Original Article

Community-acquired staphylococcal pneumonia*

Pneumonia estafilocócica adquirida na comunidade

José Wellington Alves dos Santos[1], Douglas Zaione Nascimento[2], Vinicius André Guerra[2], Vanessa da Silva Rigo[2], Gustavo Trindade Michel[3], Tiago Chagas Dalcin[2]

Abstract

Objective: Staphylococcal pneumonia typically presents high rates of morbidity and mortality. It typically occurs in cases of influenza (airborne transmission) or during episodes of bacteremia (blood-borne transmission). **Methods:** A retrospective and descriptive study was conducted in patients admitted to our hospital between January of 1992 and December of 2003. All of he patients included had been diagnosed with community-acquired pneumonia caused by *Staphylococcus aureus*. All were older than 14 years of age, and none were intravenous drug users. **Results:** Community-acquired pneumonia was identified in 332 cases, of which 24 (7.3%) were identified as cases of staphylococcal pneumonia. Age ranged from 14 to 89 years. Fifteen patients were male, and nine were female. Twelve patients met the criteria for severe pneumonia. Chest X-rays showed unilateral consolidation in 14 cases, bilateral consolidation in 10, pleural effusion in 15, rapid radiological progression of pulmonary lesions in 14, cavitation in 6 and pneumothorax in 1. Most of the patients presented comorbidities, of which diabetes mellitus was the most common. Twelve patients presented complications such as empyema and septic shock. Four patients died, translating to a mortality rate of 16.6% in our sample. **Conclusions:** The clinical presentation of pneumonia caused by *S. aureus* is similar to that of pneumonia caused by other etiological agents. Radiological findings, epidemiological data and risk factors provide important clues to the diagnosis. These factors are important for clinical suspicion, since *S. aureus* is not typically addressed in empirical treatment.

Keywords: Staphylococcal pneumonia; Staphylococcal infections; Community-acquired infections.

Resumo

Objetivo: A pneumonia estafilocócica geralmente apresenta uma elevada taxa de morbidade e mortalidade. Normalmente ocorre em infecções por influenza (via aerógena) ou durante episódios de bacteremia (via hematogênica). **Métodos:** Um estudo retrospectivo e descritivo foi realizado com os pacientes que foram admitidos em nosso hospital entre janeiro de 1992 e dezembro de 2003 com diagnóstico de pneumonia adquirida na comunidade causada por *Staphylococcus aureus*. Todos eles eram maiores de 14 anos e não usuários de drogas endovenosas. **Resultados:** De um total de 332 casos de pneumonia adquirida na comunidade, foram encontrados 24 pacientes (7,3%) com pneumonia estafilocócica. A idade mínima e máxima eram de, respectivamente, 14 anos e 89 anos. Quinze pacientes eram homens e nove eram mulheres. Doze pacientes preenchiam critérios para pneumonia grave. O radiograma de tórax evidenciou consolidação unilateral em 14 casos, bilateral em 10, derrame pleural em 15, rápida progressão radiológica das lesões pulmonares em 14, presença de cavitação em 6 e pneumotórax em 1 paciente. A maioria dos pacientes apresentou co-morbidades e diabetes mellitus foi a mais freqüente. Doze pacientes apresentaram complicações como empiema e choque séptico. Houve quatro óbitos, o que representou 16,6% da amostra. **Conclusões:** A apresentação clínica da pneumonia causada por *S. aureus* é similar à apresentação das pneumonias originadas por outros agentes etiológicos. Os achados radiológicos, os dados epidemiológicos e os fatores de risco fornecem importantes indícios para o diagnóstico. Estes fatores são importantes para uma suspeição clínica, já que o *S. aureus* normalmente não é incluído nos tratamentos empíricos.

Descritores: Pneumonia estafilocócica; Infecções estafilocócicas; Infecções comunitárias adquiridas.

