

# Pneumonia, meningitis, and endocarditis caused by *Staphylococcus aureus* in a patient living with HIV/AIDS

Pneumonia, meningite e endocardite por *Staphylococcus aureus* em paciente vivendo com HIV/aids



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Submitted: 10 April 2025

Accepted: 7 June 2025

Published: 25 August 2025

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DOI: 10.5935/2764-734X.e20250664-en

## ABSTRACT

Invasive *Staphylococcus aureus* infections, in particular those caused by methicillin-resistant strains (MRSA), are a major clinical challenge, especially in immunocompromised individuals. Patients living with HIV/AIDS are at increased risk of MRSA colonization and infection with potentially severe and multisystemic clinical presentations. This report describes the case of a 43-year-old man who initially presented with skin lesions and then developed severe systemic pneumonia, meningitis, and infective endocarditis caused by MRSA. The patient was treated with prolonged antibiotic therapy and had a favorable outcome after 2 months of hospitalization.

**Headings:** Methicillin-Resistant *Staphylococcus aureus*; Pneumonia; Meningitis; Bacterial; Endocarditis; Bacterial; AIDS; Case Report.

## RESUMO

As infecções invasivas por *Staphylococcus aureus*, especialmente as causadas por cepas resistentes à meticilina (MRSA), representam um importante desafio clínico, sobretudo em indivíduos imunocomprometidos. Pacientes vivendo com HIV/aids apresentam risco aumentado de colonização e infecção por MRSA com potenciais apresentações clínicas graves e multissistêmicas. Este relato descreve o caso de um homem de 43 anos que, a partir de lesões cutâneas, evoluiu com quadro sistêmico grave de pneumonia, meningite e endocardite infecciosa causadas por MRSA. O paciente foi tratado com antibioticoterapia prolongada e obteve desfecho favorável após dois meses de internação.

**Descritores:** *Staphylococcus aureus* resistente à meticilina; Pneumonia; Meningite Bacteriana; Endocardite Bacteriana; AIDS; Relato de Caso.

## INTRODUCTION

Treating *Staphylococcus aureus* infection involving bacteremia is a considerable challenge owing to its severity and potential for complications, including multisystem involvement with high mortality and morbidity. HIV-related immunosuppression is an aggravating factor in this context, because the function of TCD4<sup>+</sup> lymphocytes is disrupted leading to reduced production of interferon-gamma which is essential for infection control<sup>1</sup>, and because of the increased prevalence of colonization by methicillin-resistant *Staphylococcus aureus* (MRSA) in this patient population<sup>2</sup>.

The aim of this report is to present the case of a patient living with HIV/AIDS (PLWHA) whose *S. aureus* skin infection developed into pneumonia, meningitis, and endocarditis. This condition stands out for its diverse clinical presentation and the consideration of differential diagnosis

