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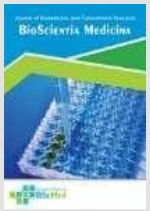

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Leukopenia as a Prognostic Factor in Severe Community-Acquired Pneumonia with Sepsis: A Case Report

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A B S T R A C T

Background: Community-acquired pneumonia (CAP) is a major cause of sepsis, and severe CAP with sepsis is associated with significant morbidity and mortality. Leukopenia, a decrease in white blood cell count, has been identified as a potential prognostic factor in sepsis, suggesting a poorer outcome. This case report aims to evaluate the role of leukopenia in predicting the clinical course and outcome of a patient with severe CAP and sepsis. **Case presentation:** A 73-year-old male presented with complaints of shortness of breath, cough, fever, and altered mental status. He was diagnosed with severe CAP with sepsis and sepsis-associated encephalopathy (SAE). Laboratory investigations revealed leukopenia. The patient's clinical condition improved over 10 days of treatment, coinciding with an improvement in his white blood cell count. **Conclusion:** This case report highlights the potential prognostic value of leukopenia in patients with severe CAP and sepsis. The patient's clinical improvement paralleled the recovery of his white blood cell count, suggesting that leukopenia may serve as a marker of disease severity and treatment response. Further studies are needed to validate these findings and establish the role of leukopenia in the management of severe CAP with sepsis.

1. Introduction

Community-acquired pneumonia (CAP) remains a significant public health concern, associated with considerable morbidity and mortality worldwide. It is a leading cause of hospitalization and death due to infectious diseases, particularly among older adults and those with underlying comorbidities. Sepsis, a life-threatening condition characterized by organ dysfunction resulting from a dysregulated host response to infection, is a frequent complication of CAP. Severe CAP, defined by the presence of specific clinical criteria, is associated with an increased risk of sepsis and adverse outcomes. Leukopenia, a decrease in the number of circulating white blood cells, has been recognized as a potential prognostic factor in sepsis. Studies have suggested that leukopenia may be associated with a higher risk of mortality in patients with sepsis, including those with CAP. However, the precise role of leukopenia in predicting the clinical course and outcome of severe CAP with sepsis remains unclear.[1,2]

This case report presents a 73-year-old male patient admitted with severe CAP, sepsis, and sepsis-associated encephalopathy (SAE). The patient's laboratory workup revealed leukopenia, prompting an evaluation of its potential prognostic significance. The case highlights the clinical course and outcome of the patient, emphasizing the correlation between

leukopenia and disease severity. Community-acquired pneumonia (CAP) is a major cause of morbidity and mortality globally, affecting millions of people each year. It is a leading cause of hospitalization and death due to infectious diseases, particularly among older adults and those with underlying comorbidities. The incidence of CAP varies depending on factors such as age, geographic location, and the presence of risk factors. In the United States, the estimated annual incidence of CAP is approximately 5-11 cases per 1,000 adults, resulting in over 1 million hospitalizations each year. The incidence is higher in older adults, with rates exceeding 20 cases per 1,000 individuals over the age of 65. Globally, the burden of CAP is even greater, particularly in low- and middle-income countries, where access to healthcare and preventive measures may be limited. Several factors increase the risk of developing CAP, including; Age: Older adults are more susceptible to CAP due to age-related decline in immune function and the increased likelihood of having underlying comorbidities; Smoking: Smoking is a well-established risk factor for respiratory infections, including CAP; Chronic Lung Diseases: Individuals with chronic lung diseases such as chronic obstructive pulmonary disease (COPD) and asthma are at increased risk of CAP; Immunodeficiency: Immunodeficiency, whether due to underlying medical conditions or immunosuppressive medications, increases the risk of CAP; Other Comorbidities: Other comorbidities such as diabetes mellitus, heart failure, and chronic liver disease have been associated with an increased risk of CAP. CAP typically occurs when microorganisms from the upper respiratory tract or the environment are aspirated into the lower respiratory tract, overwhelming the host's defense mechanisms. The most common pathogens implicated in CAP include *Streptococcus pneumoniae, Haemophilus influenzae, Mycoplasma pneumoniae, Chlamydophila pneumoniae*, and respiratory viruses. The inflammatory response triggered by the invading pathogens leads to the characteristic symptoms of CAP, such as cough, fever, shortness of breath, and chest pain. In severe cases, the inflammatory response can become dysregulated, leading to sepsis and organ dysfunction.[3,4]

