Literature Review

Interventional Approach on Lung Abscess

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Abstract

Lung abscess is a necrotic liquefaction process containing necrotic debris or fluid from the lung parenchyma tissue, creating a cavity of more than 2 cm caused by bacterial infection. The most common etiology of lung abscess is oral aspiration. With a high incidence of tuberculosis in Indonesia, Mycobacterium tuberculosis may also cause cold abscesses, although rarely reported. Several things can increase the risk of developing a lung abscess, such as oral aspiration, sepsis, and history of previous lung infection. The treatment for lung abscess was classified into two groups, the pharmacology group which uses antibiotics including clindamycin, ampicillin-sulbactam, moxifloxacin, carbapenem, and piperacillin-tazobactam; and the other group is non-pharmacology therapy including drainage which is indicated for patient with a size cavity of more than 6 cm. There are several options for drainage such as percutaneous or endoscopic drainage. Bronchoscopy may serve as a diagnostic and also intervention tool in lung abscess.

Keywords: lung abscess, lung abscess treatment, lung cavity

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INTRODUCTION

Lung abscess is an infectious process in the lung parenchyma that produces single or multiple cavities characterized by air-fluid levels.[1,2] The more dominant cavities are usually characterized by a diameter of more than 2 centimeters (cm).[3] Cavities resulting from the liquefaction of necrotic lung parenchymal tissue contain both necrotic debris and fluid caused by the infectious process. The incidence of lung abscess is more common in the *pre*-antibiotic era, so bacterial pneumonia infections may lead to lung abscess formation both with and without empyema. This is due to the limited treatment during the time.[4]

Microaerophilic streptococci are the most common etiology of lung abscess and about 60–80% of lung abscess etiologies are anaerobic germs.[5] Aspiration pneumonia is a risk factor for lung abscess. One possible reason is that lung abscess-related pathogens are mostly anaerobic bacteria originating from the upper airway including nasopharynx, tongue, buccal mucosa, and gum folds.[6]

Before the discovery of antibiotics, drainage was the only therapy for lung abscess. The first case found in 1696 showing a good response to surgery was reported by Baglivi. Schulz reported a mortality rate of 29–35% in 306 cases of lung abscess in 1901. After the discovery of antibiotics, about 80–90% of primary lung abscess was treatable without the need for surgery and reported mortality rate decreased to 10–15%.[6] One of nonpharmacological treatments or interventions in lung abscess is drainage which is indicated for abscess with size greater than 6cm.[3] Pharmacologically, lung abscess can be treated with antibiotics such as clindamycin, betalactam/betalactamase inhibitors combined with methicillin-resistant *Staphylococcus aureus* (MRSA) antibiotics, and metronidazole that can also be combined with ceftriaxone.[3,4]

DEFINITION OF LUNG ABSCESS

An abscess is a collection of pus that can be located in any part of the body.[7] A lung abscess is a process of necrotic liquefaction of lung parenchymal

tissue, creating a cavity of more than 2 cm filled with necrotic debris and fluid caused by bacterial infection.[4] Multiple lung abscess may also develop, although it is usually characterized by a single dominant abscess.[3] The prevalence of lung abscess is currently less frequent than in the pre-antibiotic era due to inadequate management of pneumonia which leads to development of lung abscess in the pre-antibiotic era, however it still is considered a significant source of morbidity and mortality.[3,4]

Aspiration pneumonia is a risk factor for lung abscess. One possible reason is that lung abscess-related pathogens are mostly anaerobic bacteria originating from the upper airway including nasopharynx, tongue, buccal mucosa, and gum folds.[6] Patient with esophageal motility disorder, esophageal stricture and gastroeshophageal reflux is also at risk for lung abscess.[3] In addition, patient who frequently falls unconscious due to alcohol intoxication, drug overdose, or under the influence of sedation, anaesthesia and opioids or older patient with neurological disorder are also at risk for lung abscess formation.[8,9]