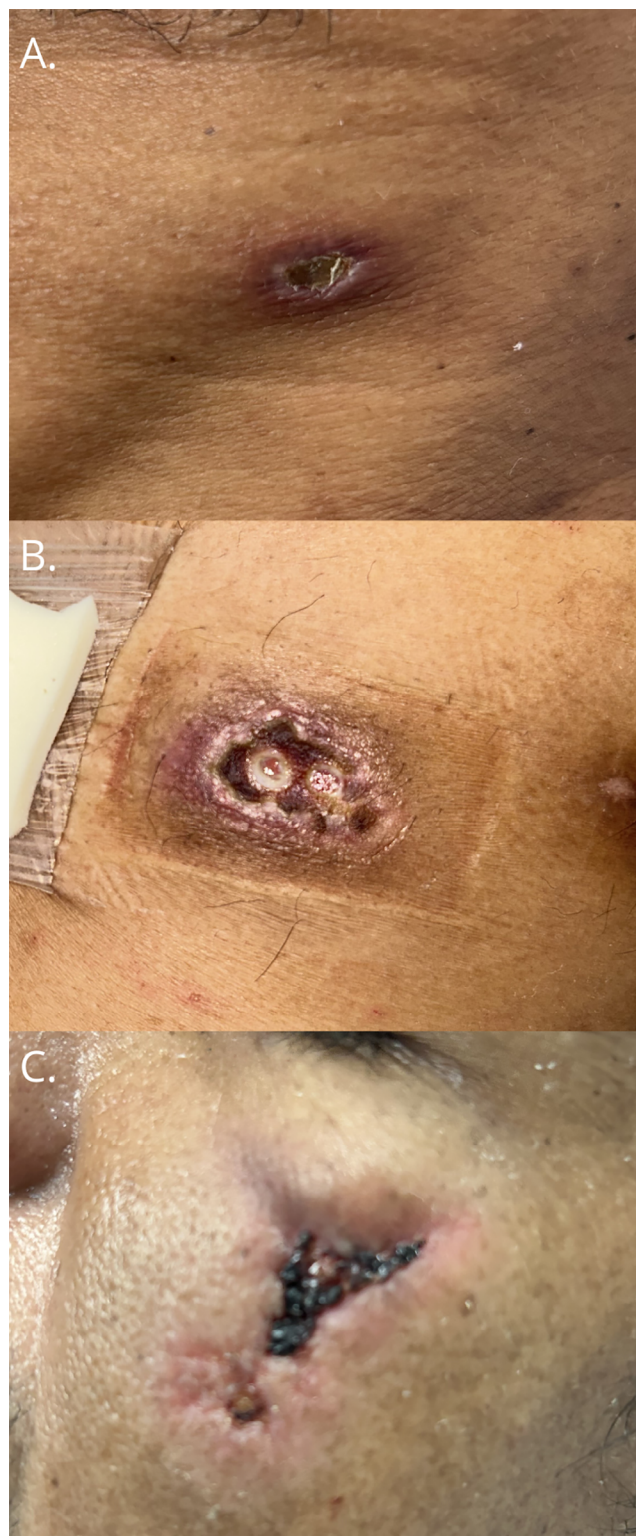
with other opportunistic infections related to severe immunosuppression.

## CASE REPORT

A 43-year-old male PLWHA since 2007 attended the emergency room due to ulcerated and crusted skin lesions for 20 days. He reported that the onset of the condition was a single, painful lesion in the inguinal region, with a pustular appearance, which regressed spontaneously. He noticed a widespread rash on the upper abdomen, face, buttocks, and limbs 10 days later, forming erythematous nodules that progressed to pustules with a yellowish secretion and then to ulcers covered in black crusts. During this period, he also experienced episodes of febrile with a maximum temperature of 39 °C, a productive cough with greenish sputum, dyspnea, and pleuritic pain as well as six tonic-clonic convulsive seizures witnessed by family members. He was born and lived in São Paulo and had been homeless for 8 years; however, he was living in a brick house for the last 5 years with his healthy wife and son. The diagnosis of HIV infection was made in the context of a focal neurological condition attributed to neurotoxoplasmosis. Since then, he had been taking phenytoin for epilepsy. His last antiretroviral regimen (which he followed inconsistently) included tenofovir, lamivudine, dolutegravir, and etravirine. The last documented TCD4+ lymphocyte count was 12 cells/mm<sup>3</sup>, and the viral load in recent tests was 118,891 copies/mL. He was a former cocaine user (abstinent for 8 years) and reported daily consumption of spirits but denied using injectable drugs.

