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Aspiration-Related Pulmonary Syndromes

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Aspiration of foreign matter into the airways and lungs can cause a wide spectrum of pulmonary disorders with various presentations. The type of syndrome resulting from aspiration depends on the quantity and nature of the aspirated material, the chronicity, and the host responses. Aspiration is most likely to occur in subjects with a decreased level of consciousness, compromised airway defense mechanisms, dysphagia, gastroesophageal reflux, and recurrent vomiting. These aspiration-related syndromes can be categorized into airway disorders, including vocal cord dysfunction, large airway obstruction with a foreign body, bronchiectasis, bronchoconstriction, and diffuse aspiration bronchiolitis, or parenchymal disorders, including aspiration pneumonitis, aspiration pneumonia, and exogenous lipoid pneumonia. In idiopathic pulmonary fibrosis, aspiration has been implicated in disease progression and acute exacerbation. Aspiration may increase the risk of bronchiolitis obliterans syndrome in patients who have undergone a lung transplant. Accumulating evidence suggests that a causative role for aspiration is often unsuspected in patients presenting with aspiration-related pulmonary diseases; thus, many cases go undiagnosed. Herein, we discuss the broadening spectrum of these pulmonary syndromes with a focus on presenting features and diagnostic aspects.

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ABBREVIATIONS: BOS = bronchiolitis obliterans syndrome; GER = gastroesophageal reflux; GERD = gastroesophageal reflux disease; HRCT = high-resolution CT; IPF = idiopathic pulmonary fibrosis

Aspiration is defined as the entrance of foreign matter into the airways and lungs.[1,2] It is a common event and can occur in healthy individuals. For example, radiotracer studies have shown that nearly one-half of healthy subjects experience aspiration of pharyngeal secretions during sleep.[3,4] Although aspiration generally triggers coughing, it can be silent, causing difficulties in recognizing aspiration as the cause of undiagnosed respiratory diseases.[5-10] For example, aspiration was suspected clinically in only 9% of 59 patients in whom aspiration was confirmed on lung biopsy.[11]

Aspiration syndromes, such as airway obstruction from an inhaled foreign body, aspiration pneumonitis, and aspiration pneumonia, are well recognized.[1,12,13] Aspiration pneumonitis is defined as acute lung injury occurring after inhalation of a large volume of acidic gastric contents. Aspiration pneumonia refers to an infectious process secondary to aspiration of colonized oropharyngeal secretions. In recent years, however, it has become apparent that the spectrum of aspiration-related pulmonary syndromes is broader and more varied in clinical and radiologic presentation than

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previously thought. Herein, we provide an overview of these aspiration-related pulmonary disorders, focusing particularly on those entities not widely appreciated and on recent advances in our understanding of aspiration-related pulmonary syndromes, which can be broadly grouped into those predominantly affecting the airways or the lung parenchyma (Table 1).

Epidemiology

Aspiration-related pulmonary syndromes are encountered in subjects of any age, from infancy to the aged. However, specific pulmonary syndromes are more likely to be encountered in certain age groups or in clinical contexts in which there are risk factors for aspiration. For example, foreign body aspiration is encountered most commonly in young children and the elderly, particularly those with impaired mental status or swallowing mechanism.[14,15] Aspiration pneumonitis typically occurs in the setting of depressed consciousness from general anesthesia or drug overdose, thus predisposing to regurgitation and inhalation of a large volume of gastric contents. Aspiration pneumonia is a relatively common form of pneumonia in the elderly with chronic medical disorders and in those residing in nursing homes.[9]

Risk Factors for Aspiration

Major risk factors for aspiration include depressed consciousness, compromised airway defenses, dysphagia, gastroesophageal reflux disease (GERD), and recurrent vomiting (Table 2).[13,16] States of depressed consciousness include general anesthesia, alcohol intoxication, and drug overdose. Under these conditions, swallowing mechanisms and airway defenses are impaired. Airway defenses are also impaired in subjects with vocal cord immobility, oropharyngeal deformities caused by surgery or radiation therapy, or endotracheal intubation.

