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Review article

The pathology of pulmonary bacterial infection

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Introduction

In its role as a portal between the ambient environment and the internal milieu, the lung is the most frequent site of bacterial infection. A variety of factors predispose to pulmonary bacterial infection, including distortions in lung anatomy, decreased mucociliary clearance, and abnormal immunity.

In addition to community acquired pneumonias, mechanical ventilation which introduces a foreign body into the proximal airways and may impair normal swallowing function, predisposes to bacterial pneumonias by virulent bacteria including staphylococcal and gram-negative organisms.

The clinical history, radiographic findings, non-invasive sampling of secretions, and serological findings are generally sufficient to diagnose typical bacterial infections, and lung biopsy is rarely required. However, it is imperative that pathologists be acquainted

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with the histopathological features of infection and its non-infectious mimics.

The epidemiology of bacterial pneumonia

Pneumonia is the world's leading cause of death among children under 5 years of age, and the most common reason for children to be hospitalized in the U.S. In adults, pneumonia accounts for most hospital admissions.[1] About 1 million adults in the U.S. are hospitalized with bacterial pneumonia every year and ~50,000 die from the disease. Half of all non-immunocompromised adults hospitalized for severe pneumonia in the U.S. are younger adults (18–57 years of age) and ~50% of deaths from bacteremic pneumococcal pneumonia occur in this age group.

For most patients, a causative microbe is never identified and these infections are treated empirically. However, antibiotic resistance is increasing amongst the bacteria that commonly cause pneumonia due to the overuse and misuse of antibiotics in the ambulatory and in patient settings. Consequently, new and more effective antibiotics are needed.

Pneumonia is the most common cause of sepsis and septic shock accounting for half of cases. Hospital-acquired pneumonia has a higher mortality rate than any other hospital-acquired infection and requires broad antibiotic coverage. Mechanical ventilation creates a high risk for virulent bacterial infections, as ventilator-associated pneumonia is more likely to be caused by antibiotic-resistant microbes and accounts the greatest antibiotic use in the critically ill.

Adults who survive pneumonia may have decreased exercise ability, cardiovascular disease, cognitive decline, and diminished quality of life that persists for months to years. In 2011, bacterial pneumonia had an aggregate cost of nearly $10.6 billion for 1.1 million hospital stays in the U.S. Finally, the death rate from bacterial pneumonia in the U.S. has shown little improvement since effective antibiotics became available more than half a century ago.

The anatomy of pulmonary defense

The histopathological features of bacterial infection reflect the dynamic interactions of bacterial virulence and host defenses.[2] Most pulmonary bacterial pathogens reach the lung via airborne droplet spread, micro-aspiration of pathogens that have colonized the oropharynx, or spread to the lungs via the pulmonary or systemic blood supply. Two systems of pulmonary lymphatic channels drain the lung either centrifugally towards the hilum, or centripetally along the convexities of the pleural surfaces before coursing to the hilar lymph nodes. From the lymph nodes, organisms can enter the systemic circulation and spread widely throughout the body, or course to the pleura to produce an empyema.

Bacteria are small ($< 5\ \mu M$) and can penetrate to the distal gas-exchanging surfaces of the lung, although the majority are excluded by the defenses of the upper airways or deposit along the conducting airways to be cleared by the mucociliary escalator. Humoral factors, including sIgA and defensins released by airway cells, limit microbial penetration into tissues. Airway mucosal dendritic cells (DC) trap bacteria antigens and transport them to regional lymph nodes, where they may be processed and present to both T- and B-lymphocytes, evoking adaptive immunity.[3]

The alveolus is under normal conditions maintained sterile by resident macrophages that scavenge inhaled particulates and secrete monokines, including IL-10 and TGF-β, that locally suppress inflammation and promote immunotolerance, but when the alveolar lining is injured, or the number of invading organisms exceed the phagocytotic capacities of resident alveolar macrophages, neutrophils and exudate monocytes are rapidly recruited to sites of infection.[4] Even small numbers of virulent pathogens can greatly amplify inflammation via the release of chemokines, cytokines, and complement, by host immune cells. For this reason, it may require a careful search and extensive tissue sectioning to identify bacteria in tissues. If antibiotic treatment has been instituted, it may be impossible to identify bacterial forms. The host defenses that promote the clearance of infection can also damage the lung.

Acute bacterial bronchopneumonia

Acute bronchopneumonia is the most common pattern of pulmonary infection. Most gram-positive and gram-negative bacteria elicit exudation of blood neutrophils into the bronchi and surrounding alveolar spaces in response to complement fragments and chemokines. Bronchopneumonia generally results from microaspiration of pathogens that have colonized the oropharynx. At times, the aspiration of colonized food particles carry bacteria the lung. Terminal episodes of aspiration often show colonies of gram-positive *Aerococci*, previously referred to as “gaffkya,” (Fig. 1) and their appearance is both common and characteristic in autopsy lungs.

The pyogenic bacteria are distinguished by their propensity to evoke acute neutrophilic inflammation and “pus.” Pyogenic infections as well as other acute necrotizing bronchopneumonias progress to *organizing pneumonia*, characterized by a fibrohistiocytic response that obliterates small airways along with inflammation of the surrounding alveolar interstitium. This reaction is non-specific, and “organizing pneumonia” or “bronchiolitis-obliterans-organizing-pneumonia,” is a rubric for the generic lesion that may be due to infection, non-infective inflammatory disorders, or may be idiopathic.[2] It is important for the surgical pathologist to convey clearly to the treating clinicians that a diagnosis of “organizing pneumonia” does not necessarily indicate a specific etiology.

Pneumococcal pneumonia

Streptococcal pneumonia (pneumococcal pneumonia) is a community-acquired pneumonia that classically produces a lobar pneumonia that heals by resolution, i.e., without necrosis or scarring.[5] In some cases, pneumococcal pneumonia

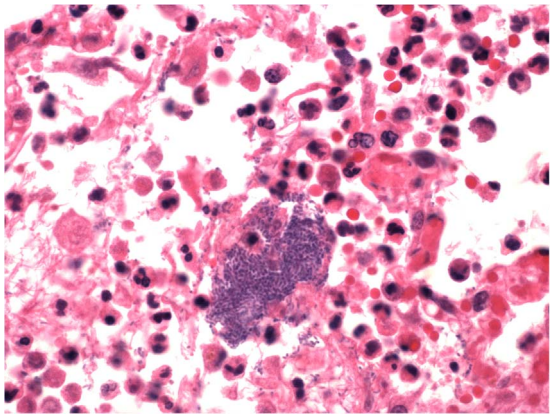

Fig. 1. Terminal aspiration showing intraluminal colony of gram-positive *Aerococcus spp.* (Gaffkya).