Official journal of the Spanish Society of Chemotherapy

Special issues in pneumonia 2021

Michael S. Niederman[1]
Catia Cilloniz[2]

Aspiration pneumonia

[1]Division of Pulmonary and Critical Care Medicine, New York Presbyterian/Weill Cornell Medical Center, New York, New York, USA.
[2]Pulmonology Department, Hospital Clinic of Barcelona, CIBERES, IDIBAPS, Spain. Spanish Society of Pneumology and Thoracic Surgery (SEPAR)

Revista Española de Quimioterapia
doi:10.37201/req/s01.17.2022

ABSTRACT

The growing population of older people worldwide represents a great challenge for health systems. The elderly are at increased risk of infectious diseases such as pneumonia, which is associated with increased morbidity and mortality related mainly to age-related physiological changes in the immune system (immunosenescence), the presence of multiple chronic comorbidities, and frailty. In pneumonia, microaspiration is recognized as the main pathogenic mechanism; while macroaspiration which refers to the aspiration of a large amount of oropharyngeal or upper gastrointestinal content passing through the vocal cords and trachea into the lungs is identified as "aspiration pneumonia". Although there are strategies for the prevention and management of patients with pneumonia that have been shown to be effective in older people with pneumonia, more research is needed on aspiration pneumonia, its risk factors and outcomes, especially since there are no specific criteria for its diagnosis and consequently, the studies on aspiration pneumonia include heterogeneous populations.

Keywords: pneumonia, aspiration, elderly

ISN'T ALL PNEUMONIA PATHOGENICALLY ASPIRATION?

The answer to this question is yes. Microaspiration is recognized as the main pathogenic mechanism in pneumonia where particulate material and microorganisms are able to enter upper airways and then reach the lower airways and respiratory tract; while macroaspiration which refers to the aspiration of a large-volume of oropharyngeal or upper gastrointestinal content passing through the trachea and larynx into the lungs describes the term "aspiration pneumonia" [1]. Approximately, between 10% to 30% of hospitalized patients with a diagnosis of community-acquired pneumonia have an illness related to aspiration [2–4]. However, numbers related to aspiration in patients with hospital-acquired pneumonia are scarce. The mortality rate of patients with aspiration pneumonia is higher in comparison to non-aspiration pneumonia. Recently, Gupte et al. [5] reported the burden of mortality from aspiration pneumonia in the United States, with an average of 58,000 deaths per year. The authors also reported 76% of the deaths related to aspiration pneumonia occurred in the group of adults aged ≥75 years old.

The clinical presentation of aspiration pneumonia can be influenced by factors such as bacterial virulence to which the patient is exposed (i.e inoculum size, resistance to antibiotics), risk of recurrent aspiration (more than one episode of pneumonia) and site of acquisition of the aspiration (community, nursing home, hospital) all of which would influence the microbial etiology, therapy and management of the patient [1].

Aspiration events can involve only the airways or the lung parenchyma, or can involve both. The lung infection caused by aspiration can cause unilateral or bilateral infiltrates, usually in gravity-dependent segments of the lung. The basal segments of the lower lobes are affected in individuals in an upright or semi-recumbent position at the time of aspiration (Figure 1A); whereas the posterior segments of the upper lobes are affected in individuals not able to move or change positions in bed (bed bound) (Figure 1B). It is important to known that in central airways, the right bronchus is wider and more straightly aligned with the trachea than the left main bronchus, making this the preferential side for aspirated material to go. Thus, aspiration pneumonia is more common in the right lobes than in the left lobes.

Two clinical consequences can be associated with aspiration; aspiration pneumonia (lung infection caused by a specific

Correspondence:
Professor. Michael S. Niederman, MD, MACP, FCCP, FCCM, FER
Division of Pulmonary and Critical Care Medicine, New York Presbyterian/Weill Cornell Medical Center, New York, New York.
Tel: (+34) 93-227-5549
E-mail: msn9004@med.cornell.edu