CLASSIFICATION

Lung abscess can be divided based on their duration, progression, formation process, and etiology. Based on duration, lung abscess is divided into acute and chronic lung abscess. Acute lung abscess occurs less than 6 weeks, while chronic lung abscess occurs longer than 6 weeks. Based on its causes, lung abscess is classified into primary and secondary lung abscess. Primary lung abscess occurs purely due to oropharyngeal aspiration without underlying lung disease which affects people with proper immunity, while secondary lung abscess occurs due to obstruction of the main airway due to masses, or as a result of complication of intrathoracic surgery, as well as in patient with low immunity such as patient with *Human Immunodeficiency Virus* (HIV) or receiving immunosuppression therapy.[3,4]

Based on its formation process, it is divided into hematogenic and bronchogenic process. The hematogenic process occurs through a systemic spread from other infectious sites such as abdominal sepsis, endocarditis, and thromboembolic sepsis, while the bronchogenic process means that lung abscess occurs due to inhalation or aspiration of oropharyngeal secretions.[3,4,9,10] Based on its etiology, lung abscess is classified into: polymicrobial etiology, such as anaerobic bacteria (*Bacteroides, Prevotella, Peptostreptococcus, Fusobacterium* or *streptococcus)* and the microbial group which caused by *Staphylococcus aureus, Klebsiella pneumonia* and *Streptococcus pyogenes.*[9]

ETIOLOGY

The most common microorganism causing lung abscess is anaerobic bacteria, reported in 60-80% of cases.[5] Primary lung abscess is usually caused by anaerobic bacteria that are considered normal flora in gum folds. These *anaerobic* bacteria are also referred to as non-specific etiology including gram-negative (*Bacteroides fragilis, Fusobacterium capsulatum*) and gram-positive (*Pepto-streptococcus* and *Microaerophilic streptococcus*) bacteria. The most common cause of primary lung in immunocompetent patient is anaerobic bacteria and *Microaerophilic streptococcus.*[3]

Lung abscess may also be caused by *aerobic* bacteria such as *Staphylococcus aureus* (including *methicillin-resistant staphylococcus aureus* [MRSA]), *Streptococcus pyogenes*, *Streptococcus pneumonia, Klebsiella pneumonia, Pseudomonas aeruginosa, Haemophilus influenzatype B, Escherichia coli* and *Legionella.*[3,6] The most common cause in immunocompromised cases is *Pseudomonas aeruginosa* with other gram-negative rods but can also co-infect with mycobacteria and fungi.[8]

RISK FACTORS

There are several factors affecting lung abscess formation, such as patient with immunocompromised conditions or *Acquired Immune Deficiency Syndrome* (AIDS), post lung transplantation, or patient who receives immunosuppression medication. Other risk factors

include condition with a high risk of aspiration, for example in seizures, bulbar dysfunction, alcohol intoxication, and other cognitivedisorders.[9] Aspiration risk is also present in patients with esophageal motility disorders, strictures due to esophageal tumor, and patients with gastroesophageal reflux conditions.[3]

Other conditions affecting lung abscess include abdominal sepsis, endocarditis-related infection, thromboembolic sepsis and the use of unhygienic nasal cannula that is not regularly replaced. In addition, following conditions may also affect lung abscess formation including history of lung diseases such as bronchiectasis, cystic fibrosis, bulla emphysema, bronchial obstruction due to tumors, foreign body aspiration, pulmonary contusion and congenital malformations such as vasculitis and cystitis conditions.[10]

PATHOGENESIS

Aspiration of oropharyngeal secretions is a common occurrence, but is not always associated with the frequency of lower respiratory tract infections. In cases of poor immunity, the infection may occur due to poor host defense mechanism against pathogens. This is rarely the case in people with good immunity. Since oropharyngeal secretions are the most common cause of abscess formation in the lung, bacteria originating from the oral cavity can also be found in lung as described in Figure 1A.[11] The average bacterial density in saliva is about 10^8/ml with anaerobic and microaerophilic organisms.[6]