Introduction

Staphylococcal pneumonia accounts for 1% to 10% of all cases of community-acquired pneumonias (CAP) and presents high mortality rates.[1-6]

In 55% of cases, infection results from aspiration of naso-oropharyngeal secretions colonized by *Staphylococcus aureus*, which usually occurs after infection with the influenza virus. Influenza virus vaccination programs, in the fall or in general, should be directed at elderly individuals (≥65 years of age), since it is cost-effective in these patients.[7] In the remaining cases of staphylococcal pneumonia, infec-

* Study carried out at the Santa Maria University Hospital of the Federal University of Santa Maria, Santa Maria, Brazil.
1. Head of the Pulmonology Department. Santa Maria University Hospital of the Federal University of Santa Maria, Santa Maria, Brazil.
2. Medical Student. Federal University of Santa Maria, Santa Maria, Brazil.
3. Professor of Pulmonology. Federal University of Santa Maria, Santa Maria, Brazil.
Correspondence to: José Wellington Alves dos Santos. Rua Venâncio Aires, 2020/403, Centro, CEP 97010-004, Santa Maria, RS, Brasil.
Tel 55 55 3220-8585. E-mail: jwasb@terra.com.br
Financial support: None.
Submitted: 28 September 2007. Accepted, after review: 10 January 2008.

tion can occur by hematogenous dissemination, secondary to the infection of skin or soft tissues, as well as of the genital tract (after septic abortion).[8,9] Its presentation is typically severe, with a clinical course that varies from subacute to fulminant, regardless of the previous health status of the patient.[2,10]

There have been few case-series studies that exclusively address community-acquired staphylococcal pneumonia.[4,6,7] The objective of this study was to describe the clinical, radiological and epidemiological characteristics of staphylococcal pneumonia in a study of 24 cases diagnosed in immunocompetent patients, nonusers of intravenous drugs, from the community and requiring hospitalization.

Methods

Between January of 1992 and December of 2003, we retrospectively selected all patients aged ≥14 years, diagnosed with CAP and admitted to the Santa Maria University Hospital (a tertiary hospital with 400 beds) for inclusion in the study. We then identified the patients with community-acquired staphylococcal pneumonia, as diagnosed through culture of blood samples, pleural fluid, fine-needle aspiration biopsy samples or tracheal aspirate. All of these patients stated that they were not intravenous drug users. Clinical, radiological and laboratory data used in the study were obtained from medical charts and radiology files recorded in standard protocol.

Pneumonia was defined as a chest X-ray finding of new and persistent infiltrate accompanied by signs and symptoms of acute infection of the lower respiratory tract. To be considered CAP, the infection should affect patients from the community or occur within less than 48 h after hospital admission, and other conditions that result in similar clinical/radiological findings must be ruled out.[11,12] Severe

Table 1 - Principal characteristics of 24 cases of staphylococcal pneumonia.

Gender/ age (years)	Point of entry/origin	Comorbidity	Complication	Severe	Length of hospital stay (days)	Outcome	Antibiotic sensitivity
M/70	Lung	COPD/DM/CVD		No	31	Discharge	MSSA
M/80	Lung	DM/ND		No	33	Discharge	MSSA
F/70	Lung	DM	Shock	Yes	44	Discharge	MSSA
M/53	Lung	Alcoholism/COPD		Yes	2	Death	MSSA
F/54	Impetigo	DM/CVD	AKI	Yes	30	Discharge	MSSA
M/52	Impetigo	DM/ND		No	33	Discharge	MSSA
M/32	Impetigo		Shock	Yes	2	Death	MSSA
M/46	Abscess	DM	Empyema	No	35	Discharge	MSSA
F/22	Abscess		Empyema	Yes	38	Discharge	MSSA
F/29	Abscess			No	33	Discharge	MSSA
F/14	Cellulitis			Yes	32	Discharge	MSSA
F/40	Abortion		Empyema	No	45	Discharge	MSSA
F/35	Abortion			No	21	Discharge	MSSA
M/58	Unknown	ND	Shock	Yes	1	Death	MSSA
M/26	Unknown	ND		No	21	Discharge	MSSA
M/25	Unknown	ND		No	45	Discharge	MSSA
M/45	Unknown	Alcoholism	Empyema	No	21	Discharge	MSSA
M/43	Unknown	Alcoholism	AKI	Yes	1	Death	MSSA
M/66	Unknown	COPD/NHR	Empyema	Yes	30	Discharge	MRSA
M/89	Unknown	COPD		No	41	Discharge	MSSA
M/40	Unknown	DM		Yes	21	Discharge	MSSA
F/39	Unknown		Empyema	No	33	Discharge	MSSA
M/23	Unknown		Empyema	Yes	54	Discharge	MSSA
F/48	Unknown			Yes	27	Discharge	MSSA

M: male; F: female; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; CVD: cardiovascular disease; MRSA: methicillin-resistant *Staphylococcus aureus*; ND: neurological disease; AKI: acute kidney injury; MSSA: methicillin-sensitive *S. aureus*; and NHR: nursing home residence.

