Bacterial Pneumonia in Elderly Japanese Populations

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ABSTRACT: Bacterial pneumonia is one of the most important infectious diseases in terms of incidence, effect on quality of life, mortality, and impact on society. Pneumonia was the third leading cause of death in Japan in 2011. In 2016, 119 650 Japanese people died of pneumonia, 96% of whom were aged 65 years and above. The symptoms of pneumonia in elderly people are often atypical. Aspiration pneumonia is seen more frequently than in young people because of swallowing dysfunction in the elderly. The mortality rate is also higher in the elderly than in young people. In Japan, the population is aging at an unprecedented rate, and pneumonia in the elderly will be increasingly important in medicine and medical economics in the future. To manage pneumonia in the elderly, it is important to accurately evaluate its severity, administer appropriate antibiotic treatment, and implement effective preventive measures.

KEYWORDS: elderly pneumonia, mortality, community-acquired pneumonia, hospital-acquired pneumonia, nursing and health care–associated pneumonia

Introduction

Bacterial pneumonia is one of the most important infectious diseases in terms of incidence, effect on quality of life, mortality, and impact on society. Infectious pneumonia is defined as an acute infectious inflammation of the lung parenchyma. The respiratory symptoms of pneumonia include cough, sputum production, dyspnea, and chest pain, whereas general symptoms such as fever, malaise, anorexia, and impaired level of consciousness may occur. Generally, crackles are heard on chest auscultation. In severe cases, there may be respiratory dysfunction and shock. Laboratory testing often shows leukocytosis with neutrophil predominance and elevated markers of inflammatory response, such as C-reactive protein, erythrocyte sedimentation rate, and procalcitonin. Chest x-ray often shows infiltrates and air bronchograms.

In Japan, bacterial pneumonia is classified as community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), or nursing and health care–associated pneumonia (NHCAP).[1] Although this classification influences choice of treatment to some extent, the medical staff must also evaluate the disease severity in each patient. In HAP and NHCAP, resistant bacteria are frequently the causative organisms, and the mortality rate is higher than that of CAP. As the elderly are often encountered in these health care settings, prudent attention to these factors is required for proper treatment.

Regarding the incidence of pneumonia in Japan, according to the report of the Ministry of Health, Labor and Welfare in 2014, the treatment rate of pneumonia in hospitalized patients (ie, the number of patients treated per day out of 100 000 people) was 34.6. The rate for outpatient treatment of pneumonia was 8.2.

In hospitalized elderly patients, the rate of treatment for pneumonia is higher than that for bronchial asthma, chronic obstructive pulmonary disease, and lung cancer. Pneumonia is thus a common disease in elderly Japanese individuals. In Japan, where the elderly aged 65 years and older receive a high rate of medical treatment and where the population is aging, it is obvious that pneumonia will be an increasingly important disease in the future.

In Japan, it is estimated that population aging has been advancing at an unprecedented rate against the background for many years of a declining birth rate. Therefore, pneumonia in the elderly is increasingly important in terms of both medical care and economic considerations. This review addresses aspects of bacterial pneumonia in the elderly that will become increasingly important in Japan in the future.

Epidemiology of Pneumonia in the Elderly

The aging of the population in Japan is progressing at an unprecedented rate compared with the rest of the world. According to the National Institute of Population and Social Security Studies "Japanese Population Estimate (in January 2012),"[2] the population of Japan will decrease from 128 060 000 in 2010 to 86 740 000 in 2060, whereas the number of elderly individuals, 65 years old and older, is estimated to increase from 29 480 000 to 37 410 000 over the same 50-year period. Under these circumstances, the proportion of the population more than 65 years old was projected to reach 26.7% in 2015 according to the Statistics Bureau of the Ministry of Internal Affairs and Communications.[3] The National Institute of Population and Social Security Research estimates that the proportion of elderly in Japan's population will reach 39.9% in 2060.