Sepsis is a life-threatening condition characterized by organ dysfunction resulting from a dysregulated host response to infection. It is a frequent complication of CAP, particularly in patients with severe disease. Severe CAP is defined by the presence of specific clinical criteria, such as an elevated respiratory rate, hypoxemia, multilobar infiltrates on chest radiographs, and altered mental status. The pathophysiology of sepsis involves a complex interplay of inflammatory mediators, immune cells, and coagulation factors. The systemic inflammatory response can lead to widespread endothelial dysfunction, microvascular thrombosis, and impaired tissue perfusion, ultimately resulting in organ dysfunction. Leukopenia, a decrease in the number of circulating white blood cells, has been recognized as a potential prognostic factor in sepsis. Studies have suggested that leukopenia may be associated with a higher risk of mortality in patients with sepsis, including those with CAP. However, the precise role of leukopenia in predicting the clinical course and outcome of severe CAP with sepsis remains unclear. Several mechanisms may contribute to the development of leukopenia in sepsis, including increased consumption of white blood cells, impaired production in the bone marrow, redistribution of leukocytes from the circulation to the tissues, and the effects of bacterial toxins or pathogens on leukocyte function. In patients with CAP, leukopenia has been associated with increased mortality, particularly in those with severe disease. The presence of leukopenia may reflect the severity of the inflammatory response and the degree of immune dysregulation in sepsis. It may also indicate an impaired ability to mount an effective immune response against the invading pathogens. Sepsis-associated encephalopathy (SAE) is a diffuse cerebral dysfunction that can occur in patients with sepsis. It is characterized by altered mental status, ranging from mild confusion to coma. The pathophysiology of SAE is complex and not fully understood, but it is thought to involve a combination

of factors, including inflammation, microcirculatory dysfunction, and neurotransmitter imbalances. SAE is associated with increased mortality and long-term cognitive impairment in patients with sepsis. The presence of SAE in patients with severe CAP and sepsis may further complicate their clinical course and increase their risk of adverse outcomes.[5,6]

The diagnosis and management of severe CAP with sepsis require prompt recognition and aggressive treatment. The Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) have published guidelines for the diagnosis and treatment of CAP, including criteria for identifying severe CAP. These guidelines emphasize the importance of early and appropriate antibiotic therapy, supportive care, and management of complications such as sepsis and SAE. The initial evaluation of patients with suspected CAP should include a thorough history and physical examination, chest radiograph, and laboratory studies, including complete blood count, blood cultures, and inflammatory markers. In patients with severe CAP, additional investigations such as arterial blood gas analysis and blood lactate measurement may be necessary. Empirical antibiotic therapy should be initiated promptly in patients with suspected CAP, with the choice of antibiotics guided by the severity of illness, risk factors for multidrug-resistant organisms, and local antibiotic resistance patterns. In patients with severe CAP and sepsis, broad-spectrum antibiotics covering both typical and atypical pathogens should be administered intravenously. Supportive care is essential in the management of severe CAP with sepsis and may include oxygen supplementation, intravenous fluids, and mechanical ventilation if necessary. The management of SAE focuses on supportive care and treatment of the underlying sepsis.[7,8]

Several factors have been associated with increased mortality in patients with severe CAP and sepsis, including; Age: Older adults have a higher risk of mortality from severe CAP and sepsis; Comorbidities: The presence of underlying comorbidities such as chronic lung disease, heart failure, and diabetes mellitus increases the risk of mortality; Severity of Illness: The severity of pneumonia and sepsis, as assessed by clinical criteria and laboratory parameters, is a strong predictor of mortality; Leukopenia: Leukopenia has been identified as a potential risk factor for mortality in patients with severe CAP and sepsis; Sepsis-Associated Encephalopathy (SAE): The presence of SAE is associated with increased mortality in patients with sepsis. Severe CAP with sepsis is a life-threatening condition associated with significant morbidity and mortality. Leukopenia has been identified as a potential prognostic factor in sepsis, suggesting a poorer outcome.[9,10] This case report aims to evaluate the role of leukopenia in predicting the clinical course and outcome of a patient with severe CAP and sepsis.

2. Case Presentation

A 73-year-old male presented to the emergency department with a 3-day history of progressive shortness of breath. The shortness of breath had been persistent and worsened significantly the day before his admission. In addition to his breathing difficulties, the patient experienced an altered mental state with poor responsiveness, prompting his family to seek immediate medical attention. He was initially taken to the emergency department of a private hospital in Padang, where a chest X-ray was performed and subsequently referred to Dr. M. Djamil General Hospital for further evaluation and treatment.

The patient's family reported that he had been experiencing a cough for the past week. The cough was characterized by thick, yellowish sputum, and occurred intermittently. There was no history of coughing up blood. Along with the cough, the patient had been experiencing intermittent low-grade fevers for the past three days, without chills. He also reported a decreased appetite over the past week but denied any weight loss. His current weight was recorded as 55 kg. There were no complaints of nausea, vomiting, or changes in bowel or bladder habits.

The patient was retired and had previously worked as a farmer. He had a history of smoking, starting at

the age of 25 and continuing for 38 years, with a smoking intensity of 12 cigarettes per day. He had successfully quit smoking 20 years prior, classifying him as a former smoker with a moderate Brinkman index. He lived in a permanent residence with four family members, with adequate ventilation and lighting. The patient's medical history was significant for hypertension, which was being managed with regular antihypertensive medication. He denied any history of malignancy, tuberculosis, asthma, or other lung diseases. There was no family history of lung disease. He had not been hospitalized in the past three months.

