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Per-Oral Endoscopic Myotomy in Achalasia and Lung Abscess: A Case Report

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Abstract: A lung abscess is defined as an infectious process with suppuration and cavitation. Lung abscess is more frequent in patients predisposed to aspiration due to achalasia. In the pre-antibiotic era, the mortality of patients with lung abscess was higher whereas today with the appropriate antibiotic therapy we can save these patients. The emergence of antibiotic-resistant strains is becoming a concern in such patients. Achalasia is an esophageal motility disorder characterized by loss of peristalsis and insufficient relaxation of the lower esophageal sphincter (LES). Per-oral endoscopic myotomy (POEM) should be considered the preferred treatment for achalasia because of its low invasiveness and high efficacy. The authors report a challenging case of a woman with achalasia, dysphagia, cough, weight loss who progressed to lung abscess caused by Pseudomonas aeruginosa and Klebsiella pneumoniae treated with antibiotics and POEM. This case report contributes to expanding knowledge on the management of lung abscess and achalasia, highlighting the importance of treatment with antibiotic therapy and POEM. Early treatment contributes to improving outcome and cutting socio-economic costs. Key facts to ameliorate to improve prognosis and length of hospital admission could be a swifter diagnosis and consensus on the antibiotic therapy.

Keywords: Lung abscess; Achalasia; Per-oral Endoscopic Myotomy; POEM; *Pseudomonas aeruginosa*; *Klebsiella pneumoniae*; Antibiotic therapy.

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1. Introduction

Lung abscesses are classified as either primary or secondary. Primary lung abscesses are the result of aspiration of oral flora-comensal pathogens, principally anaerobic agents and are usually associated with dental disease or situations which predispose towards bronchoaspiration such as achalasia or altered mental status (alcoholism, epilepsy, stroke, central nervous system depressor medication, general anesthetic). Secondary lung abscesses imply the presence of conditions conducive to local infection, including immunodeficiency virus infection (HIV), iatrogenic immunosuppression or diabetes, and those which lead to structural bronchial obstruction (neoplasm, aspirated foreign bodies and bronchostenosis). Patients with chronic lung disease, increasing age, history of aspiration or risk of aspiration caused by reduced consciousness (due to sedative or antipsychotic medications, cardiac arrest), structural or motor diseases of the pharynx and esophagus, neuromuscular disorders, are at higher risk of developing lung abscess. Lung abscesses are incapacitating clinical conditions which manifest slowly several weeks with reduced physical capacity. They have risk of several complications and high socio-economic costs [1-8].

Achalasia is an uncommon disorder, but its frequency appears to be rising. Achalasia results from progressive degeneration of ganglion cells in the myenteric plexus in the

esophageal wall leading to esophageal dilatation. The etiology of primary or idiopathic achalasia is unknown. Secondary achalasia is due to diseases that cause esophageal motor abnormalities (Chagas disease, Amyloidosis, Sarcoidosis, Neurofibromatosis, Eosinophilic esophagitis, Multiple endocrine neoplasia, Sjögren's disease, Fabry disease). Achalasia has an insidious onset and disease progression is gradual. Patients are most commonly present with dysphagia to solids and liquids, regurgitation and weight loss. Achalasia can be treated with POEM, pneumatic dilatation, botulinum toxin injection or surgical myotomy (laparoscopic Heller myotomy and Nissen fundoplication). POEM is a newer endoscopic technique that has been gaining increasing use as an alternative to traditional esophageal myotomies [9-14].

The authors aim to raise awareness about the importance of early diagnosis and appropriate treatment of lung abscess and achalasia with antibiotics and POEM to prevent complications.

2. Case Report

A 79-year-old woman has achalasia (the diagnosis was made one year before) medicated with omeprazole 20 mg, domperidone 10 mg, lercanidipine 10 mg, nitroglycerine 0,5 mg. She was admitted to the hospital with a six months history of dysphagia, cough, weight loss. She denied previous episodes of aspiration pneumonia. Laboratory findings showed anemia, leukocytosis, neutrophilia and elevated C-reactive protein without respiratory failure and with no other significant abnormalities. Tests for Influenza, Respiratory Syncytial Virus and SARS-Cov 2, Legionella/Pneumococos urinary antigen, HIV infection were negative. An x-ray (Figure 1) and computed tomography (CT) scan (Figure 2) of the chest revealed cavitated lesion right upper lobe (94 mm x 42 mm) with hydroaerial level (55 mm x 27 mm) suggestive of lung abscess.