Lipoproteins within *Staphylococcus aureus* will stimulate chemokines and cytokines derived from macrophages which sequentially cause an influx of monocytes and neutrophils at the site of infection. This will lead to increased levels of tissue factor (FJ) and inhibitor of plasminogen activator (PAI-1) which will further activate coagulation, inhibit fibrinolysis leadingto fibrin deposition and cause cavity formation and provide life support for the bacteria to survive by forming a fibrin capsule as illustrated in Figure 1B.[11] Cavity formation usually takes about 1–2 weeks. A lung abscess forms after the inflammatory process produces necrotizing tissue with a cavity that will be surrounded by regenerated epithelium until a lung abscess forms.[12]

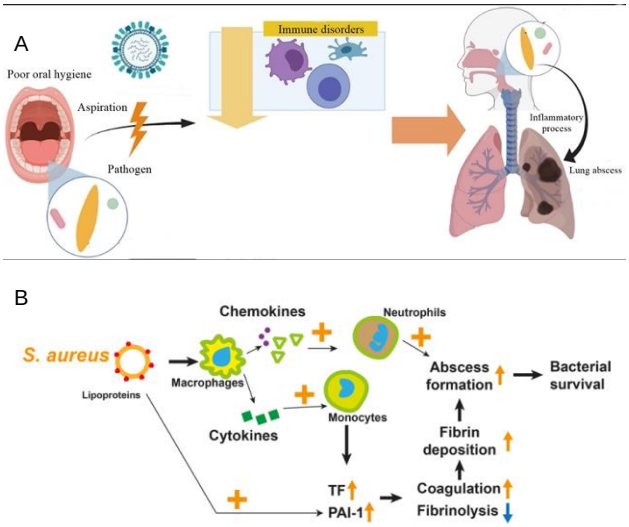

Figure 1. A) Illustration of the pathogenesis of lung abscess; B) Pathogenesis of abscess formation caused by *Staphylococcus aureus.*[11]

DIAGNOSIS APPROACH

The clinical manifestations of lung abscess are similar to those of other pulmonary infections with cough, purulent sputum production, pleuritic chest pain, fever, and haemoptysis. In anaerobic infection, clinical symptoms may deteriorate over a long period of time and can even be asymptomatic, whereas infections caused by aerobic germs are usually more acute. The history of the disease course should be explored such as when symptoms began, risk factors, predisposing factors, comorbidities, and previous pulmonary infections.[3,13]

Vital signs usually include fever and increased respiratory rate.[3] Physical examination may reveal rales as well as decreased breath sounds due to consolidation. Bad breath odor or poor oral hygiene can also be a sign of lung abscess. This is because aerobic bacteria are unable to produce sputum with odor *in vitro* or *in vivo* so it is likely that it is caused by anaerobic bacteria that infect lung tissue and form a lung abscess.[12,13]

Laboratory tests may reveal leukocytosis.[4] A blood culture may be ordered to identify secondary lung abscess. Gram staining of sputum usually shows neutrophil dominance with various types of

flora and bacteria. Sputum culture test may also be run in order to determine the pathogen causing the lung abscess. Cultures derived from alveolar rinse specimens usually reveal aerobic organisms since it is usually difficult to obtain and very sensitive to antibiotics which are usually administered before the patient took the test.[3]

On chest x-ray examination, one or more cavities with thick walls can be found, usually in dependent parts of the lung such as the upper lobe or posterior segment of the lower lobe. Primary lung abscess caused by aspiration is usually found in the posterior segment of the upper lobe and the superior segment of the lower lobe.[3,13] Another marker of lung abscess is the"*air-fluid level*" as shown in Figure 2.[14] A computed tomography scan (CT-scan) examination may facilitate in diagnosing and determining the size and location of the lung abscess, as well as identifying any other abnormalities or cavities. If cavities are found in nondependent parts of the lung such as the right middle lobe or the anterior segment of the upper lobe, the possibility of malignancy cannot be ruled out.[12,13]