On examination, the patient appeared severely ill and was somnolent, with a Glasgow Coma Scale (GCS) score of 10 (E3M4V3). His vital signs were as follows; Blood pressure: 110/76 mmHg with a mean arterial pressure (MAP) of 87 mmHg; Heart rate: 110 beats per minute; Respiratory rate: 32 breaths per minute; Temperature: 38°C; Oxygen saturation: 88% on room air. The patient's body mass index (BMI) was calculated to be 20.20 kg/m^2 based on his height (165 cm) and weight (55 kg). Physical examination revealed no other significant abnormalities. Lung examination revealed symmetrical chest expansion during both quiet breathing and deep inspiration. Palpation was difficult to assess due to the patient's decreased level of consciousness. Percussion of the chest wall was resonant bilaterally. Auscultation revealed brochovesicular breath sounds with rhonchi in both lung fields, predominantly in the right lower lobe. No wheezing was noted. Examination of the extremities revealed warm skin and a capillary refill time of fewer than 2 seconds.

The chest X-ray taken at the private hospital prior to the patient's transfer showed multilobar infiltrates predominantly in the basal regions, along with cardiomegaly (Figure 2). Upon arrival at Dr. M. Djamil General Hospital, blood samples were immediately collected for arterial blood gas (ABG) analysis and a complete blood count. Blood cultures were also obtained from both arms. Empirical antibiotic therapy was initiated, and intravenous fluids were administered. The complete blood count revealed leukopenia (1,900/mm^3), thrombocytopenia (140,000/mm^3), and an elevated total bilirubin level (1.8 mg/dL). Procalcitonin was also significantly elevated (62.09 ng/mL). ABG analysis showed respiratory alkalosis with an elevated lactate level (2.5 mmol/L) and a normal PaO_2/FiO_2 ratio (Table 1).

Based on the patient's clinical presentation, which included an altered mental state (GCS 10), an elevated respiratory rate (32 breaths/min), leukopenia (1,900/mm^3) (Figure 1), and the presence of multilobar infiltrates on the chest X-ray, a working diagnosis of severe community-acquired pneumonia (CAP) was established. The Pneumonia Severity Index (PSI) score was calculated to be 113, and the CURB-65 score was 3, both indicating a high severity of illness. The patient also met the criteria for sepsis, with the altered mental status attributed to sepsis-associated encephalopathy (SAE). Meningoencephalitis was considered a differential diagnosis. However, a consultation with the neurology department did not reveal any signs of meningeal irritation, lateralizing signs, or pathological reflexes, making meningoencephalitis less likely. Initial management included oxygen supplementation via nasal cannula at 4 liters/minute (FiO_2 30%), intravenous fluid administration with 0.9% NaCl at 500 cc every 8 hours, and empirical antibiotic therapy with intravenous ampicillin-sulbactam 3 grams every 8 hours and levofloxacin 750 mg every 24 hours. N-acetylcysteine 200 mg every 12 hours and paracetamol 500 mg every 6 hours were also administered. A nasogastric tube (NGT) was inserted to prevent aspiration and facilitate nutritional support, and a urinary catheter was placed for fluid balance monitoring.

On day 4 of hospitalization, the patient's mental status showed improvement, although he remained somnolent, with a GCS score of 12 (E3M5V4). His respiratory symptoms were also less severe. His vital signs were as follows; Blood pressure: 120/80 mmHg; Heart rate: 80 beats per minute; Respiratory rate: 25 breaths per minute; Temperature: 36.8°C; Oxygen

saturation: 95% with nasal cannula at 4 liters/minute. His fluid balance over 24 hours was positive at +200 cc. Repeat laboratory tests showed a slight improvement in leukopenia (2,500/mm^3) and thrombocytopenia (149,000/mm^3). However, procalcitonin remained elevated (2.83 ng/mL). By day 5, the patient had regained full consciousness, and his respiratory symptoms continued to improve. His vital signs were as follows; Blood pressure: 130/90 mmHg; Heart rate: 75 beats per minute; Respiratory rate: 24 breaths per minute; Temperature: 37.2°C; Oxygen saturation: 97% with nasal cannula at 4 liters/minute. His fluid balance over 24 hours was positive at +250 cc. Sputum culture obtained on admission grew *Staphylococcus haemolyticus*, which was sensitive to vancomycin, tetracycline, and tigecycline. Blood cultures from both arms remained negative. Based on the culture results, the patient's antibiotic therapy was adjusted to intravenous vancomycin 1 gram every 12 hours. Previous antibiotics were discontinued, and other supportive therapies were continued based on the patient's symptoms. On day 7, a repeat chest X-ray was performed to assess the progression of the pneumonia. The X-ray showed a worsening of the infiltrates in the right lung, which was inconsistent with the patient's clinical improvement. By day 10, the patient's respiratory symptoms had significantly improved. His vital signs were as follows; Blood pressure: 130/90 mmHg; Heart rate: 75 beats per minute; Respiratory rate: 24 breaths per minute; Temperature: 37.2°C; Oxygen saturation: 97% on room air. Repeat laboratory tests showed further improvement in leukopenia (3,500/mm^3) and a decrease in procalcitonin (1.26 ng/mL). The patient's overall clinical condition had significantly improved, and he was deemed stable for discharge. He was discharged home with oral antibiotic therapy and scheduled for follow-up appointments at the pulmonology clinic.