Figure 1. Chest X-Ray cavitated lesion right upper lobe.

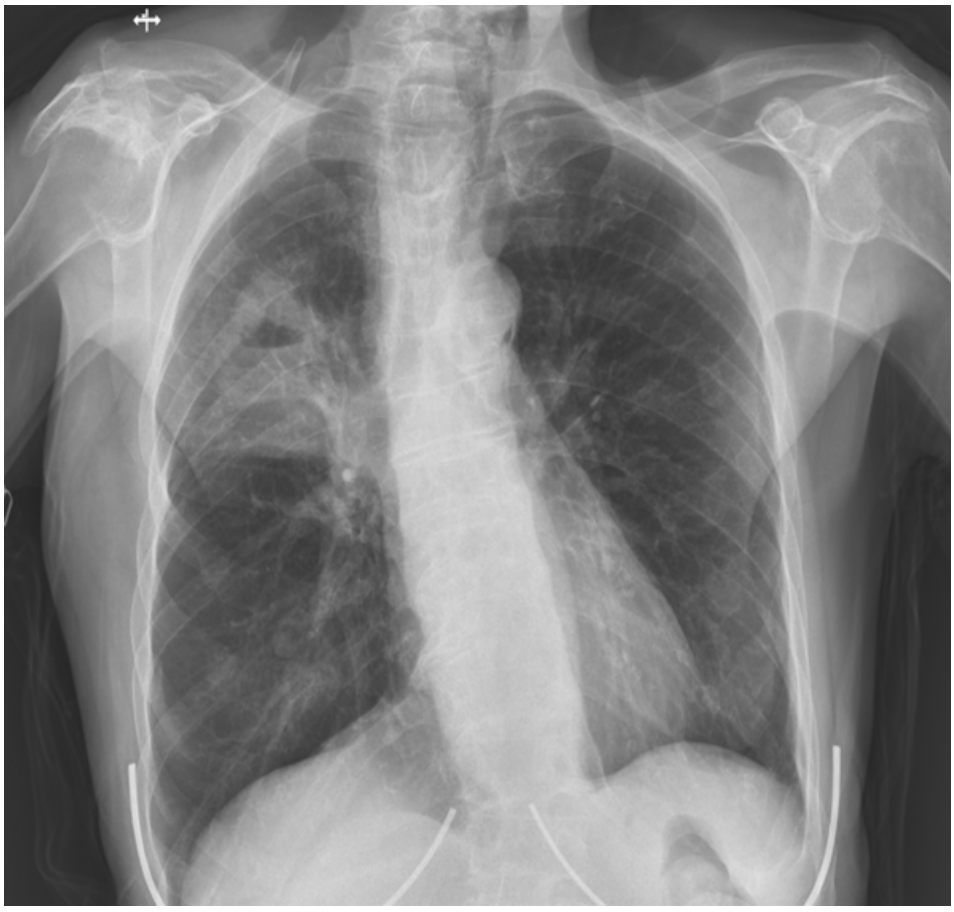
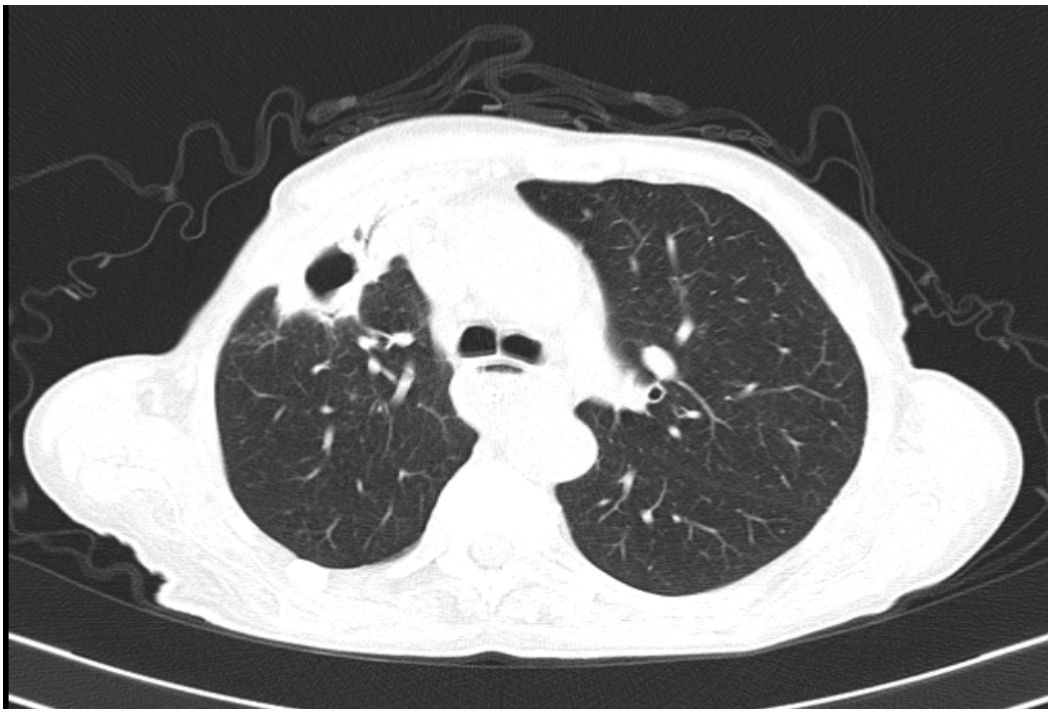