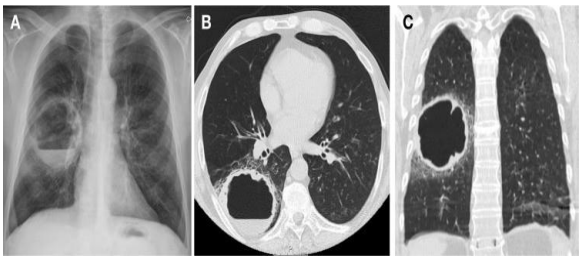

Figure 2. A) Chest-Xray examination; B) and C) CT-scan showing the cavities in the lung abscess.[14]

TREATMENT

Pharmacological Treatment

The treatment for lung abscess is classified into two groups: pharmacological and non-pharmacological management. Pharmacological management is the administration of antibiotics. About 95% of patients have a good response to antibiotics. Penicillin has been the first choice of antibiotic in lung abscess treatment, even though anaerobic bacteria can produce betalactamase and penicillin is not able to counter the effects of betalactamase.[3] Clindamycin was then developed and in clinical trials proved superior to penicillin.[4]

Clindamycin can be administered at a dose of 600mg/8 hours *intravenously* (IV) daily followed by 300mg/6 hours *orally* (PO) daily. Betalactam/betalactamase inhibitors are potentially combined with antibiotics that can treat methicillin-resistant *Staphylococcus aureus* (SARM) bacteria such as vancomycin. Amoxicillin-clavulanate 625 mg and 1000 mg PO every 8 hours can be continued if the patient's condition is stable.[3,4] If the abscess is caused by methicillin-sensitive *Staphylococcus aureus* (SASM) bacteria, cefazolin 2 g/8 hours IV or nafsilin 2 mg IV every 4 hours or oxacillin 2 mg every 4 hours can be administered, dose adjustment in patients with renal abnormalities is required.[9]

Ampicillin-sulbactam 3g/6-8h IV showed similar efficacy to clindamycin (with or without cephalosporins). Some data suggest that with fluoroquinolone antibiotics (moxifloxacin or levofloxacin), moxifloxacin 400 mg PO once daily is clinically proven to have similar efficacy and safety to ampicillin-sulbactam. Carbapenems including ertapenem can be given 1 g/24 hours IV, imipenem-cilastatin 500-1000 mg/6 hours IV, or meropenem 1 g/8 hours IV.[3,8] Another alternative therapy is tazobactam piperacillin 3.375 mg IV every 6 hours.[10]

Metronidazole should not be ordered as monotherapy since it lacks the ability to fight microaerophilic *Streptococcus* bacteria that often cause primary lung abscess, although metronidazole can fight anaerobic bacteria. The results of monotherapy studies using metronidazole are also unsatisfactory and not better than clindamycin. Metronidazole can be administered in some cases together with ceftriaxone antibiotics at a standard dose of 500 mg IV/PO every 6–8 hours.[3,4]

Antibiotics should be administered until there is an improvement in imaging or a shrinking lung abscess. Some studies recommend the evaluation of thoracic photographs every week or two weeks.[4] Age and size of abscess are significantly associated with radiologic improvement time. Persistent fever is usually due to antibiotic-resistant pathogens or diagnoses other than lung abscess. Most lung abscess can be drained through tracheobronchial

branching of the main airway. Surgery is not required if the patient has shown clinical improvement and less sputum production.[3]

Nonpharmacological Treatment

The indication for intervention in lung abscess is when patient's clinical condition does not improve with antibiotics.[15] The duration of pharmacological therapy ranges between 3–4 weeks to 14–16 weeks. Clinical improvement may be observed within 3–4 days of treatment and complete improvement takes 7–10 days. Another indication for intervention is lung abscess with size greater than 6 cm which rarely respond to antibiotic therapy alone without additional interventions such as surgery or drainage, patient with poor cough reflexes, lung abscess caused by antibiotic-resistant microorganisms and bronchopleural fistula.[3]

