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More than Meets the Eye: Bacteremic Pneumococcal Pneumonia as the Initial Presentation of Multiple Myeloma

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Male, 60-year-old
Final Diagnosis: *Streptococcus pneumoniae* bacteremia • multiple myeloma
Symptoms: Chills • cough • fever
Medication: —
Clinical Procedure: Bone marrow biopsy • CT scan • serology
Specialty: Hematology • Infectious Diseases • General and Internal Medicine

Objective: Challenging differential diagnosis

Background: Increased susceptibility to bacterial infections is a hallmark of multiple myeloma (MM). Invasive infections with *Streptococcus pneumoniae* may be the first manifestation of underlying MM. Clinicians treating patients with invasive *S. pneumoniae* infections may consider searching for underlying MM in the presence of certain diagnostic findings.

Case Report: A previously healthy 60-year-old man was referred from his general physician because of fever, cough, and chills despite treatment with clarithromycin. The patient had experienced night sweats, weight loss, and recurrent episodes of fever and cough during the last 3 months. Examination was significant for left-sided pulmonary rales. A chest X-ray showed a retrocardiac consolidation of the left lower lobe. The patient was started on empirical antimicrobial therapy for community-acquired pneumonia. Subsequently, blood and sputum cultures were positive for *S. pneumoniae*. Given the history of night sweats and weight loss, the discrepancy between elevated total protein and low albumin levels, and the diagnosis of pneumococcal bacteremia, multiple myeloma (MM) was suspected and confirmed by immunofixation and bone marrow biopsy.

Conclusions: This case showed that clinicians should be vigilant for features of MM, which are encountered during history (e.g., weight loss, bone pain) or routine laboratory workup (e.g., unexplained anemia, renal failure, hypercalcemia, or a discrepancy between elevated total protein and low albumin levels) in elderly patients presenting with invasive pneumococcal disease.

MeSH Keywords: Herpes Simplex • Multiple Myeloma • Pneumococcal Infections • Pneumonia, Bacterial

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/927904

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Background

Streptococcus pneumoniae is an important human pathogen responsible for approximately 2 million death per year worldwide [1]. It is included in the list of 12 antibiotic-resistant "priority pathogens" of the World Health Organization that pose the greatest threat to human health. Invasive pneumococcal disease (IPD) is a result of a breach of epithelial or endothelial barriers (tissue invasion) and is defined by an isolation of *S. pneumoniae* from normally sterile sites (e.g., blood, pleural space, or cerebrospinal fluid) [1,2]. Bacteremia and pneumonia are the most common manifestations of IPD, and they are associated with admission to an Intensive Care Unit in one-fourth of cases [3]. Several risk factors have been recognized, such as age, certain comorbidities, and immunosuppression.

Multiple myeloma (MM) is a clonal plasma cell proliferation disorder that is often preceded by a premalignant stage termed monoclonal gammopathy of undetermined significance (MGUS) [4]. Infections constitute one of the major complications with MM and even with MGUS and cause early morbidity and mortality [5–7]. In the United States, an estimated 32 270 new MM cases and associated 12 830 deaths will occur in 2020 [8]. Augustson et al. [5] analyzed 3107 newly diagnosed MM patients and found that 299 (10%) died within 60 days, with bacterial infections causing 135 (45%) of the early deaths. Higher disease burden, relapsed disease, and high-dose chemotherapy are important factors that determine infection risk [9].

Only a few case reports document IPD as the first manifestation of underlying MM [10]. The aim of the present report is to raise awareness of MM as a possible underlying disease in patients presenting with IPD and highlight features of MM encountered during history or routine laboratory workup.

Case Report

A previously healthy 60-year-old man was referred from his general practitioner due to recurrent episodes of fever and cough during the past 2.5 months. The most recent episode of fever, cough, and chills occurred 6 days before admission and did not response to treatment with clarithromycin. The patient reported that the first episode started shortly after a cruise trip to the Baltic Sea.