Figure 2. Computed tomography scan of the chest cavitated lesion right upper lobe (94 mm x 42 mm) with hydro-aerial level (55 mm x 27 mm).



Empiric antibiotic therapy with amoxicillin+clavulanic acid 2,2 g intravenous (iv) every 8 hours was started. The patient was admitted for diagnostic investigation. Hemocultures, bacilloscopies, gastric aspirate polymerase chain reaction for *Mycobacterium tuberculosis* were negative. On the 8th day of hospitalization, after isolation of *Pseudomonas aeruginosa* in sputum samples, antibiotic therapy was changed to piperacillin+tazobactam 4,5 g iv every 8 hours for six weeks. On the 10th day of hospitalization, fibre-optic bronchofibroscopy was performed and excluded neoplasm. The biological product with positive culture result was broncho-alveolar aspirate with *Klebsiella pneumoniae*. Nasogastric tube diet was needed for fifteen days. She maintened lansoprazole 30 mg once a day, lercanidipine 10 mg once a day and domperidone 10 mg every 8 hours. On the 16th day of hospitalization she tolerated oral diet, apyrexia and decrease of inflammatory markers. After six weeks of antibiotic therapy, clinical, laboratory and radiological improvement was observed (Figure 3).

She was discharged on the 45th day of hospitalization. At follow-up visit after 3 months, she had dysphagia, normal laboratory tests and radiological improvement (Figure 4). Spirometry was normal. Upper digestive endoscopy revealed a dilated esophagus, the contracted LES could be traversed easily with gentle pressure on the endoscope, the esophageal and gastric mucosa were normal (Figure 5). At follow-up visit after 6 months, contrast esophagram, upper digestive endoscopy and esophageal manometry were performed and findings were suggestive of achalasia. Contrast esophagram revealed a narrowed esophagogastric junction, esophageal aperistalsis and dilated esophagus. Upper digestive endoscopy revealed a dilated esophagus with erythema and ulceration, LES does not open spontaneously to allow effortless passage of the endoscope into the stomach but could be traversed easily with gentle pressure on the endoscope (Figure 6). Manometry revealed a incomplete relaxation of the LES and aperistalsis of the esophagus. POEM was performed in four consecutive steps (Figure 7). First, a mucosal incision was made to allow the gastroscope to enter the submucosal space to create the submucosal tunnel. The location of the mucosal incision was determined by the level of the esophagogastricjunction (EGJ) and the length of the submucosal tunnel required.

Figure 3. Computed tomography scan of the chest after six weeks of antibiotic therapy radiological improvement of lung abscess right upper lobe.