The air-fluid level may be an indication for drainage. Abscess drainage can be performed percutaneously or endoscopically. Percutaneous drainage is less invasive but possesses high benefits and effectiveness. However, in certain conditions such as coagulation disorders, infections around thoracic sites, or when a lot of lung tissue needs to be saved, endoscopic techniques are the right choice than percutaneous drainage.[3]

Bronchoscopy is beneficial for both diagnosis and therapy that is facilitating drainage of lung abscess. Lung abscess can be managed with antibiotics and drainage. The drainage usually involves a medical rehabilitation team to perform chest physiotherapy and postural drainage. Surgical intervention is considered when the condition does not improve with antibiotics and postural drainage alone. Bronchoscopy is not only performed to obtain sample but also to proceed with endoscopic drainage procedure.[16] Endoscopic procedure is also currently recognized as indication for patient with lung abscess located away from the pleura and pose a high risk for percutaneous drainage.[17]

A drainage endoscopy procedure is performed using a bronchoscope toidentify the segment of the bronchus where the abscess cavities are located.[18] The guidewire used is usually rigid. The guidewire is then inserted and the bronchoscope is slowly removed and a small catheter, usually an endovascular *pigtail* catheter of 110cm in length and 6F size, is inserted and retained in the lung abscess and left until it is externally fixed to the nostril to prevent accidental dislodgement.[15,18]

After the catheter is fixed, a CT-Scan may be run to evaluate the placement of the drainage catheter, and then the components of lung abscess can be removed through the drainage and the clinician can insert intracavitary antibiotics directly. In a study conducted by Unterman et al, evaluation after catheter placement was done using fluoroscopy. After that, intracavitary antibiotics were administered at a dose of 80–160 mg gentamicin 2–4 times a day. The catheter can be removed after clinical improvement, the study showed that usually the catheter can be left for 2–6 days with a median of 4 days and also to observe the improvement of infection markers.[15,18]

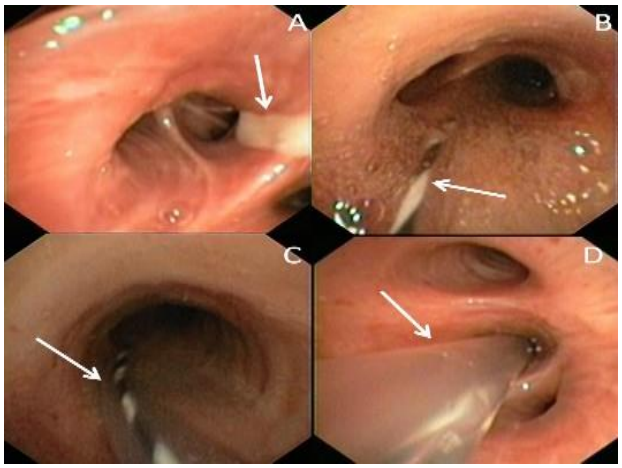

Figure 3. A) Bronchoscopy showing the bronchus segment where the lung abscess is located; B) The white arrow shows the guidewire inserted in the bronchial segment where the lung abscess is located; C) The catheter is inserted through the guidewire; D) The catheter is inserted at the abscess site.[18]

Percutaneous drainage procedure was first introduced in 1938 as a management of tuberculous cavities. It was later used as a pyogenic abscess management before the antibiotic era. Percutaneous drainage may be used as alternative therapy when the patient is not eligible for surgery. Another indication is when there is no *air-fluid level* and it appears homogeneous indicating a high-pressure difference and endobronchial decompression which

increases the risk of action. Percutaneous drainage can also prevent haemoptysis. Percutaneous drainage is not recommended in patients with massive haemoptysis and unstable hemodynamics.[19]