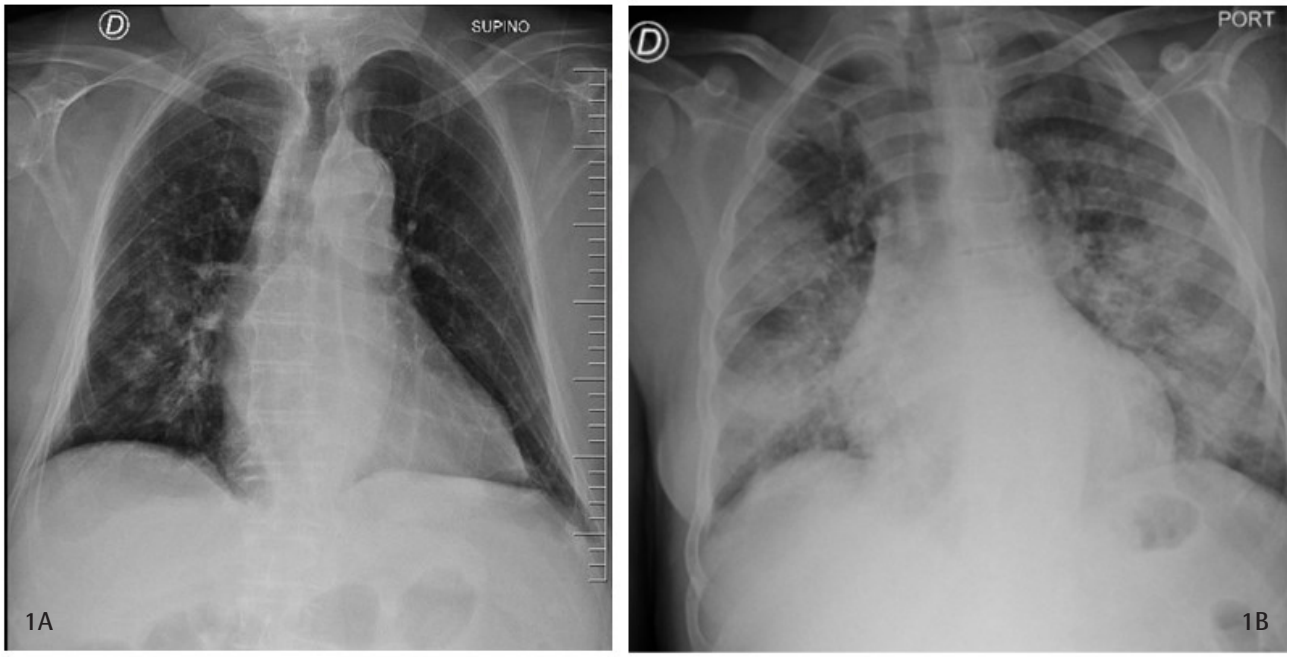

Figure 1 **A) The chest X-ray shows an alveolar inflitrate at right lower lobe, in a 86 year-old patient with moderate cognitive impartiment. The patient live in a nursing-home, present episodes of vomiting and was disoriented.**
B) The chest X-ray shows a bilateral lung infiltrates, respiratory failure, and acute respiratory distress in a 80 year-old patient with repetive episodes of aspiration.

microorganism) and chemical pneumonitis (chemical injury causing inflammation by aspiration of the acid gastric content) [1]. In addition, aspiration of solid material can lead to foreign body aspiration and local endobronchial obstruction.

RISK FACTORS RELATED TO ASPIRATION PNEUMONIA

The factors related to macroaspiration and development of pneumonia include: impaired swallowing (dysphagia, chronic obstructive pulmonary disease, neurological diseases such as stroke or dementia, need of mechanical ventilation), impaired consciousness (acute stroke, head injury, brain lesions, seizures and the effect of some agents that can induce impaired consciousness such as alcohol, drugs, anesthesia or sedatives), increased chance of gastric contents reaching the lung (reflux and tube feeding), and impaired cough reflex (medications, stroke, dementia, impaired consciousness and alcohol). Also, poor dentition in elderly patients could increase the risk of aspiration pneumonia because of the growth of potentially pathogenic anaerobic bacteria.

As we mentioned before, aspiration pneumonia could be multifactorial (Figure 2). Oropharyngeal dysphagia is a relevant risk factor for aspiration pneumonia that is an important area of investigation. In a prospective cohort study of pneumonia patients from Spain [6], of the 134 pneumonia patients analyzed, 55% presented with oropharyngeal dysphagia, and this group of patients was older and often in nursing-homes. Pneumonia was most severe in patients with oropharyngeal dysphagia and has a higher 30-day mortality compared with pneumonia patients without oropharyngeal dysphagia. Similarly, a case- control study [7] that included 36 pneumonia cases and 72 controls (patients with no pneumonia) found that the case group presented with a higher proportion of dysphagia (92% vs 40%, p0.001) than the control group. In this study, oropharyngeal dysphagia was strongly associated with the risk of pneumonia (OR 11.9, 95% CI 3.03–46.9, p0.001).