On admission, he was in a regular general state, pale, dehydrated, tachypneic (32 breaths/min), tachycardic (119 beats/min), normotensive, afebrile, and without desaturation. Breathing sounds were normal, without effort; there were no murmurs on cardiac auscultation. He was alert and opened his eyes spontaneously, obeyed commands but had mild disorientation and confused speech. Monoparesis was observed in the left arm, with no signs of meningeal irritation. On the skin, multiple lesions measuring approximately 3 × 3 cm were spreading over the face, abdomen, buttocks, perianal, and pelvic regions, with some being ulcerated and others covered with crusts (Figure 1). Thus, it was decided to open a “care protocol for sepsis” of cutaneous focus, and antibiotic therapy was immediately instituted with oxacillin and ceftriaxone after blood samples were taken for culture. Initial laboratory tests showed anemia (Hb: 8.8 g/dL), increased C-reactive protein (203.6 mg/L, normal upper limit of 5.0 mg/L), and a slight increase in canalicular enzymes.

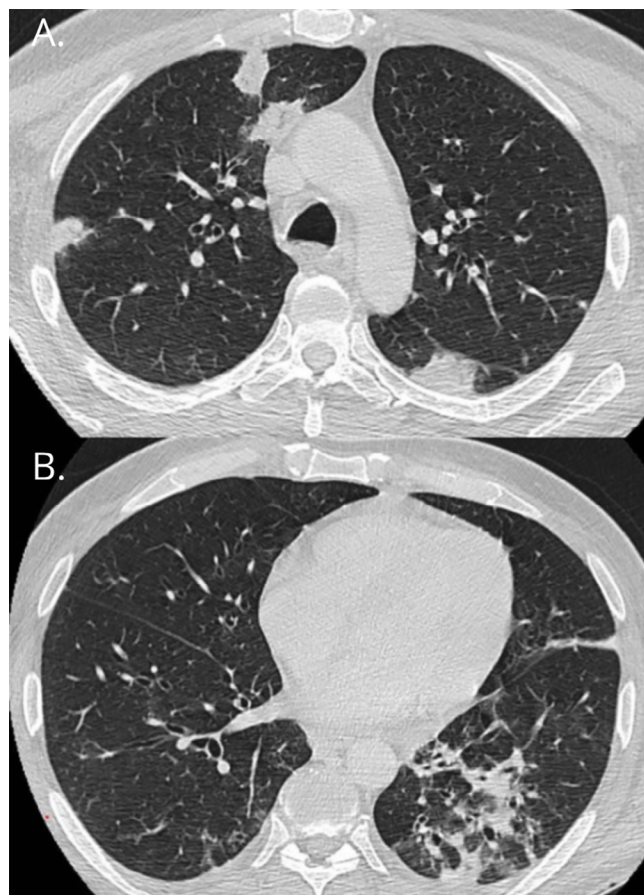
He underwent chest, brain, and abdominal computed tomography (CT), wherein consolidations and nodules



**Figure 1.** Skin lesions in the neck region (A), lateral aspect of the left hemithorax (B), and left malar region (C).

without cavitation were observed with a random distribution in the lungs (Figure 2); the brain images indicated sequelae; and there were no significant abdominal alterations. Considering the history of convulsive seizures





**Figure 2.** CT scans showing solid nodular opacities in both lungs (A) and a focus of consolidation in the left lower lobe (B).

and nonspecific CT images, the patient underwent lumbar puncture for cerebrospinal fluid collection (CSF) - the results of three sequential samples are listed in Table 1. Histologically, one of the biopsied ulcerated skin lesions showed skin without epidermis and with necrosis extending to the deep dermis as well as numerous bacterial colonies. The results of the blood cultures collected on hospital admission showed MRSA growth in two samples, whose antibiogram is detailed in Table 2. Antibiotic therapy was changed to vancomycin, and fundoscopy (normal) and a transthoracic echocardiogram were performed, the latter reporting “preserved ejection fraction of 64%. Mitral and tricuspid valves with thin leaflets, preserved opening and mobility. Aortic valve with thin leaflets, preserved opening. Presence of a filamentary and mobile image adhered to the ventricular face of the non-coronary leaflet, measuring approximately 32 mm, which may correspond to vegetation”. The blood cultures that were collected every other day became negative on day 11 after the introduction of vancomycin. The direct test for acid-fast bacilli and the rapid molecular test for the detection of *Mycobacterium*