On presentation, the patient was febrile (temperature 40.1°C), tachycardic (109 beats/min), normotensive (138/81 mmHg), and tachypneic (28 breaths/min), and basal rales were noted over the left lung on auscultation. Additionally, the patient had perioral grouped blisters extending to the nasal orifices. Laboratory tests were significant for leukocytosis (13×10^9/L, normal range [3.5–10]$\times10^9$/L), elevated C-reactive protein (303 mg/mL, normal range <10 mg/L) and total protein (97 g/L, normal range 64–83 g/L), low albumin (26 g/L, normal range 35–52 g/L), and moderate hyponatremia (sodium 127 mmol/L, normal range 135–145 mmol/L). A chest X-ray showed a retrocardiac consolidation of the left lower lobe (**Figure 1**). The patient was diagnosed with community-acquired pneumonia and started on empirical antimicrobial therapy with piperacillin/tazobactam plus clarithromycin. On the next day, blood and sputum cultures were positive for *S. pneumoniae*, and the patient was de-escalated to intravenous benzylpenicillin and later to oral amoxicillin and treated for a total duration of 14 days.

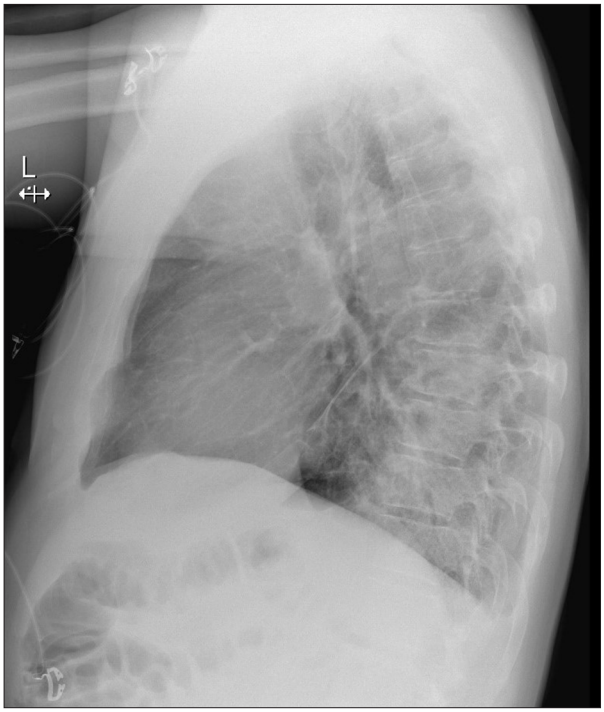

Figure 1. Lateral chest X-ray demonstrating a retrocardiac consolidation of the left lower lobe.

Additionally, due to a presumed cutaneous herpes simplex type 1 (HSV-1) infection, the patient was treated with valaciclovir. This diagnosis was later confirmed by a positive HSV-1 polymerase chain reaction result based on a swab taken from a perioral blister.

Given the recurrent episodes of fever and cough, the *S. pneumoniae* bacteremia, and the extensive HSV-1 infection, a detailed history was again undertaken, which revealed night sweats and a weight loss of 4 kg within the past 4 weeks. An HIV test was negative. Given the discrepancy between the elevated total protein and low albumin levels and the diagnosis of pneumococcal bacteremia, MM was suspected. Serum electrophoresis followed by immunofixation identified an IgG kappa monoclonal gammopathy (M-protein 31 g/L, free light-chain

