Austrian syndrome – an exceeding rare condition

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Streptococcus pneumoniae (pneumococcus) was first isolated in 1880 by George Miller Sternberg in the United States and by Louis Pasteur in France, followed by its association with arthritis, otitis media, lobar pneumonia, meningitis, and endocarditis[1]. Classical Austrian syndrome (AS) includes the triad of endocarditis, meningitis, and pneumonia by pneumococcus, a condition with approximately 80 case descriptions [2-7]. The main risk factors are alcoholism, immunosuppression, smoking, aging, and drug abuse. This challenging and severe entity may evolve clinically unsuspected, being undetected or misdiagnosed in cases with neither complementary evaluations nor autopsy studies [3]. Worthy of note was the increase of AS case reports since 2015 (~30/80), despite the global program of vaccination against pneumococcal infections [1,2,4-7]. Prevention with the new pneumococcal conjugate vaccine is mandatory in risk groups[,7,8]. One can hypothesize enhancing clinical awareness and accurate evaluation to explain it. Hence, the publishing of single case studies of this rare syndrome should be stimulated. One hundred and forty years after the first isolations of pneumococcus, brief comments on recent reports of AS seem appropriate in the context of a respiratory viral pandemic. Besides the lungs, COVID-19 also affects the heart and the central nervous system, and patients with *S. pneumoniae* coinfections have been described in several regions[5,8-10]. Patients with COVID-19 and hypoxemic pneumonia are suspected of having bacterial co-infection that must be treated, mainly in cases with the presence of elevated D-dimers [9]. Without accurate studies, including autopsies, one cannot know the real coinfection rate.

Exceeding rare has been the concomitant COVID-19 in people with a confirmed diagnosis of AS similar to a 75-year-old woman (pneumococcal pneumonia, meningitis, and mitral valve endocarditis), which was treated with intravenous ceftriaxone. Besides drug-induced agranulocytosis, she had severe clinical deterioration due to COVID-19 [5]. Her comorbidities were chronic obstructive pulmonary disease, hypothyroidism and hypertension. There was sepsis, right upper lobar pneumonia, and acute kidney injury. The PCR in CSF, blood cultures, and urinary antigens were positive for *S. pneumoniae*. Furthermore, after the general status deterioration, she tested positive for SARS-CoV-2. The authors commented on the difficulty to ascertain if the SARS-CoV-2 infection was at admission and therefore she likely contracted the virus during her inpatient stay [5].

Arias-Morales *et al*. reported a 49-year-old woman with a history of diabetes, alcoholism, hepatitis C, immunosuppression (HIV-positive), smoking, and drug abuse [2]. She was hypoxemic, lethargic, with diffuse interstitial lung changes, atelectasis of left lower lobe, aortic valve vegetation, and pneumococci in sputum and blood cultures. Because of penicillin allergy, she started on intravenous vancomycin, further changed to moxifloxacin and metronidazole, and obtaining a successful clinical improvement. She also developed acute renal failure and needed intermittent hemodialysis support.

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The authors emphasized the good outcome despite risk factors and multiorgan failure [2]. Jesus *et al*. previously reported a healthy 67-year-old woman with sudden coma, hypoxemia, tachycardia, hypotension, acute renal failure, meningitis, and the presence of pneumococcus in cultures of blood, cerebrospinal fluid and the bronchial secretions [4]. Imaging studies showed bilateral lung consolidation and vegetation in the mitral valve. She underwent intensive care support, and ceftriaxone based on the sensitivity tests. Even with the resolution of lung and kidney changes, she died on the 18th day of admission. The authors highlighted the severe course of the syndrome in this elderly woman without any of the classical risk factors, but presenting with persistent lymphopenia[4]. Rodríguez Nogué et al. reviewed the literature on AS and reported the case of a 44-year-old Spanish male without risk factors for pneumococcal infection except for diabetes [6]. He had bilateral pneumonia, meningitis, and endocarditis in the aortic valve, and was treated by ceftriaxone, ampicillin and vancomycin. Besides, he underwent a mechanic prosthesis valve change, and evolved with left hypoacusis and cortical brain infarction [6]. Their review included data of 74 confirmed cases of AS published before May 2018. Patients: 48 (64.87%) males; age ranges: ≤. 40 (16.22%), 40-64 (71.62%), and ≥ 65 (12.16%) years; site of endocarditis: aortic (49.32%), aortic and mitral (13.70%), mitral (28.77%), pulmonary (one), mitral and tricuspid (two), and tricuspid (three) cases [6]. Surgical valve procedures occurred in 57.58% of patients, and the authors emphasized the role of early cardiac surgery to decrease premature mortality and complications risk. Ictus affected near 23% of patients and loss of hearing is a complication in up to 36%, both related to physiopathological phenomena in meningitis, endocarditis or pneumonia. Invasive pneumococcal infection is prevalent in elderly people with comorbidities, and the relative risk increases from 4.4 to 7.6 comparing between one and three risk factors. Alcoholism was a risk factor in only approximately 38 % of the individuals, while diabetes played a major role under 64 years, mainly in those aged less than 40 years [6]. The authors called attention to earliest cardiac imaging study in cases of pneumonia or meningitis by pneumococcus, aiming to rule out the hypothesis of acute endocarditis [6]. Shin *et al*. reported a 43-year-old alcoholic male with fever, confusion, pain and edema in the left foot, systolic aortic murmur, hypoxemia, and bilateral pulmonary infiltrates [7]. Blood cultures revealed pneumococcus, the echocardiogram showed aortic vegetation, and the analysis of cerebrospinal fluid (CSF) was consistent with bacterial meningitis. His treatment with ceftriaxone was guided by sensitivity test, and he also underwent cardiac surgery to repair the aortic valve and ventricular wall destroyed by the infection. The intensive management was unsuccessful, following septic and hemorrhagic shock. The authors focused the early cardiac evaluation in cases of pneumococcal pneumonia [7]. Final comments on the complete autopsy study by Dos Santos *et al*. in a 23-year-old alcoholic male non-vaccinated against pneumococcus seem to be useful in this setting [3]. He presented longstanding fever before accentuated headache, and CSF changes of bacterial meningitis, initially treated with penicillin, aminoglycoside and chloramphenicol, without clinical improvement. He further developed an aortic murmur of double valve lesion and had sudden precordial pain followed by circulatory shock. Autopsy study revealed turbid CSF, diffuse brain edema, hyperemia, and arachnoiditis; myocardial infarction by an embolus with pneumococcus in the anterior descendent coronary; mitral and aortic vegetations with purulent exudates; bronchopneumonia and diffuse alveolar edema; liver congestion, macro vesicular fatty changes, focal necrosis and Mallory bodies; and spleen hyperplasia, with septic infarctions and huge abscess [3]. The authors stressed the role of the early diagnosis and prompt antimicrobial treatment of this severe entity scarcely described, at least in part due to clinical under-recognition. They also highlighted preventive measures against invasive pneumococcal infections [3].

The aim of the commented articles on AS is to enhance the awareness of all the care health workers about this multi-organ involvement with an elevated lethality rate. Less than 3% of native valve endocarditis is due to *S. pneumoniae*, and less than 1% of patients with pneumococcal

endocarditis have the AS [5]. Nevertheless, the association of pneumonia and sepsis should be an indicator for a transesophageal echocardiogram, while neck stiffness and changes of consciousness level are clues for CSF evaluations [5].

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