lung abscess 2

by ccpulmo@gmail.com 1

Submission date: 11-Feb-2023 02:28AM (UTC-0800)
Submission ID: 2011558091
File name: Lung_abscess_-_Template_JRI_no_ref.docx (1.87M)
Word count: 3900
Character count: 22497

Original Article

LUNG ABSCESS

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Abstract ← **Arial 10pt, bold, justify**

Lung abscess is a necrotic liquefaction process containing necrotic debris or fluid from the lung parenchyma tissue which creates a cavity with a size of more than 2 cm caused by bacterial infection. The most common etiology of lung abscess is caused by oral aspiration, mostly in people with poor oral hygiene. Several things can increase the risk of developing a lung abscess, such as oral aspiration, sepsis, and a history of previous lung infections. The clinical manifestations of lung abscess are similar to other lung disease symptoms such as cough, purulent phlegm, pleuritic chest pain, fever, and hemoptysis. The treatment for lung abscess was classified into two groups, the pharmacology uses of antibiotics like clindamycin, ampicillin-sulbactam, moxifloxacin, carbapenem, and piperacillin-tazobactam. The other group is nonpharmacology therapy including drainage which is indicated for a patient with a size cavity more than 6 cm.

Keywords: Lung abscess, lung cavity, lung abscess treatment

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Submitted: Janury 26th, 2023
Accepted:
Published:

J Respirol Indones. 2023
Vol. XX No. XX: XXX-XXX
https://doi.org/10.36497/respirsci.v1i2.20

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 can progress to lung abscess formation both with and without empyema. This is due to the limited treatment during that time.[4]

Lung abscess can be divided based on the duration of the lung abscess, the progressivity of the lung abscess, and the process of spread.[3] The causative agents of lung abscess are usually anaerobic bacteria that can also be normalflora in the gum folds.[4] In the pre-antibiotic era the pathogens causing lung were caused by a single type of bacteria whereas today the etiology is more often due to the polymicrobiome.[3] 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. This can be the reason, pathogens that cause lung are mostly from the upper airway and anaerobic bacteria originating from the nasopharyngeal space, tongue, buccal mucosa, and gum folds.[6] The condition of patients with altered consciousness with any underlying disease is a risk factor for lung abscess, due to the high risk of aspiration pneumonia, besides patients with esophageal motility disorders, esophageal strictures, gastroesophageal reflux is also a risk factor for lung abscess.[3]

Lung abscess management can be divided into pharmacological and non-pharmacological management. Pharmacologically, lung abscess can be given antibiotics with several choices such as clindamycin, betalactam/betalactamase inhibitors combined with antibiotics for methicillin-resistant *Staphylococcus aureus* (MRSA), and metronidazole can also be combined with ceftriaxone. The choice of antibiotics can certainly depend on several conditions and is given until there is a clinical and radiological

improvement. The duration of antibiotic administration does not have clear limits, but in general, patients usually get 6-8 weeks of therapy or more. Non-pharmacological management such as drainage in some cases with abscess sizes greater than 6 cm.[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 can also formed, although it is usually characterized by a single abscess that is more dominant.[3]The prevalence of lung is now less frequent than in the pre-antibiotic era because in the pre-antibiotic era, management was inadequate so that pneumonia caused by bacteria could form a lung abscess, but it is still a significant source of morbidity and mortality.[3,4]

Lung abscess most commonly caused by aspiration from the gastrointestinal tract, especially in patients with poor oral hygiene. In addition, patients usually tend to be unconscious due to alcohol intoxication, drug overdose, or under the influence of sedation, anesthesia and opioids. Patients with old age and neurological disorders are also risk factors 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 can be divided into acute and chronic lung abscess. Acute lung abscess occurs in not over than 6 weeks, while chronic lung abscess occurs over than 6 weeks. When classified based on the course of the lung abscess, lung abscess can also divide into primary and secondary lung abscess. Primary lung abscess occur purely due to oropharyngeal aspiration without underlying lung disease, meaning that the abscess occurs in people with good immunity, while secondary lung abscess occur due to obstruction of the main airway due to masses, or as a result of complications of intrathoracic surgery, as well as in patients with decreased immunity such as patients with *Human Immunodeficiency Virus* (HIV) infection or receiving immunosuppression therapy.[3,4]