*tuberculosis* DNA in sputum were negative, as were the direct stains for fungi and respective cultures (results obtained later). However, considering the patient’s severe immunosuppression and the solid lung nodules seen on the CT scan, a surgical biopsy was performed to rule out pulmonary involvement due to opportunistic infection. The histological study showed foci of organizing pneumonia interspersed with structures compatible with bacterial colonies (Figure 3). Both cultures of the lung tissue and the previously biopsied skin sample showed *S. aureus* growth with a resistance profile similar to that isolated from the blood. Vancomycin was maintained for five weeks, until signs of bone marrow toxicity (neutropenia and thrombocytopenia) were observed, which led to its replacement with daptomycin after confirming near-total resolution of the lung images on CT scan and the absence of brain abscesses or spinal cord involvement based on nuclear magnetic resonance imaging scans. The last CSF collection, on day 22 of hospitalization (after 18 days of treatment), showed a reduction in cellularity and a significant improvement in proteinorrachia (Table 1). There was no need for surgical treatment of the aortic valve according to the expert assessment of the cardiac surgery team, with only maintenance of clinical treatment and echocardiographic follow-up being recommended. A final transesophageal examination performed in the fifth week showed total regression of the valve vegetation, without functional sequelae. The patient was discharged after 2 months, in good general condition and without complaints, and was referred for outpatient follow-up with an infectious disease specialist at the basic health unit.

## DISCUSSION

*S. aureus* is responsible for a wide range of community and hospital infections and is a relevant pathogen for PLWHA owing to its prevalence, morbidity, and mortality. This can be explained by the high rates of MRSA colonization in this population compared with the general population (6–18 times higher)<sup>3</sup> and also by the complex interaction of risk factors associated with community exposure (as in our case, alcohol abuse and having lived on the streets)<sup>4</sup> or frequent and longer hospitalizations, implying previous selective exposure to antibiotic therapy and invasive procedures<sup>5</sup>.

The secretion of coagulases is one of the mechanisms used by *S. aureus* to facilitate the formation of microthrombi that protect it bacteria from the host’s immune response<sup>6</sup>. Another similar mechanism is the secretion of proteases that inhibit the activation and migration of inflammatory cells<sup>7</sup>. When the skin is

**Table 1.** Evolution of cerebrospinal fluid analysis results in relation to glucose and antibiotic therapy administered during hospitalization.

Test	D4	D6	D22	Reference values
<b>Cellularity</b> (number cells/mm <sup>3</sup> )	18	87	16	0 - 4
<b>Lymphocytes (%)</b>	79	85	91	50 - 70
<b>Monocytes (%)</b>	12	13	9	30 - 50
<b>Neutrophils (%)</b>	8	1	0	1 - 3
<b>Proteins (mg/dL)</b>	2808	3939	87	0 - 40
<b>Glucose (mg/dL)</b>	84	33	44	50 - 70
<b>Blood glucose (mg/dL)</b>	418	245	87	0 - 9
<b>Lactate (mg/dL)</b>	44	40	11	9 - 22
<b>Aerobic culture</b>	no growth	no growth	no growth	no growth
<b>RMT-TB</b>	not detected	not detected	not detected	not detected
<b>Mycobacteria culture</b>	no growth	no growth	no growth	no growth
<b>Antibiotic therapy</b>	oxacillin and ceftriaxone	oxacillin and ceftriaxone	vancomycin	-

Legend: D4/D6/D22 - 4th/6th/22nd day of hospitalization; RMT-TB - rapid molecular test for the detection of *Mycobacterium tuberculosis* DNA.