In percutaneous drainage procedure, the patient is in decubitus position and then Ultrasound (USG) or CT-Scan guidance is used to mark and determine the location of catheter insertion, followed by aseptic septic measures and local anesthesia using lidocaine before aspiration and thoracocentesis using a 14G needle. Then, a 14F trocar is placed and the abscess is drained out, after that normal saline is used to irrigate the abscess until it becomes clear. The irrigation with normal saline 5–15 mL is continued daily to improve recovery process.[17,19,20]

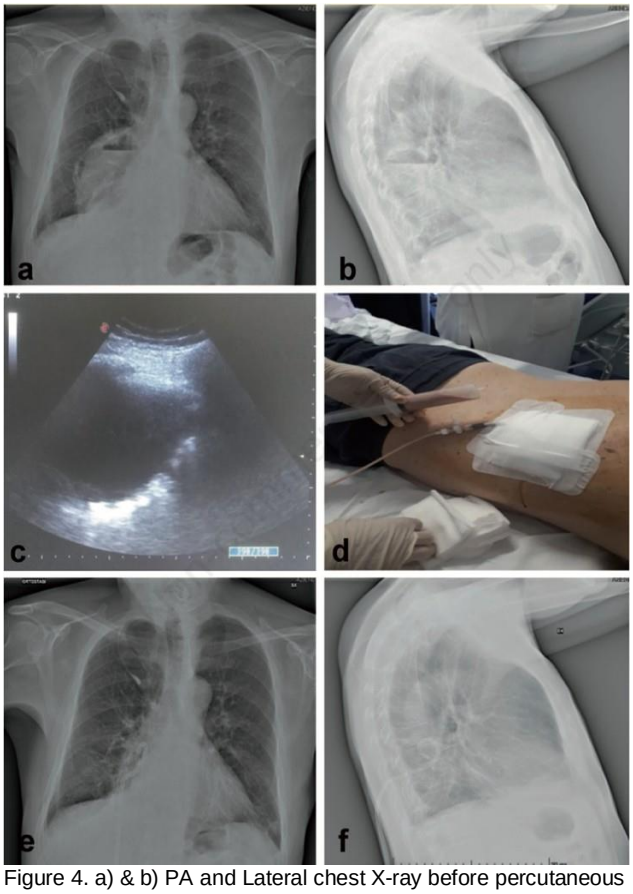

Figure 4. a) & b) PA and Lateral chest X-ray before percutaneous drainage; c) Thoracic ultrasound before percutaneous drainage; d) Percutaneous drainage; e) & f) PA and lateral chest X-ray 5 days after percutaneous drainage.[20]

Percutaneous drainage has advantages, especially in complicated lung abscess that do not improve with pharmacological management, but this method is not widely practiced due to the risk of complications associated with trocar insertion.[17,19,20] It also may lead to complications including pneumothorax, empyema, hemothorax, and bronchopleural fistula formation. Lung abscess without intervention may also cause rupture and empyema, so percutaneous drainage procedure can increase this risk by creating a connection between the pleura and lung parenchymal tissue.[15]

Drainage can also be performed using *endobronchial ultrasonography-assisted transbronchial needle aspiration* (EBUS-TBNA) under general anesthesia and also using a 22G aspiration needle (*Vizishot* NA-201SX-4021). The EBUS scope was directed linearly to access the abscess and then the pus was aspirated using a vacuum suction. Systemic antibiotics should still be administered despite this intervention. EBUS has been reported to provide benefits as diagnostic and interventional tool for peripherally located or mediastinal abscess. The procedure takes approximately 30 minutes if performed by an experienced operator. EBUS procedure can also be considered the first stage of diagnosis in patients with suspected lung abscess in the future, and also as management if the patient is unable to undergo surgery.[21]

