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ROLE OF LOW-DOSE AZITHROMYCIN IN THE MANAGEMENT OF CYSTIC BRONCHIECTASIS: A CASE SERIES

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Abstract: Role of Low-Dose Azithromycin in The Management of Cystic Bronchiectasis: A Case Series. Bronchiectasis is an abnormal chronic and persistent dilatation of the bronchi that is accompanied by destruction of the bronchial walls due to congenital or acquired disorders such as chronic respiratory tract infections. Recurrent respiratory tract infections are characteristic of bronchiectasis. Radiological examination plays a role in diagnosis, a thin section CT to confirm a diagnosis of bronchiectasis when clinically suspected, and provides clearer information on lung morphology. The goals of treating bronchiectasis are to prevent exacerbations, reduce complaints, improve the patient's quality of life, and stop the disease from worsening. Therapy is expected to address the proven underlying cause, cutting off the vicious cycle of bronchiectasis Long-term antibiotics are considered in patients with bronchiectasis with frequent exacerbations three or more times per year to relieve symptoms and reduce the frequency of exacerbations. Macrolides are a plausible alternative antibiotic and anti-inflammatory agent with a lower burden of treatment for bronchiectasis patients. We present three cases of Bronchiectasis that were admitted to Mataram University Hospital. The three cases were given Long-term antibiotics with low-dose Azithromycin for 2 and 3 months. This report demonstrates clinical improvement in a reduction of exacerbation frequency, improvement in quality of life, decreased sputum production, and increased ability to carry out activities in patients treated with low-dose azithromycin. The most common side effect that appears in three cases is gastrointestinal disturbances.
Keywords: Low-dose Azithromycin, Long-term antibiotics, Cystic Bronchiectasis

Abstrak : Peran Azithromycin Dosis Rendah pada Penanganan *Cystic Bronchiectasis : A Case Series*. Bronkiektasis adalah dilatasi bronkus kronis dan persisten yang abnormal yang disertai dengan kerusakan dinding bronkus karena kelainan bawaan atau didapat seperti infeksi saluran pernapasan kronis. Infeksi saluran pernapasan berulang adalah karakteristik bronkiektasis. Pemeriksaan radiologi berperan dalam penegakan diagnosis, CT scan bagian tipis untuk memastikan diagnosis bronkiektasis bila dicurigai secara klinis, dan memberikan informasi yang lebih jelas tentang morfologi paru. Tujuan pengobatan bronkiektasis adalah untuk mencegah eksaserbasi, mengurangi keluhan, meningkatkan kualitas hidup pasien, dan menghentikan perburukan penyakit. Terapi diharapkan untuk mengatasi penyebab yang terbukti, memotong lingkaran setan bronkiektasis Antibiotik jangka panjang dipertimbangkan pada pasien dengan bronkiektasis dengan eksaserbasi yang sering tiga kali atau lebih per tahun untuk meredakan gejala dan mengurangi frekuensi eksaserbasi. Macrolides adalah agen antibiotik dan anti-inflamasi alternatif yang masuk akal dengan beban pengobatan yang lebih rendah untuk pasien bronkiektasis. Kami menyajikan tiga kasus Bronkiektasis yang dirawat di Rumah Sakit Universitas Mataram. Ketiga kasus diberikan antibiotik jangka panjang dengan Azithromycin dosis rendah selama 2 dan 3 bulan. Laporan ini

menunjukkan perbaikan klinis dalam penurunan frekuensi eksaserbasi, peningkatan kualitas hidup, penurunan produksi dahak, dan peningkatan kemampuan untuk melakukan aktivitas pada pasien yang diobati dengan azitromisin dosis rendah. Efek samping paling umum yang muncul dalam tiga kasus adalah gangguan pencernaan.
Kata kunci: Azithromycin dosis rendah, Antibiotik jangka panjang, *Cystic Bronchiectasis*

INTRODUCTION

Bronchiectasis is an abnormal chronic and persistent dilatation of the bronchi accompanied by destruction of the bronchial walls due to congenital or acquired disorders such as chronic respiratory tract infections (Barker & Brody, 2015). Previously, the prevalence of bronchiectasis was not widely known because the symptoms varied and the diagnosis was often not made (Barker & Brody, 2015 ; Pasteur et al, 2010). Data in the UK from 2004 to 2013 showed that the incidence of bronchiectasis increased, with an increase of 66% in women, and 50% in men, per 100,000 person-years. The population of bronchiectasis in adult men and women in the UK went up 61,7% in women, and from 61,1% in men, per 100,000 heads of population, approximately 262,900 adults were diagnosed with bronchiectasis in 2013 (Quint et al, 2016).

The pathogenesis of bronchiectasis is unknown, in many cases, each patient may differ concerning the etiology (Barker & Brody, 2015). Cole's vicious circle model of mucociliary disturbances in clearing the airways, chronic inflammation of the respiratory tissues, injury to the respiratory tissues, and bacterial colonization is used to explain the course of bronchiectasis (Barker & Brody, 2015 ; Quint et al, 2016). The diagnosis of bronchiectasis is determined from clinical findings and the results of investigations. a thin section needs to perform CT to confirm a diagnosis of bronchiectasis when clinically suspected and provide clearer information on lung morphology (Barker & Brody, 2015 ; Hill, De Soyza et al, 2021).

