

Management of Submandibular Abscess in Patients with Multiple Drug Resistance (MDR-TB)

drg. Rachendra Pratama*, drg. Farah Asnely Putri*, Sp.BM., drg. Seto Adiantoro**, Sp.BM (K)

*Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Padjadjaran University

**Oral and Maxillofacial Surgery Department, RSUP dr. Hasan Sadikin Bandung, Indonesia

Corresponding Author: rachendra19001[at]mail.unpad.ac.id

Abstract: *One of the key treatments of odontogenic infection is adequate antibiotic regimen. The host factor plays an important role in the prognosis of the patient. Patient with tuberculosis associated with malnutrition and anemia as the most common complications in TB sufferers. Multi-drug resistant (MDR-TB) defined as resistance to both isoniazid and rifampicin, the two most important first-line drugs in treating TB. Many research showed that Rifampicin were also quite effective in inhibiting the growth of orofacial bacteria. In this article, we present a case of one patient with odontogenic infection that has spread to submandible and submental spaces with history of previously failed TB treatment and currently diagnosed with MDR-TB. We performed surgical intervention by incision and drainage of pus, the provision of adequate broad spectrum antibiotic, and high calorie and high protein diet in order to ensure a better response to the treatment. Our patient showed a good and fast response to the combination of treatment that was given despite her systemic condition.*

Keywords: odontogenic infection, submandibular abscess, tuberculosis, Multiple Drug Resistance (MDRTB)

1. Introduction

Odontogenic infections are infections of the alveolar, jaw, or face that originate from the teeth or from their supporting structures and are among the most common infections encountered. The most common causes of odontogenic infections are dental caries, deep patches or failed root canal treatment, pericoronitis, and periodontal disease. The infection starts locally around the tooth and can remain localized to the area where it started, or it can spread to adjacent or distant areas. The spread of infection depends on bacterial virulence, host resistance factors (host), and regional anatomy.^{1,2}

Tuberculosis can cause a variety of laboratory abnormalities such as anemia, increased erythrocyte sedimentation, decreased albumin serum, hyponatremia, impaired liver function, leukocytosis, and hypocalcemia.³ Tuberculosis can also cause or worsen malnutrition by reducing appetite and increasing catabolism.⁴ Malnutrition related to resistance from the host plays an equally important role in the spread of odontogenic infections. Relationship between malnutrition and tuberculosis, namely the effect of tuberculosis on nutritional status and the effect of malnutrition on clinical manifestations of tuberculosis as a result of immune system weakness.^{5,6} Malnutrition is also a major risk factor for active onset of tuberculosis and also can worsen the prognosis of TB disease.⁷ Malnutrition influences cell-mediated immunity (CMI) and CMI is the body's main defense system against TB.⁸

Multi drug resistance tuberculosis is defined as resistance to isoniazid and rifampin, which are the 2 most effective first-line drugs for TB. In 2006, an international survey found that 20% of *M tuberculosis* isolates were MDR. As host factor play an important role in the severity of infections, systemic disease like tuberculosis can altered the host response to any treatment given. It may affect the likeliness of a TB patient to be infected due to the low immune

system, higher chance of leukocytosis, lower albumin serum level that has a deep correlation with infection and difficulties in absorption of drugs. The purpose of writing this journal is to add insight into the management of dental emergencies in submandibular abscess cases extending to the submental region in patients with multiple drug resistance (MDRTB) with the using of antibiotics according to empiric as well as adequate incision and drainage also education and nutritional improvement.^{7,8,9}

2. Case Report

Female patients aged 25 years came to the emergency room at Hasan Sadikin Hospital (RSHS) in Bandung with complaints of swelling in the lower right jaw extending to the chin. \pm 1 month before hospitalization, the patient complained of toothache in the lower right jaw area, but she did not seek any treatment. About 7 days before admission, she complained of toothache in the right lower jaw area. Within 3 days, a painful swelling occurred. After the swelling got much bigger and the pain increased 4 days later, she went to a private clinic and directly referred to the Hasan Sadikin Hospital Emergency Department for further treatment. This patient has a history of Multiple Drug Resistance-TB and currently on her 5th month of TB treatment.