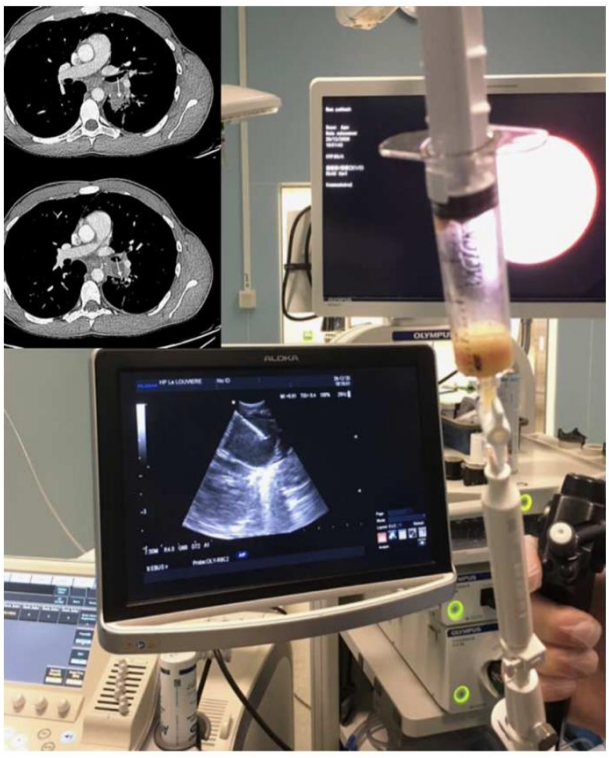

Figure 5. Procedure of EBUS-TBNA showed a pus was aspirated using a vacuum suction.[21]

Kurimoto et al reported a successful procedure using endobronchial ultrasonography with a guide sheath (EBUS-GS). The primary benefit of this procedure is the reversibility, meaning after identifying the lesion, it can be converted to drainage the abscess. After the probe is placed in the lesion of the lung abscess using radial EBUS and the pus was drained through the guide sheath by removing the echo probe, the negative pressure aspirated the content of the guide sheath, then the drainage was successful. If there is a suspicion of malignancy differential diagnose with lung abscess, EBUS-GS may be elected because when the drainage of the pus is successful, the drainage can be continued, but if the drainage is failed then it can be switched into transbronchial biopsy (TBB) to diagnose the possibility of malignancy.[22]

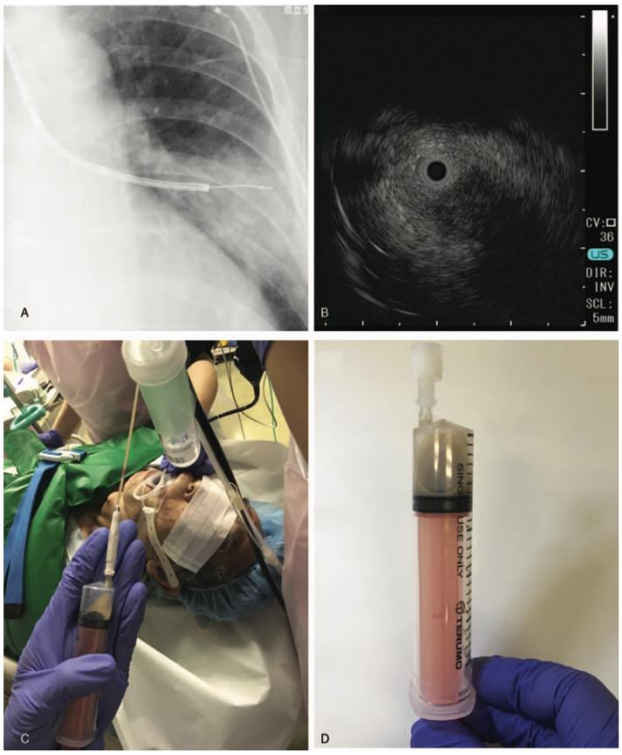

Figure 6. A) Fluoroscopic showing the guide sheath placed; B) The USG located the lesion using radial EBUS; C) Pus aspirated into syringe using EBUS-GS procedure; D) The pus was collected.[22]