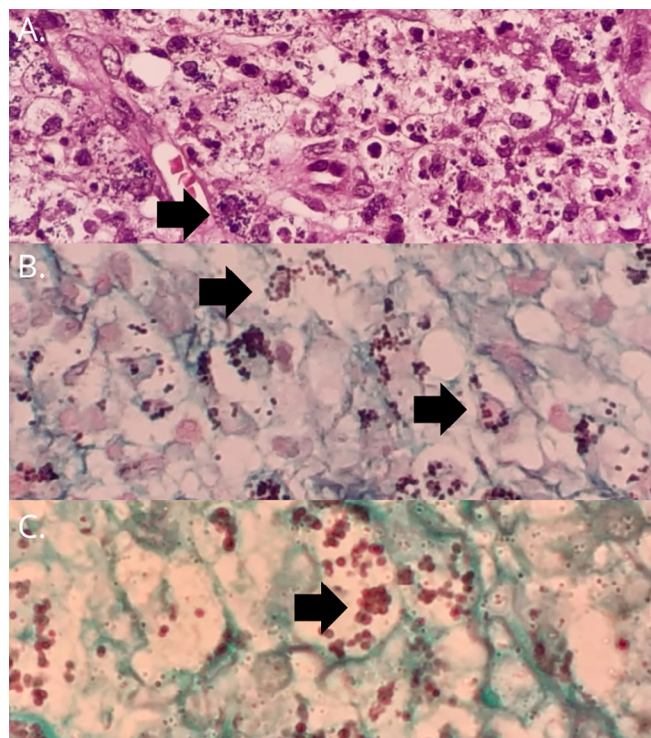
**Table 2.** Result of the antibiogram performed based on the growth of *Staphylococcus aureus* in peripheral blood cultures seeded in automated BD Bactec FX™ and Phoenix™ media.

Microorganism	Antimicrobial tested	MIC	Sensitivity profile
<b><i>Staphylococcus aureus</i></b>	ciprofloxacin	<=0,5	I
	clindamycin	>2	R
	daptomycin	<=1	S
	erythromycin	>4	R
	gentamicin	<=1	S
	levofloxacin	<=0,5	I
	linezolid	<=1	S
	oxacillin	>2	R
	penicillin	>1	R
	sulfamethoxazole + trimethoprim	<=1/19	S
	tigecycline	<=0,25	S
	vancomycin	<1	S

Legend: MIC - Minimum Inhibitory Concentration; S: sensitive to standard dose; I: sensitive by increasing exposure; R: resistant (according to EUCAST, BrCAST version, available at: <https://brcast.org.br/documentos/documentos-3/>).

involved, the secretion of coagulases and  $\alpha$ -hemolysin is a critical factor in the pathogenesis of the infection<sup>8</sup> as it causes dermonecrosis that can be clinically confused with cutaneous tuberculosis, Herpes Zoster, and malignant syphilis in the context of immunosuppression<sup>9</sup>. In the lungs, necrotizing processes are more commonly related to MRSA that produce Panton-Valentine leukocidin (PVL), a cytotoxin that induces necroptosis in lung tissue<sup>10</sup>. The solid nodules biopsied were demonstrated to result from metastatic infections (septic emboli); however, other diagnostic hypotheses had been previously raised, such as fungal infection (especially histoplasmosis)<sup>11</sup> and mycobacterial infection, especially in a PLWHA. The involvement of the central nervous system (CNS),

marked by high proteinorrhacia, was the only one not microbiologically confirmed in the present case, possibly because the CSF was collected while the patient already was on antibiotic therapy, reducing the sensitivity of the culture. The cytochemical analysis of CSF showing very high protein without corresponding increase in cellularity is known as albuminocytological dissociation and is caused by the inflammatory potential without the cellular effectiveness that is typical of immunodepression. This finding also allows us to consider the differential diagnosis of CNS infection by *M. tuberculosis*, which must be ruled out using bacilloscopy, molecular testing, and specific culture for mycobacteria and by observing the clinical response to the antimicrobial treatment. We believe that the increase