Extra-oral examination has showed a swelling in the right lower jaw that was extended to the chin region. The swelling were reddish, warm, localized, with fluctuation and pain on palpation (Figure 1). Intra oral examination has revealed that gingiva was generally hyperemic (Figure 2). The result of chest radiograph has showed that there was signs of active TB with right pleural effusion (Figure 3). In the panoramic picture there were radiolucency in the apical area of the teeth 46, 47 and 48 (figure 4). We diagnose this patient with submandibular abscess extended to submental due to necrosis of pulp 47, radices of teeth 46, and chronic periodontitis of teeth 48. The diagnosis also included necrosis

of pulp 28, radices of teeth 36, and Multiple Drug Resistant Pulmonary Tuberculosis (MDRTB). The dental emergency procedure was incision and drainage of the pus and extraction of teeth 28,36,46,47,48 (Figure 5,6)

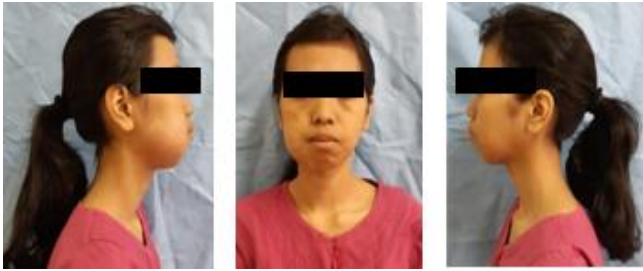


Figure 1: Facial profile and swelling in the right lower jaw extending to the chin area with a size of 4x2x2 cm that was reddish, warm, localized, with fluctuation and pain on palpation

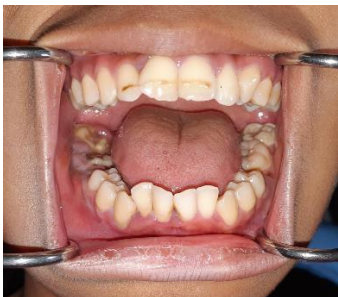


Figure 2: Intra oral examination shows a swelling of gingiva and vestibule of the 46-48 region. A slight decrease in mouth opening was also noted in this patient



Figure 3: Chest radiography shows signs of active TB with right pleural effusion



Figure 4: Panoramic features diffuse radiolucency in the apical area of the teeth 36, 46, 47



Figure 5: Tapping of the pus in the submandibular and submental regions



Figure 6: Exploratory actions through submandibular and submental spaces



Figure 6: Post Penrose drain application and extraction of the causative teeth

Emergency actions that have been taken were infusion of lincosamine 16 gtt / min, tapping of pus in submandibular and submental regions, administration of 1 gram ceftriaxone, metronidazole 500 mg, omeprazole 40 mg, and ketorolac 30 mg intravenously. We performed incisions through the submandibular and submental regions and drainage of the pus. As a source control measure, teeth 28, 36, 46, 47, 48 were extracted. Penrose drain was inserted to ensure optimum drainage of pus and wound was closed with gauze. Patients were given instructions on a high calorie and high protein diet and oral hygiene maintenance (gargling using 0.12% chlorhexidine 2 times daily for 1 week and regular brushing). To manage the trismus and ensure an adequate drainage of the pus, we instructed the patient to practice mouth opening using stick as often as possible.

Continuous medication and diet intervention to the patient proved to have a good result as the swelling in submandible and submental area had begun to shrink the following day. We also monitored an improvement to the trismus problem as the interincisal opening has increased to 3 cm. The penrose drain was removed 3 days later after our patient showed no more sign of infection.



Figure 7: Follow up day 2

3. Discussion

Definition

Infection is the process of entry of microorganisms into the body; these microorganisms penetrate and destroy the host slowly so that they multiply. Spread of infection can occur because the spaces in the head and neck region is only separated by loose connective tissue.¹⁴

Submandibular abscesses are defined as the formation of abscesses in the potential space in the submandibular region accompanied by sore throat, fever and limited mouth opening movements. In general, the source of infection in the submandibular space comes from the infection process of the teeth, floor of the mouth, pharynx and submandibular

lymph nodes. It may also be the continuation of infection from another deep neck space.¹⁴

The causative bacteria are usually a mixture of aerobic and anaerobic bacteria. The most common of aerobic bacteria are *Streptococcus* sp, *Staphylococcus* sp, *Neisseria* sp, *Klebsiella* sp, *Haemophilus* sp. In cases originating from dental infections, anaerobic bacteria are often found in groups of gram-negative rods, such as *Bacteroides melaninogenesis*, *Eubacterium*, *Peptostreptococcus* and the rarest is *Fusobacterium*.¹⁴

