Sobreinfección por Pneumocystis jirovecii y Staphylococcus aureus resistente a meticilina tras infección por SARS-CoV2

Pneumocystis jirovecii and methicillin-resistant Staphylococcus aureus superinfection, a challenge in a post-COVID-19 scenario.

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ABSTRACT

We present a case of an 87-year-old nonsmoker female who recovered after infection by SARS-CoV-2 and was readmitted two weeks later due to respiratory sepsis. Radiological imaging showed a significant radiological worsening with extensive areas of bronchopneumonia and ground-glass opacities suggestive of organizing pneumonia. Empirical treatment with meropenem 1g/8h was started; however, clinical worsening persisted with tachypnea and desaturation requiring heated high-flow nasal cannula oxygen therapy, with poor response. Methicillin-resistant Staphylococcus aureus was isolated both in nasal screening swab and sputum, and RNA polymerase chain reaction in induced sputum was positive for P. jirovecii. Serum (1-3)-beta-D-glucan was normal, and blood cultures were sterile. Antibiotic therapy was adjusted with intravenous linezolid 600mg/12h and trimethoprim-sulfamethoxazole 320/1600mg/6h, plus methylprednisolone 40mg/day. Unfortunately, the patient had no response to optimized treatment and finally died. Clinicians should be aware of opportunistic and resistant microorganisms superinfections in relation to SARS-CoV-2 infection, even more, when corticosteroids are widely used.

Keywords: corticosteroids; MRSA; organizing pneumonia; Pneumocystis jirovecii; SARS-CoV-2.

Palabras clave: corticosteroides; SARM; neumonía organizada; Pneumocystis jirovecii; SARS-CoV-2.

INTRODUCCIÓN

Coronavirus disease 2019 (COVID-19) is caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In the early stage, prevail infection and viral replication, while during late-stage prevail the inflammatory response. Symptoms and complications are consequences of these complex pathophysiological mechanisms. Additionally, the presence of bacterial or fungal co-infection has been reported for up to 8% of hospitalized patients[1]. Computed tomography (CT) represents a useful tool for monitoring COVID-19. Different imaging patterns have been reported, especially the presence of peripheral and multilobar ground-glass opacities (GGO), linear consolidation and reverse halo sign. These findings suggest the association with the development of secondary organizing pneumonia (OP), a well-known entity related to infections (virus, bacterial, fungi), drugs, and toxics[2,3].

CASE REPORT

An 87-year-old female nonsmoker and non-vaccinated against SARS-CoV-2 with a history of diabetes mellitus type 2, hypertension, coronary heart disease, and previous hospitalization due to bilateral pneumonia by SARS-CoV-2 treated with dexamethasone 6mg per day. Ceftriaxone 2g per day was associated empirically without any bacterial isolations. Additionally, low-flow nasal cannulas were needed for respiratory support. Before discharge, a SARS-CoV-2 PCR test was performed with a negative result and antibody seroconversion for COVID-19 was objectified. She was re-admitted to our center due to worsening dyspnea and malaise two weeks later. Physical examination showed a poor general state, with blood pressure 109/40 mmHg, 72 bpm, 36.4ºC, 40 breaths per minute, and 65% SpO2 on room air recovered to 91% with a non-rebreathing mask of 15L/min. Extensive pulmonary dry crackles. Laboratory tests showed arterial blood gas pH 7.46, partial O2 pressure (pO2) 77 mmHg, pCO2 28 mmHg, lactate 3.0 mmol/L, hemoglobin 9.7 g/dL, 411,000/µL platelets, 13,500/µL leukocytosis, 1,000/µL lymphocytes, INR 1.25, fibrinogen >1000 mg/dL, D-dimer 2979 ng/mL, glucose 201 mg/dL, creatinine 0.74 mg/dL, AST 31 UI/L, LDH 542 U/L, CRP 30 mg/dL, procalcitonin 0.56 µg/L. CT angiography of pulmonary arteries ruled out pulmonary embolism but showed a significant radiological worsening with extensive consolidations in the upper lobes and bilateral GGO in the lower lobes (Fig. 1). Nasopharyngeal PCR test for SARS-CoV-2 was negative, blood cultures were sterile and pneumococcal and legionella urine antigens were negative. Empirical treatment with meropenem 1g/8h was started; however, clinical worsening persisted with tachypnea and desaturation requiring heated high-flow nasal cannula oxygen therapy with a fraction of inspired oxygen at 100%, but poor response. MRSA was isolated both in nasal screening swab and sputum culture, and a non-automated RNA polymerase chain reaction (PCR) in induced sputum was positive for PJ. Serum (1-3)-beta-D-glucan and galactomannan antigen were normal (<2.5 pg/mL and 0.13 ng/mL, respectively). Antibiotic therapy was adjusted with intravenous linezolid 600mg/12h and trimethoprim-sulfamethoxazole 320/1600mg/6h, plus methylprednisolone 40mg/day. Unfortunately, the patient had no response to optimized treatment and finally died.