In particular, the growth of the old-old population of 75 years or older is remarkable and it is speculated that this trend will continue in the future.[4]

From a medical economic viewpoint, the rapid aging of the Japanese population is likely to change the relative incidence of particular diseases, which will have a major influence on Japanese medical care. According to reports in 2012,[5] medical expenses for those aged 65 years or older were 56.3% of the national total and those for people 75 years or older were 34.6% of the total. As the population in Japan is projected to age, it is urgent to address prevention as well as effective treatment of pneumonia in the elderly.

According to Japanese statistics,[4] the current most common causes of death are malignant neoplasm, heart disease, pneumonia, and cerebrovascular disease, with pneumonia surpassing cerebrovascular disease in 2011.

In 2015, 120 953 people died of pneumonia, accounting for 9.4% of total deaths.[6] Of those deaths from pneumonia, 96% were among those aged 65 years or older.[7] It is presumed that the main explanation for the increasing number of deaths from pneumonia in Japan is the aging of the population.

In addition, the death rate due to senescence has increased markedly in recent years and it seems that there is a close correlation between senility and pneumonia. For example, aspiration resulting in pneumonia may be more likely to occur as a result of senescence. Conversely, repeated bouts of pneumonia contribute to progressive senescence. In this way, even though pneumonia may not be the direct cause of death in elderly patients, previous episodes of pneumonia may have contributed to their physical decline and subsequent death.

CAP in the Elderly

Community-acquired pneumonia is a pneumonia that occurs in a person with only minor or no comorbidities. It occurs in community-dwelling individuals but may still be classified as CAP if it develops within 48 hours after hospital admission for some other cause.

According to a multicenter collaborative study in Japan,[8] the number of adults with CAP is estimated to be 1 880 000 people a year, with 70% of those affected being elderly. The death rate from CAP is estimated at 74 000 a year. Community-acquired pneumonia may present with typical pneumonia symptoms, such as cough, sputum production, fever, dyspnea, and chest pain. However, the elderly do not always have typical respiratory symptoms, complaining instead of nonspecific symptoms, such as an anorexia and decrease in activity.

In a series of 127 cases of pneumonia in elderly Japanese patients, 12 (9.4%) had a diagnosis of pneumonia on computed tomography that could not be diagnosed on chest radiography.[9] Therefore, one should not hesitate to order chest computed tomography if CAP is suspected in an elderly person with a normal chest x-ray.

Health Care–Associated Pneumonia in the Elderly

Hospital-acquired pneumonia is defined as pneumonia that develops after more than 48 hours of hospitalization. A subset of HAP is ventilator-associated pneumonia, occurring at least 48 hours after tracheal intubation and use of a ventilator. The definition of NHCAP includes pneumonia in patients (1) receiving long-term care in a health care facility or nursing home, (2) who are within 90 days of hospital discharge, (3) receiving ongoing nursing care at home, or (4) undergoing ongoing intravascular treatment, such as hemodialysis, antibiotics, cancer chemotherapy, and immunosuppressants. The JRS (Japanese Respiratory Society) Guidelines for the Management of Pneumonia in Adults[1] indicates a death rate from HAP of 30.4% and from NHCAP of 15.5%, similar to values in the United States.

Many patients who develop HAP and NHCAP are elderly, and, as with CAP in the elderly, they often do not exhibit typical respiratory symptoms. They may have nonspecific symptoms such as anorexia, incontinence, and decreased activity.

Compared with CAP, HAP and NHCAP are more frequently caused by antibiotic-resistant bacteria and have a higher mortality rate. The main pathogenic mechanisms of NHCAP are as follows: (1) aspiration pneumonia, (2) secondary bacterial pneumonia after viral infection such as influenza, (3) pneumonia with resistant bacteria related to intravascular treatment, and (4) infection that develops in immunosuppressed patients. Of these risk factors, the most common in elderly people is aspiration.