Another retrospective study [8] that investigated the risk of aspiration pneumonia in patients receiving antipsychotic drugs during hospitalization, reported that of the 146,552 hospitalizations, antipsychotics were used in 10,377 (7.1%) hospitalizations. Aspiration pneumonia occurred in 557 (0.4%) hospitalizations, but the incidence of aspiration pneumonia was 0.3% in unexposed individuals and 1.2% in those with antipsychotic exposure (OR3.9, 95% C = 3.2-4.8). The use of antipsychotics was significantly associated with aspiration pneumonia (aOR1.5, 95% CI = 1.2-1.9).

THE MICROBIOLOGY OF ASPIRATION IS CHANGING

Several studies have demonstrated that the lung microbiome of the individuals with chronic lung diseases differs in diversity and in abundance from lung microbiome of healthy

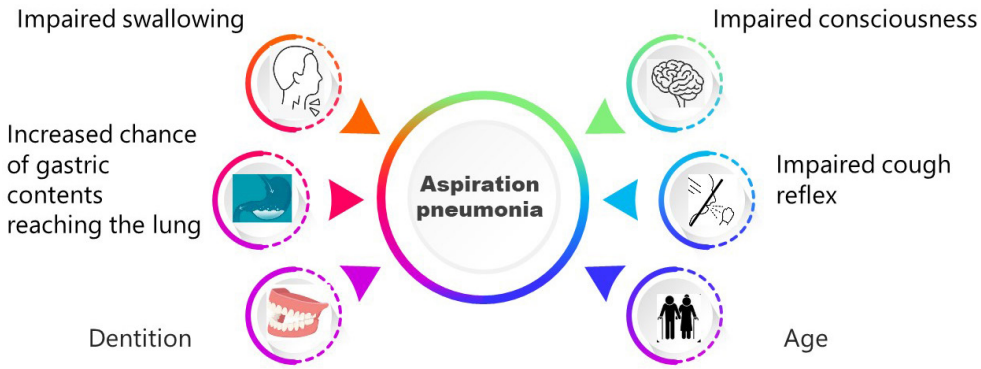

Figure 2 | **Risk Factors for Aspiration Pneumonia**

individuals. We now know that the lung microbiome plays a central role in modulating local inflammation and immune response in lung infections [9]. The lung microbiome shifts in composition during infection or an exacerbation of chronic lung diseases and can become less diverse,which in turn can impair host defenses. Bacteria such as *Prevotella*, *Veillonella*, *Streptococcus*, *Fusobacterium* and *Haemophilus* are common in the normal lung microbiome, and are part of a dynamic community that maintains a constant equilibrium in healthy lungs and these organisms are involved in lung immunity. This equilibrium is disturbed by acute infections, such as pneumonia, or chronic lung diseases. Dysbiosis is the term used to describe this disequilibrium, and is reflected by changes in microbial communities. The risk factors for dysbiosis in aspiration pneumonia and the mechanisms that cause disease are only partly understood [10].

Microbial etiology of aspiration pneumonia has changed over time. Currently, microorganism such as *Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae,* and *Enterobacteriaceae* are the most common organisms. In a recent retrospective multi-institutional joint research from Japan were **1,800 patients with pneumonia were included, the ratio of aspiration pneumonia to total pneumonia** cases increased with age, and 38% of the patients had aspiration pneumonia [11]. There were significant differences between the microbial etiology between patients with aspiration pneumonia and patients without aspiration pneumonia, with a higher frequency of *S. aureus*, *Klebsiella* spp., and *Escherichia coli*, and a lower frequency of *S. pneumoniae*, and *H. influenzae* in the aspiration group. The detection rate of anaerobic bacteria was low in both groups.

Another prospective study that investigated the etiology of hospitalized patients with severe aspiration pneumonia, reported that the three most common microorganism were gram negative bacteria (*E. coli*, *K. pneumoniae, Serratia* spp. and *Proteus* spp.), *S. aureus* and *S. pneumoniae* [12]. Anaerobes were uncommon.

