudinal cohort study. Lancet Respiratory Medicine, 5(4), 269-281

- Esmail, A., Barry, C. E. III, Young, D. B., & Wilkinson, R. J. (2014). The ongoing challenge of latent tuberculosis. *Philosophical Transactions of the Royal Society B: Biological Sciences, 369*(1645), 20130437.
- Floyd, K., Glaziou, P., Houben, R., Sumner, T., White, R. G., & Raviglione, M. (2018). Global tuberculosis targets and milestones set for 2016-2035: definition and rationale. International Journal of Tuberculosis and Lung Disease, 22(7), 679-689.
- Katz, D. E., & E. D. H. (2011). Protein-Energy Malnutrition and Risk of Infection. Annual Review of Nutrition. 121–148.
- Lange, C., Abubakar, I., Alffenaar, J. W., Bothamley, G., Caminero, J. A., Carvalho, A. C., et al. (2014). Management of patients with multidrug-resistant/extensively drug-resistant tuberculosis in Europe: a TBNET consensus statement. European Respiratory Journal, 44(1), 23-63.
- Lee, M., Lee, J., Carroll, M. W., Choi, H., Min, S., Song, T., Via, L. E., Goldfeder, L. C., Kang, E., Jin, B., Park, H., Kwak, H., Kim, H., Jeon, H.-S., Jeong, I., Joh, J. S., Chen, R. Y., Olivier, K. N., Shaw, P. A., ... Barry, C. E. (2012). Linezolid for Treatment of Chronic Extensively Drug-Resistant Tuberculosis. New England Journal of Medicine, 367(16), 1508–1518. https://doi.org/10.1056/nejmoa1 201964
- Mustofa, S., & Antoni, A. (2023). Case Report: Unilateral Secondary Spontaneous Pneumothorax caused by Pulmonary Tuberculosis in a Heavy Smoker. *Sriwijaya Journal of Medicine*, 6(3), 87–93.
- Mustofa, S., Faisal, M. E. P. A., Soemarwoto, R. A. S., Rusmini, H., & Silaen, D. T. (2023). Tuberkulosis Paru Dengan Pneumonia Komunitas, Paraparese Inferior, Dan Penyakit Jantung Koroner: Laporan Kasus. *Jurnal*

- Kedokteran Universitas Lampung, 7(1), 18-24.
- Mustofa, S., Herdato, M. J. D., Morfi, C. W., Saputra, T. A., Pratama, A., Tria, M., Putranata, N. R., Sanjaya, R. P., & Erumbia, I. A. (2023). Peningkatan Pengetahuan Mengenai Manajemen Tatalaksana Terhadap Pasien Penyakit Paru Obstruktif Kronik (PPOK) dan Tuberkulosis Paru (TB) Pada Tingkat Fasilitas Kesehatan Pertama (FKTP) di Kabupaten Lampung Tengah. JPM (Jurnal Pengabdian Masyakat) Ruwa Jurai, 8(2), 86-90.
- Mustofa, S., Megantoro, G. K., Gozali, A., Saputra, T. T., & Sanjaya, R. P. (2023). SINDROM OBSTRUKSI PASCA TUBERKULOSIS DENGAN LULUH LOBUS: LAPORAN KASUS. Jurnal Ilmu Kedokteran dan Kesehatan, 10(7), 2426-2430.
- Mustofa, S., Putri, N. S. P. D. L., Togihon, L., Aryana, W. F., Sanjaya, R. P., & Saputra, T. T. Pengaruh Pemberian (2023).Ekstrak Biji Kopi Robusta (Coffea canephora) Lampung terhadap Aktivitas Enzim Katalase Hippocampus Tikus Putih (Rattus norvegicus) Jantan Galur Sprague dawley Diinduksi yang Monosodium Glutamat. MAJORITY, 12(1), 42.
- Nahid, P., Mase, S. R., Migliori, G. B., Sotgiu, G., Bothamley, G. H., Brozek, J. L., et al. (2019). Treatment of Drug-Resistant Official Tuberculosis. An ATS/CDC/ERS/IDSA Clinical Practice Guideline. American Journal of Respiratory and Critical Care Medicine, 200(10), e93e142.
- Noviyanti, D. W., & Saftarina, F. (2024).
 Penatalaksanaan Holistik Pasien
 Perempuan Usia 55 Tahun Dengan
 Penyakit Paru Obstruktif Kronis
 (PPOK) dan Riwayat Tuberculosis
 (TB) Paru melalui Pendekatan
 Dokter Keluarga di Wilayah
 Puskesmas Pasar Ambon. *Medical*

- Profession Journal of Lampung, 14(7), 1440-1455.
- Pontali, E., Visca, D., Centis, R., D'Ambrosio, L., Spanevello, A., Migliori, G. B. (2013). Multi- and extensively drug-resistant tuberculosis: advances in diagnosis and management. Future Microbiology, 8(4), 451-462.
- Poty, P. M., Mustofa, S., Kurniawaty, E., & Soleha, T. U. (2024). Mekanisme Kerja & Penggunaan Klinis N-Acetylcystein (NAC) Pada Penyakit Paru & Saluran Napas. *Medical Profession Journal of Lampung*, 14(5), 912-918.
- Singh, V., & Chibale, K. (2021).

 Strategies to combat multi-drug resistance in tuberculosis. *Accounts of chemical research*, *54*(10), 2361-2376.
- Soemarwoto, R. A., Rusmini, H., Messah, A. D. V., Dilangga, P., Wibowo, A., & Mustofa, S. (2024). Role of matrix metalloproteinase-1 (MMP-1) on lung remodelling in post pulmonary tuberculosis squelae.
- Syal, R., et al. (2014). Hematological profile in patients of pulmonary tuberculosis." International Journal of Research in Medical Sciences. 605–607.
- Udwadia, Z. F., & Mullerpattan, J. B. (2014). Multidrug-resistant

- tuberculosis management in India: past, present, and future. *Journal of Thoracic Disease*, 6(3), 146-154.
- World Health Organization. (2022).

 WHO consolidated guidelines on drug-resistant tuberculosis treatment.
- World Health Organization. (2020).
 Global Tuberculosis Report 2020.
 Geneva: World Health
 Organization. Available at: WHO
 Global TB Report.
- Xie, Y. L., Chakravorty, S., Armstrong, D. T., Hall, S. L., Via, L. E., Song, T., et al. (2017). Evaluation of a rapid molecular drug susceptibility test for tuberculosis. *New England Journal of Medicine, 377*(11), 1043-1054.
- Zignol, M., Dean, A. S., Alikhanova, N., Andres, S., Blanc, L., Cirillo, D. M., et al. (2016). Population-based resistance Mycobacterium of tuberculosis isolates pyrazinamide and fluoroquinolones: results from a multicountry surveillance project. Lancet Infectious Diseases, *16*(10), 1185-1192.