The goals of treating bronchiectasis are to prevent exacerbations, reduce complaints, improve the patient's quality of life, and stop the disease from worsening (Barker & Brody, 2015 ; Polverino et al, 2017). Therapy is expected to address the proven underlying cause and cut off the vicious cycle of bronchiectasis (De Soyza et al, 2021).

Long-term antibiotics are considered in patients with bronchiectasis with frequent exacerbations three or more times per year to relieve symptoms and reduce the frequency of exacerbations (De Soyza et al, 2021; Polverino et al, 2017).

A study in the Netherlands showed that azithromycin 250 mg daily for 12 months reduced exacerbations, improved quality of life, and improved FEV1 (McShane et al, 2013 ; Altenburg et al, 2013). This report demonstrates three cases given Long-term antibiotics with low-dose Azithromycin at Mataram university hospital.

CASE SERIES

From May 1, 2022 to December 31, 2022, a total of three patients presented to the Pulmonary Division at Mataram university hospital with diagnose bronchiectasis. The patients in the respective cases will be denoted as Case 1 ,Case 2, and Case 3. There were two male patients, ages 58 and 46, and one female patient, age 57 years old. Of the three cases, case 1 and case 3 was hospitalization for respiratory illness, whereas case 2 were diagnosed following their referral topulmonary outpatient clinic for a history of a chronic cough and recurrent hemoptysis. In all of the three cases, Chest CT was performed with result Cystics type bronchiectasis (infected). Each patient's history and clinical summary with the included workup are presented below and can be visualized in Table 1.

Table 1. Patient profile, clinical history, and medical work-up

	Case 1	Case 2	Case 3
Age/Sex	58 years old male	46 years old male	57 years old female
Visit type	Inpatient/outpatient	Outpatient	Inpatient/outpatient
Chest CT	Cystic bronchiectasis (infected bronchiectasis) Pneumonia especially dextra	Cystic bronchiectasis (infected) Thickening of the left posterior basal pleura	Cystic bronchiectasis (infected); and suspicion of pneumonia dextra
Chest X-ray	Bilateral bronchopneumonia, with bronchiectasis	N/A	bilateral pneumonia with bronchiectasis
Laboratory Work up	- PCR MTB sputum examination was not detected - Fungi identification using KOH results in positive, - anti-HIV (RAPID) nonreactive - gram staining found gram-positive coccus, gram-positive diplococcus, gram-positive streptococcus, gram-positive staphylococcus, found gram-negative bacilli, gram-negative coccus, gram diplococcus negative.	PCR MTB sputum examination was not detected	PCR MTB sputum examination was not detected
Comorbidities	- Probable pulmonary mycosis - Type II diabetes mellitus	- Recurrent hemoptysis	- Mild persistent asthma being partially controlled

CASE 1.

A 58-year-old man came through the emergency room at the Mataram university hospital with complaints of severe shortness of breath coughing up approximately 200 ml of sputum all day, greenish yellow in color, fever, fatigued and limited activity. In the last two months, the patient has been hospitalized three times and has been treated in the ICU because of respiratory failure. This patient has a history of recurrent respiratory tract infections and chronic cough with a large amount of mucopurulent sputum, especially in the morning. History of uncontrol Diabetes Mellitus Type-2 with HbA1C 13.2%, no history of tuberculosis. Active smokers with 40 packs per year.

On examination, the general condition was found to be moderately ill, with Glasgow Coma Scale (GCS) E4V5M6, blood pressure 127/50mmHg, respiratory rate 26 times/minute, pulse 115 times/minute, temperature 38.9^{o}C, oxygen saturation 89% room air, after administration oxygen supplementation by nasal cannula 4lpm oxygen saturation 96%. coarse crackles and wheezing were found in all lung fields. Other systemic examinations were within normal limits. The results of blood tests were Hb 11.3 g/dl, leukocytes 7.860/mm3, EOS type count% 0.4%, BASO% 0.3, NEUT% 58.5%, LYMPH% 29.1%, MONO% 11.7, platelets 289,000/mm3. Blood gas analysis pH 7.46, pCO2 37, pO2 143, HCO3 26.3, BE 2.5, SaO2 99%, FiO2 49%. Fungi identification using KOH results in positive, anti-HIV (RAPID) nonreactive, PCR MTB sputum not detected, gram staining found gram-positive coccus, gram-positive diplococcus, gram-positive streptococcus, gram-positive staphylococcus, found gram-negative bacilli, gram-negative coccus, gram diplococcus negative.