CAP was defined as presenting at least one of the two major criteria (requiring mechanical ventilation; and being in septic shock) or two of the minor criteria (respiratory rate > 30 breaths/min; multilobar involvement; arterial oxygen tension/fraction of inspired oxygen ratio < 250; confusion or disorientation; leukopenia; thrombocytopenia; hypothermia; and hypotension warranting aggressive fluid replacement).[12]

Patients who presented any of the following characteristics were excluded from the study: HIV-positivity; neoplasia; chronic use of corticosteroids (>20 mg/day of prednisone or equivalent); intravenous drug use; bacterial endocarditis; or an incomplete medical chart.

A microbiological evaluation was performed using the sputum and blood samples collected from all of the patients at hospital admission, as well as samples of pleural fluid, tracheal secretions and transcutaneous pulmonary aspirate, collected as necessary. Specimens were collected in sterile containers and sent to the laboratory for later processing. Evaluation of sputum microbiology, pleural fluid and transcutaneous pulmonary aspirate was carried out through direct analysis (Gram, Ziehl-Neelsen and 10% potassium hydroxide staining), as well as through culture for bacteria (blood agar, MacConkey agar and chocolate agar media), mycobacteria (Löwenstein-Jensen medium) and fungi (Sabouraud agar medium). Quantitative cultures for gram-positive and gram-negative germs were performed in the evaluation of the tracheal aspirate culture. Blood cultures were analyzed 48-72 h after incubation. Characteristic colonies of gram-positive cocci, together with positive catalase and coagulase, were considered indicative of *S. aureus* infection. Sensitivity to antibiotics was determined by the diffusion on Mueller-Hinton agar technique, according to standards previously described by Jorgensen et al.[13] Patients in whom *S. aureus* was isolated only in sputum were not included in the study.

The study of 332 cases of pneumonia was approved by the Ethics in Research Committee of our Institution.

Table 2 - Clinical and laboratory characteristics of 24cases of staphylococcal pneumonia.

Symptoms	n	%
Dyspnea	21	87.5
Fever > 37.8 °C	19	79.1
Cough	19	79.1
Pleuritic chest pain	18	75.0
Expectoration	14	58.2
Hemoptysis	5	20.8
Laboratory variables		
Leukocyte count > 12,000/mm^3	17	78.8
Urea > 30 mg	11	45.8
Hematocrit < 30%	5	20.8
Creatinine > 100 µmol/L	4	16.6
Glycemia > 13.9 mmol/L	4	16.6
Arterial pH < 7.35	4	16.6
PaO_2/FiO_2 < 250 mmHg	4	16.6
SBP < 90 mmHg	5	20.8

PaO_2/FiO_2: arterial oxygen tension/fraction of inspired oxygen ratio; and SBP: systolic blood pressure.

Results

Through the application of the methods described, we selected 332 cases diagnosed with CAP in adults hospitalized at the University Hospital during the study period. Among these cases, and meeting criteria described above, *S. aureus* was isolated in 24 patients (7.3%).

Individual characteristics of the 24 patients with staphylococcal pneumonia are specified in Table 1. Mean age was 45.7 years (range, 14-89 years). Fifteen cases (62.5%) were in males, and 9 cases (37.5%) were in females. Mean hospitalization stay among patients who were discharged was 33 days (range, 21-54 days). There were 4 deaths, corresponding to 16.6% of the cases.

Table 3 - Radiological characteristics and pulmonary involvement in 24 cases of staphylococcal pneumonia.