Aspiration pneumonia generally occurs because of swallowing dysfunction. The prevalence of cerebrovascular disease, dementia, and Parkinson disease or other neurologic disorders in the elderly increases the likelihood of a decreased swallowing reflex. This may occur even in the absence of obvious neurologic deficits, as apparently asymptomatic cerebral infarction may cause aspiration of oral secretions because of decreased swallowing and cough reflexes, resulting in pneumonia.[10]

It is speculated that aspiration is commonly involved in the pathogenesis of HAP and NHCAP in the elderly.[10,11] This is because underlying conditions associated with aspiration pneumonia overlap conditions occurring in patients with HAP and NHCAP, conditions which are seen less frequently in patients with CAP.

Elderly people may have a decreased cough reflex, so that silent aspiration may occur unnoticed by health care staff or family members. In addition, after a stroke, whether ischemic or hemorrhagic, the elderly patient may have swallowing dysfunction with a decreased deglutition reflex, increasing the risk of overt aspiration. Activities of daily living (ADLs) also decline in weak elderly people, especially those with cerebrovascular disease and dementia.[12] They may therefore not be able to maintain good oral hygiene, increasing the chance of pneumonia occurring as a result of subclinical aspiration of saliva with bacterial overgrowth.

Tube feedings, whether through a nasogastric tube or percutaneous endoscopic gastrostomy, are widely used in hospitals and nursing homes. These may be effective for nourishment

and hydration for bedridden elderly people with poor ADL in whom oral intake is insufficient. But, although it might seem that this would reduce the risk of aspiration, thereby decreasing the risk of pneumonia, tube feedings are in fact recognized as a common cause of aspiration.[13] Patients receiving tube feedings are still at risk of aspiration of oral secretions because of swallowing dysfunction, along with the possibility of poor oral hygiene.

Pathogenic Bacteria in Pneumonia in the Elderly

In a survey of the causal bacteria responsible for pneumonia in elderly Japanese patients,[14–16] the most frequently detected organisms were *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, Pseudomonas aeruginosa*, normal oral flora, and *Klebsiella*. In any study in Japan, *S pneumoniae* has been the most frequently detected pathogenic species. Oral bacteria and anaerobic bacteria have been detected at a rate of 10% or more, suggesting that pneumonia caused by bacteria from the oral cavity is common.[17]

According to a meta-analysis of research in Japan,[1] the most common organisms causing CAP are *S pneumoniae* (18.8%), followed by *H influenzae* (7.6%) and *Staphylococcus aureus* (4.2%).

However, bacteria responsible for HAP and NHCAP tend to include more antibiotic-resistant strains than those seen in CAP. According to an analysis of HAP in Japan,[1] methicillin-resistant *S aureus* accounts for 17.5%, *P aeruginosa* 13.9%, and methicillin-sensitive *S aureus* 6.5%. A similar analysis of NHCAP[1] reported *S pneumoniae* in 16.4% of cases, *Klebsiella* in 9.6%, and methicillin-resistant *S aureus* in 9.6%. However, it should be noted that in about half of cases, the bacteria responsible for aspiration pneumonia could not be identified.

Treatment and Management of Pneumonia in the Elderly

If multidrug-resistant bacteria are not assumed to be the causative organisms in elderly patients with pneumonia, it is usually not necessary to use broad-spectrum antibiotics.[14] Rather, narrow-spectrum antimicrobial drugs effective for the likely causative bacteria, including coverage of anaerobic bacteria, are regarded as the first choice for lower respiratory tract infection. In a Japanese study,[14–16] elderly patients with pneumonia had an initial response rate of about 85% when treated with β-lactam antibacterial agents along with a -lactamase inhibitor or with ceftriaxone and/or clindamycin. However, in-hospital mortality or 30-day mortality in that study was reported to be 10% or more.