Table 1. Timeline of disease.

Days before admission	Symptoms
7	Cough with thick yellowish sputum decreased appetite
3	Shortness of breath, fever
1	Worsening shortness of breath altered mental status
Admission	Severe shortness of breath, productive cough, altered mental status, fever (38°C), tachycardia (110 bpm), tachypnea (32 breaths/min), hypotension (110/76 mmHg), hypoxemia (SpO_2 88%), leukopenia (1,900/mm^3), thrombocytopenia (140,000/mm^3), elevated bilirubin (1.8 mg/dL), elevated procalcitonin (62.09 ng/mL), respiratory alkalosis with elevated lactate (2.5 mmol/L)
Day 4	Improved mental status, decreased respiratory distress, leukopenia (2,500/mm^3), thrombocytopenia (149,000/mm^3), elevated procalcitonin (2.83 ng/mL)
Day 5	Full consciousness, decreased respiratory distress, normal vital signs, positive sputum culture for Staphylococcus haemolyticus
Day 7	Improved chest radiograph
Day 10	Significant clinical improvement, resolution of leukopenia, normal vital signs, discharge from hospital

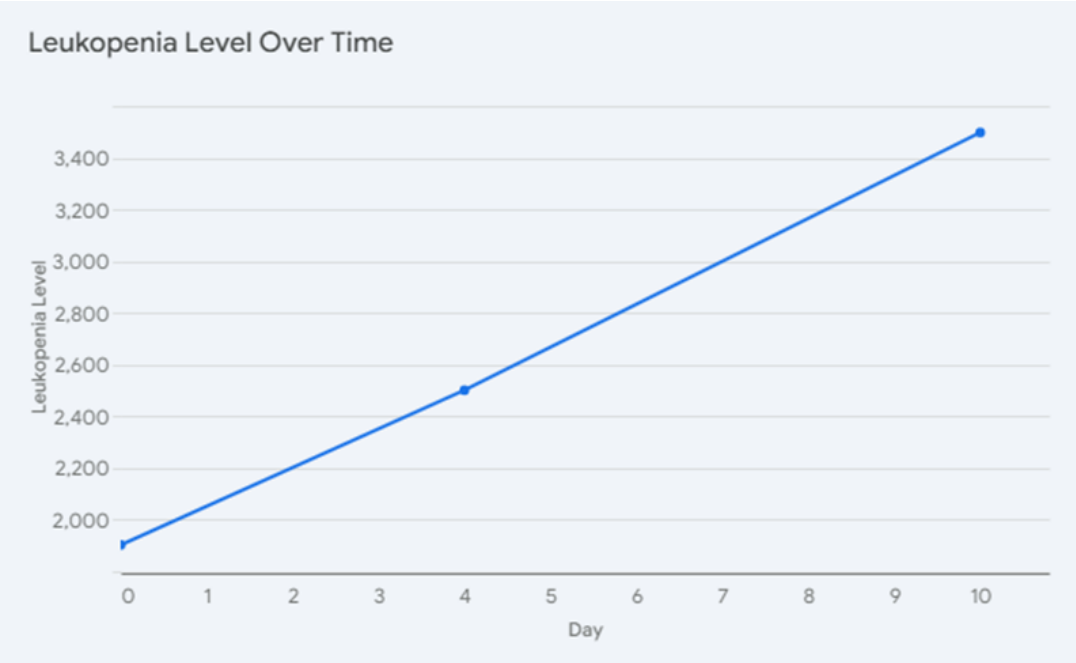
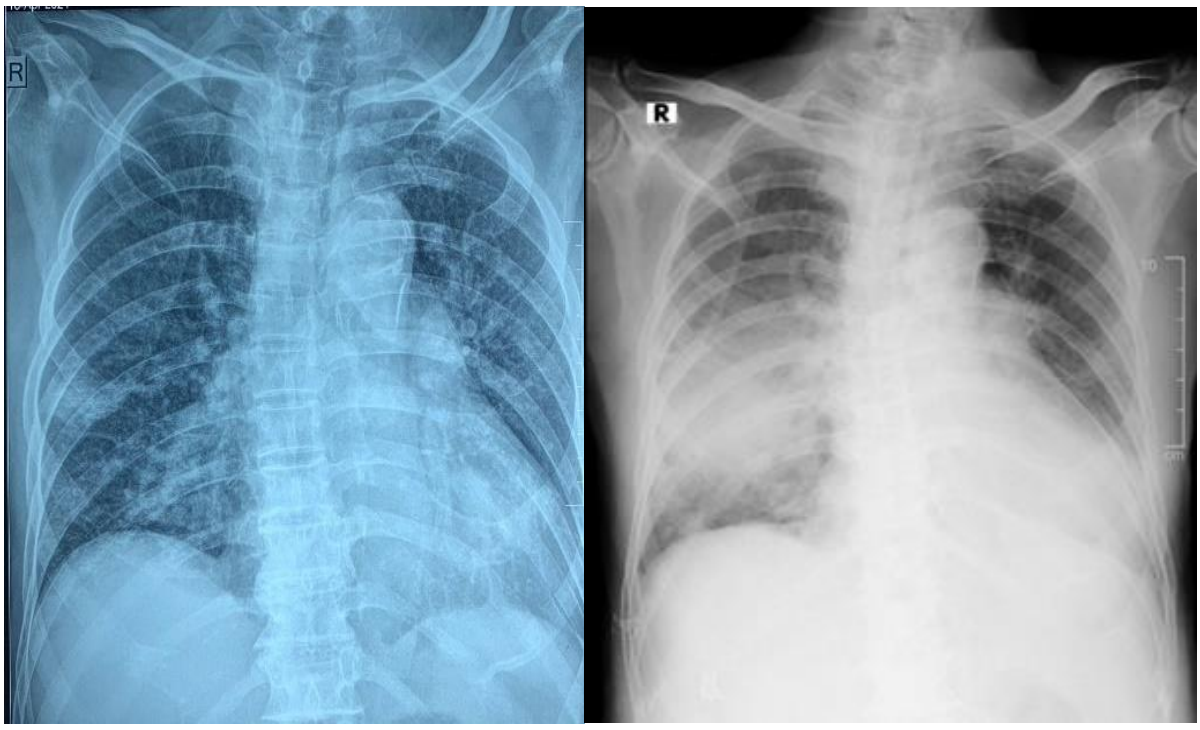