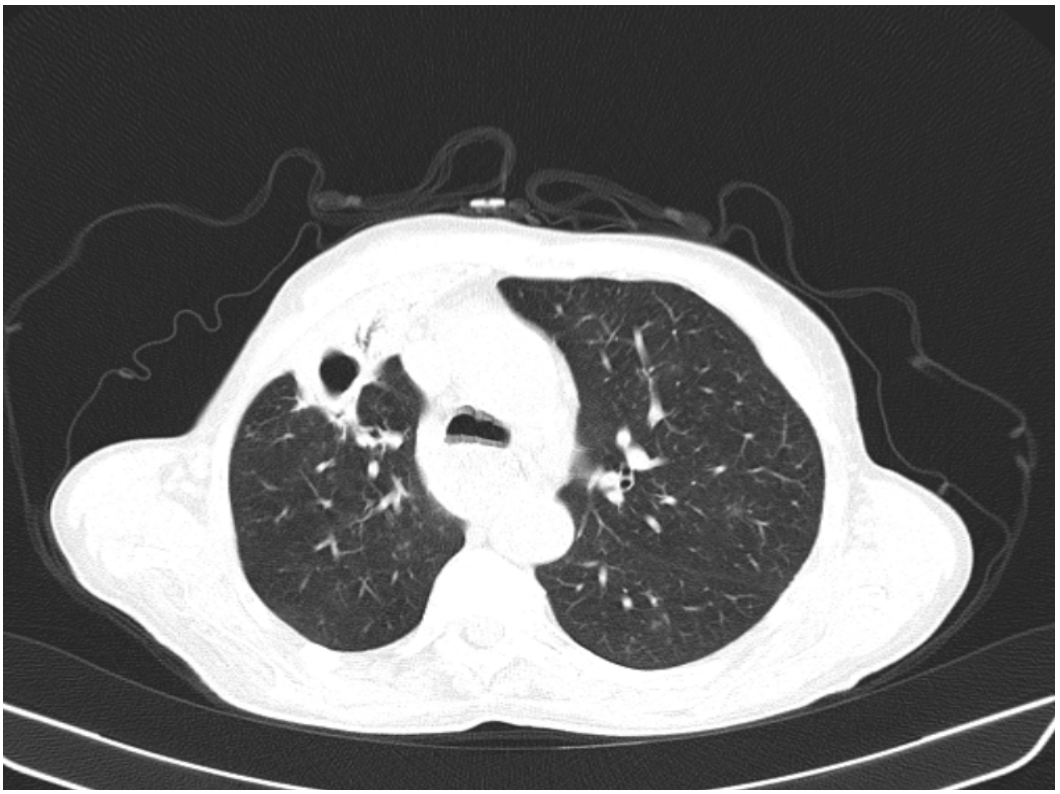


Figure 4. Follow-up after 3 months: computed tomography scan of the chest abscessed lesion already in the resolution phase right upper lobe.