TABLE 1] Aspiration-Related Pulmonary Syndromes

Syndrome
Airway
Vocal cord dysfunction
Foreign body aspiration (mechanical obstruction)
Bronchiectasis
Bronchoconstriction (eg, exacerbation of asthma)
Diffuse aspiration bronchiolitis
Bronchiolitis obliterans syndrome
Parenchyma
Aspiration pneumonitis
Aspiration pneumonia
Exogenous lipoid pneumonia
Interstitial lung disease

TABLE 2] Risk Factors for Aspiration-Related Pulmonary Syndrome

Risk Factor
Depressed consciousness (eg, sedation, anesthesia, alcohol intoxication, drug overdose)
Compromised airway defenses (eg, vocal cord paralysis, endotracheal intubation)
Dysphagia
Neurologic disorders (eg, stroke, multiple sclerosis, Parkinson's disease, dementia)
Altered upper aerodigestive tract (eg, cancer, prior surgery, radiation therapy)
Esophageal diseases (eg, cancer, prior surgery, motility disorders, tracheoesophageal fistula)
Gastroesophageal reflux disease
Recurrent vomiting

Dysphagia can be caused by neurologic disorders, such as stroke; neuromuscular disorders, especially those with bulbar involvement; or upper aerodigestive alterations related to prior surgery or radiation therapy.[16,17] Aspiration complicates many genetic or metabolic disorders associated with significant neurologic compromise and dysphagia, particularly in children (eg, familial dysautonomia [Riley-Day syndrome]).

GERD is a common disorder in the Western world, with symptoms experienced by 10% to 20% of the adult population at least once a week, and it can underlie occult aspiration.[18] Esophagogastric sphincter dysfunction, motility disorders involving the esophagus or stomach, postsurgical anatomic alterations, and obesity (increased gastric pressure) augment the likelihood of gastroesophageal reflux.[19] If typical symptoms of GERD are absent, or symptoms do not respond to empirical medical therapy, diagnostic testing for GERD, such as ambulatory esophageal pH testing or upper GI endoscopy, may be needed.

Pathophysiology

When aspiration occurs in healthy subjects, the amount of aspirated material is usually minimal and cleared without clinical sequelae. When aspiration results in adverse clinical consequences, the character of the evolving illness is determined by the nature and volume of the aspirated material, the chronicity, and the host responses.

In patients with GERD, laryngeal injury with mucosal damage results from direct exposure to refluxed gastroduodenal contents that include acid, pepsin, and bile

acids.[20] In experimental animals, airway hyperresponsiveness can be elicited by acid stimulation of the sensory nerves innervating the larynx and trachea, which is principally induced by breakdown of the airway epithelial barrier.[21] Aspiration of solid or semisolid material into the airways causes mechanical obstruction, resulting in acute respiratory distress or sometimes asphyxia, depending on the location of the obstruction and the size of the foreign body. However, a small-sized foreign body may be inhaled without the subject being aware, especially in the setting of alcohol or drug intoxication. If the foreign body is retained, bronchial obstruction leads to persistent cough, recurrent postobstructive pneumonias, and bronchiectasis. The nature of the foreign body will also influence the resulting injury. Sharp inorganic objects may cause direct physical injury to the airways, whereas organic material, such as nuts or meat, elicits a granulomatous inflammatory reaction with localized bronchial stenosis in addition to mechanical obstruction.[15,22]

Aspiration of large amounts of gastric acid induces a chemical injury to the airways and lung parenchyma. A cascade of inflammatory response follows this initial injury and includes recruitment of inflammatory cells and release of various inflammatory mediators.[16,23] With massive gastric acid aspiration, acute lung injury occurs, with diffuse alveolar damage and progressive hypoxemia. In contrast, recurrent small-volume aspirations of refluxed gastric contents during sleep appear to result in chronic and less severe forms of lung injury, such as diffuse aspiration bronchiolitis or chronic exogenous lipoid pneumonia (when oil-based substances [eg, mineral oil laxative] are aspirated).

Aspiration pneumonia results from the inhalation of oropharyngeal secretions containing pathogenic microbes. In this regard, there has been increasing interest in the nature of the lung microbiome. Although the lungs were previously thought to be sterile, studies using culture-independent techniques have demonstrated a diverse population of bacteria in the lungs of healthy individuals.[24,25] This lung microbiome derives mostly, but not entirely, from the mouth.[25] Entrance of oral microbes into the lung likely perturbs the existing lung microbiome, which can be modified by preexisting respiratory conditions and host immune responses. Colonization of the oropharynx with pathologic microbes occurs in the aged, particularly those with comorbidities.[16] Decreased salivary clearance and poor oral hygiene likely contribute to this development.[9] Impaired cough reflex and immune defense, not uncommon in the elderly, are additional factors that promote the development of pneumonia after aspiration of pathologic microbes.

