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Case Report
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Invasive Pneumococcal Disease Associated with Austrian Syndrome

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Abstract

Austrian syndrome (AS) is named in honor of the eminent doctor Robert Austrian, an American physician specializing in infectious diseases who described this pathology in 1957. AS is a clinical entity caused by disseminated *Streptococcus pneumoniae* infection and is usually characterized by the triad of pneumonia, endocarditis, and meningitis. Before the discovery of penicillin, *S. pneumoniae* was one of the most common causes of endocarditis, but today it represents fewer than 1% of such cases. Current estimates place the occurrence rate of AS at 0.9-7.8 cases per 10 million people per year, with a mortality rate of approximately 32%. Alcohol abuse is the main risk factor, but it appears in only 40% of patients with AS. Additionally, 14% of AS patients have no associated risk factors. The majority of patients with AS are males, and it generally appears in middle age. AS more frequently affects the native valve, and in 50% of cases, the aortic valve is damaged. Timely and appropriate antimicrobial treatment and early surgery for endocarditis both decrease the risk of mortality. We present a case of a patient without predisposing factors who presented with this clinical entity and had a satisfactory outcome.

Keywords: Austrian syndrome, meningitis, endocarditis, pneumonia

Introduction

Austrian syndrome is named in honor of the eminent doctor Robert Austrian, an American doctor specializing in infectious diseases, who described this pathology in 1957 (1). Austrian syndrome is a clinical entity caused by disseminated Streptococcus pneumoniae infection and is usually characterized by the triad of pneumonia, endocarditis and meningitis. Before the discovery of penicillin, *Streptococcus pneumoniae* was one of the most common causes of endocarditis, but today it represents less than 1% (2). Currently it is estimated that there are 0.9-7.8 cases per 10 million people each year who have Austrian Syndrome, with a mortality rate of around 32% (3). Alcohol abuse is the main risk factor but it appears in only 40% of the patients. Additionally, only 14% of patients do not have any risk factor. The majority of the patients are males and it generally appears in people who are middle aged. It more frequently affects the native valve and in 50% of cases, the aortic valve is injured (3,4). Proper antimicrobial treatment and early surgery of endocarditis, both decrease the risk of mortality. We present a case of a patient without predisposing factors who presented this clinical entity with a satisfactory outcome.

Case Report

A 57-year-old patient with no past medical history was admitted by ambulance to Emergency Room (ER) in November 2019 with altered mental status. According to the family's account, two weeks before, the patient had an isolated episode of self-limited diarrhea and vomiting with appearance of a cold sore. Also, he was absent-minded and disoriented the day before.

Emergency medical services reported that the patient was found collapsed on the floor by his wife, with a Glasgow Coma Scale (GCS) of 12.

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On arrival at the ER, was febrile with a body temperature of 39.2 ºC. His heart rate was 116 beats per minute with a blood pressure of 136/73 mmHg [mean arterial pressure (MAP): 94]. His respiratory rate was 30 breaths per minute with an oxygen saturation of 99% in room air. He was agitated with a GCS of 10 (E3V2M5). His pupils were anisocoric with non-reactive mydriasis. The neck was stiff with positive signs of Brudzinski and Kernig. The rest of the examination was unremarkable. Initial blood test confirms systemic infection with abnormal complete blood count: hemoglobin=10.2 g/dL, white blood cell count: $8.2x10^3$/uL (85,9% neutrophils) and platelet count: $130x10^3$/uL. C-reactive protein was 20.3 mg/dL, procalcitonin was 6.2 ng/mL, and lactate was 2 mmol/L. Prothrombin activity: 52% [the international normalized ratio (INR: 1.54)]; Other blood examinations were unremarkable. The patient received a sedative (Midazolam 10 mg intravenous) due to significant agitation and cranial computed tomography (CT) scan was performed. After the patient´s stabilization, he was admitted to the intensitive care unit (ICU) where orotracheal intubation was performed (GCS decreased to 7) and broad-spectrum antibiotic treatment (Cefotaxime 2 gr/6 hours + Vancomycin 1500 mg/8 hours + Ampicillin 2 gr/4 hours + Acyclovir 800 mg/8 hours) for suspected meningitis was initiated. In addition, medication with inotropic drug (Norepinephrine 10 mL/h perfusion) was added to control the marked hypotension [mean arterial pressure (MAP: 54)], refractory to fluid therapy. Complete microbiological traceability (blood, sputum and urine cultures, antigens in urine and viral serologies) was taken before the initiation of the antibiotic therapy. After performing a cranial CT scan and correcting the observed coagulopathy (Prothrombin Activity 52%/INR: 1.54), a lumbar puncture was performed that confirmed the presence of *S. pneumoniae* in the cerebrospinal fluid. During the patient's admission to the ICU, the presence of pneumonia was confirmed with blood cultures and rapid Pneumococcal Urinary Antigen (PUAg) test positive for *S. pneumoniae*. Subsequently, the pneumonia responded favorably to antibiotic treatment. The patient progressed well, achieving neurological recovery without any neurological consequences, and was finally discharged 14 days after admission.