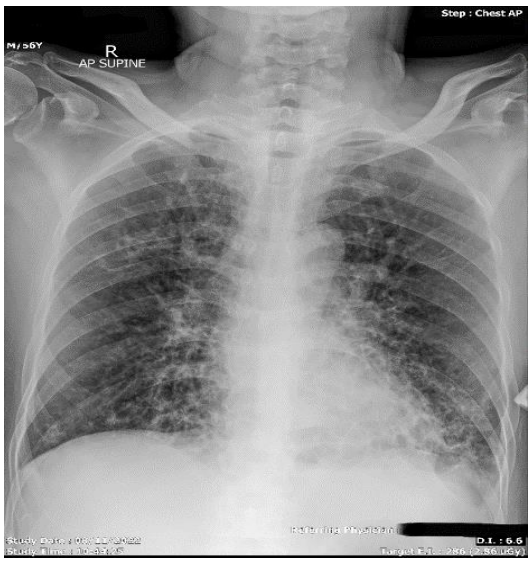

Figure 1. increase in bronchovascular markings with multiple inhomogeneous opacity in both lungs, some with a granular appearance. Bronchial dilation with peribronchial thickening and air bronchogram (+), some with cystic features in the basal aspect of the pulmo, especially the left.

A chest photo examination on November 8, 2022 (Figure 1) found the conclusion of Bilateral bronchopneumonia, with bronchiectasis. Thoracic HRCT examination on November 10, 2022 (Figure 2) found a conclusion Leading to Cystic bronchiectasis (infected bronchiectasis) Based on anamnesis, physical examination, and supporting examinations, the patient was diagnosed with infected bronchiectasis, bronchopneumonia, probable pulmonary mycosis, type II diabetes mellitus, and type 1 respiratory failure. After 5 days of treatment, the patient was stable and discharged.