In cases of HAP and NHCAP, in addition to a somewhat different range of likely pathogens, the patients' general condition may be quite poor. In many cases, it is difficult to obtain sputum for examination or to perform invasive diagnostic procedures. In such cases, as there is an increased risk of resistant bacteria, we should consider use of piperacillin/ tazobactam, carbapenem, a fourth-generation cephem, or a newer quinolone.

Complications of Elderly Pneumonia

Elderly patients with pneumonia often develop various complications in addition to pneumonia. In particular, patients with HAP/NHCAP often have underlying diseases associated with pneumonia, which cause death.

As mentioned above, the onset of HAP/NHCAP is closely related to aspiration. Risk factors for aspiration include dementia, malnutrition, cerebrovascular disease, Parkinson disease, gastroesophageal reflux disease, and so on. Therefore, it is clear that the complications of these underlying diseases are involved in the mortality of patients with pneumonia.

Actually, malignant tumor complications, such as decreased renal function, ADL, and serum albumin levels, are related to the poor prognosis in elderly patients with pneumonia.[18,19]

In addition, according to the analysis of necropsy results in a Japan study, the coexistence rate of Parkinson disease, malnutrition, osteoporosis, gastroesophageal reflux disease, and gallbladder stone was higher in patients with pneumonia than in those without pneumonia. Therefore, careful systemic management is required when treating patients with these diseases.[20]

Prevention of Pneumonia in the Elderly

As aspiration is a particular problem in the elderly, improving the swallow and cough reflexes may help prevent the development of pneumonia. Specifically, angiotensin-converting enzyme inhibitors, amantadine, and cilostazol have an effect of on improving swallowing and preventing aspiration pneumonia.[21–23]

Elderly people with good ADL can keep the oral cavity as clean as that of younger people and therefore have a lower incidence of pneumonia compared with the elderly with poor ADL.[24] For prevention of pneumonia, administering drugs for underlying diseases that also have a prophylactic effect against pneumonias is useful, as is good oral care. In patients with poor ADL, particularly those requiring tube feedings, it is important not only to use drugs to prevent pneumonia but also to reduce the risk of gastroesophageal reflux and aspiration by maintaining the patient in the sitting position during feedings. Other measures include frequent change of position to prevent pressure ulcers and aspiration of oral and nasopharyngeal secretions.[25,26]

Since October 2014, in Japan, administration of pneumococcal vaccine to elderly people aged 65 years or older has been recommended. Two kinds of vaccine, pneumococcal polysaccharide vaccine 23 (PPSV23) and pneumococcal conjugate vaccine 13 (PCV13), are available. In clinical trials among Japanese, PPSV23 contributed to suppression of acute exacerbations of chronic obstructive pulmonary disease.[27] In patients aged 75 years or older, administering both PPSV23 and influenza vaccine reduced hospitalization for pneumonia

compared with influenza vaccine alone.[28] It was also reported that giving PPSV23 to elderly patients in long-term care facilities reduced the incidence of pneumonia due to *S pneumoniae* by 63.8% and of pneumonia overall by 44.8%, hence lowering the pneumococcal pneumonia mortality rate.[29] There are as yet few clinical trials in Japan of PCV13. It is necessary to accumulate data on its use and to evaluate the optimal method of vaccine prevention of pneumonia in the elderly in Japan.

Author Contributions

NM designed the review article, reviewed the data, and wrote the manuscript. YY designed the review article and supervised the manuscript. All authors approved the final version.

Disclosures and Ethics

As a requirement of publication, authors have provided to the publisher signed confirmation of compliance with legal and ethical obligations including but not limited to the following: authorship and contributorship, conflicts of interest, privacy and confidentiality, and (where applicable) protection of human and animal research subjects. The authors have read and confirmed their agreement with the ICMJE authorship and conflict of interest criteria. The authors have also confirmed that this article is unique and not under consideration or published in any other publication. The external blind peer reviewers report no conflicts of interest.

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