Diagnostic Evaluation

Evaluation of a patient suspected of having an aspiration-related pulmonary syndrome is tailored to the individual context and the specific syndrome (based on clinical and radiologic features) being addressed. Several modalities are available to evaluate subjects with dysphagia. Videofluoroscopic swallow study (performed by a speech therapist or radiologist) is generally considered to be the procedure of choice and should assess oral, pharyngeal, and esophageal phases.[9,12,17] Other methods of evaluation include fiber-optic nasoendoscopy, motility testing, and upper GI endoscopy. Endoscopy with biopsy and ambulatory pH monitoring are useful in confirming GERD.[18,19] Evaluation for aspiration-related airway diseases usually entails visualization of the airways with laryngoscopy or bronchoscopy and pulmonary function testing. Aspiration-related parenchymal diseases, such as aspiration pneumonitis, aspiration pneumonia, and exogenous lipoid pneumonia, are generally diagnosed by clinical and radiologic findings. In occult cases, findings on lung biopsy (ie, presence of foreign matter or lipid-laden macrophages) may confirm the diagnosis.[6,11]

Airway Manifestations

Vocal Cord Dysfunction

Several laryngeal manifestations have been associated with GERD; these include chronic laryngitis, laryngospasm, vocal fold granuloma, and vocal cord dysfunction.[26,27] The most relevant of these entities to pulmonologists is vocal cord dysfunction, which is commonly misdiagnosed as asthma. Vocal cord dysfunction is characterized by episodes of airflow obstruction due to true vocal cord adduction during inspiration, occasionally during expiration, or both.[27] Vocal cord dysfunction is thought to be of psychologic origin in some patients and irritant induced (eg, laryngopharyngeal reflux) in others.[27] Because the laryngoscopic findings used in diagnosing laryngopharyngeal reflux are nonspecific, it remains unclear whether there truly is a relationship between GERD and vocal cord dysfunction. The diagnosis of vocal cord dysfunction is based on the presence of symptoms (typically noisy breathing and dyspnea), the laryngoscopic finding of paradoxical vocal cord adduction, and an abnormal flow-volume loop (plateauing of the inspiratory limb).[27] Management of vocal cord dysfunction is directed at the underlying cause,

along with supportive care that may include speech therapy.

Foreign Body Aspiration

Foreign body aspiration is potentially life threatening and occurs more commonly in children.[2,15,22] Foreign body aspiration is unusual in adults and is often overlooked as a cause of respiratory symptoms, particularly when patients do not recall the aspiration event or were unconscious at the time.[15,22,28] The majority of foreign bodies found in the airway are food particles, most commonly nuts.[15,22]

Most patients present with a nonresolving cough, sometimes associated with exertional dyspnea, chest pain, or hemoptysis. Some may present with recurrent pneumonias or persistent pulmonary infiltrates, whereas others are mistakenly given a diagnosis of asthma based on persistent wheezing. Misdiagnosis is not uncommon because of the nonspecific clinical presentation. The possibility of airway foreign body should be considered when "pneumonia" or "asthma" does not respond as expected to treatment.

Chest radiography usually reveals lobar or segmental atelectasis or hyperinflation, but may be normal.[2,29] Chest CT scanning often provides additional diagnostic information including demonstration of an intrabronchial mass, which may be mistaken for an endobronchial malignancy.[2,29] Expiratory images may show air trapping in the affected segment (or lobe). When bronchial obstruction is chronic, consolidative opacities from postobstructive pneumonia may be demonstrated along with bronchiectasis.

Bronchoscopic examination confirms the diagnosis of foreign body aspiration by visualizing the obstructing foreign body. Extraction of the foreign body can usually be accomplished by flexible bronchoscopy, although rigid bronchoscopy, or rarely surgery, may be needed in some situations, such as in patients with central airway occlusion.[14,15,28,30]

Pill aspiration represents a unique type of foreign body aspiration because some pills such as potassium and iron preparations may dissolve in the airways, causing intense bronchial inflammation and stenosis.[31,32] Thus, bronchoscopic examination may not visualize an aspirated foreign body. Prompt diagnosis of pill aspiration and timely bronchoscopy for extraction and bronchial lavage help minimize adverse sequelae.