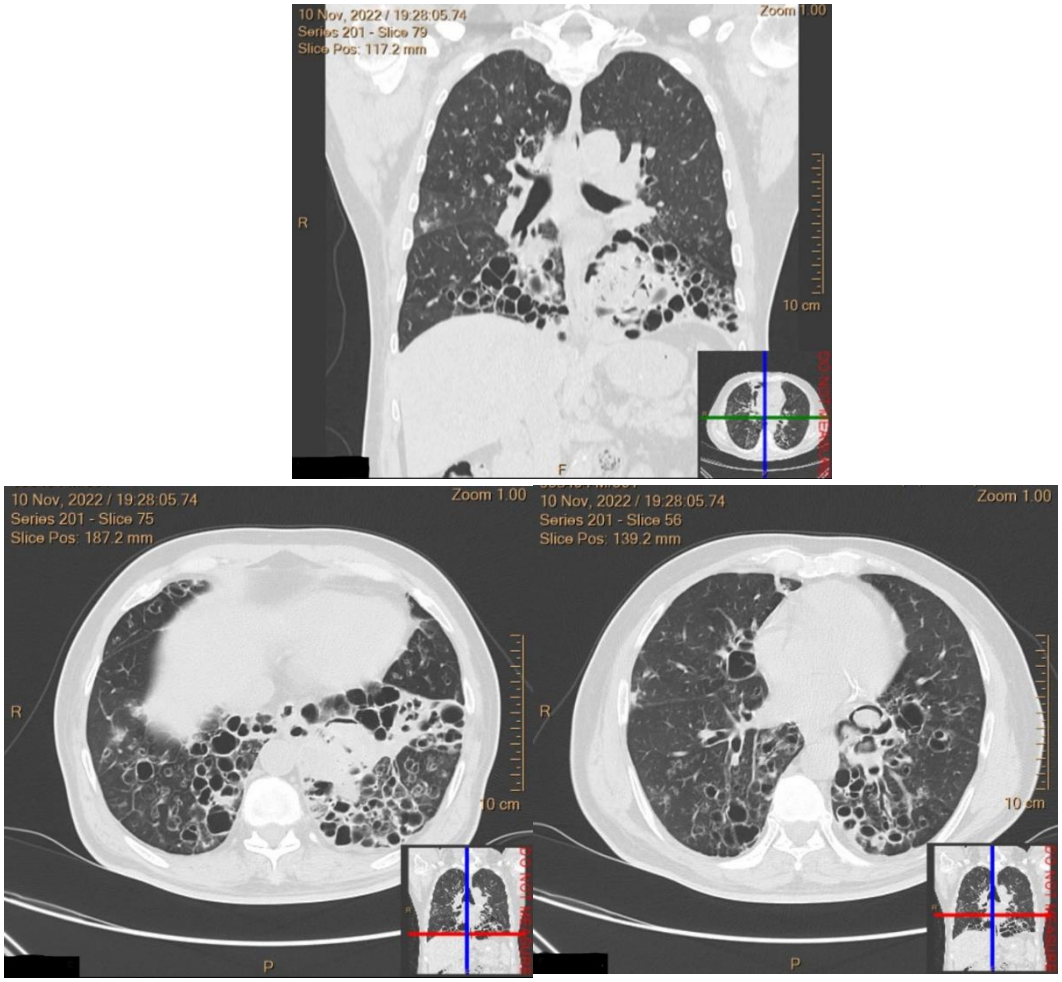

Figure 2. bronchial dilation and multiple cystic appearance in both lungs, especially on the medial and inferior pulmonary aspects, the size of the lesions varied, the walls were thin and some of them appeared to be thick walls and a honeycomb (+) appearance was seen. There is an air fluid level (+) on the cystic picture, especially on the posterior basal aspect of the pulmo. On the left side of the medial basal aspect and seen minimally on the right basal pulmo, there is a cavity with a central lesion, soft tissue density isodense is seen (43-47 HU), fungus ball and air crescent sign (+), the largest size is about 3.7 c m x 4.2 cm. Infiltrate spots (partially with ground glass opacity) are seen at the apex of the right pulmo, the inferior lobe of the right pulmo, and are faintly visible in the basal pulmo bilaterally. and with a fungus ball appearance especially on the left pulmo on the basal medial aspect, Different Diagnostic : cystic bronchiectasis and with pulmonary abscess (bilateral) suggestive of pulmonary aspergilloma/mycosis, Pneumonia especially dextra.

After undergoing treatment with fluconazole 2x100mg orally for 2 months, azithromycin 1x250mg orally for 3 months Salbutamol mdi 3x100mcg prn worsening shortness of breath, and n-acetylcysteine 3x200mg orally prn cough through policlinic every month with a diagnosis of stable bronchiectasis, probable pulmonary mycosis, DM type II, the patient came back to the pulmonary polyclinic at the Mataram university hospital with cough was rare and sputum production had decreased, the patient had also started to return to his activities properly. The patient also never felt shortness of breath got worse and had never visited the emergency room again for the past 3 months. In these 3 months, the patient has had additional complaints such as epigastric pain with nausea, bitter mouth, and sometimes vomiting. Patients were given lansoprazole 1x30 mg orally.

On examination, the general condition was good, with Glasgow Coma Scale (GCS) E4V5M6, blood pressure 117/50mmHg, respiratory rate 20 times/minute, pulse 85 times/minute,

temperature 36.6oC, 98% oxygen saturation without oxygen support. On physical examination, the lungs are within normal limits Other systemic examinations are within normal limits. Chest X-ray examination on January 31, 2023 (Figure 3) showed a suggest Cystic bronchiectasis.

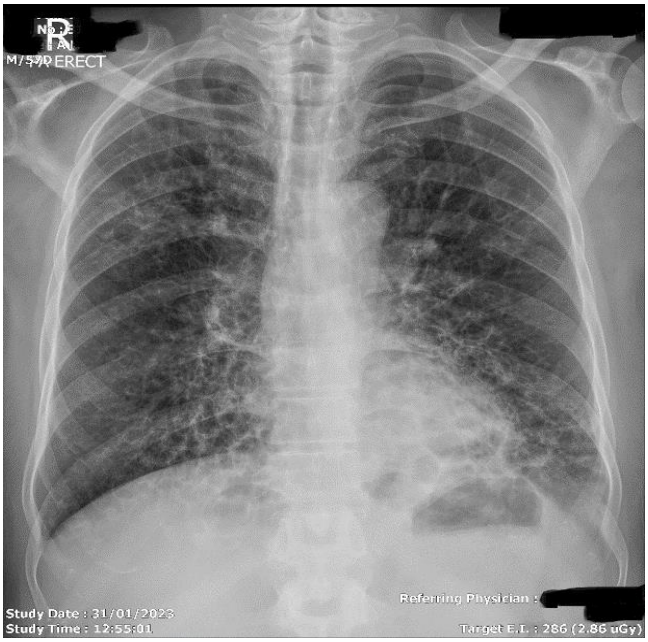

Figure 3. increase in bronchovascular markings with peribronchial thickening and air bronchogram (+), and a cystic appearance was seen in the basal aspect of both lungs, especially the left, honey comb appearance (+). Infiltrates were seen in both lungs, especially mid and medial pulmo region

CASE 2

A 46-year-old man came to the pulmonary polyclinic at Unram University Hospital with a hemoptysis of approximately 45cc fresh red blood usually appears once a week and chest tightness and dry cough. This complaint has been felt frequently patient since 10 years ago but is intermittent. The patient admitted that his weight was stable and no history of tuberculosis. The patient stated that he had never smoked. On examination, the general condition was good, with the Glasgow Coma Scale (GCS) E4V5M6, blood pressure 102/68mmHg, respiratory rate 20 times/minute, pulse 85 times/minute, temperature 36.6oC, oxygen saturation 99% room air. OPhysicalexamination of the lungs and other systemic examinations are within normal limits. Blood examination results showed Hb 11.0 g/dl, leukocytes 12,970/mm3, EOS% 0.1%, BASO% 0.3, NEUT% 74.8%, LYMPH% 16.7%, MONO% 6.9. On PCR MTB sputum examination was not detected,

Thoracic HRCT examination on May 24, 2022 (Figure 4). Impression Features Cystic bronchiectasis (infected) Thickening of the left posterior basal pleura. Based on anamnesis, physical examination, and supporting examinations, the patient was diagnosed with infected bronchiectasis and recurrent hemoptysis. Patients received Codeine 2x10mg orally prn worsening cough, azithromycin 1x250mg orally for 3 months, and tranexamic acid 3x500mg. After 3 months of a routine visit to the Mataram university hospital, the patient admitted that he had complained of hemoptysis that only appeared once in the past 3 months approximately 15cc.