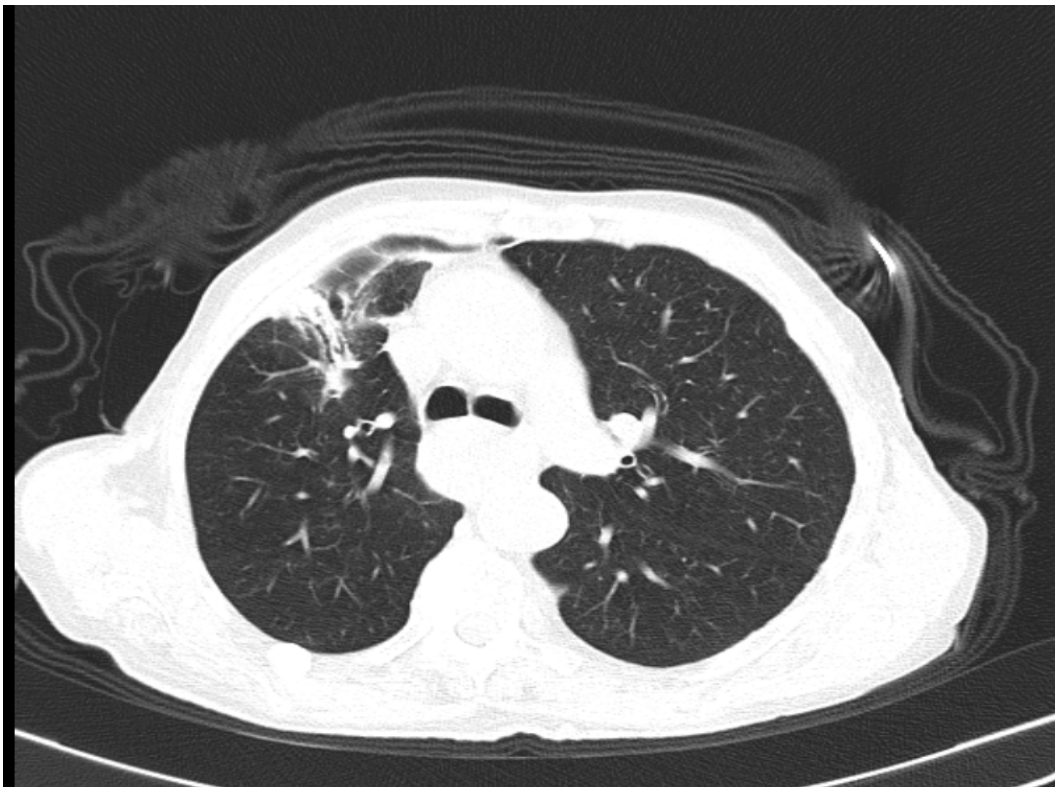


Figure 5. Follow-up after 3 months: upper digestive endoscopy revealed a dilated esophagus, the contracted LES could be traversed easily with gentle pressure on the endoscope, the esophageal and gastric mucosa were normal.

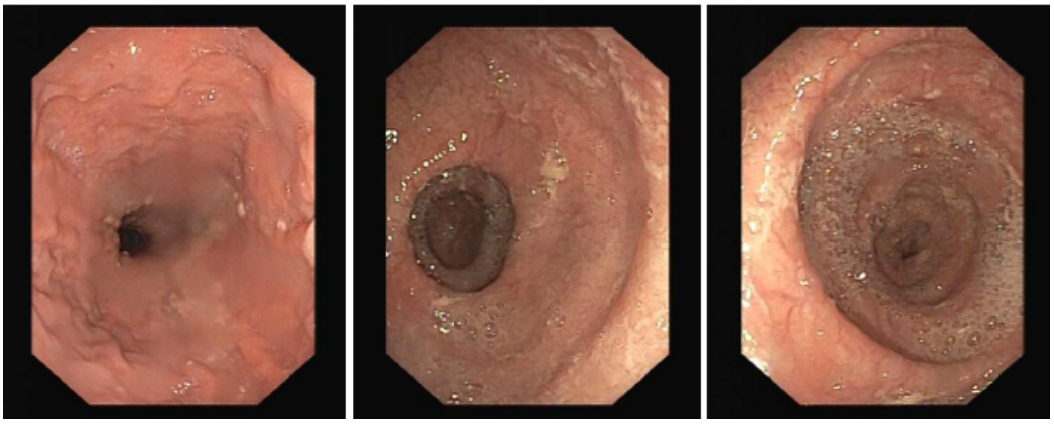


Figure 6. Follow-up after 6 months: Upper digestive endoscopy revealed a dilated esophagus with erythema and ulceration, LES does not open spontaneously to allow effortless passage of the endoscope into the stomach but could be traversed easily with gentle pressure on the endoscope.