CLINICAL FEATURES OF ASPIRATION PNEUMONIA

An interesting retrospective study from Japan [13] investigated the clinical features and outcomes of patients with aspiration pneumonia in comparison to patients with non-aspiration pneumonia. The study included a total of 214 consecutive patients with pneumonia. Of all the patients, 47% had aspiration pneumonia and 36% had health care associated pneumonia (HCAP). Aspiration was diagnosed in 34% of the CAP patients and in 70% of the HCAP patients. The authors reported three main differences between patients with aspiration pneumonia in comparison to patients without aspiration pneumonia. The first characteristic that the authors found was that patients with aspiration pneumonia had specific host factors and were older, had more frailty, had lower Body Mass Index (BMI) and were more often from nursing home. The second characteristic was related to the severity of pneumonia. Aspiration pneumonia was more severe (severity scores were higher) and more frequently needed intensive care therapy. Finally, the authors observed that patients with aspiration pneumonia had worse outcomes, these patients also presented longer length of stay, had higher rates of pneumonia recurrence and mortality. The most frequent pathogens related to aspiration pneumonia *were S. aureus, S. pneumoniae, Klebsiella* spp. and *E. coli.*

A systematic review and meta-analysis (19 studies) that investigated the outcomes of aspiration pneumonia in CAP patients reported that aspiration pneumonia increased in-hospital mortality (RR, 3.62; 95% CI, 2.65-4.96; $P < 0.001$) and 30-day mortality (3.57; 2.18-5.86; $P < 0.001$). On the other hand, the authors found that aspiration pneumonia was associated with decreased ICU mortality (RR, 0.40; 95% CI, 0.26-0.60; $P < 0.00001$) [14].

Aspiration pneumonia is an acute process that may present with mild symptoms to severe distress associated to respiratory failure. Host factors, chronic comorbidities and functional status are related to presentation and severity of aspiration pneumonia. In elderly patients aspiration pneumonia is often related to poor outcomes.

Figure 3 | **Algorithmic approach to antibiotic therapy for aspiration pneumonia [1].**

CHEMICAL PNEUMONITIS

Chemical pneumonitis is characterized by the macroaspiration of a large volume of gastric contents with a pH<2.5, leading to acute hypoxemia, fever, tachycardia, abnormal chest x-ray and the presence of crackles or wheezes on physical examination. In approximately 16% of the cases of chemical pneumonitis the patients developed acute respiratory distress syndrome (ARDS) [15].

In a study that characterized a cohort of patients who aspirate and require hospitalization, the authors reported that of the 5,584 patients at risk for ARDS and who required hospitalization, aspiration was present in 212 (4%). The authors found that patients who aspirated were with more often male, admitted from a nursing home, had a history of alcohol abuse, and had a lower Glasgow Coma Scale. Aspiration patients were sicker (higher APACHE II score), required more mechanical ventilation, developed more moderate to severe ARDS, and had higher in-hospital mortality rate [16].

RADIOGRAPHIC AND CT DIAGNOSIS

For the diagnosis of aspiration, pneumonia, it is necessary to get confirmation by chest X-ray or computed tomography (CT) scans that are considered the gold standard for the diagnosis of aspiration pneumonia. However, in some cases the chest x-ray may be negative as reported by the study of Miyashita et al. [17] that found negative chest x-ray in 28% of the pneumonia cases that CT scan confirmed. Importantly, in frail patients or in patients who are bedridden, lung ultrasound may be an alternative and complementary approach that can help with the diagnosis of pneumonia. In a patient with suggestive clinical symptoms, presence of pulmonary infiltrates especially in the lower right lobes, the diagnosis of aspiration pneumonia is highly probable [1].

THERAPY OF ASPIRATION PNEUMONIA

For the decision about antimicrobial therapy the determinant factor is the site of aspiration (community, hospital or long term care facility) and risk factors for resistant pathogens. Other determinant factors for antimicrobial therapy are the presence of an abnormal or normal chest x-ray and the severity of the presentation. An algorithmic approach to antibiotic therapy for aspiration pneumonia was proposed by Mandell and Niederman [1]. Figure 3 summarizes this algorithm.

In chemical pneumonitis antibiotics are not recommended. However, in severe cases antibiotics should initiate empirically and the duration of the antibiotics should by guide with the clinical course of the patient.

CONCLUSION

Aspiration pneumonia occurs in characteristic anatomical locations, usually with well-defined risk factors. We should distinguish infectious aspiration pneumonia from chemical aspirations. The microbial etiology of aspiration pneumonia has changed in the last few years, with anaerobes playing a less important role than in the past.