The patient returned to the ER at the beginning of January 2020 complaining of severe dyspnea and low limb edema. In addition, he presented altered mental status [GCS of 14 (O4V4M6)] and difficulty in breathing with involvement of accessory muscles. In the ER he showed severe hypotension (MAP: 56) and marked respiratory distress [respiratory rate (RR): 36; Peripheral oxygen saturation (SpO_2): 86%]. Our first diagnosis was a septic shock due to a previous history of pneumococcal meningitis and pneumonia, but serious shortness of breath and peripheral edema increased the possibility of an acute heart failure. After hemodynamic stabilization of the patient (PAM: 67; SpO_2: 95%) we admitted the patient to the ICU again. Once in the ICU, the presence of acute pulmonary edema was confirmed (Figure 1) and an echocardiography was performed, which detected significant aortic insufficiency and an image compatible with vegetation on the aortic valve (Figure 2). The next day the patient underwent urgent surgery for aortic valve replacement. The patient recovered well and upon discharge from the hospital, was referred to the cardiac rehabilitation unit.

Discussion

The groups at risk of developing invasive pneumococcal disease are children under the age of 2, older adults and the immunocompromised (5). The triad of pneumonia, meningitis and endocarditis secondary to bacteremia was first described in 1862 by Herchl after the autopsy of five patients. In 1882, Netter again revealed this clinical relationship, pointing to a clear predisposition for the aortic valve. In 1957 Robert Austrian,

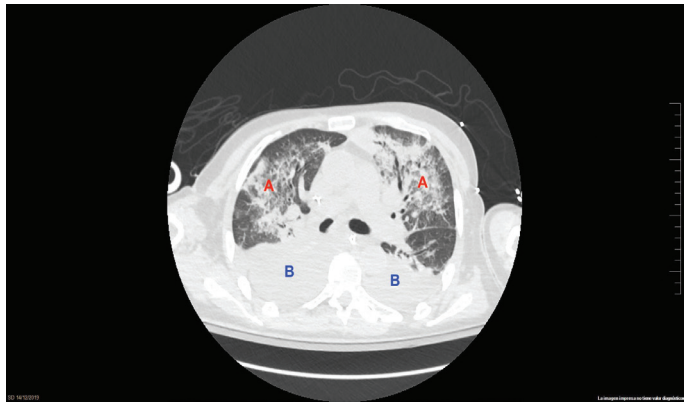

Figure 1. A. Airspace opacity in a central peribronchovascular distribution classic of acute pulmonary edema. **B.** Radiologic image compatible with bilateral pleural effusion

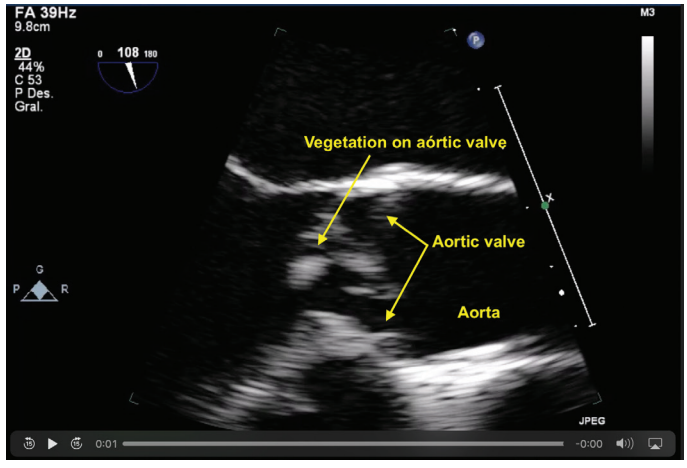

Figure 2. Ultrasonographic confirmation of the presence of vegetation on native aortic valve