Figure 1. Leukopenia level over time.



A B

Figure 2. Chest X-Ray. A. Admission. B. 7 days after admission.

3. Discussion

Severe community-acquired pneumonia (CAP) frequently progresses to sepsis, a life-threatening condition characterized by organ dysfunction resulting from a dysregulated host response to infection. The pathophysiology of sepsis involves a complex interplay of inflammatory mediators, immune cells, and coagulation factors. The systemic inflammatory response can lead to widespread endothelial dysfunction, microvascular thrombosis, and impaired tissue perfusion, ultimately resulting in organ dysfunction. In this case, the patient's initial presentation with severe CAP and sepsis was marked by several clinical and laboratory features indicative of a significant inflammatory response and potential organ dysfunction. His altered mental status, elevated respiratory rate, and hypoxemia suggested respiratory and neurological compromise. The laboratory findings of leukopenia, thrombocytopenia, and elevated procalcitonin and lactate levels further supported the diagnosis of sepsis and indicated a significant inflammatory response. The pathophysiology of sepsis in severe CAP begins with an exuberant inflammatory response to the invading pathogen. In CAP, the lungs are the primary site of infection, and the inflammatory response is initiated by the activation of alveolar macrophages and other immune cells in the lungs. These cells release a variety of inflammatory mediators, such as cytokines, chemokines, and reactive oxygen species, which recruit neutrophils and other immune cells to the site of infection. In severe CAP, the inflammatory response can extend beyond the lungs, leading to a systemic inflammatory response syndrome (SIRS). SIRS is characterized by a constellation of clinical findings, including fever, tachycardia, tachypnea, and leukocytosis or leukopenia. The systemic inflammatory response can lead to widespread activation of the endothelium, the lining of blood vessels. Endothelial dysfunction is a key feature of sepsis and is characterized by increased permeability of the endothelium, allowing fluid and inflammatory cells to leak into the tissues. This can lead to tissue edema and impaired tissue perfusion. Sepsis is also associated with abnormalities in coagulation, leading to a procoagulant state. This can result in the formation of microthrombi in the small blood vessels, further impairing tissue perfusion. The combination of endothelial dysfunction, coagulation abnormalities, and impaired tissue perfusion can lead to organ dysfunction. The lungs are often the first organs to be affected in severe CAP with sepsis, but other organs, such as the kidneys, liver, and brain, can also be involved. Sepsis-associated encephalopathy (SAE) is a common complication of sepsis and is characterized by altered mental status, ranging from mild confusion to coma. The pathophysiology of SAE is complex and not fully understood, but it is thought to involve a combination of factors, including inflammation, microcirculatory dysfunction, and neurotransmitter imbalances. The patient in this case presented with several clinical and laboratory features indicative of severe CAP and sepsis. His altered mental status, elevated respiratory rate, and hypoxemia suggested respiratory and neurological compromise. The laboratory findings of leukopenia, thrombocytopenia, and elevated procalcitonin and lactate levels further supported the diagnosis of sepsis and indicated a significant inflammatory response. The patient's altered mental status was likely due to a combination of factors, including hypoxemia, sepsis-associated encephalopathy (SAE), and the effects of inflammatory mediators on the brain. The elevated respiratory rate was a response to hypoxemia and the increased work of breathing due to pneumonia. Hypoxemia, or low blood oxygen levels, is a common feature of severe CAP and sepsis. It can result from impaired gas exchange in the lungs due to pneumonia, as well as from impaired tissue perfusion due to sepsis. Leukopenia, or a low white blood cell count, is a common finding in sepsis and can be a marker of disease severity. It may result from increased consumption of white blood cells, impaired production in the bone marrow, or redistribution of leukocytes from the circulation to the tissues. Thrombocytopenia, or a low platelet count, is also a common finding in sepsis and can be a marker