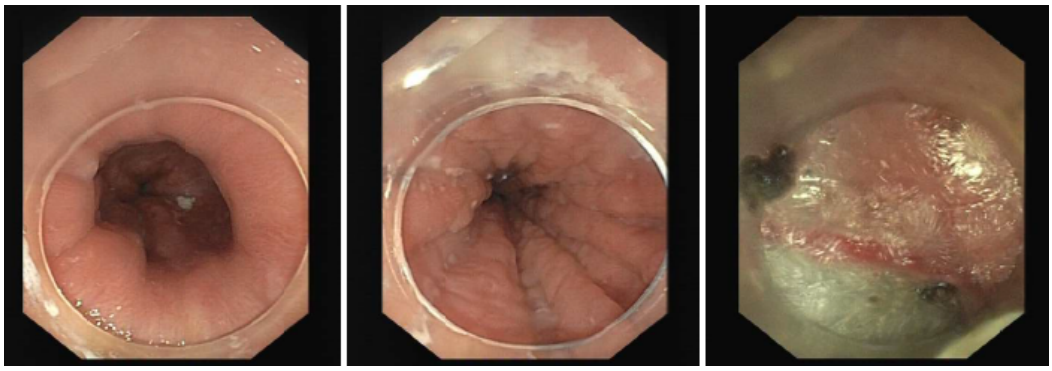
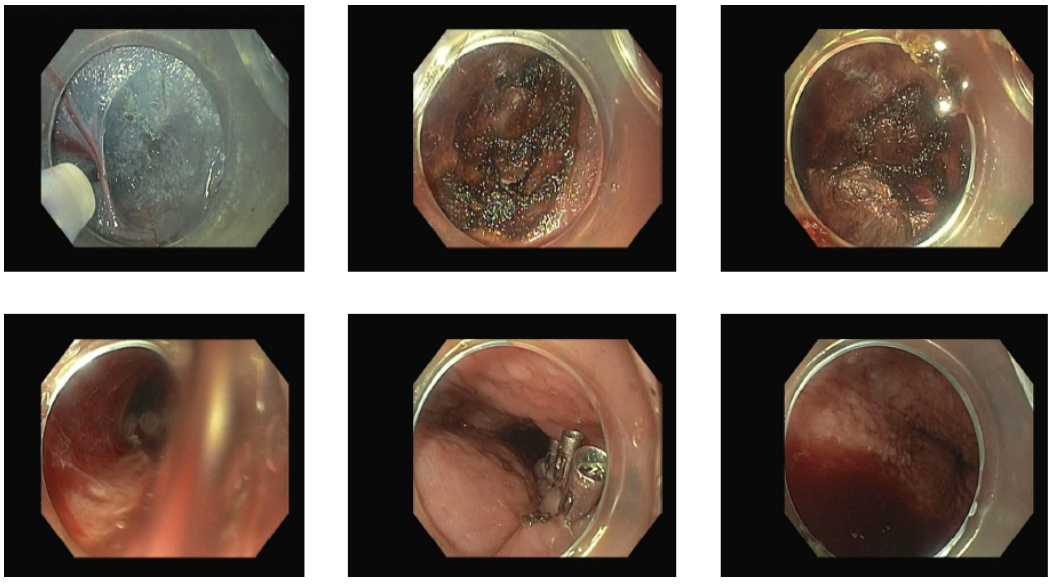


Figure 7. Endoscopic images of Per-oral Endoscopic Myotomy (POEM).



The length of the submucosal tunnel required was determined by the length of the myotomy required. A 6 to 8 cm esophageal myotomy was performed. The gastroscope

was maneuvered into the submucosal space after dissecting the submucosal fibers at the mucosal incision with the knife. Second, a submucosal tunnel was created toward the stomach using a technique similar to endoscopic submucosal dissection. Using the knife, the submucosa was dissected with a no-touch technique using spray coagulation in a plane that was located nearly on the surface of the muscularis propria.

The submucosal tunnel was extended until it is 2 to 3 cm beyond the EGJ, passing where the fibers maintain the continence of the LES. Third, selective myotomy of the inner circular muscle bundles was performed starting 2 cm distal to the mucosal incision. Circular muscle bundles were individually lifted toward the submucosal tunnel by the sharp tip of the knife and divided with spraycoagulation. In terms of length of myotomy, it was essential to achieve a 2 to 3 cm myotomy into the gastric cardia. Fourth, before closure of the mucosal incision, a careful inspection of the submucosal tunnel was performed and any bleeding was controlled. The esophageal mucosa was then inspected. Adequate LES relaxation was confirmed by a retroflexed view of the gastric cardia. Closure of the mucosal incision was performed with five endoscopic clips. No adverse events were found.

3. Discussion and Conclusion

A lung abscess should be suspected in presence of risk factors, fever, dyspnea, cough, putrid or bloody sputum, weight loss, leukocytosis and a cavitating or fluid-filled lung mass on imaging. Chest CT is the procedure of choice to distinguish differential diagnosis like lung neoplasm, empiema, tuberculosis, superinfected fungal or mycobacterial cavity, granulomatosis with polyangiitis, rheumatoid arthritis, sarcoidosis, silicosis, pulmonary langerhans cell histiocytosis. infected lung cyst or bulla, hydatid cyst. Endobronchial cancer can cause a postobstructive lung abscess, so it is possible for both malignancy and infection to be present. After obtaining samples of blood and sputum, empiric antibiotic therapy should be initiated because delayed therapy correlates with increased mortality. Antibiotic choices can be revised based on culture results. Antimicrobial resistance is a universal problem [1-8].