Deep neck space infections can cause different complications that can be life threatening such as upper airway obstruction and mediastinitis.¹⁴ The tip of the root of the second and third molars is located behind the lower mylohyoid line (the attachment site of the mylohyoid muscle) which is located in the inner aspect of the mandible, so that if the second and third molars are infected and form abscesses, the pus can spread to the submandibular space and can expand into the parapharyngeal space.¹⁵

Management

Our patient reported that she had a history of exposure to Tuberculosis (TB) 3 times in the last 4 years. She failed to comply and finish her first regiment treatment and was dropped out in Oktober 2016. After that she continued having the symptom of TB and then she take the treatment of her TB again and relaps again. When the patient has a history of incomplete TB treatment, the patient should be indicated as having Multiple Drug Resistant (MDRTB). Patients who are at risk of MDRTB are divided into three main groups: patient contact with drug-resistant TB, who was previously treated, and who had failed treatment. Close contact with patients with drug-resistant TB is more likely to have been infected with resistant strains of TB, and if they have active TB it should be considered to have drug-resistant strains.¹⁶ Patients who have received TB treatment in the past include those who have relapsed (have TB disease again after being declared "cured" in the past) and those who are lost to follow-up (did not complete TB treatment as recommended in the past). Nearly one-third of all patients who fail or recur will have MDRTB type.¹⁶ Therefore it is important to get a history of accurate TB treatment because this is a very strong risk factor for drug-resistant TB.¹⁷

Patient with multi-drug resistant (MDR-TB) defined as resistance to both isoniazid and rifampicin, the two most important first-line drugs. Our patient is in her 5th month of MDR-TB treatment and were given Rifampicin and isoniazid with the standard dose of 10 mg/kg rifampicin. Although regularly consuming antibiotic, it was no longer effective in suppressing bacterial infections alas the spread of the infections were fast to the head and neck spaces. According to Noor Abdullah Sulaiman's research in 2019, rifampicin antibiotics are quite effective in inhibiting the growth of orofacial bacteria so that the development of infection could be inhibited. In patients with MDRTB and extensive abscesses, it is necessary to adjust antibiotics by considering the history of previous treatment.¹⁸ Recently, several studies have suggested that the standard dose of 10 mg/kg rifampicin is suboptimal and at the lower end of the

dose-response curve. This standard suboptimal dose of rifampicin can contribute to the emergence of new cases of MDRTB.¹⁹

Another factor for the rapid expansion of infection in this patients is the factor of malnutrition and malabsorption due to TB itself. Nutritional status parameters that are often used are albumin levels and body mass index.^{7,8,9} Tuberculosis can cause or worsen malnutrition by reducing appetite and increasing catabolism.⁸ Research in India shows that TB sufferers are at seven times the risk of having a BMI <18.5 kg / m² and a middle arm circumference <24 cm.⁸ This patient has 36 kg of body weight and 162 cm of height, with BMI score of 13.7, indicating malnutrition. Activating the immune response during infection will increase energy consumption. Therefore malnutrition can result in weakness of immune system in protecting the body from ongoing infection. Malnutrition is also a major risk factor for active onset of tuberculosis and can also worsen the prognosis of TB disease.⁸

Malnutrition influences cell-mediated immunity (CMI) and CMI is the main body's defense system against TB.³⁰ Active tuberculosis is associated with cachexia, weight loss, low serum leptin concentrations. Leptin is the main mediator between nutrition and immunity.¹¹ When there is interference with leptin, anorexia will occur which allows a state of decline in nutritional status.³¹ Anorexia causes abnormalities in poor nutritional status by reducing energy intake. In addition to anorexia, disruption of nutrient absorption and increased catabolism affect poor nutritional status.¹¹ This consideration is one of the reasons for hospitalization to improve general conditions especially the nutrition of the patient. Patient education about the

importance of nutritional improvement also plays an important role in the patient's recovery. Aside from providing her diet during her hospitalization, we also emphasize on the importance of a better daily nutritional intake to the patient and the family. Further follow up to the internist is suggested to this patient.¹¹ Micronutrient deficiency is the most common cause of secondary immunity and tuberculosis. In tuberculosis patients there are several micronutrient deficiencies such as zinc, vitamin A and selenium.⁹ This causes disruption of the body's immune response.^{9,10} Zinc deficiency causes a decrease in phagocytic activity and reduces the number of T cells in circulation.¹⁰ Zinc has an important role in the contribution of macrophages against body defenses at the site of infection.¹⁰ Vitamin A deficiency affects the normal functioning of B and T lymphocytes, macrophage activity, mucosal and epithelial defenses and antibody response.