Bronchiectasis

Bronchiectasis, defined by irreversibly widened bronchi due to damage to the bronchial walls, usually arises from some combination of bronchial obstruction and infection.[33] Aspiration has been identified as the cause in 4% to 18% of patients (more commonly in children) with non-cystic fibrosis bronchiectasis.[34-36] However, it is unclear from these studies how the causal relationship between aspiration and bronchiectasis was established. Some investigators used 24-h ambulatory esophageal pH monitoring, upper GI contrast study, and the location of the bronchiectasis (ie, predominantly lower lobes) in implicating aspiration.[35] Nonetheless, it would appear that identifying the underlying cause, such as aspiration, would be essential in optimally managing patients with bronchiectasis.

Bronchoconstriction

In patients with GERD, aspiration of gastric acid triggers bronchoconstriction and cough.[37,38] The prevalence of GERD is higher in subjects with asthma than in the general population.[39] One study found GERD to be the most common identifiable cause underlying refractory asthma.[40] However, studies investigating the role of acid-suppressive therapy (eg, proton pump inhibitors) in the management of asthma have yielded inconsistent results.[39,41,42] Although treatment of symptomatic GERD in subjects with asthma is reasonable, treatment of asymptomatic GERD does not appear to be justified, even in patients with poorly controlled asthma.[39,42]

Diffuse Aspiration Bronchiolitis

Bronchiolitis refers to a broad spectrum of disorders characterized by inflammation and fibrosis of the bronchioles (internal diameter of ≤ 2 mm).[43] Aspiration is an underappreciated cause of bronchiolitis.[6,44] "Diffuse aspiration bronchiolitis" is a term used previously to describe chronic bronchiolar inflammation with foreign body reaction noted at the autopsies of chronically debilitated elderly subjects manifesting diffuse micronodular opacities on chest radiography.[45] Recent experience suggests that diffuse aspiration bronchiolitis can be seen in adults without apparent risk factors for aspiration. Barnes and colleagues[6] reported four patients ranging in age from 41 to 59 years with persistent respiratory symptoms and diffuse pulmonary opacities caused by chronic occult aspiration that was eventually diagnosed by surgical lung biopsy. None of them had dysphagia or neurologic disorders. Although three subjects had a history of GERD, only one had active symptoms of gastroesophageal reflux (GER). High-resolution CT (HRCT) scanning demonstrated diffuse centrilobular nodules with a tree-in-bud pattern (Fig 1), contrary to the findings expected of aspiration pneumonia (ie, patchy bronchopneumonic

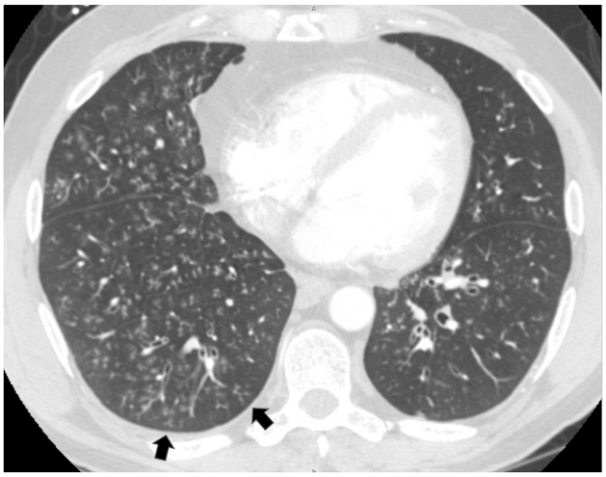

Figure 1 – *High-resolution CT (HRCT) scan of diffuse aspiration bronchiolitis. An HRCT scan of the chest shows micronodular opacities throughout both lungs, more numerous in the right lung. "Tree-in-bud" branching opacities (arrows) are seen in peripheral lung zones.*

infiltrates involving dependent lung zones). Recurrent occult aspiration was likely related to GER that occurred during sleep.