In this case, a woman with achalasia, dysphagia, cough, weight loss for several months had a lung abscess caused by *Pseudomonas (P.) aeruginosa* and *Klebsiella (K.) pneumoniae* with good response after antibiotics therapy. No need to drainage of the abscess or surgical procedure. Treatment of achalasia was crucial with proton pump inhibitor, prokinetic, calcium channel blocker, nitrate and POEM. *P. aeruginosa* and *K. pneumoniae* are uncommon agents in community-acquired lung abscess which is caused most frequently by anaerobes that make up the flora of the gingival crevice. Infections with *P. aeruginosa* and *K. pneumoniae* are usually acquired in the hospital setting. In this case, achalasia was a risk factor to co-infection *P. aeruginosa* and *K. pneumoniae.* They occur frequently in patients with impaired host defenses (diabetes mellitus, alcoholism, malignancy, chronic obstructive pulmonary disease, glucocorticoid therapy, immunodeficiency) or prior antibiotic use that were excluded [1-8].

Nosocomial colonization of the upper respiratory tract is common in hospitalized patients. Isolation of *P. aeruginosa* and *K. pneumoniae* from the sputum of a hospitalized patient without other signs and symptoms of infection may not be indicative of an infection. Changes in clinical status such as new fever, new leukocytosis, new abnormality on chest imaging, and worsened respiratory status are suggestive of infection in patients chronically colonized. In this case, a woman with cough, weight loss, leukocytosis, elevated C-reactive protein, cavitated lesion right upper lobe with hydro-aerial level suggestive of lung abscess helped the diagnosis of *P. aeruginosa* and *K. pneumoniae* co-infection rather than colonization [1-8].

The choice of empiric therapy depends on numerous factors, such as local resistance rates of *P. aeruginosa* and *K. pneumoniae*, prior culture susceptibility results, allergies and the availability in the local hospital formulary. Prior broad-spectrum antibiotic therapy is the major risk factor for the development of multidrug resistance. Emergence of antibiotic resistance results in increased length of hospitalization, increased rates of morbidity and

mortality and higher costs. Antibiotics active against *P. aeruginosa* are the antipseudomonal penicillins in combination with a beta-lactamase inhibitor like piperacillin-tazobactam used in this case, cephalosporins with antipseudomonal activity (ceftazidime, cefepime), ciprofloxacin, carbapenem. For patients who are allergic to penicillin, should be use quinolone plus metronidazole. Switch from iv to oral agents once the patient has defervesced and become clinically stable. In this case, patient did not tolerate oral medication due to dysphagia caused by achalasia so oral agents were not a choice. Antibiotic therapy should be used until CT shows a stable residual lesion like in this case that required six weeks of antibiotics. Further respiratory sampling via flexible bronchoscopy is usually indicated like in this case. Most patients with lung abscess do well with prolonged course of antibiotics [1-8].

In literature several factors are associated with increased abscess-related mortality and may warrant a more aggressive approach. These include older populations, large cavity size, longer duration of symptoms prior to therapy, lower lobe location, association with malignant disease and multiple abscesses. Patients who require surgery are immunocompromised or have malignancy that were excluded in this case. Major considerations in patients with a delayed response after antibioterapy. An associated condition that precludes response, such as obstruction with a foreign body or neoplasm. Erroneous microbiologic diagnosis with infection due to bacteria, mycobacteria or fungi that are not being treated. Failure of medical therapy despite appropriate antibiotics. Drainage may be required to facilitate recovery. This is more typical in patients with large cavities but there is no clear size cut-off that mandates intervention, and drainage has been reported to be helpful even for some smaller abscesses that fail to improve with antibiotics. An alternative, nonbacterial cause of cavitary lung disease, such as cavitating neoplasm or vasculitis. Conditions that mimic an abscess such as an infected cyst or empyema. Patients who fail to improve by 7 to 10 days despite appropriate antimicrobial therapy may need a drainage procedure or surgery. Percutaneous drainage is preferred. Patients continue with their systemic antimicrobial until the abscess cavity closes or is small and stable. For patients who fail to improve clinically or radiographically with antibiotic therapy with or without catheter drainage or who develop complications during therapy (significant hemorrhage, bronchopleural fistula), surgery may very rarely be indicated [1-8].

A number of interventions have been proposed to prevent aspiration. Semi-recumbent position (30 to 45 degree) for preventing aspiration events. Enteral feeding with nasogastric tubes are efficient for delivering nutrition and oral medications in patients with dysphagia, but have not been shown to reduce the incidence of aspiration compared with oral feeding. Postpyloric tubes (nasoduodenal, jejunal) may reduce aspiration compare with gastric tubes. Thickened liquids may improve swallowing safety. Prokinetics have been associated with lower rates of aspiration (metoclopramide and domperidone) due to nausea and dysphagia control. Regular oral care can improve oral health [1-8].