The principles of MDR-TB treatment itself must include at least four drugs that must be given to MDRTB patients. This also includes injections for at least 7 months, and at least three possible effective drugs in the advanced phase for a total of 18-21 months of treatment. Ideally, this should include all drugs from Group 1 (pyrazinamides and ethambutol), second-line injections (from Group 2), last generation quinolones (moxifloxacin or levofloxacin - from Group 3), and additional drugs from groups 4 and 5 to complete the regimen adequate and adequate. Ethionamide / prothionamide seem to be the most effective group 4 drug. Injecting agents are prescribed for a minimum of 7 months, and ideally for at least 4 months after the patient gets a negative result on TB examination.¹⁷

WHO 2014		WHO 2016	
Group	Drugs	Group	Drugs
Group 1	Isoniazid Rifampicin Ethambutol Pyrazinamide Rifabutin, rifapentine		
Group 2	Streptomycin Kanamycin Amikacin Capreomycin	Group A*	Levofloxacin Moxifloxacin Gatifloxacin
Group 3	Levofloxacin Moxifloxacin Gatifloxacin	Group B	Amikacin Capreomycin Kanamycin (streptomycin) [†]
Group 4	Ethionamide Prothionamide Cycloserine Terizidone <i>p</i> -Aminosalicylic acid	Group C*	Ethionamide/prothionamide Cycloserine/terizidone Linezolid Clofazimine
Group 5	Bedaquiline Delamanid Linezolid Clofazimine Amoxicillin/clavulanate Imipenem/cilastatin Meropenem High-dose isoniazid Thioacetazone Clarithromycin	Group D	D1 Pyrazinamide Ethambutol High-dose isoniazid D2 Bedaquiline Delamanid D3 <i>p</i> -Aminosalicylic acid Imipenem-cilastatin [†] Meropenem [†] Amoxicillin-clavulonate [†] (thioacetazone)

Figure 7: MDRTB treatment protocol¹⁷

Incisions through the submandible and submental spaces were made for the purpose of evacuating the abscess which were done under local anesthesia. The administration of antibiotics should be based on the results of bacteria culture and sensitivity tests for bacteria that cause infection. Beside rifampicin, they were resistant against some important drugs like Amikacine, Ampicillin, Ciprofloxacin, Erythromycin, Oxacillin.²¹ The test result of bacteria culture and sensitivity usually take several days to process and as we understand the history of resistancy in this patient, we then decided to give the antibiotic empirically. The combination of ceftriaxone and metronidazole were proven to be effective in treating odontogenic infections. Aneesh Sebastian et al in 2019 said that Metronidazole and cephalosporin were sensitive enough to anaerobic group. Close monitoring of the patient response to the antibiotic is important and it may be adjusted after the sensitivity test result have been obtained.²⁰

The outcome of our patient is similar to the case report done by Marcelo Guzmán-Letelier in 2017. The use of empiric antibiotic for odontogenic infection were still quite effective despite of several antibiotic resistance in MDRTB.

4. Conclusion

Empiric antibiotic administration with evacuation of pus, and improving the patient nutrition was still quite successful in the management of submandibular abscesses that extends to the submental in patients with MDR-TB.