The diagnosis of diffuse aspiration bronchiolitis can be confirmed by lung biopsy, bronchoscopic or surgical, that demonstrates granulomatous inflammation and multinucleated giant cells associated with the presence of foreign material.[6,11] It should be noted that the presence of foreign material on the lung biopsy can be easily overlooked by pathologists, resulting in misdiagnosis.[11] The management of diffuse aspiration bronchiolitis focuses on addressing the underlying cause, usually GERD or dysphagia. Fundoplication has been performed in patients with GERD and aspiration bronchiolitis that is recurrent despite medical therapy.[6]

Bronchiolitis Obliterans Syndrome

Lung transplantation is an accepted treatment strategy for end-stage lung disease. Bronchiolitis obliterans syndrome (BOS) remains a major cause of morbidity and mortality in lung allograft recipients.[46,47] BOS is defined by persistent airflow limitation compared with the recipient's peak baseline values after lung transplant. Underlying this airflow obstruction is a histopathologic pattern of dense fibrous scarring constricting the small airways.

A high prevalence of GER has been reported in lung allograft recipients, and aspiration has been implicated as a contributor to the development of BOS.[46,48] Aspiration related to GERD has been associated with a worse outcome among lung allograft recipients, possibly because of recurrent microaspiration.[46,47,49] Studies have reported a decreased rate of lung function decline after laparoscopic fundoplication in lung allograft recipients who had GERD.[50,51] Further exploration is needed to assess the effects of GERD and aspiration on the clinical course and outcome of lung allograft recipients.

Parenchymal Lung Manifestations

Aspiration Pneumonitis

Two aspiration-related pulmonary syndromes that are most familiar to physicians are aspiration pneumonitis and aspiration pneumonia. Aspiration pneumonitis refers to acute lung injury occurring after inhaling a large volume of regurgitated gastric contents.[16] This syndrome typically occurs in patients who have altered consciousness, such as that resulting from sedation, general anesthesia, drug overdose, seizure, massive stroke, or traumatic brain injury.[13,52] Although the initial lung injury is chemical (related to low pH) in nature, a superimposed bacterial infection may ensue at later stages, especially in the presence of gastric acid-suppressive therapy such as proton pump inhibitors or enteral feedings that promote colonization of gastric contents with pathogenic bacteria.

Aspiration pneumonitis presents acutely with cough, dyspnea, and wheezing following regurgitation and aspiration. Hypoxemia and hypotension may follow over the next several hours and may progress to ARDS.[53] However, aspiration may not be recognized in some patients, such as those undergoing general anesthesia, who may present with new radiologic opacities and decreasing arterial oxygen saturation.[13] There is subsequent progression to diffuse air-space consolidation in the following 24 to 48 h.[2,13]

The diagnosis of aspiration pneumonitis is not difficult when regurgitation and aspiration are witnessed with the development of expected clinical and radiologic features. Even in the presence of witnessed aspiration, however, aspiration pneumonitis often does not ensue. In unwitnessed aspiration, the diagnosis is supported by documenting the presence of bilious fluid or particulate matter in the airways during bronchoscopy or on examination of respiratory secretions. Several potential biomarkers of gastric aspiration, such as pepsin and lipid-laden macrophages, can be sought in respiratory secretions or BAL specimens obtained bronchoscopically.[13] However, the use of these biomarkers remains controversial, and none has been deemed a validated diagnostic tool. In many cases, the diagnosis of aspiration pneumonitis remains a clinical determination based on the clinical context (eg, general anesthesia) and the acute development of respiratory symptoms and

diffuse pulmonary opacities in the absence of another explanation.

The management of aspiration pneumonitis is mainly supportive and includes suctioning of the aspirated material bronchoscopically or via an endotracheal tube when placed for protection of the airway.[13,16] Supplemental oxygen is needed as gas exchange becomes impaired, sometimes requiring mechanical ventilatory support. Prophylactic use of antimicrobial therapy in this setting is generally not recommended unless evidence of superimposed infection ensues in the following days.[13,16] The role of corticosteroid therapy in the treatment of aspiration pneumonitis remains controversial.[16]

Aspiration Pneumonia

Aspiration pneumonia refers to an infection that develops after the entrance of pathologic oropharyngeal microbes into the lung.[16] Aspiration pneumonia is one of the common forms of community-acquired and health-care-associated pneumonias.[9,54] A multicenter study from Japan noted that 18% of patients with community-acquired and health-care-associated pneumonias had aspiration pneumonia.[55] The disease was diagnosed based on the presence of risk factors for aspiration combined with evidence of gravity-dependent opacities on chest CT scan.