Esophageal manometry is required to establish the diagnosis of achalasia. Upper endoscopy should be performed to exclude malignancy at the esophagogastric junction that can mimic achalasia [9-14]. Pharmacologic therapy is the least effective treatment option in patients with achalasia, but should be considered in patients who are unable to tolerate invasive therapy. Because nitrates are short-acting, sublingual isosorbide dinitrate (5 mg) is administered 10 to 15 minutes before meals. Sublingual nitroglycerin 0.4 mg is an alternative. Nitrates relax the smooth muscle of the LES. Treatment with sublingual nitroglycerin may result in short-term symptomatic improvement but the benefit is not durable. Side effects such as headache and flushing are common. Several studies have described variable efficacy rates for treatment with calcium channel blockers for achalasia [9-14].

Treatment of achalasia is aimed primarily at decreasing the resting pressure in the LES. This can be accomplished by mechanical disruption of the muscle fibers of the LES (pneumatic dilation, surgical myotomy, peroral endoscopic myotomy (POEM) or by pharmacologic reduction in LES pressure (injection of botulinum toxin or oral nitrates). No

treatment can reverse the degeneration of ganglion cells, restore the lost esophageal neurons and normalize esophageal function. Available treatments do not normalize swallowing, they improve symptoms by reducing esophageal obstruction. The efficacy of all treatments tends to decrease with time. Patients will require long-term follow-up and will frequently need repeated or alternative treatments [9-14].

For patients who have surgical risk, preferred options for treatment include pneumatic dilation, laparoscopic Heller myotomy (LHM) with a partial fundoplication or POEM. POEM has been proposed as the procedure of choice for achalasia because can deliver a longer myotomy of the LES that is generally not possible with pneumatic dilation or LHM and a longer myotomy might be more effective at controlling symptoms. POEM is a natural orifice transluminal endoscopic surgery (NOTES) that can be performed in most patients who have symptomatic, manometrically proven primary idiopathic achalasia [9-14]. In this case, she performed contrast esophagram, upper endoscopy and esophageal manometry that confirmed achalasia and POEM procedure was carried out in four consecutive steps: 1) mucosal incision and entry into the submucosa, 2) creation of a submucosal tunnel, 3) myotomy, and 4) closure of the mucosal incision. No adverse events were found.

The use of POEM is supported by clinical trials and observational data from highly specialized centres. POEM is a safe procedure and is highly efficacious in the management of achalasia that is associated with a low rate of postoperative adverse events. Pneumoperitoneum, pneumothorax, inadvertent mucosotomy, mediastinitis are rare. Bleeding during submucosal tunneling is not uncommon. Small vessels can be prophylactically coagulated with the electrocauteryknife itself. The most common late adverse event associated with POEM is gastroesophageal reflux (GER) so pharmacologic acid suppression should be considered. Patients with achalasia should be informed that POEM and LHM are equally effective in relieving swallowing difficulties but POEM results in more reflux and LHM has more adverse events. The choice may depend on available local resources and patient/surgeon preference. Patients with one of the following conditions should not undergo POEM: severe erosive esophagitis, significant coagulation disorders, liver cirrhosis with portal hypertension, prior therapy that may compromise the integrity of the esophageal mucosa or lead to submucosal fibrosis (radiation, endoscopic mucosal resection or radiofrequency ablation). Previous therapies for achalasia, such as pneumatic balloon dilation, botulinum toxin injection or surgical myotomy are not contraindications to POEM [9-14].

Without treatment, patients with achalasia can develop progressive dilation of the esophagus. Late- or end-stage achalasia is characterized by esophageal tortuosity and severe dilation or megaesophagus (diameter >6 cm). Approximately 10 to 15% of patients who have undergone treatment for achalasia will develop late- or end-stage achalasia and a few require esophagectomy. The risk of esophageal cancer is increased in patients with achalasia but the absolute risk is low so do not perform endoscopic surveillance in patients with achalasia. Follow-up visits to reassess symptoms in patients with a history of achalasia is crucial because esophageal dilatation can occur over time. Intervening before severe dilatation occurs may prevent end-stage complications and the need for esophagectomy [9-14].

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Research Ethics Committee Approval: Written informed consent was obtained from the patient for the publication of anonymized clinical data and images. The study followed the ethical guidelines established by the Declaration of Helsinki.

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Conflicts of Interest: None.

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