References

- [1] Management of Submandibular Abscess with Limited Resources Jyoti Sharma, Amiya R. Patnaik, Neerja Banerjee, Rajesh Sood. 2018. Department of Anesthesia, PGIMS, Rohtak, Haryana, Department of Anesthesia, PGIMER and Dr RML Hospital, New Delhi, India
- [2] Candamourty R, Venkatachalam S, Babu MR, et al. Ludwig's Angina—An emergency: A case report with literature review. *Journal of natural science, biology, and medicine*. 2012 Jul;3(2):206
- [3] Zumla A, Chakaya J, Centis R, et al. Tuberculosis treatment and management—an update on treatment regimens, trials, new drugs, and adjunct therapies. *The Lancet Respiratory Medicine*. 2015 Mar 1;3(3):220-34.
- [4] Kant S, Gupta H, Ahluwalia S. Significance of nutrition in pulmonary tuberculosis. *Critical reviews in food science and nutrition*. 2015 Jun 7;55(7):955-63.
- [5] Chandra RK, Newberne PM. Nutrition, immunity, and infection: mechanisms of interactions. *Springer Science & Business Media*; 2012 Dec 6.
- [6] Chandrasekaran P, Saravanan N, Bethunaickan R, et al. Malnutrition: modulator of immune responses in tuberculosis. *Frontiers in immunology*. 2017 Oct 18;8:1316.
- [7] Kawai K, Villamor E, Mugusi FM, et al. Predictors of change in nutritional and hemoglobin status among adults treated for tuberculosis in Tanzania. *NIH Public Access*. 2011;15(10):1380–9.
- [8] Bhargava A, Chatterjee M, Jain Y, Chatterjee B, et al. Nutritional Status of Adult Patients with Pulmonary Tuberculosis in Rural Central India and Its Association with Mortality. *PLoS One*. 2013;8(10):1–11.
- [9] Oliveira MG, Delogo KN, Oliveira HM, et al. Anemia in hospitalized patients with pulmonary tuberculosis. *Jornal Brasileiro de Pneumologia*. 2014 Aug;40(4):403-10
- [10] Miyata S, Tanaka M, Ihaku D. The prognostic significance of nutritional status using malnutrition universal screening tool in patients with pulmonary tuberculosis. *Nutrition Journal*; 2013;12(1):1.
- [11] Zheng Y, Ma A, Wang Q, et al. Relation of Leptin, Ghrelin and Inflammatory Cytokines with Body Mass Index in Pulmonary Tuberculosis Patients with and without Type 2 Diabetes Mellitus. *PLoS One*. 2013;8:1–7.
- [12] WHO. 2017 Zignol M, Gemert WV, Falzon D, et al. Surveillance of anti-tuberculosis drug resistance in the world: an updated analysis, 2007-2010. *Bulletin of the world Health Organization*. 2012; 90: 111-9.
- [13] Jaganath D, Mupere E. Childhood tuberculosis and malnutrition. *The Journal of infectious diseases*. 2012 Dec 15;206(12):1809-15.
- [14] Pellechia R, Holmes H, Barzani G, et al. Antimicrobial therapy and surgical management of odontogenic infections. *A Textbook of Advanced Oral and Maxillofacial Surgery*. 2016 Aug 31; 3:1.
- [15] AL-Muflahi MS, Bahannan AA. Deep Neck Space Abscess; Clinical Presentation, Etiology and Morbidity; A Retrospective Review. *Yemeni Journal of Medical and Health Research*. 2014; 6(1&2).
- [16] Wilson JW, Tsukayama DT. Extensively drug-resistant tuberculosis: principles of resistance, diagnosis, and management. In *Mayo Clinic Proceedings*. Elsevier. 2016 Apr 1 (Vol. 91, No. 4, pp. 482-495)
- [17] World Health Organization. WHO treatment guidelines for drug-resistant tuberculosis, 2016 update. WHO/HTM/ TB/2016.04 [Internet]. Geneva: World Health Organization; 2016 [cited 2017 May 1]. Available from: <http://www.who.int/tb/areas-of-work/drug-resistant-tb/treatment/resources/en/>
- [18] Becerra MC, Appleton SC, Franke MF, et al. Tuberculosis Burden In Households of Patient with Multipledrug-Resistant and Extensively Drug-Resistant Tuberculosis: A Retrospective Cohort Study. *Lancet*. 2011; 377 (9760):147-152
- [19] Pinto Lancelot, Dick Menzies. Treatment of Drug-Resistant Tuberculosis. *Respiratory Epidemiology and Clinical Unit, Montreal Chest Institute, Montreal, QC, Canada; Departement of Epidemiology and Biostatistics, McGill University, Montreal, QC, Canada*. 2011
- [20] Sulaiman Abdullah Noor et al. Orofacial Space Infections, Etiology, Microbiological Susceptibility and Surgical Management. *Ghazi al-Hariri Surgical Specialities Hospital, Baghdad, Iraq*. 2019.
- [21] *International Journal of Current Microbiology and Applied Sciences* ISSN: 2319-7706 Volume 5 Number 8 (2016) pp. 197-203