of disease severity. It may result from consumption of platelets due to coagulation abnormalities or from impaired production in the bone marrow. Procalcitonin is a protein that is produced in response to bacterial infections and is often elevated in sepsis. It can be a useful marker for distinguishing bacterial infections from other causes of inflammation. Lactate is a byproduct of anaerobic metabolism and is often elevated in sepsis due to impaired tissue perfusion. It can be a marker of disease severity and is used to guide resuscitation efforts.[11,12]

Leukopenia, a decrease in the number of circulating white blood cells, has been recognized as a potential prognostic factor in sepsis. Several studies have suggested that leukopenia may be associated with a higher risk of mortality in patients with sepsis, including those with CAP. However, the precise role of leukopenia in predicting the clinical course and outcome of severe CAP with sepsis remains unclear. Several mechanisms may contribute to the development of leukopenia in sepsis, including increased consumption of white blood cells, impaired production in the bone marrow, redistribution of leukocytes from the circulation to the tissues, and the effects of bacterial toxins or pathogens on leukocyte function. In patients with CAP, leukopenia has been associated with increased mortality, particularly in those with severe disease. The presence of leukopenia may reflect the severity of the inflammatory response and the degree of immune dysregulation in sepsis. It may also indicate an impaired ability to mount an effective immune response against the invading pathogens. In this case, the patient's initial leukopenia was quite severe (1,900/mm^3), which raised concerns about his prognosis. However, his white blood cell count gradually recovered as his clinical condition improved. This suggests that leukopenia may serve as a dynamic marker of disease severity and treatment response in patients with severe CAP and sepsis. Leukopenia is a decrease in the number of white blood cells (leukocytes) circulating in the bloodstream. White blood cells are an essential part of the immune system, playing a crucial role in defending the body against infection and other foreign invaders. Leukopenia can impair the body's ability to fight off infection, making individuals more susceptible to severe illness and complications. Sepsis is a life-threatening condition that arises when the body's response to an infection becomes dysregulated, leading to widespread inflammation and potential organ damage. In severe sepsis, the inflammatory response can be so overwhelming that it impairs the function of vital organs, such as the lungs, kidneys, and heart. Leukopenia is frequently observed in patients with sepsis and is often associated with a poorer prognosis. In sepsis, white blood cells are recruited to the site of infection to fight off the invading pathogens. However, the intense inflammatory response can lead to increased consumption and destruction of these cells, resulting in leukopenia. The bone marrow is responsible for producing white blood cells. In sepsis, the inflammatory response can suppress bone marrow function, leading to decreased production of white blood cells and subsequent leukopenia. During sepsis, white blood cells may be redistributed from the circulating blood to the tissues, where they are needed to fight the infection. This can result in a temporary decrease in the number of white blood cells in the bloodstream, leading to leukopenia. Some bacterial toxins and pathogens can directly damage white blood cells or interfere with their function, contributing to leukopenia. Community-acquired pneumonia (CAP) is a common cause of sepsis. In patients with severe CAP, the inflammatory response can be particularly intense, increasing the likelihood of developing sepsis and its associated complications. Leukopenia has been identified as a potential prognostic marker in patients with severe CAP and sepsis. Studies have shown that patients with leukopenia at the time of diagnosis or during the course of their illness have a higher risk of mortality compared to those with normal white blood cell counts. The presence of leukopenia in severe CAP and sepsis may reflect the severity of the inflammatory response and the degree of immune dysregulation. It may also indicate an impaired ability to mount an

effective immune response against the invading pathogens. In this case, the patient's initial leukopenia was quite severe (1,900/mm^3), which raised concerns about his prognosis. However, his white blood cell count gradually recovered as his clinical condition improved. This suggests that leukopenia may serve as a dynamic marker of disease severity and treatment response in patients with severe CAP and sepsis. The improvement in the patient's white blood cell count likely reflects a combination of factors, including the resolution of the infection, the restoration of bone marrow function, and the return of white blood cells from the tissues to the circulation.[13,14]