**Figure 3.** Histological sections of the lung biopsy: chronic inflammatory process with histiocytic reaction corresponding to organizing pneumonia. Rounded and clustered structures can also be seen in the cytoplasm of histiocytes and in alveolar spaces, compatible with colonies of gram-positive bacteria (black arrows) stained with hematoxylin and eosin (A), Grocott (B), and Brown-Brenn (C).

in cellularity that occurred between days 4 and 6 of hospitalization (Table 1) was indicative of the progression of meningeal involvement in the absence of adequate treatment, since the patient was still taking oxacillin and ceftriaxone. Meanwhile, the lower glycorrachia values confronted to the serum glucose values indicated better glycemic control throughout hospitalization.

The diagnosis of infective endocarditis in this case meets the guidelines updated in 2023 by the European Society of Cardiology<sup>12</sup> through two major criteria (typical microorganism and echocardiographic finding) and two minor criteria (fever and evidence of vascular dissemination by embolism). These same guidelines, however, point out three reasons why urgent surgical treatment of the aortic valve could have been indicated in order to reduce the high risk of embolization to the CNS: the size of the vegetation (greater than 10 mm), persistently positive blood cultures for more than a week of adequate antibiotic therapy and the previous occurrence of embolic phenomena<sup>12</sup>. Hemodynamic stability during the patient's good clinical evolution certainly contributed to this

conservative decision; however, it is worth emphasizing that early surgery, if applicable, is a good option for patients with low surgical risk<sup>12</sup>.

According to reports by Rivera<sup>13</sup> and Pandey<sup>14</sup>, the concomitance of pneumonia, meningitis, and endocarditis in the same patient brings us back to the clinical triad initially described by Heschl in 1862, later taken up by Sir William Osler who in 1881 associated it with the presence of bacteria, at the time described as "micrococci" (characterizing what we know as "Osler's triad"). In 1882, Netter documented a clear predisposition for the aortic valve in this context, while Robert Austrian's publication in 1957<sup>15</sup> added the predilection of *Streptococcus pneumoniae* as the most frequent infectious agent. This led the clinical triad of pneumonia, meningitis and endocarditis due to *S. pneumoniae* to receive the eponym "Austrian syndrome", an entity with the largest number of reports in the literature. Therefore, our case report is an example of the Osler triad caused by MRSA, with the particularity of occurring in PLWHA.

## CONCLUSION

As stated in Robert Austrian's original paper<sup>15</sup>, Sir William Osler himself argued "meningitis is a very rare complication of pneumonia and may occur separately from endocarditis; but in a case of inflammation of the lungs and particularly if the apex is involved (...), the development of an irregular temperature with cerebral symptoms must suggest the possibility of endocardial damage, with secondary meningeal inflammation." This was most likely the pathophysiology of the case we reported herein. Taking this into account, echocardiographic investigation in patients with pneumonia, fever, and neurological symptoms has proven to be extremely important, with a clear impact on the clinical (or possibly surgical) management of the case. Moreover, we highlight the importance of considering pyogenic agents, such as *S. aureus*, in the differential diagnosis of multisystem infections in patients with suppressed immunity in addition to the wide range of opportunistic agents usually investigated.

*"This case report deserved an official declaration of acknowledgement and ethical approval by its institution of origin and was peer-reviewed before publication, whilst the authors declare no fundings nor any conflicts of interest concerning this paper. It is noteworthy that case reports provide a valuable learning resource for the scientific community but should not be used in isolation to guide diagnostic or treatment choices in practical care or health policies. This Open Access article is distributed under the terms of the Creative Commons Attribution License (CC-BY), which allows immediate and free access to the work and permits users to read, download, copy, distribute, print, search, link and crawl it for indexing, or use it for any other lawful purpose without asking prior permission from the publisher or the author, provided the original work and authorship are properly cited."*



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