Radiological characteristics:	n	%
Homogeneous consolidation	21	87.5
Pleural effusion	15	62.5
Radiological deterioration after hospital admission	14	58.3
Cavitation	6	25.0
Nodule	3	12.5
Pneumatoceles	1	4.1
Spontaneous pneumothorax	1	4.1
Pulmonary involvement		
Multilobar	15	62.5
Unilobar	9	37.5
Unilateral	14	58.3
Bilateral	10	41.6

Table 4 - *Staphylococcus aureus* isolation site.

Isolation site	n	%
Blood culture	12	50.0
Pleural fluid	9	37.5
Sputum	4	16.6
Tracheal secretion	2	8.3
Fine-needle aspiration biopsy	1	4.1

Fifteen patients (62.5%) presented comorbidities: diabetes mellitus in 7 (29.15%); neurological disease in 5 (20.85%); chronic obstructive pulmonary disease (COPD) in 4 (16.5%); alcoholism in 3 (12.5%); and cardiovascular disease in 2 (8.5%). Five patients (20.85%) presented multiple comorbidities.

The principal clinical manifestation was dyspnea, which was present in 21 cases (87.5%). Symptoms such as fever, cough, pleuritic chest pain and expectoration are also noteworthy. Five patients (20.8%) presented hemoptysis. The most common laboratory alteration was leukocytosis, which occurred in 17 cases (78.8%). Clinical and laboratory characteristics are listed in Table 2.

Radiological findings were quite heterogeneous (Table 3). Homogeneous alveolar consolidation was the most common radiological characteristic, being present in 21 cases (87.5%). Multilobar involvement occurred in 15 cases (62.5%), whereas bilateral involvement was observed in 10 cases (41.6%). Pleural effusion was present in 15 patients (62.5%), nodules in 3 patients (12.5%), cavitation in 6 patients (25%), pneumothorax and pneumatoceles in one case (4.1%) each. Rapid radiological progression of pulmonary lesions after hospital admission was found in 14 patients (58.3%).

Nine cases (37.5%) presented an associated focus of extrapulmonary infection caused by impetigo (in 3), abscess (in 3), septic abortion (in 2) and cellulitis (in 1). Hematogenous dissemination was considered as the probable origin of pneumonia in all 9 of those cases. There were four cases (16.6%) with a recent history of upper respiratory tract infection, and airborne transmission was considered the most probable route in those cases. The probable route of transmission was not defined in 11 patients (45.8%).

The pathogen most often isolated, in blood culture, as well as in the culture of pleural fluid, was *S. aureus* (in 50.0% and 37.5% of the cultures, respectively). Four patients presented positive sputum and blood culture. In one case, fine-needle aspiration biopsy was the only elucidative diagnostic measure (Table 4). There were 23 cases (95%) of methicillin-sensitive *S. aureus* (MSSA) and only one case of methicillin-resistant *S. aureus* (MRSA),