Aspiration pneumonia generally occurs in the absence of witnessed aspiration and often without the patient being aware of the aspiration (eg, patients with stroke). Patients with community-acquired aspiration pneumonia are older, have more comorbidities, and have a higher mortality rate compared with those with non-aspiration-related pneumonia.[54]

Patients with aspiration pneumonia typically present in an indolent manner with cough productive of purulent sputum, dyspnea, and fever evolving over an interval of several days to weeks. Many will have experienced weight loss and have anemia on presentation. Chest radiography will usually reveal patchy alveolar opacities in a bronchopneumonia pattern, predominantly in the dependent portion of the lung.[2] Those with a prolonged course preceding medical evaluation may show radiologic evidence of necrotizing bronchopneumonia, lung abscess, and even empyema.

Most patients with community-acquired aspiration pneumonia have a mixed infection with anaerobic and aerobic bacteria, whereas those with a health-care-associated form of pneumonia will more likely have gram-negative infections, including *Pseudomonas aeruginosa*.[13,16] The choice of antibiotics depends on the setting in which the aspiration occurred, the individual context, and the severity of illness. In view of the rising resistance to antimicrobial agents, local data on antimicrobial susceptibility patterns will also need to be taken into account.

Exogenous Lipoid Pneumonia

Exogenous lipoid pneumonia is an uncommon condition that results from the entrance into and accumulation of lipid-containing material in the lung.[56] In contrast, "endogenous" lipoid pneumonia is a histopathologic lesion of lipid accumulation within intra-alveolar macrophages, typically seen in the setting of postobstructive pneumonia.

Exogenous lipoid pneumonia can be seen in an acute form related to aspiration of a large quantity of a petroleum-based product as accidental inhalation and as an occupational hazard in fire-eaters ("fire-eater's pneumonia").[56,57] Chronic exogenous lipoid pneumonia is more difficult to diagnose because of the nonspecific clinical presentation and the absence of a recognizable aspiration event. It is caused by recurrent aspiration or inhalation of mineral oil or similar substances that are ingested or applied intranasally. Presenting symptoms are similar to those of other aspiration syndromes and include cough, dyspnea, and sometimes chest pain, but one-half or more may be asymptomatic.[56,57]

Chest radiographic findings are generally nonspecific and include patchy parenchymal opacities that may be poorly defined, consolidative, or of an interstitial pattern.[56,57] The most frequent findings on HRCT scan include consolidation, ground-glass opacities, mass-like lesions, and septal thickening.[56,57] The most characteristic CT scan findings are areas of fat attenuation within consolidation or mass-like opacities that may mimic a lung neoplasm (Fig 2).[2,57,58]

Diagnosis of exogenous lipoid pneumonia can be based on characteristic chest CT scan findings (opacities containing fat attenuation) combined with a history of exposure to oily substances, most commonly mineral oil ingestion. In other circumstances, additional diagnostic evidence is needed, typically histopathologic confirmation by bronchoscopic or surgical lung biopsy. Histologically, chronic exogenous lipoid pneumonia is characterized by the presence of numerous lipid-laden (lipid vacuoles) macrophages within the alveolar spaces, giant cell granulomas, inflammatory cellular infiltration, and a variable amount of fibrosis.[2,59] Cytologic demonstration of lipid-laden macrophages in BAL has also