Based on the process of lung abscess formation, it can be divided into hematogenic and bronchogenic process. The hematogenic process occurs through a systemic spread process from other infectious sites such as abdominal sepsis, endocarditis, and thromboembolic sepsis, while the bronchogenic process means that lung abscess occur due to inhalation or aspiration of oropharyngeal secretions.[3,49,10] Based on their etiology, lung abscess is divided into two groups: polymicrobiological etiology, such as anaerobic bacteria (*Bacteroides, Prevotella, Peptostreptococcus, Fusobacterium* or *streptococcus)*. While the monomicrobiology group can be caused by *Staphylococcus aureus, Klebsiella pneumonia* and *Streptococcus pyogenes.*[9]

ETIOLOGY

The most common microorganisms causing lung are anaerobic bacteria, reported about 60-80% of cases.[5] Primary lung abscess are usually caused by anaerobic bacteria that are normal flora in the gum folds. These *anaerobic* bacteria are also referred to as non-specific etiologic causes consist of gram-negative (*Bacteroides fragilis, Fusobacterium capsulatum*) and gram-positive (*Pepto-streptococcus* and *Microaerophilic streptococcus*) bacteria. The most common causes of primary lung in immunocompetent patients are anaerobic bacteria and *Microaerophilic streptococcus.*[3]

Lung abscess can 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 things that increase the risk of lung abscess formation, such as patients with immunocompromised conditions *Acquired Immuno Deficiency Syndrome* (AIDS), after lung transplantation, or patients who receive immunosuppression drugs). Other conditions that are risk factors for lung abscess formation are patients 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 tumors, and patients with gastroesophageal reflux conditions.[3]

Other conditions that are at risk of abscess formation are patients with abdominal sepsis, infections that cause endocarditis, thromboembolic sepsis and the use of unhygienic nasal cannulas because they are not replaced regularly. In addition, patients who have previous lung diseases such as a history of bronchiectasis, cystic fibrosis, bulla emphysema, bronchial obstruction due to tumors, a history of *corpus alienum,* 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 mechanisms 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 possessed by *Staphylococcus aureus* will stimulate chemokinesand cytokines derived from macrophages which sequentially then 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 leading to 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]

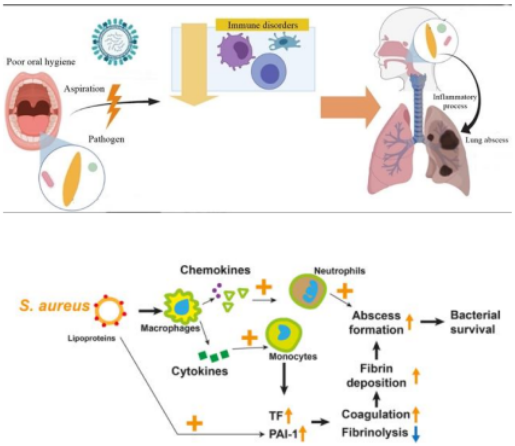


Figure 1A. Illustration of the pathogenesis of lung abscess;1B. Pathogenesis of abscess formation caused by *Staphylococcus aureus*.[11]

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 hemoptisis. In conditions of anaerobic infection, clinical symptoms may worsen 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 frequency.[3] Physical examination may reveal rales as well as decreased breath sounds due to consolidation. Bad breath odor or poor oral hygiene can be a sign of a 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 done to see if there is a secondary lung abscess. Gram staining of sputum usually shows neutrophil dominance with various types of flora and bacteria. Sputum culture can also be done to determine the pathogen causing the lung abscess. Cultures derived from alveolar rinse specimens usually find aerobic organisms because anaerobic bacteria are usually difficult to obtain and are very sensitive to antibiotics that are usually given before the patient is asked for an examination sample.[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 can help to diagnose and determine the size and location of the lung abscess, as well as to evaluate whether there are 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]