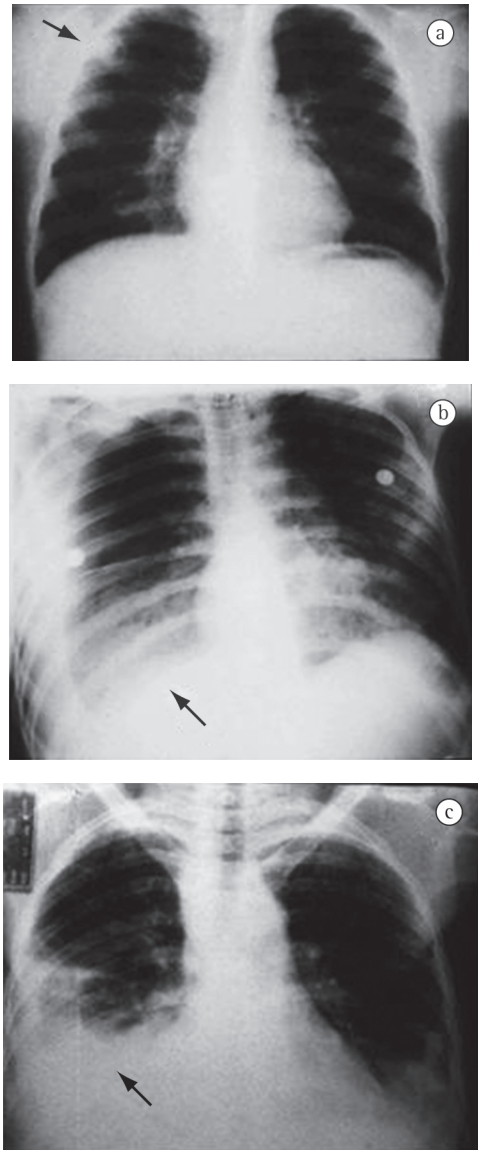

Figure 1 - Chest X-rays selected from among the cases: a) cavity with well-defined borders adjacent to the pleura in the right upper lobe; b) extensive alveolar opacity with air bronchogram in the right lower lobe; and c) alveolar opacities in the lower lobes, with pleural effusion on the right.

which was in an elderly patient residing in a nursing home.

Regarding severity, 12 patients (50%) met the criteria for severe pneumonia and were admitted to the intensive care unit (ICU). Of these, 10 were under 60 years of age and 7 presented a preexisting chronic disease. Twelve cases (50%) presented complications such as empyema, in 7 cases (29.1%), septic shock in 4 (16.6%) and acute kidney injury (AKI) in 3 (12.5%). Two patients presented septic shock associated with AKI.

Discussion

As an etiology of CAP, *S. aureus* is uncommon in patients who are not hospitalized and is more relevant in patients who require hospitalization.[14,15] The percentage found in this study sample is in accordance with the variation shown in other studies.[1-6,16-19] The infection typically affects elderly individuals with preexisting chronic pathologies such as COPD, cardiovascular diseases, alcoholism and diabetes mellitus, as well as hemodialysis patients with chronic kidney disease.[2,4,6] Young or previously healthy individuals can also be affected, principally when they present predisposing factors such as skin infections (impetigo, abscess, cellulitis, furunculosis or infected wound) or infections of the genital tract associated with septic abortion, all of which represent hematogenous dissemination of the infection.[5,8,9]

Most of the patients evaluated in the present study presented a predisposing factor for acquiring staphylococcal pneumonia (skin infection, septic abortion or a history of viral infection of the upper respiratory tract). However, a significant number of the affected individuals were previously healthy. It is also noteworthy that 1% to 50% of the adult population present intermittent *S. aureus* infection in the nasal vestibule, whereas 10 to 20% present permanent colonization, translating to a greater risk of developing staphylococcal pneumonia for both groups.[20,21]

Predisposition to pneumonia after previous influenza virus infection of the upper respiratory tract merits some attention. It is believed that the bronchial surface becomes more vulnerable to secondary bacterial infection, allowing the aspiration of oropharyngeal contents contaminated with *S. aureus*.[9,10] In addition to increasing susceptibility of the patient to *S. aureus*-related pneumonia, infection with the influenza virus also increases the severity of the *S. aureus* infection, as well as increasing the risk of superinfection.[22]

Symptomatology is typically acute, with variable intensity and frequency. The most common symptoms are dyspnea, fever, cough and pleuritic chest pain accompanied by leukocytosis and bacteremia.[23] Hemoptysis, also observed by some authors,[8] is an uncommon finding.

The radiological presentation varies (Figure 1), ranging from alveolar consolidation or isolated cavity to multiple consolidations, cavitary nodules or a miliary pattern. Other characteristics observed are pneumatoceles, pneumothorax, pleural effusion and rapid radiological progression of lesions after hospital admission.[5,10,20] In a study that evaluated radiological characteristics of staphylococcal pneumonia in adults and children, pneumatoceles was observed in 41% of the cases, pneumothorax in 20%, pleural effusion in 33% and bilateral consolidations in 35%.[24] Some of these characteristics, except for cavitations, which are seen in one fourth of the cases of *S. aureus* infection, can be common to other types of bacterial pneumonias such as those related to infection with *Streptococcus pneumoniae* or *Legionella pneumophila*. Pneumothorax and pneumatoceles, typical findings in children, are not common in adults and, when present, are clinical indicators of staphylococcal infection.[24-26] In the present study, it is important to highlight the high incidence of involvement of the pleural space, the bilateral consolidation, the rapid radiological progression of lesions after hospital admission and the cavitations. Pneumothorax and pneumatoceles are rare findings.[25,26] In order to suspect *S. aureus*-related CAP, it is essential to identify risk factors for this etiology, since this infection has quite diverse clinical symptoms and radiological presentations.