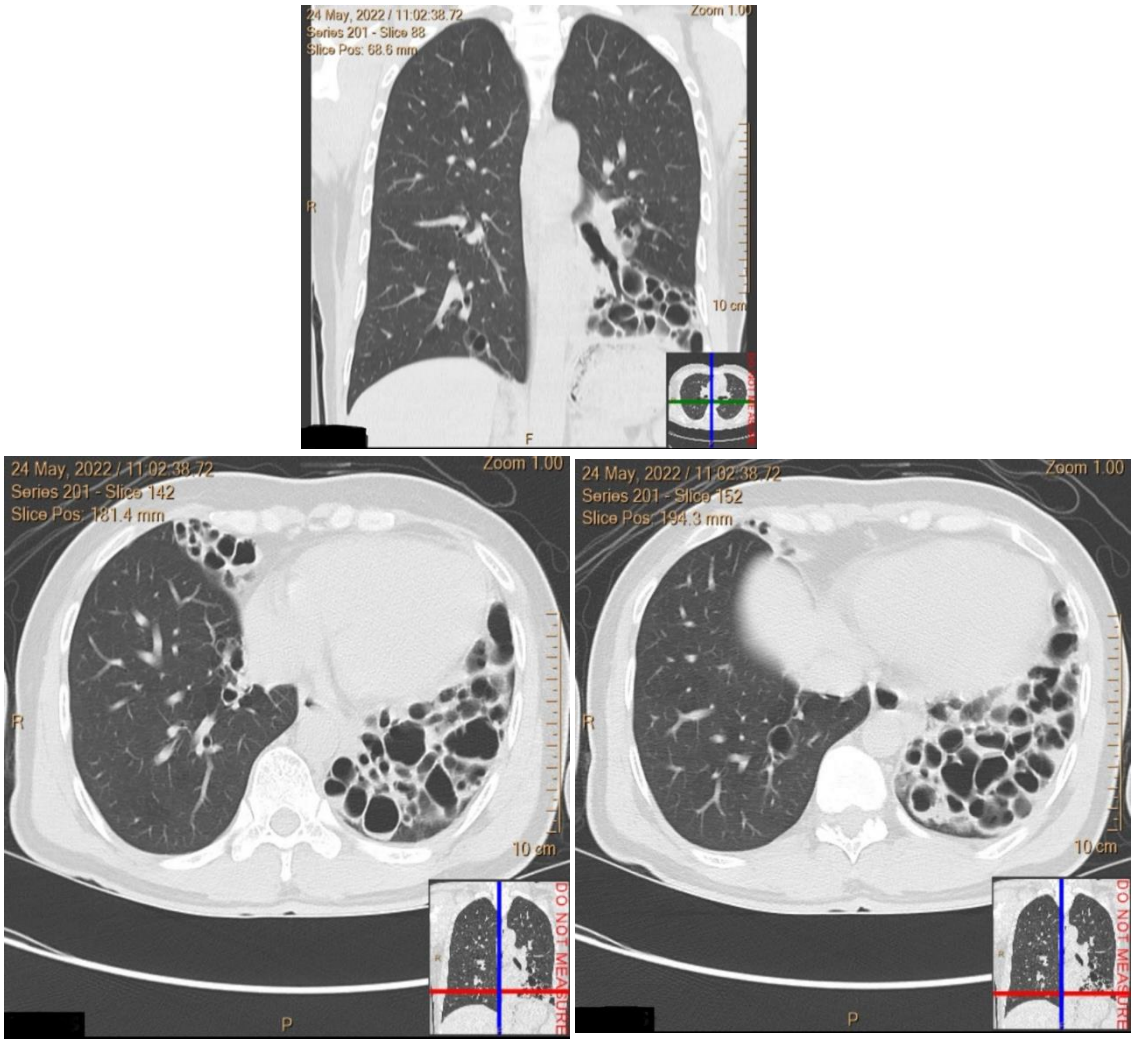

Figure 4. Multiple cystic features in both lungs, especially the medial aspect, especially the left, with varying sizes, thin walls and some with thick walls and a honeycomb (+) appearance. There is an air fluid level (+) on a cystic view with a thick wall on the left basal aspect of the pulmo.

Other complaints such as shortness of breath, limited activity, and sputum production were denied by the patient. On examination, the general condition was good, with Glasgow Coma Scale (GCS) E4V5M6, blood pressure 107/62mmHg, respiratory rate 20 times/minute, pulse 88 times/minute, temperature 36.6^{o}C, oxygen saturation 98% without oxygen. Physical examination of the lungs and other systemic examinations are within normal limits.