Sepsis-associated encephalopathy (SAE) is a diffuse cerebral dysfunction that can occur in patients with sepsis. It is characterized by altered mental status, ranging from mild confusion to coma. The pathophysiology of SAE is complex and not fully understood, but it is thought to involve a combination of factors, including inflammation, microcirculatory dysfunction, and neurotransmitter imbalances. SAE is associated with increased mortality and long-term cognitive impairment in patients with sepsis. The presence of SAE in patients with severe CAP and sepsis may further complicate their clinical course and increase their risk of adverse outcomes. In this case, the patient's initial presentation with altered mental status raised the suspicion for SAE. The absence of meningeal signs or focal neurological deficits on examination and the lack of findings suggestive of an alternative cause for his encephalopathy further supported the diagnosis of SAE. Sepsis-associated encephalopathy (SAE) is a serious neurological complication that can occur in individuals with sepsis. It is characterized by a diffuse dysfunction of the brain, leading to a wide range of neurological symptoms, from mild confusion and disorientation to delirium, seizures, and even coma. Sepsis triggers a systemic inflammatory response, releasing inflammatory mediators that can cross the blood-brain barrier and affect brain function. These mediators can disrupt neuronal signaling, cause swelling in the brain, and contribute to the development of SAE. Sepsis can also disrupt the delicate balance of blood flow within the brain. The inflammatory response can damage blood vessels, leading to impaired blood flow, oxygen delivery, and nutrient supply to brain cells. This microcirculatory dysfunction can contribute to neuronal dysfunction and the development of SAE. Neurotransmitters are chemical messengers that transmit signals between nerve cells in the brain. Sepsis can disrupt the balance of neurotransmitters, leading to abnormal brain activity and contributing to the neurological symptoms of SAE. The blood-brain barrier is a protective mechanism that separates the circulating blood from the brain tissue, regulating the passage of substances into the brain. Sepsis can disrupt the integrity of the blood-brain barrier, allowing toxins and inflammatory mediators to enter the brain, further contributing to neuronal dysfunction and SAE. The clinical manifestations of SAE can vary widely depending on the severity of the encephalopathy and the individual patient. This can range from mild confusion and disorientation to delirium, stupor, and coma. Patients with SAE may experience difficulties with attention, memory, and executive functions such as planning and decision-making. SAE can cause changes in psychomotor activity, such as restlessness, agitation, or slowed movements. Patients with SAE may experience sleep-wake cycle disruptions, including insomnia or excessive sleepiness. In some cases, SAE can lead to seizures, although this is less common. Diagnosing SAE can be challenging, as there is no single specific test. A confirmed diagnosis of sepsis is a prerequisite for diagnosing SAE. The presence of altered mental status, as evidenced by changes in consciousness, behavior, or cognitive function, is a key feature of SAE. It is important to exclude other potential causes of encephalopathy, such as metabolic disturbances, drug toxicity, or primary neurological conditions. Neuroimaging studies, such as magnetic resonance imaging (MRI) or computed tomography (CT) scans of the brain, may be performed to rule out other structural brain abnormalities. Electroencephalography (EEG) can be

used to assess brain activity and may reveal abnormalities suggestive of SAE. SAE is associated with increased mortality in patients with sepsis. The severity of encephalopathy is a strong predictor of outcome, with patients experiencing more severe neurological impairment having a higher risk of mortality. Even in patients who survive sepsis, SAE can lead to long-term cognitive impairment. Studies have shown that individuals who have experienced SAE may have persistent difficulties with memory, attention, and executive functions, affecting their quality of life and functional independence. The management of SAE focuses primarily on supportive care and treatment of the underlying sepsis. Maintaining adequate oxygenation, hydration, and nutrition is crucial in managing patients with SAE. Aggressive treatment of the underlying sepsis is essential to improve outcomes in SAE. This includes prompt administration of antibiotics, source control measures to address the infection, and supportive care to maintain organ function. There is ongoing research into neuroprotective strategies that may help to mitigate brain injury in SAE. However, currently, no specific neuroprotective therapies have been definitively proven to improve outcomes in SAE.[15,16]

The management of severe CAP with sepsis and SAE requires a multifaceted approach, including prompt initiation of appropriate antibiotic therapy, supportive care, and close monitoring for complications. In this case, the patient received empirical antibiotic therapy with ampicillin-sulbactam and levofloxacin, which was later adjusted to vancomycin based on the sputum culture results. The choice of antibiotics was guided by the severity of the illness, risk factors for multidrug-resistant organisms, and local antibiotic resistance patterns. Supportive care is essential in the management of severe CAP with sepsis and SAE. This may include oxygen supplementation, intravenous fluids, and mechanical ventilation if necessary. The management of SAE focuses on supportive care and treatment of the underlying sepsis. The prompt initiation of appropriate antibiotic therapy is critical in the management of severe CAP with sepsis. Empirical antibiotic therapy should be started as soon as the diagnosis is suspected, even before the results of microbiological cultures are available. The choice of antibiotics should be guided by the severity of illness, risk factors for multidrug-resistant organisms, and local antibiotic resistance patterns. Once the results of microbiological cultures are available, antibiotic therapy should be tailored to the specific pathogen(s) identified. This is known as targeted antibiotic therapy and helps to ensure that the patient is receiving the most effective antibiotics for their infection. The duration of antibiotic therapy for severe CAP with sepsis is typically 7-10 days, but it may be longer depending on the patient's clinical response and the severity of the illness. Oxygen supplementation is often required in patients with severe CAP with sepsis to maintain adequate oxygenation. This may be delivered via nasal cannula, face mask, or mechanical ventilation, depending on the severity of respiratory distress. Intravenous fluids are used to maintain adequate hydration and blood pressure in patients with severe CAP with sepsis. The type and amount of fluids administered will depend on the patient's individual needs and the severity of their illness. Mechanical ventilation may be required in patients with severe CAP with sepsis who develop respiratory failure. Mechanical ventilation helps to support breathing and maintain adequate oxygenation. Source control refers to measures taken to address the underlying cause of the infection. In the case of severe CAP with sepsis, this may involve drainage of pleural effusions or abscesses, if present. Vasopressors are medications that help to increase blood pressure in patients with sepsis who develop hypotension. They work by constricting blood vessels and increasing the heart's pumping action. Inotropes are medications that help to increase the heart's pumping action in patients with sepsis who develop heart failure. They work by increasing the force of contraction of the heart muscle. Corticosteroids are sometimes used in the management of severe CAP with sepsis to help reduce inflammation. However, their use is controversial, and