CONFLICTS OF INTEREST

Authors declare no conflicts of interest

REFERENCES

1. Mandell LA, Niederman MS. Aspiration Pneumonia. N. Engl. J. Med. 2019; 380: 651–663.
2. DiBardino DM, Wunderink RG. Aspiration pneumonia: a review of modern trends. J Crit Care 2015; 30: 40–48.
3. Reza Shariatzadeh M, Huang JQ, Marrie TJ. Differences in the features of aspiration pneumonia according to site of acquisition: community or continuing care facility. *J Am Geriatr Soc* 2006; 54: 296–302.
4. Suzuki J, Ikeda R, Kato K, Kakuta R, Kobayashi Y, Ohkoshi A, et al. Characteristics of aspiration pneumonia patients in acute care hospitals: A multicenter, retrospective survey in Northern Japan. PLoS One 2021; 16: e0254261.
5. Gupte T, Knack A, Cramer JD. Mortality from Aspiration Pneumonia: Incidence, Trends, and Risk Factors. Dysphagia 2022; .
6. Cabre M, Serra-Prat M, Palomera E, Almirall J, Pallares R, Clavé P. Prevalence and prognostic implications of dysphagia in elderly patients with pneumonia. Age Ageing 2010; 39: 39–45.
7. Almirall J, Rofes L, Serra-Prat M, Icart R, Palomera E, Arreola V, Clavé P. Oropharyngeal dysphagia is a risk factor for community-acquired pneumonia in the elderly. Eur Respir J 2013; 41: 923–928.
8. Herzig SJ, LaSalvia MT, Naidus E, Rothberg MB, Zhou W, Gurwitz JH, Marcantonio ER. Antipsychotics and the Risk of Aspiration Pneumonia in Individuals Hospitalized for Nonpsychiatric Conditions: A Cohort Study. J Am Geriatr Soc 2017; 65: 2580–2586.
9. Man WH, de Steenhuijsen Piters WAA, Bogaert D. The microbiota of the respiratory tract: gatekeeper to respiratory health. Nat. Rev. Microbiol. 2017; 15: 259–270.
10. Wu BG, Segal LN. The Lung Microbiome and Its Role in Pneumonia. Clin. Chest Med. 2018; 39: 677–689.
11. Suzuki J, Ikeda R, Kato K, Kakuta R, Kobayashi Y, Ohkoshi A, et al. Characteristics of aspiration pneumonia patients in acute care hospitals: A multicenter, retrospective survey in Northern Japan. PLoS One. 2021 Jul 30;16(7):e0254261. doi: 10.1371/journal.pone.0254261.
12. El-Solh AA, Pietrantoni C, Bhat A, Aquilina AT, Okada M, Grover V, Gifford N. Microbiology of severe aspiration pneumonia in institutionalized elderly. Am J Respir Crit Care Med 2003; 167: 1650–1654.
13. Hayashi M, Iwasaki T, Yamazaki Y, Takayasu H, Tateno H, Tazawa S, et al. Clinical features and outcomes of aspiration pneumonia compared with non-aspiration pneumonia: a retrospective cohort study. J Infect Chemother 2014; 20: 436–442.
14. Komiya K, Rubin BK, Kadota JI, Mukae H, Akaba T, Moro H, et al. Prognostic implications of aspiration pneumonia in patients with community acquired pneumonia: A systematic review with meta-analysis. Sci Rep. 2016 Dec 7;6:38097. doi: 10.1038/srep38097.
15. Gajic O, Dabbagh O, Park PK, Adesanya A, Chang SY, Hou P, Anderson H, et al. Critical Illness and Injury Trials Group: Lung Injury Prevention Study Investigators (USCIITG-LIPS). Early identification of patients at risk of acute lung injury: evaluation of lung injury prediction score in a multicenter cohort study. Am J Respir Crit Care Med 2011; 183: 462–470.
16. Izcovich A, Ragusa MA, Tortosa F, Lavena Marzio MA, Agnoletti C, Bengolea A, et al. Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review. PLoS One. 2020; 15(11): e0241955.
17. Miyashita K, Nakatani E, Hozumi H, Sato Y, Miyachi Y, Suda T. Risk Factors for Pneumonia and Death in Adult Patients With Seasonal Influenza and Establishment of Prediction Scores: A Population-Based Study. Open Forum Infect Dis 2021; 8: ofab068.