CASE 3

A 57-year-old woman came through the emergency room at the Unram Hospital with complaints of shortness of breath, coughing up greenish-yellow phlegm, weakness, and limited activity. Since 15 years ago, the patient had complaints of shortness of breath which often recurred. The patient admitted that shortness of breath was often experienced during rainy and cold weather. In this one year patients experience 4 times respiratory tract infections. The patient's husband is an active smoker and the patient has been frequently exposed to cigarette smoke from her husband since 35 years of marriage, with no history of tuberculosis.

On examination was found to be in moderate general illness, with Glasgow Coma Scale (GCS) E4V5M6, blood pressure 110/80mmHg, respiratory rate 24 times/minute, pulse 108 times/minute, temperature 37.4oC,

oxygen saturation 94% room air. On physical examination of the lungs, coarse crackles were found in all right lung fields and the basal areas of the right and left lungs. Other systemic examinations are within normal limits. Blood examination results showed Hb 10.8 g/dl, leukocytes 10,610/mm3, EOS% 0.2%, BASO% 0.1, NEUT% 82.2%, LYMPH% 9.9%, MONO% 7.6, platelets 500,000/mm3.

PCR MTB sputum examination was not detected. Chest X-ray examination on December 28, 2022 (Figure 5) showed a conclusion of bilateral pneumonia with bronchiectasis. Thoracic HRCT examination on December 29 20,22 (Figure 6) Impression leads to Cystic bronchiectasis (infected); and suspicion of pneumonia dextra. Based on anamnesis, physical examination, and supporting examinations, the patient was diagnosed with infected bronchiectasis and community-acquired pneumonia. After a treatment within 9 days, the patient is stable and discharged.

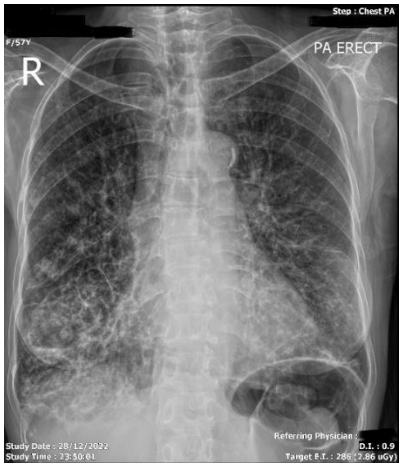

Figure 5. inhomogeneous opacity in both lungs, especially the media and basal pulmonary aspects with peribronchial thickening and air bronchograms. with bronchiectasis

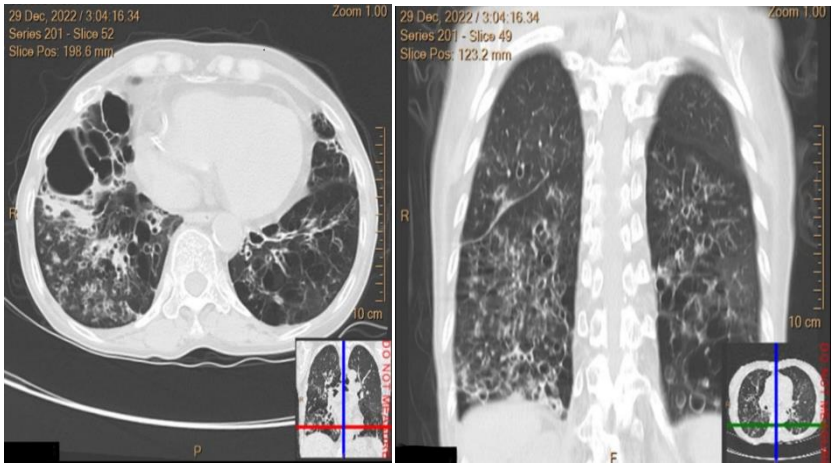

Figure 6. HRCT Thorax Multiple cystic features appeared in both lungs, especially on the pulmonary posterobasal aspect. The size of the lesions varies, most of the walls are thin and some have thick walls and a honeycomb (+) appearance is seen. There is an air fluid level (+) on the cystic picture, especially in cysts with rather thick walls on the posterobasal aspect of the pulmo. There was fibrosis and patchy infiltrates with ground glass opacity infiltrates in the right pulmo posterobasal and left perihilar infiltrates.

During 2 months of treatment with a diagnosis of stable bronchiectasis, mild persistent asthma being partially controlled, and Gastroesophageal Reflux Disease. Patients received azithromycin 1x250 mg orally continued for up to 3

months, lansoprazole 1x30 mg, sucralfate syrup 3x1 orally, Budesonide 160 mcg, and Formoterol Fumarate 4.5 mcg 2x1 puff. The patient admits that there are no complaints of shortness of breath, the cough is greatly reduced, the patient can carry out normal activities, the sputum production is greatly reduced, the patient has not visited the emergency room for the past 2 months, and other complaints of heartburn and nausea are sometimes felt. On examination, the general condition was good, with Glasgow Coma Scale (GCS) E4V5M6, blood pressure 127/61mmHg, respiratory rate 20x/minute, pulse 89x/min, temperature 36.6oC, oxygen saturation 98% without oxygen. Physical examination of the lungs, and other systemic examinations are within normal limits.