Among patients with severe CAP, staphylococcal infection is one of the most common etiologies. It is a high-risk disease, even when it affects young or previously healthy patients. In case of clinical suspicion, the patient should be hospitalized, even if not meeting the criteria for hospitalization in the first evaluation, since the disease has a complicated course. Suppurative lesions, persistent fever, the need for mechanical ventilation and ICU admission are common.

It is estimated that bacteremia occurs in 20 to 30% of all cases of staphylococcal pneumonia.[27] However, in our study, bacteremia was found in 50% of the cases. This high incidence was probably due to the presence of an extrapulmonary focus of bacteremia in a significant proportion of the patients (37.5%), as well as to the inclusion criteria used, which demand that, in addition to blood cultures, cultures of pleural fluid, tracheal secretions and transcutaneous pulmonary aspirate be performed when necessary. Under these conditions, blood culture positivity tends to be higher, making blood culture an effective instrument in diagnosis. As a prognostic factor, bacteremia has been shown to be an independent predictor of mortality in CAP, as it might also be in staphylococcal pneumonia.[28]

The invasive procedures used in the present study were thoracocentesis and fine-needle aspiration biopsy, both of which increased the diagnostic accuracy. Blood culture and sputum examination are quite useful. However, they are not always elucidative. Principally in sputum samples, there is considerable oropharyngeal contamination with *S. aureus*, and it is not possible to distinguish between colonization and infection. Since the frequency of complications is high and the clinical course is aggressive, the use of invasive procedures for suspected staphylococcal infection is fully justified. These methods have great value, since they allow clinical specimens to be obtained directly from the infectious focus.[12,27]

The incidence of *S. aureus* infection in CAP is low. Therefore, it is not usually treated with the empirical treatments recommended in the related guidelines. However, effective antistaphylococcal antibiotics should be included in the initial therapeutic regimen of patients presenting radiological and epidemiological characteristics suggestive of such etiology. In addition, the choice of antibiotic therapy should be guided by the pattern of local sensitivity and by the presence of risk factors for MRSA, such as comorbidities, residence in nursing homes, drug use, recent hospitalization and previous use of antibiotic therapy.[29] Most of the patients in our sample were infected with MSSA. Only one case of MRSA infection was found, and that was in an elderly patient with COPD who was a resident of a nursing home. The majority of the patients were young adults with no history of hospitalization or of recent intravenous drug use.

In other case-series studies, mortality ranges from 30 to 40%, reaching 100% among severe cases. Decreased level of consciousness, hypotension, preexisting chronic disease and being over 60 years of age are all associated with a worse prognosis. Of the four deaths observed in this study, three occurred in patients with subjacent comorbidities. However, they were all in individuals under the age of 60, and the deaths all occurred in the first 48 h after hospital admission (they all presented severe respiratory failure upon hospital admission), which demonstrates the severity of the evolution and the fulminant course of the disease, regardless of the age of the patient. The high morbidity rate associated with the frequent presence of complications (in half the cases of this study, 7 of which, notably, presented empyema), as well as the prolonged hospital stays, should be emphasized. Another severe potential complication is necrotizing pneumonia due to staphylococcal infection, which frequently evolves to bronchopleural fistula and respiratory insufficiency. Early identification of this potentially fatal complication is indispensable, since immediate surgical treatment involving resection of the necrotic tissue can improve the prognosis.[30]

In conclusion, staphylococcal pneumonia generally presents a variety of clinical findings and a course that ranges from subacute to fulminant. Radiological findings such as cavitation, pleural effusion, bilateral consolidations and rapid radiological progression of pulmonary lesions are common. In addition, pneumothorax and pneumatoceles are quite characteristic. When such findings are accompanied by a history of infection with influenza, skin infection or infection of the genital tract after septic abortion, staphylococcal etiology is likely. When these characteristics are seen and the pneumonia is severe, invasive diagnostic methods are quite useful and should be used in early diagnosis.

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