they are typically reserved for patients who do not respond to other therapies. Patients with severe CAP with sepsis are at risk for developing organ dysfunction, including respiratory failure, kidney failure, and shock. Close monitoring of organ function is essential to identify and manage complications promptly. SAE is a common complication of sepsis and can lead to altered mental status, ranging from mild confusion to coma. Close monitoring of neurological status is essential to identify and manage SAE promptly. Other potential complications of severe CAP with sepsis include acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC), and septic shock.[17,18]

Several factors have been associated with increased mortality in patients with severe CAP and sepsis, including older age, the presence of comorbidities, the severity of illness, leukopenia, and SAE. In this case, the patient had several risk factors for adverse outcomes, including his age, history of smoking, and the presence of SAE. However, his clinical condition gradually improved with appropriate treatment, and he was able to be discharged home after 10 days of hospitalization. The patient's recovery may be attributed to several factors, including the prompt initiation of appropriate antibiotic therapy, supportive care, and the absence of other significant comorbidities. The resolution of his leukopenia may also have contributed to his favorable outcome. The prognosis of severe CAP with sepsis is influenced by a multitude of factors that interact in complex ways. Identifying these factors is crucial for risk stratification, treatment optimization, and informed decision-making. Advanced age is a well-established risk factor for adverse outcomes in severe CAP with sepsis. Older adults tend to have decreased physiological reserve, impaired immune function, and a higher prevalence of comorbidities, all of which contribute to increased susceptibility to severe infections and their complications. The presence of underlying comorbidities, such as chronic lung diseases (COPD, asthma), cardiovascular diseases (heart failure, coronary artery disease), diabetes mellitus, and chronic kidney disease, significantly worsens the prognosis of severe CAP with sepsis. Comorbidities can impair immune function, compromise organ reserve, and increase the risk of complications. The severity of both pneumonia and sepsis is a strong predictor of outcome. Clinical markers of severity include altered mental status, tachypnea, hypoxemia, and hypotension. Laboratory markers, such as leukopenia, thrombocytopenia, elevated procalcitonin, and elevated lactate, also reflect the severity of the inflammatory response and organ dysfunction. Leukopenia, a decrease in the number of circulating white blood cells, has emerged as a potential prognostic marker in severe CAP with sepsis. It may reflect the severity of the inflammatory response, impaired immune function, or the effects of bacterial toxins or pathogens on leukocyte function. Studies have shown that patients with leukopenia at the time of diagnosis or during the course of their illness have a higher risk of mortality compared to those with normal white blood cell counts. SAE, a diffuse cerebral dysfunction associated with sepsis, is another significant prognostic factor in severe CAP with sepsis. It can manifest as altered mental status, ranging from mild confusion to coma. The presence of SAE is associated with increased mortality and long-term cognitive impairment in patients with sepsis. In the presented case, the patient had several risk factors for adverse outcomes, including his age (73 years), history of smoking, and the presence of SAE. However, his clinical condition gradually improved with appropriate treatment, and he was able to be discharged home after 10 days of hospitalization. The patient received empirical antibiotic therapy with ampicillin-sulbactam and levofloxacin promptly after admission, which was later adjusted to vancomycin based on the sputum culture results. The early initiation of appropriate antibiotic therapy is crucial in controlling the infection and preventing its progression. The patient received comprehensive supportive care, including oxygen supplementation, intravenous fluids, and nutritional support. Supportive care is essential in maintaining organ

function and preventing complications in severe CAP with sepsis. The patient did not have any other significant comorbidities besides hypertension, which was well-controlled. The absence of comorbidities likely contributed to his favorable outcome, as comorbidities can worsen the prognosis of severe CAP with sepsis. The patient's initial leukopenia gradually resolved as his clinical condition improved. The resolution of leukopenia may have contributed to his favorable outcome, as leukopenia can be a marker of disease severity and impaired immune function.[19,20]

4. Conclusion

This case report highlights the potential prognostic value of leukopenia in patients with severe CAP and sepsis. The patient's clinical improvement paralleled the recovery of his white blood cell count, suggesting that leukopenia may serve as a marker of disease severity and treatment response. Further studies are needed to validate these findings and establish the role of leukopenia in the management of severe CAP with sepsis.

5. References

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