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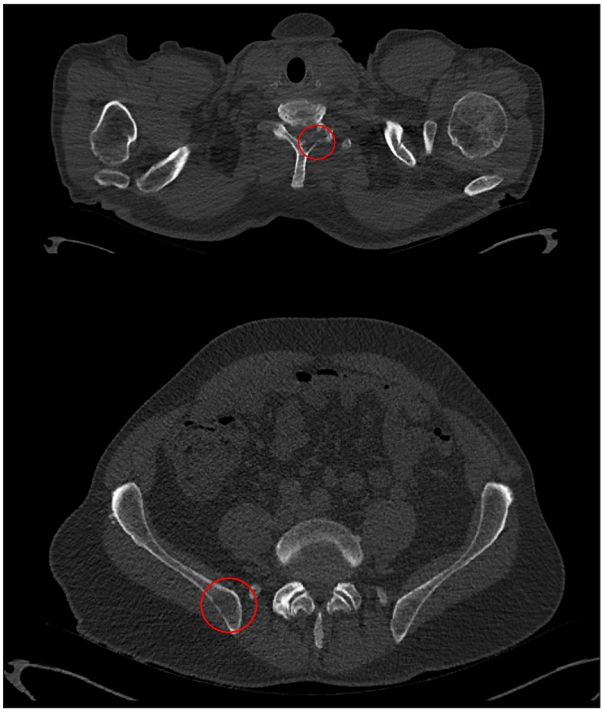

Figure 2. Whole-body low-dose computed tomography scan showing an osteolytic bone lesion in the seventh cervical vertebra and the right pelvis (red circles).

kappa 500.2 mg/L, free light-chain lambda 8.8 mg/L, kappa/lambda ratio 56.84). Bone marrow biopsy revealed a plasma cell infiltration of >60%. Whole-body low-dose computed tomography scan demonstrated 4 lytic lesions in the pelvis and 1 in the cervical spine (**Figure 2**). Hence, in accordance with the Revised International Myeloma Working Group diagnostic criteria [4], a diagnosis of MM IgG kappa was established. After the patient's recovery from the bacteremic pneumonia, standard induction treatment with bortezomib, lenalidomide, and dexamethasone was initiated, and the patient was scheduled for an autologous hematopoietic stem cell transplantation.

Treatment with intravenous immunoglobulin to prevent recurrent bacterial infections was discussed, and the patient received the 13-valent pneumococcal vaccination 1 month after discharge.

Discussion

An increased risk of bacterial and viral infections causing substantial morbidity and early mortality secondary to impaired humoral and cellular immune responses is well documented in patients with MM [5,6]. In particular, the burden of IPD including bacteremia is significantly higher (674 cases/100 000 per year *vs.* 11 cases/100 000 per year in the general adult population) [11]. However, despite this well-documented association, case reports of patients presenting with IPD as the first sign of underlying MM are rare. Kalambokis et al. [10] analyzed data from 17 cases presenting with an acute bacterial infection as the first manifestation of MM. *Streptococcus pneumoniae* was isolated as the causative pathogen in 65% of the cases (11/17) and was associated with bacteremia, septic arthritis, pneumonia, meningitis, and rarely cellulitis. In a large Swedish population-based study, Blimark et al. [6] showed that patients with MM had an increased risk of pneumonia and septicemia.

Susceptibility to infections is increased in MM patients for several reasons, including a diminished secretion of polyclonal immunoglobulins. In case of *S. pneumoniae* infection, antibody-dependent humoral immunity is crucial [12]. Strategies to prevent infections with *S. pneumoniae* therefore include administration of pneumococcal vaccines and intravenous immunoglobulin replacement [13], although vaccine responses may be impaired [14] and the benefit of intravenous immunoglobulin may be confined to patients with stable MM and recurrent serious infections or specific antibody deficiencies [15].

Conclusions

This case report highlights the importance of a thorough history and interpretation of laboratory tests in the context of IPD. Given the low incidence of underlying MM [16] and the variety of other predisposing diseases such as lymphoma, HIV, common variable immunodeficiency [17], or specific polysaccharide antibody deficiency [18], screening for MM is not justified in all patients without an apparent predisposing factor presenting with IPD.

However, clinicians should be vigilant for certain features of MM in elderly patients presenting with IPD that are encountered during history (e.g., weight loss, fatigue, bone pain), physical examination (e.g., peripheral neuropathy), and routine laboratory workup (e.g., unexplained anemia or renal failure, hypercalcemia, and a discrepancy between an elevated total protein and low albumin level) [19].

In conclusion, physicians treating IPD in an elderly patient without a readily identifiable predisposing disease may consider searching for underlying MM to facilitate the diagnosis in an earlier stage.

Conflicts of Interest

None.

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