reported a total of eight cases, of which six of them died, revealing that the fatal outcome of these patients was commonly the rupture of the aortic valve (1). This association is currently a clinical rarity, however, there is no data on its incidence. The physiopathology is not clear, but it is believed to be caused by *S. pneumoniae* bacteremia originating in any area, the most common being the sinuses or in cases of pneumonia, and here the cardiac valve was affected which, compromised the other systems by embolisms (6). The risk factors for developing Austrian syndrome are as follows; immunosuppressive conditions such as HIV infection, malignancies, organ transplants, chronic steroid use, age: in the early or the late stages of life, cardiovascular diseases such as heart failure and cardiomyopathies, chronic lung disease such as chronic obstructive pulmonary disease and asthma, cirrhosis, chronic renal failure, nephrotic syndrome, sinus and ear infections, influenza virus AH1N1 infection, diabetes, malnutrition, alcohol abuse, cocaine and intravenous drug use, pregnancy, lack of pneumococcal vaccination and cerebrospinal fluid fistula (7). In case of our patient there was no known history of any medical problems. Austrian Syndrome can be fatal if appropriate treatment is not administered early (8,9). In a recently published review of 111 cases of *S. pneumoniae* endocarditis in Spain, Austrian syndrome appears to be a poor prognostic factor and was present in 43.5% of patients with *S. pneumoniae* endocarditis. Pneumonia was reported to be the first clinical manifestation of Austrian syndrome in almost half of the cases (10). Austrian syndrome is characterized by implication of the left chambers of the heart, especially the aortic valve, and is highly aggressive, with almost constant valve destruction. *S. pneumoniae* endocarditis mainly affects native valves, although data on the most commonly affected valves are contradictory and vary among series of cases (10). The clinical profile presentation is an average age of 52 years, with 75% of men affected. There may be a delay of up to 4 or 6 weeks in the diagnosis of the disease. Predisposing cardiac lesions are not frequent and more than half of the patients present a systemic pathology that makes them susceptible to infection. Subacute presentation is a rare form, which was described by Robert Austrian, being more common in older patients, where the course of the disease is usually indolent. The treatment of choice continues to be penicillin, and the decrease in the incidence of *S. pneumoniae* endocarditis has been related to the effectiveness of antibiotic treatment. Owing to cases of moderate resistance to penicillin, third generation cephalosporins have been successfully used, except in rare cases of total resistance in which, vancomycin is the treatment of choice. In our case, we started with a treatment that includes third generation cephalosporin (Cefotaxime) + Vancomycin + Ampicillin amplifying the coverage for treatment of the herpes simplex virus by Acyclovir. Given the aggressiveness of the disease, which produces severe local destruction, surgical treatment is necessary in most patients, as seen in our patient who developed valve damage despite being on adequate antibiotic treatment. Surgical management with valve replacement should be carried out as soon as possible to avoid the development of cardiogenic shock. Despite correct antibiotic treatment and basic support measures, the main prognostic factor of the disease is valve destruction and this is the main cause of death (1). In the Robert Austrian series of case studies, 6 of the 8 patients died per clinic, due to secondary complications of valve destruction therefore the author concludes that antibiotic treatment serves to improve survival, but not to prevent valve rupture, and that patients who develop such a complication have a poor prognosis (1).

In conclusion, Austrian syndrome is a very rare pathology at present, but it is a critical condition and is often only diagnosed when complications arise at a late stage. It is important to maintain close clinical observation especially in the presence of signs of severe sepsis with suspected *S. pneumoniae* infection with or without predisposing factors. An early diagnosis, early initiation of antibiotic treatment and timely surgical management are the only factors that have been shown to decrease mortality and improve patient prognosis.

Ethics

Informed Consent: The patient and his family was informed orally about the suspected diagnosis, about the most appropriate investigation tests and treatment that require. Also the signed the informed consent to complete all of procedures.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.G., B.D.T.M., L.G.P.R., A.G.O., Concept: A.G., F.M.M.C., E.G., M.A.G., H.A.V., L.G.P.R., Design: A.G., F.M.M.C., E.G., M.A.G., L.P.L., H.A.V., E.C.G., L.G.P.R., J.L.G.F., A.G.O., Data Collection or Processing: A.G., F.M.M.C., B.D.T.M., M.A.G., S.R.S., E.C.G., A.G.O., Analysis or Interpretation: A.G., F.M.M.C., B.D.T.M., M.A.G., S.R.S., E.C.G., A.G.O., Literature Search: A.G., F.M.M.C., E.G., L.P.L., S.R.S., H.A.V, L.G.P.R., J.L.G.F., Writing: A.G., B.D.T.M., H.A.V., A.G.O.

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