Atypical Pneumonia in the ICU

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Introduction

Severe pulmonary infections with respiratory failure are a common feature in the ICU either as a primary reason for admission or as a complication. In many cases bacterial causes can readily be identified. When Gram stains of pulmonary secretions reveal many leukocytes without bacteria the presence of atypical pneumonia should be considered. This rather outdated but common term is used for pulmonary infiltrative infections caused by Legionella pneumophila, Mycoplasma pneumoniae, Chlamydia psittaci, Coxiella burneti, (para)influenza virus, adenovirus and several other micro-organisms. Not much is known about the incidence of atypical pneumonias in the ICU. Sporadic cases of atypical pneumonia are not rare and may give rise to such severe complications that intensive treatment is necessary. They usually cause diagnostic confusion and initial therapeutic anxiety also because extrapulmonary manifestation may be the most impressive presenting symptoms. In the following, infections due to Mycoplasma pneumoniae and Legionella pneumophilia will be briefly discussed.

Mycoplasma Pneumoniae Infections

Mycoplasma pneumoniae infections usually run a benign, often subclinical course with upper respiratory tract infection and bronchitis. Clinically apparent pneumonias develop in 3–10% of infected patients and may account for up to 20% of all pneumonia cases in the general population and even for up to 50% in isolated populations [1, 2]. Most frequently, children and young adults are infected but the disease may occur at all ages. The typical course of a Mycoplasma pneumonia is benign with spontaneous resolution and this course may be shortened by appropriate antibiotic agents such as erythromycin or tetracyclins. However, life-threatening infections can occur and the wide spectrum of pulmonary manifestations also include rapidly progressive pneumonias [3], multilobar pulmonary involvement, adult respiratory distress syndrome (ARDS) [4–6] and extensive interstitial pneumonia with severe hypoxemia [7], conditions usually requiring mechanical ventilation and carrying a high risk of mortality. The onset of acute respiratory deterioration may be abrupt and rapid [5]. Other pulmonary lesions that have been published are lung abscesses [1–3], Swyer-

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James syndrome [1], pneumatoceles [1, 2] and pleural effusions [1, 2]. Some have reported acute exacerbations of chronic lung disease [1].

The infiltrates on the chest roentgenogram are characteristically unilateral segmental areas of consolidated bronchopneumonia mostly involving the lower lobes. Although pathognomonic signs are lacking, it has been suggested that segmental or patchy infiltrates and centrally dense infiltrates are helpful diagnostic signs [8]. Bilateral infiltrates occur in up to almost half of the cases and often extend from the hilar areas. Also, reticulo-nodular patterns, multiple segmental infiltrates, unilobar and multilobar infiltrates and complete consolidation of one lung has been described [2]. Progression of pulmonary infiltrates to involve new parenchymal areas during antimicrobial therapy has been observed as well as relapsing or recurrent pneumonia [2]. Generally, resolution of pulmonary infiltrations runs a protracted course.

The protean manifestations of M. pneumoniae infection include a large number of extrapulmonary conditions. Among these are hemolytic anemia, diffuse intravascular coagulation, thrombocytopenic purpura, myalgia, arthralgia, polyarthritis, pericarditis, myocarditis, gastro-enteritis, hepatitis, pancreatitis, Stevens-Johnson syndrome and skin rashes. Some cases with cardiovascular collapse, shock and acute renal failure have been reported [3]. In fatal cases a high incidence of vascular thrombosis has been observed [3].

Severe neurologic complications have been reported including aseptic meningitis, meningo-encephalitis, transverse myelitis, Guillain-Barré syndrome, hemiplegia, brainstem involvement, cranial nerve lesions and cerebellar ataxia [1, 2, 9, 10].

In a retrospective study of 560 patients infected with M. pneumoniae, neurological complications were observed in 27 patients (4.8%) including 18 with (meningo) encephalitis [9]. Mortality in this group was 22%. In half of the cases of nervous system involvement symptoms appear to have been preceded by upper airway or pulmonary infections. Many of these patients may require intensive treatment and admission to the ICU.

In our 6 bed Medical Intensive Care Unit we have observed 8 cases of severe M. pneumoniae infection in the last 3 years (age 26–87 years). All required mechanical ventilation and 2 required hemodialysis. In almost all patients an underlying chronic medical condition was present, and 3 patients did not survive.

Although 7 patients had clinical and radiological signs of pulmonary infiltrates 2 patients presented with shock and 2 with severe neurologic symptoms (encephalitis with coma and seizures, Guillain-Barré syndrome). One patient developed ARDS and 2 acute renal failure. Prior to the diagnosis, positive cultures with mainly gram-positive micro-organisms had been isolated from the sputum in 6 patients. Although it has been suggested that mixed or superinfections are uncommon [2], our results indicate that this may not be true in the ICU. In fact, the diagnosis of Mycoplasma infection, either serologically or by culture of the micro-organism, was usually only considered when seemingly adequate antibiotic therapy had failed, chest abnormalities and fever did not resolve or recurred and the sputum Gram stain yielded many granulocytes without bacteria. Six out of 8 patients happened to be treated with antibiotics active against micro-

organisms other than M. pneumoniae so that M. pneumoniae infections could be secondary in these patients.