Large cavities >6 cm caused by resistant organisms, obstructing neoplasms, massive hemoptysis, bronchopleural fistula with or without empyema and/or extensive necrosis with or without drainage are indications for lung resection (such as segmentectomy, lobectomy, or pneumonectomy). [3,8] Currently, surgical management is reported to be performed only in 10–15% of patients who do not improve with pharmacologic management.[4] When pharmacologic management does not result in effective outcomes, surgical intervention in the form of lung resection is an option, but mortality rates remain around 15–20%.[18]

A case report showed that opening the top of the abscess or debridement of the abscess may have a risk of complications such as air leakage, but it may close spontaneously. If the air leak persists and does not close, endoscopic insertion of a one-way valve in the bronchial segment may provide positive outcome. Lobectomy also has good outcomes for fulminant and lobar gangrene. This case report also shows that 12 out of 13 patients who underwent surgical intervention improved, concluding that lobectomy can be performed routinely in patients with lung abscess that do not improve with pharmacological therapy.[23]

Patients who do not show clinical improvement within two weeks should be evaluated for other possible diagnoses or complications. It may be performed through sputum culture or samples obtained from bronchoscopy. When the regimen fails, it is usually due to poor drainage, endobronchial obstruction due to neoplasm or foreign body, deteriorating imaging of chest x-ray in one third of patients within the first week. The exact amount of time taken for the cavities to fully close is approximately 4 weeks and the surrounding infiltrates take twice as long to improve. Radiologic improvement takes longer than clinical improvement.[4]

Medical Rehabilitation

Medical rehabilitation in patients with lung abscess aims to improve ventilation and oxygenation, bronchial hygiene and exercise lung tolerance. This physiotherapy program consists of several interventions such as secretion mobilization, breathing training, chest cavity development training, physical mobilization exercises, and posture retraining with various objectives and doses or frequencies such as if we aim to reduce tightness during activity then the required intervention is pursed

lip breathing with frequency of 10 sets, 3–4 times a day for 4 weeks; if the aim is to remove sputum, the intervention is postural drainage with manual chest percussion and acapella with seated position every 4 hours for 4 weeks; if the aim is to improve ventilation and increase chest wall expansion, the intervention is posterolateral chest wall mobilization and chest wall expansion exercise for 15–20 minutes, 2 times a day for 4 weeks.[24]

PROGNOSIS

Comorbidities and predisposing factors affect the prognosis of patient with lung abscess. Patient with predisposing factors such as pneumonia, neoplasm, impaired consciousness, and also anemia has higher mortality rate.[3,9] In addition, patient with poor immune system such as malnutrition and old age also has worse prognosis. Lung abscess caused by *Pseudomonas aeruginosa, Staphylococcus aureus,* and Klebsiella *pneumonia* are also associated with worse prognosis.[3] The general prognosis of lung abscess is usually good.[25]

CONCLUSIONS

Before antibiotic, surgery was the sole treatment for lung abscess, with reported mortality between 29–35%. Post-antibiotics, mortality reduced up to 10–15% with 80–90% of cases were managed without surgery. Nonpharmacological intervention such as abscess drainage is prompted when antibiotics fail or in cases of large abscesses (>6cm), poor cough reflexes, antibiotic-resistant strains or bronchopleural fistula. Percutaneous or endoscopic drainage can also be an option to manage the lung abscess. Bronchoscopy facilitates diagnosis and therapy, especially for centrally located abscesses. Endoscopic ultrasonography-assisted transbronchial needle aspiration (EBUS-TBNA) may serve as both alternative diagnostic and interventional tool.[21] Surgical intervention may be an option in unresponsive cases with pharmacological management. A comprehensive approach, integrating antibiotics, drainage procedure and surgery ensure effective lung abscess management.

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