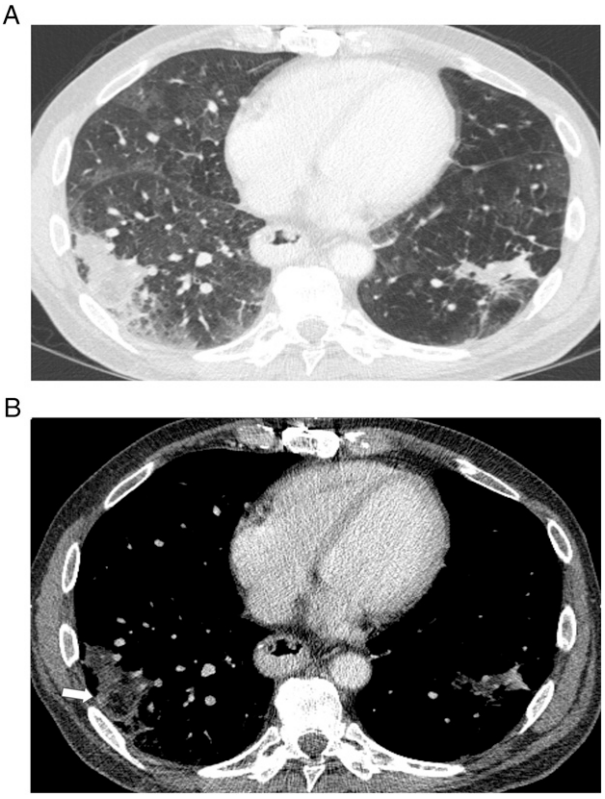

Figure 2 – *HRCT scan of exogenous lipoid pneumonia. A, An HRCT scan of the chest on lung window setting shows irregular mass-like opacities bilaterally. B, A fat density (arrow) is present within the right lung mass. See Figure 1 legend for expansion of abbreviations.*

been proposed for diagnostic use but remains controversial because this finding is nonspecific.[56,60]

Cessation of exposure to oily substances generally suffices in managing patients with exogenous lipoid pneumonia. In patients with extensive lung disease, corticosteroid therapy has been used but is of unclear benefit.

Interstitial Lung Disease

The role of aspiration has been implicated in fibrotic interstitial lung diseases, particularly idiopathic pulmonary fibrosis (IPF), which is a disorder characterized by progressive parenchymal fibrosis resulting in respiratory failure.[61] GERD is highly prevalent in patients with IPF, and a potential causal relationship between GERD and IPF has been pondered for a number of years.[61-63] Savarino and colleagues[64] reported increased distal as well as proximal esophageal acid exposure in patients with IPF compared with those with non-IPF interstitial lung diseases and healthy volunteers. In addition, patients with IPF had more bile acids and pepsin in their BAL fluid than did comparison groups, suggesting aspiration of gastric refluxate.

Several studies have reported an association between the treatment of GERD and clinical end points in IPF. For example, Raghu and colleagues[65] described four patients with IPF whose clinical course stabilized or improved over a 4-year period with the use of medical and/or surgical therapies for GERD. The use of acid-suppressive therapy has also been associated with longer survival in patients with IPF and a slower rate of decline in pulmonary function.[66,67] International guidelines on the diagnosis and management of IPF published in 2011 recommended treatment of asymptomatic GERD in the majority of patients with IPF, but acknowledged that the quality of evidence was low.[61]

During the clinical course of IPF, some patients experience acute worsening of their respiratory status, accompanied by increased gas exchange impairment and new pulmonary opacities. Many of these episodes have no identifiable cause (eg, pneumonia, heart failure, pulmonary embolism), have been termed "acute exacerbation" of IPF, and commonly result in death.[68,69] Occult aspiration of gastric contents has been proposed as one possible mechanism leading to these acute exacerbations. Lee and colleagues[70] reported a higher level of pepsin in the BAL of patients with IPF experiencing an acute exacerbation compared with stable control subjects. These results suggest that occult aspiration may play a role in some cases of acute exacerbation of IPF.

Similar questions regarding the role of GERD and aspiration in other interstitial lung diseases have arisen. In scleroderma, those with interstitial lung disease have been reported to have a higher number of acid and nonacid GER episodes.[71] The severity of interstitial lung disease assessed by HRCT scanning correlated with the number of reflux episodes. Christmann and colleagues[72] reviewed the available literature on the relationship between GER and scleroderma and recommended "aggressive treatment" of GER for all patients with scleroderma-associated interstitial lung disease. To date, there is no definitive evidence (ie, clinical trials) that treatment aimed at GERD (including fundoplication) improves the clinical course of patients with scleroderma-associated interstitial lung disease or IPF.

Conclusions

Aspiration can be clinically occult and elicits a broad spectrum of pulmonary syndromes. Integration of the clinical context (including risk factors for aspiration) and awareness of clinicoradiologic findings associated with these disorders will facilitate recognition of these diverse syndromes, which often go undiagnosed.

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