DISCUSSION

Bronchiectasis is generally divided into bronchiectasis due to cystic fibrosis and non-cystic fibrosis bronchiectasis. Non-cystic fibrosis bronchiectasis is a chronic inflammatory condition that results from recurrent inflammatory, recurrent obstruction of the small and medium bronchi, leading to persistent bronchial dilation and architectural distortion which affects a heterogeneous population with many causes (Barker & Brody, 2015 ; Pasteur et al, 2010). Lung infection or tissue injury makes the bronchial walls weak due to the loss of their muscular and elastic elements with an inflammatory response mechanism involving neutrophils, lymphocytes, and macrophages as well as inflammatory products secreted by microorganisms and the body's defenses (proteases, collagenases, and free radicals) (Quint et al, 2016; Chalmers et al, 2015).

Neutrophil elastase (NE) reduces the speed of mucociliary clearance and increases mucus secretion, causing mucus stasis so that respiratory tract infections will often occur and will then spin again like a vicious circle (Barker & Brody, 2015 ; Quint et al, 2016). Repeated exacerbations and chronic colonization of pathogens in bronchiectasis will increase the release of pro-inflammatory cytokines which can trigger the continuous release of reactive oxygen species (ROS) and increase levels of oxidative stress markers (Quint et al, 2016; Chalmers et al, 2015). Recurrent respiratory infections are the most common cause of non-cystic fibrosis bronchiectasis (Barker & Brody, 2015 ; Quint et al, 2016; Chalmers et al, 2015).

In case 1 and case 3 main complaint is Shortness of breath and chronic cough with the production of large amounts of mucopurulent sputum. In case 2 hemoptysis and recurrent coughing without sputum or minimal sputum production. All three cases have a history of Recurrent respiratory tract infections. All three cases show characteristic complaints of bronchiectasis. Other significant symptoms that can be found in bronchiectasis patient is chronic airway obstruction, progressive respiratory depression that worsens from year to year, and chronic cough with the production of large amounts of mucopurulent sputum (McShane et al, 2013; King, 2009 ; Chalmers & Sethi, 2017). A lot of sputum production, especially in the morning after accumulating during deep sleep, is often experienced by patients with bronchiectasis. In some patients with bronchiectasis, they may also complain of recurrent coughing without sputum or minimal sputum production and sometimes accompanied by coughing up hemoptysis with varying amounts of blood streaks to large clots (McShane et al, 2013; Chalmers & Sethi, 2017). The condition of acute exacerbation of bronchiectasis is characterized by an increase in cough intensity, tightness, volume, and change in sputum color, fever, coughing up blood, and chest pain (Barker & Brody, 2015 ; McShane et al, 2013 ; King, 2009). Shortness of breath and wheezing can be found if the disease gets progressive (McShane et al, 2013 ; Chalmers & Sethi, 2017).

X-rays or plain chest radiographs were performed to screen for early disease and exacerbations. In case 1 and case 3, there was Bronchial dilation with

peribronchial thickening and air bronchogram (+) with cystic features with conclusion bronchopneumonia, with bronchiectasis. Due to the limited specificity and sensitivity of the chest X-ray examination, a follow-up examination of the thorax HRCT was carried out in the three patients. In all three cases, the result was cystic-type bronchiectasis confirmed as a diagnosis by clearer information on lung morphology with HRCT (Barker & Brody, 2015 ; De Soyza et al, 2021). The PCR SPUTUM MTB examination was carried out on the three patients and the results of MTB were not detected, which means that tuberculosis was not the cause of bronchiectasis and was diagnosed in all three cases. Other tests such as spirometry, full blood count test, serum total IgE, and assessment of sensitization to A. fumigatus, Serum IgG, IgA, and IgM, sputum cultures, screening for Cystic Fibrosis and Primary ciliary dyskinesia cannot be performed due to limited supporting examination facilities.

The diagnosis of bronchiectasis is determined in three cases from clinical findings and the result of other investigations. The goals of treating bronchiectasis are to prevent exacerbations, reduce complaints, improve the patient's quality of life, and stop the disease from worsening (Barker & Brody, 2015 ; Polverino et al, 2017). Therapy is expected to address the proven underlying cause and cut off the vicious cycle of bronchiectasis (De Soyza et al, 2021). Therapy can be in the form of giving antibiotics to inhibit infections that cause damage to the airways. Antibiotics are used for Pseudomonas and/or MRSA eradication, suppression of chronic bacterial colonization, or for the management of exacerbations (King, 2009). Bronchiectasis patients who are experiencing an exacerbation are advised to administer antibiotics for 14 days (Polverino et al, 2017). A sputum culture examination is needed to determine the type of germ and clinical evaluation of the patient (De Soyza et al, 2021; Polverino et al, 2017). If sputum cultures are not available or in cases of high risk of Pseudomonas aeruginosa colonization, it is preferable to use antibiotics that include pseudomonas aeruginosa (Al-Jahdali et al, 2017).