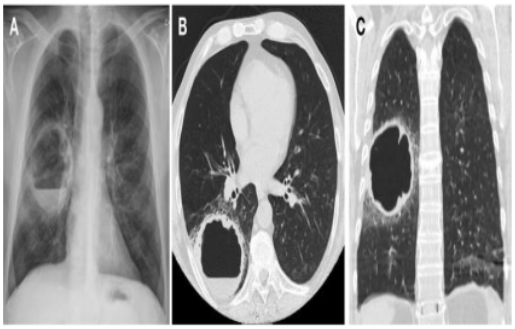


Figure 2A. Chest-Xray examination, B and C. CT-scan showing the cavities in the lung abscess.[14]

TREATMENT

Pharmacological treatment

The treatment for lung abscess can be divided into two groups, as a 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 antibiotic in lung abscess, even though anaerobic bacteria can produce betalactamase, while penicillin are not able fight the effects of betalactamase.[3] Clindamycin then emerged and in clinical trials proved superior to penicillin.[4]

Clindamycin can be given 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 given, 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 given as monotherapy because it does not have the ability to fight microaerophilic *Streptococcus* bacteria that are often a component in the flora that causes 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 given in some cases together with ceftriaxone

antibiotics at a standard dose of 500 mg IV/PO every 6-8 hours.[3,4]

Antibiotics can be given until there is an improvement in imaging, namely the image of a shrinking lung abscess. Some studies recommend the evaluation of thoracic photographs every one week or two weeks.[4] Age and abscess size 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 drainedthrough tracheobronchial branching of the main airway, if the patient is clinically improved and sputum production is good then surgery is notrequired.[3]

Nonpharmacological treatment

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 about 29-35% in 306 cases of lung abscess in 1901. After the discovery of antibiotics about 80-90% of primary lung can be managed well without the need for surgery and reported mortality rates decreased to 10-15%.[6] One of the nonpharmacological treatments or interventions in lung abscess is abscess drainage.[3]

The indication for intervention in lung abscess is when the clinical condition does not improve with antibiotics.[15] The duration of pharmacological therapy can be 3-4 weeks to 14-16 weeks. Clinical improvement usually starts to be seen in 3-4 days and complete improvement takes 7-10 days. Another indication for intervention is lung abscess with size greater than 6 cm which is rarely respond well to antibiotic therapy alone without additional interventions such as surgery or drainage, patients 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 done percutaneously or endoscopically. Percutaneous drainage is more minimally invasive but it also has high benefits and effectiveness. However, in certain conditions such as coagulation disorders, infections around the thoracic sites, or when a lot of lung tissue needs to be saved, endoscopic techniques are the right choice compared to percutaneous drainage.[3]

Bronchoscopy has benefits not only for diagnosis but also for therapy, which can assist the lung abscess drainage. Lung abscess can bemanaged with antibiotics and drainage. This 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 culture but also to proceed with endoscopic drainage procedures.[16] It is also now recognized that endoscopic procedures are indicated

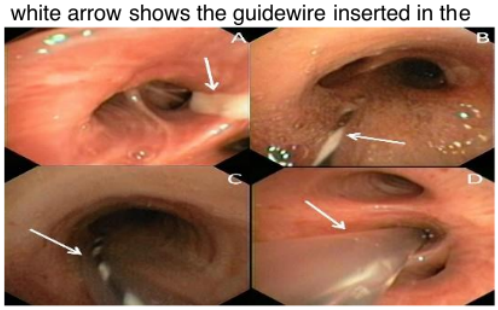
for patients with lung abscesses that are centrally located away from the pleura and pose a high risk of percutaneous drainage.[17]

A drainage endoscopy procedure is performed using a bronchoscope to identify 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 can be performed to evaluate the placement of the drainage catheter, and then the components of the 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 medianof 4 days and also see the improvement of infection

markers.[15,18]

Figure 3A. 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 procedures were 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 can be analternative 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 increases the risk of action. Percutaneous drainage can also prevent hemoptysis. Percutaneous drainage is not recommended in patients with massive hemoptysis and unstable hemodynamics.[19]

In the percutaneous drainage procedure, the patient has positioned decubitus, and then marking is done with ultrasound (USG) or CT-Scan guidance to find the location where the catheter will be inserted, after which aseptic septic measures and local anesthesia using lidocaine before aspiration and thoracocentesis using a 14G needle. Then the action continued with the installation of a 14F trocar and the abscess was drained out, after that using normal saline fluid the abscess was irrigated until it became clear. Then irrigate every day using normal saline 5-15 mL to speed up the repair process. [17,19,20]