A high index of clinical suspicion in the ICU and awareness of the clinical manifestations of M.pneumoniae infection is essential for obtaining a correct diagnosis. Laboratory diagnosis include isolation of the micro-organism from pulmonary secretions or (rarely) from cerebro-spinal fluid and serological techniques (CBR, Elisa-IgM, IF-IGM, cold agglutinins).

Legionella Infections

Pneumonia caused by Legionella pneumophila and other Legionella species is recognized to occur in sporadic, endemic and epidemic form. In the latter two an environmental source of the bacteria (such as heat exchange devices or potable water sources) is usually implicated, as has been documented in several outbreaks [11, 12]. Sporadic cases are not rare and now seem to outweigh the total number of endemic cases [11]. The total spectrum of the clinical manifestation of legionellosis is not known exactly but may range from asymptomatic or mild, flu-like illness to a fulminant pneumonia that can be fatal. Legionella pneumonias account for up to 15% of community-acquired adult primary pneumonias admitted to the hospital [13]. Most cases occur in middle aged or older patients among whom males predominate. Cigarette smokers and patients with serious underlying disease or on immunosuppressive therapy have increased susceptibility to infection [14–17]. In many although not all reported series the majority of patients had severe underlying disease. The illness may also be more severe in immunocompromised hosts. Increasing age and chronic bronchitis or emphysema are associated with increased risk of death [16].

The symptoms may be of gradual onset or may present abruptly with malaise, headache, nausea, vomiting, unproductive cough, diarrhea, lethargy and high fever with chills often in repeated episodes. Diarrhea is present in nearly half of the cases and may be a helpful diagnostic clue [18]. Upper respiratory symptoms are unusual [15] while pleuritic chest pain is not uncommon. Progressive pulmonary involvement may evolve into acute respiratory failure. It is estimated that 15–30% of the patients need mechanical inspiratory support [16, 18, 19]. Abscess formation has been observed especially in immunocompromised hosts [14, 20] but also without underlying disease [21].

There is no characteristic radiographic appearance although patchy and mottled interstitial infiltrates or (often nodular) areas of consolidation are most often seen usually progressing to more widespread and multilobar involvement. Early in the course the majority of patients has unilateral involvement with subsequent spread to contiguous areas or to the opposite lung. Pleural effusions may ocur as well as cavitations [17, 18, 22, 23].

In some patients the disease runs a fulminant course with serious multisystem illness involving extensive pneumonia, diarrhea, encephalopathy, shock and acute renal failure. Mortality of hospitalized patients has been reported to exceed 20% [18]. Many patients, also in milder cases, have extrapulmonary manifestations of the disease including hypotension, renal failure, hematuria, myoglo-

binuria, myalgia, myositis, rhabdomyolysis, acute pancreatitis, pericarditis, hepatic dysfunction, thrombocytopenia, diffuse intravascular coagulation, hyponatremia, hypophosphatemia and hypoplastic anemia [18, 22, 24, 25]. Nervous system involvement is also common with symptoms including headache, desorientation, confusion, hallucinations, obtundation, delirium, stupor, seizures and peripheral neuropathy [15, 18, 22, 25].

In the last 6 years 10 patients (age 46–80 years, 8 males) with documented Legionella pneumonia have been observed in our unit. All patients needed mechanical ventilatory support and 5 patients survived. In 6 patients a chronic underlying medical condition was present. In 4 patients clinical signs of septic shock were apparent, usually with an extremely high cardiac output and acute renal failure necessitating hemodialysis developed in 2 patients. Two patients had seizures and 4 other had mild signs of nervous system involvement. Thrombocytopenia was documented in 5 patients and overt diffuse intravascular coagulation developed in one patient. Bradyarrhythmias were observed in 3 patients and in one of them peri- and myocarditis was documented on autopsy.

Diagnosis of Legionella infections can be made by culture of blood, sputum, bronchoscopically obtained pulmonary secretions, pleura exsudate or pulmonary tissue as in 5 of our patients. Direct immunofluorescence examination or a Dieterle silver stain of biopsy or autopsy material often demonstrates the organism (2 patients). Direct immunofluorescent antibody examination can also be used to identify the micro-organism in sputum or other material. Finally, a serologic diagnosis can be made by indirect immunofluorescent antibody examination. However, seroconversion in Legionnaire's disease may be delayed [26].

Erythromycin intravenously is generally given as the drug of choice. The addition of rifampicin may be considered in slowly responding or severe cases [14] but should not be used alone because resistance may rapidly develop. However the efficacy of adding rifampicin to erythromycin therapy is primarily based on theory and experience rather than convincing data.

In conclusion both Mycoplasma and Legionella infections appear to induce multisystem illness although pulmonary symptoms almost always predominate. Severe and life-threatening complications occur and warrant admission to the ICU often causing diagnostic problems. The importance of recognizing these infections is that they are treated best with antibiotics not usually administered for common types of pneumonia.

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