Long-term antibiotics are considered in patients with bronchiectasis with frequent exacerbations three or more times per year to relieve symptoms and reduce the frequency of exacerbations (De Soyza et al, 2021; Polverino et al, 2017). Inhaled/nebulized antibiotics can reduce the number of bacteria, reduce exacerbations, improve quality of life, and reduce inflammation and purulence of sputum (De Soyza et al, 2021). Inhaled colistin for adults with bronchiectasis and chronic P. aeruginosa infection inhaled gentamicin as a second-line alternative and macrolides (azithromycin, erythromycin) in whom an inhaled antibiotic is contraindicated, not tolerated or not feasible (De Soyza et al, 2021; Polverino et al, 2017).

Azithromycin or erythromycin can be given to patients without P. aeruginosa colonized, inhaled gentamicin as a second line alternative, doxycycline as an alternative in patients intolerant of macrolides or in whom they are ineffective for Non- P.aeruginosa colonized patient (De Soyza et al, 2021; Polverino et al, 2017). Inhaled antibiotics take a long duration of daily administration, there is also a risk of bronchospasm and additional administration of airway clearance will result in a large treatment burden and increase the risk of non-adherence. Macrolides are a plausible alternative with a lower burden of treatment but have less evidence in the context of chronic P. aeruginosa infection (Contarini et al, 2018).

In the three cases, exacerbations complained of more than 3 times in one year. The condition of acute exacerbation of bronchiectasis is characterized by an increase in cough intensity, tightness, volume, and change in sputum color, fever, coughing up blood, and chest pain (Barker & Brody, 2015 ; McShane et al, 2013 ; King, 2009). So they were given long-term antibiotic treatment with macrolide as an alternative antibiotic and antiinflammatory agent with a lower

burden of treatment for bronchiectasis patients, the macrolide used low dose azithromycin 1x250mg orally for 3 months.

Mechanism of action of macrolides in respiratory diseases by modifying mucus production, inhibiting biofilm production, suppressing inflammatory mediators, reducing leukocyte recruitment and function, and inhibiting superoxide and nitric oxide production can be useful as anti-inflammatory, immunomodulating, reducing ROS production, and as antimicrobial in the management of bronchiectasis (Wong & Jones, 2013). A study in New Zealand showed that azithromycin 500 mg 3 times a week for 6 months reduced exacerbations, improved quality of life, and reduced inflammatory markers such as C-reactive protein and leukocytes (Wong et al, 2012). The Bronchiectasis and Low-dose Erythromycin Studies (BLESS) study in Australia, namely giving oral erythromycin 400 mg twice per week for 12 months reduced exacerbations, reduced sputum volume, and improved FEV1 (Serisier, 2013).

In observation after 2 and 3 months of treatment with low dose azithromycin 1x250mg orally. In case 1 cough was rare and sputum production had decreased, the patient had also started to return to his activities properly. The patient also never felt shortness of breath got worse and had never visited the emergency room again for the past 3 months In these 3 months, the patient has had additional complaints such as epigastric pain with nausea, bitter mouth, and sometimes vomiting, patients were given lansoprazole 1x30 mg orally. In case 2 the patient admitted that he had complained of coughing up blood for the past 3 months and only appeared once in the color fresh red approximately 15cc, before taking azithromycin daily patient can complain of hemoptysis once every week. In case 3 The patient admits that there are no complaints of shortness of breath, the cough is greatly reduced, the patient can carry out normal activities, the sputum production is greatly reduced, the patient has not visited the emergency room in the past 2 months, other complaints of heartburn and nausea are sometimes felt. These interventions with low-dose azithromycin resulted in a reduction of exacerbation frequency, improvement in quality of life, decreased sputum production, and increased ability to carry out activities. Side effects of macrolides include gastrointestinal disturbances, hepatotoxicity, cardiovascular risk, germ resistance, and hearing loss. The adverse events with macrolides are not significant to lead to withdrawal (Chalmers & Sethi, 2017 ; Serisier et al, 2013). The most common side effect that appears in three cases is gastrointestinal disturbances. This case series contained certain limitations, other tests such as spirometry, bronchoscopy, serum total IgE, assessment of sensitization to A. fumigatus, Serum IgG, IgA, and IgM, sputum cultures, screening for Cystic Fibrosis and Primary ciliary dyskinesia cannot be performed due to limited supporting examination facilities.

CONCLUSION

The pathogenesis of bronchiectasis is unknown, in many cases, each patient may differ concerning the etiology. Therapy is expected to address the proven underlying cause, cutting off the vicious cycle of bronchiectasis. Azithromycin is recommended as a second line of treatment and as a substitute when Inhaled/nebulized antibiotics are not available. Low-dose azithromycins are a plausible alternative antibiotic and anti-inflammatory agent with a lower burden of treatment for bronchiectasis patients. Low dose azithromycin 1x250mg orally in 2 and 3 months resulted in a reduction of exacerbation frequency, improvement in quality of life, decreased sputum production, and increased ability to carry out activities with the most common side effect appearing in three cases are gastrointestinal disturbances. As a suggestion for further cases, further investigation to discover the underlying etiology of bronchiectasis should be done to improve treatment for a patient with bronchiectasis.

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