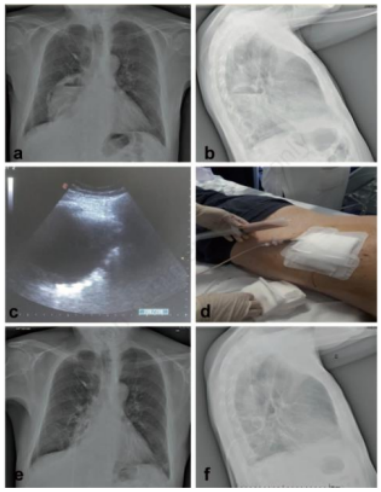


Figure 4A&B PA and Lateral chest X-ray before percutaneous drainage. C. Thoracic ultrasound before percutaneous drainage. D. Percutaneous drainage, E&F PA and lateral chest X-ray 5 days after percutaneous drainage.[20]

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] Percutaneous drainage has some risk of complications such as pneumothorax, empyema, hemothorax, and bronchopleural fistula formation. This is because lung abscess without intervention also have a risk of complications to rupture and cause empyema, so percutaneous drainage procedures can increase this risk by creating a connection between the pleura and lung parenchymal tissue.[15]

Drainage can also be done 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 abscess fluid or pus was aspirated using a vacuum suction. Systemic antibiotics were still given despite this intervention. EBUS has been reported to have benefits as a diagnostic and interventional tool for peripherally located or mediastinal. This takes approximately 30 minutes if performed by an experienced operator.

This 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]

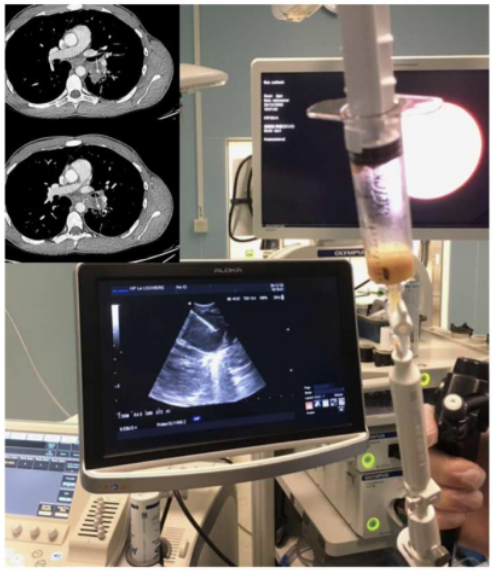


Figure 5. Procedure of EBUS-TBNA showed a pus was aspirated using a vacuum suction.[21]

Kurimoto et al reported a successful procedure using endobronchial ultrasonography with a guide sheath (EBUS-GS). The benefit using this procedure is the reversibility, meaning after located the lesion using EBUS-GS, then the procedure can be converted into 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, means the drainage was successfully done. If there was a suspicion of malignancy differential dignose with lung abscess, EBUS-GS can be chosen because when the drainage of the pus was successful, the drainage can be continued, but if the drainage pus was failed the procedure can be switched into transbronchial biopsy (TBB) to diagnose the possibility of malignancy.[22]

Figure 6A. 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 >6cm caused by resistant organisms, obstructing neoplasms, massive hemoptysis, bronchopleural fistula with or without empyema and/or extensive necrosiswith 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 can have a good 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, thus concluding that lobectomy can be performed routinely in patients with

lung that do not improve with pharmacological therapy.[23]

Patients who do not show clinical improvement within two weeks need to beevaluated for other possible diagnoses or complications. This can be found by performing culture on sputum results or on samples obtained from bronchoscopy. When medical management fails, possible problems are usually due to poor drainage, endobronchial obstruction due to neoplasm or foreign body, chest x-ray usually showing the worsen 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 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 reduces tightness during activity the intervention required is pursed lip breathing with frequency 10 sets, 3-4 times a day for 4 weeks, if the aim is secret mobilization, 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 well expansion, the intervention can be done is posterolateral chest wall mobilization and chest wall expansion exercise 15-20 minutes, 2 times a day for 4 weeks.[24]

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