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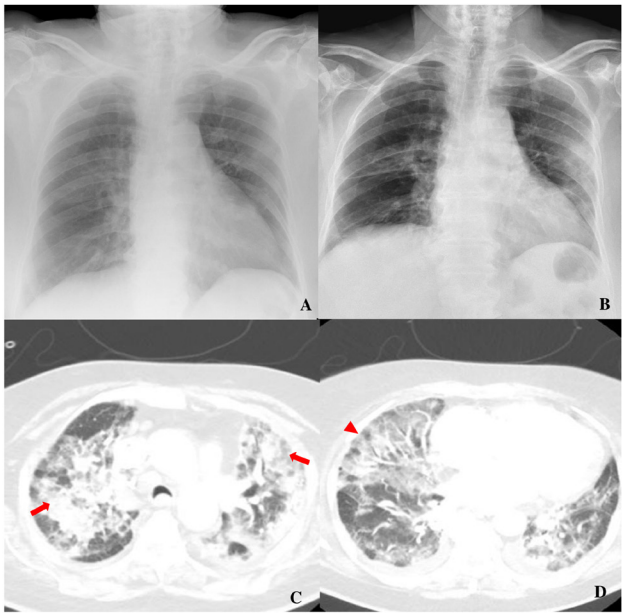

Figure 1. Chest X-ray showing bilateral ground-glass opacities related to SARS-CoV-2 (a) with favorable evolution (b), during the first admission.
Computed tomography demonstrates areas of bilateral consolidation suggesting bronchopneumonia superinfection in the upper lobes (red arrows), and areas mimicking organizing pneumonia in lower lobes (redhead arrow) (c,d).

DISCUSSION

Pneumocystis jirovecii pneumonia (PJP) is an opportunistic fungal entity classically associated with human immunodeficiency virus (HIV)-infected patients; however, in the last decades, PJP has been related to non-HIV-immunocompromised patients in the setting of hematological or solid malignancies, organ transplantation, and corticosteroids or immunosuppressive therapy. PJ caused interstitial pneumonia with nonspecific and insidious onset, bilateral reticulonodular infiltrates in chest radiography, and typically presented with elevated LDH, low serum albumin, and CD4+ lymphocyte count <200 cells/μL. The gold standard test for diagnosis relies on visualizing PJ in respiratory samples or biopsy. Other diagnostic tools are molecular and serology tests. PCR test for *P. jirovecii* can be performed in non-invasive samples and presents a high sensitivity but low specificity, so it might detect colonization. PJ colonization has been demonstrated in both HIV and non-HIV patients in different types of samples, lung tissue, bronchoalveolar fluid, sputum, and others. Among non-HIV patients, colonization might be more prevalent than previously thought (reaching up to 13-23%), being the use of corticosteroids (prednisone 20mg/day or higher dose), older age, and chronic comorbidities the main risk factors for both colonization and disease development. PCR test interpretation should be individualized depending on the right clinical context before starting treatment[4]. On the other hand, (1-3)-beta-D-glucan is part of most fungi' walls and presents a good sensibility and specificity in detecting fungal infection, especially in HIV patients; but it may present false-negative results[4,5]. Finally, trimethoprim-sulfamethoxazole constitutes the first-line treatment, regardless of severity. Additionally, prednisone has demonstrated an improvement in survival, and it is recommended in moderate to severe disease (pO2 less than 70 mmHg or an alveolar-arterial oxygen gradient of greater than 35 mmHg)[5,6].

Methicillin-resistant *Staphylococcus aureus* represents a major health problem in community-associated and hospital-associated infections, with significant morbidity and mortality worldwide. Further, it represents a diagnostic and therapeutic challenge for clinicians[7]. Although empirical antibiotic coverage for MRSA is recommended in patients at risk due to the burden of the disease, the main issue in daily practice concerns which patients really require empirical coverage[7,8]. A meta-analysis, comprising 5163 patients, has evaluated the role of nasal screening in rule-out MRSA pneumonia. The data found showed that the prediction of MRSA pneumonia by nasal screening swab for MRSA presented a sensitivity, specificity, positive predicted value, and negative predicted value of 70.9% (95% CI, 58.8%–80.6%), 90.3% (86.1%–93.3%), 44.8% and 96.5%, respectively. Thus, MRSA nasal swab test might represent an inexpensive, rapid, and cost-effective tool for rule-out MRSA pneumonia and/or deescalating empirical anti-MRSA therapy, avoiding possible drug-adverse reactions and antimicrobial resistance[8]. Linezolid both orally or intravenously has demonstrated a proper tissue penetration, and it might be considered a first-choice regimen for MRSA pneumonia[7].

In the setting of the current pandemic, the potential relationship between PJ and MRSA has been evaluated related to SARS-CoV-2 infection. On the one hand, Alanio *et al.*[9] evaluated in a prospective cohort the presence of PJ in 108 non-HIV COVID-19 patients admitted to the intensive care unit (ICU), founding a total of 10 patients (9.3%) with positive PCR for PJ, from those (1-3)-beta-D-glucan was measured in 9 patients being negative in 7/9 patients (78%). Similar data for fungal co-infection (~7%) were reported for the *Influenza* virus in previous works. On the other hand, Punjabi *et al.*[10] evaluated the prevalence of MRSA in patients hospitalized with COVID-19 pneumonia in a retrospective cohort of 472 patients, showing a prevalence for MRSA of 0.6% to 5.7% from day 3 to day 28 of hospitalization, respectively; pointing out a timeline relationship between a prolonged hospital stay and the risk of colonization or superinfection, especially in ICU patients. Our clinical case showed an elderly with a recently SARS-CoV-2 infection treated with corticosteroids, who was re-admitted due to respiratory sepsis in the setting of superinfection by PJ and MRSA, showing a fatal outcome.

CONCLUSION

Superinfection by opportunistic or resistant microorganisms should be considered in the SARS-CoV-2 scenario, even more, due to the wide use of corticosteroids.

CONFLICT OF INTEREST
The authors declare that they have no conflict of interests.

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ETHICAL ASPECTS
All participants submitted a consent form to be included in this study.

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