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CASE REPORT

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Severe Austrian Syndrome in an Immunocompromised Adult Patient – A Case Report

Ioana Raluca Chirteș[1*], Dragos Florea[2], Carmen Chiriac[1,3], Oana Maria Mărginean[1], Cristina Mănășturean[3], Alexander A Vitin[4], Anca Meda Georgescu[1,3]

[1] University of Medicine and Pharmacy of Tirgu Mures, Romania

[2] National Institute of Infectious Diseases "Prof. Dr Matei Bals", Laboratory of Molecular Biology, Bucharest, Romania

[3] Mures County Hospital, Infectious Diseases Clinic I, Tirgu Mures, Romania

[4] Department of Anesthesiology & Pain, Medicine University of Washington Medical Center, Seattle WA, USA

Abstract

Background: Known also as Osler's triad, Austrian syndrome is a complex pathology which consists of pneumonia, meningitis and endocarditis, all caused by the haematogenous dissemination of Streptococcus pneumoniae. The multivalvular lesions are responsible for a severe and potential lethal outcome.

Case report: The case of a 51-year-old female patient, with a past medical history of splenectomy, is presented. She developed bronchopneumonia, acute meningitis and infective endocarditis as a result of Streptococcus pneumoniae infection and subsequently developed multiple organ dysfunction syndromes which led to a fatal outcome. Bacteriological tests did not reveal the etiological agent. The histopathological examination showed a severe multivalvular endocarditis, while a PCR based molecular analysis from formalin fixed valvular tissue identified Streptococcus pneumoniae as the etiologic agent.

Conclusions: The presented case shows a rare syndrome with a high risk of morbidity and mortality. Following the broad-spectrum treatment and intensive therapeutic support, the patient made unfavourable progress which raised differential diagnosis problems. In this case, the post-mortem diagnosis demonstrated multiple valvular lesions occurred as a result of endocarditis.

Keywords: Austrian syndrome, multivalvular endocarditis, *Streptococcus pneumoniae*, splenectomy

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Introduction

Austrian syndrome is defined as a triad of pneumonia, endocarditis and meningitis, caused by invasive *Streptococcus pneumoniae* infection. Since the introduction of antibiotics, the incidence is small, occurring in about 3 % of the total cases of endocarditis, compared to 10-15 % in the pre-antibiotic era [1-3].

The pneumococcal endocarditis evolves aggressively with rapid valvular destructions and is associated with a 63% mortality rate in non-surgical cases and 32% mortality rate in early-surgical intervention cases [4].

The portal of entry is the respiratory tract. The aortic valve is mostly affected, varying from 46.7 % to 77.4 %, leading to life-threatening complications. The mitral valve can be affected in 31.4 % to 56.7 % of cases [5-6].

Several studies have demonstrated an association between invasive disease and specific pneumococcal serotypes. According to the European Centre for Disease Prevention and Control, the most likely causes of invasive pneumococcal disease are the serotypes 3, 8, 22F, 19A, 7F, 12F, 1, 9N, 15A, 24F. Host factors which increase the risk of invasive pneumococcal disease are alcohol abuse, chronic pulmonary diseases, systemic corticotherapy, diabetes mellitus, haematological neoplasias, chronic renal failure, pregnancy and the postpartum period, asplenia, influenza infection, solid organ or hematopoietic cell transplantation, HIV in-

* Correspondence to: Ioana Raluca Chirteș, Infectious Diseases Clinic I, Tîrgu-Mureș, Romania, Str. Gheorghe Doja, Nr. 89, Târgu Mureș. Romania E-mail: itodoran@yahoo.com

fection and other condition associated with immunodeficiency [7-8].

Strains of *S. pneumoniae* resistant to penicillin are continually being reported extending to 24 % of all known strains in the USA and 58 % in some European countries [1, 9].

The etiological treatment for penicillin-resistant strains includes ceftriaxone or cefotaxime plus vancomycin [10]. Mortality rate ranges from 63 % up to 80 % of patients who underwent medical treatment, compared to 32 % in those who benefited from combined medical-surgical therapy [11].

In accordance with the American College of Cardiology and the American Heart Association Task Force on Practice accepted guidelines, surgical intervention should be taken into consideration once a diagnosis of bacterial endocarditis has been reached [12-13].

This report aimed to highlight the importance of early detection and adequate management of the invasive pneumococcal disease and to reconsider *S. pneumoniae* as a possible etiologic agent of infective endocarditis in patients with associated risk factors. Consent to publish the case was given by the treating physician.

Case Report

A 51-year-old female patient was admitted to the Infectious Diseases Clinic I, Tîrgu-Mureș, Romania, having been transferred from the county hospital in Alba Iulia due to the sudden onset of fever, chills, headache, vomiting and altered states of consciousness. The patient was splenectomised seven years ago with idiopathic thrombocytopenic purpura. No pneumococcal vaccination was recorded. The patient was hypertensive and reported that she neither consumed alcohol or smoked cigarettes.

The patient had recently been hospitalised for left upper lobe pneumonia as well as for lumbar discopathy and had received lumbar steroid injections for low back pain.

Upon admission, the patient was confusion and had motor aphasia, neck stiffness, discrete left peripheral facial paralysis, left flank pain on palpation, tachypnea, disseminated bronchial rales, bilateral crackles, heartbeat was 117 beats/minute, temperature of 35.3°C, oxygen saturation (SaO2) of 77 % - 84 %, blood pressure of 107/74 mmHg.

The magnetic resonance imaging (MRI) scan, performed during a previous hospitalization four days ago previously, highlighted an apparently well-defined focal image with fine internal septum located adjacent to the right iliac wing, the sacral wing, and the lateral contour of the right sacroiliac joint in contact with the psoas muscle with a demarcation plane against it, apparently without bone invasion. This mass measured 3.5 cm long and 3.00 cm wide (Fig.1).

Blood samples were collected on admission. Laboratory data revealed a leucocytosis of 23860/µl, with a left shift, 87% neutrophils, inflammatory syndrome, 30 mg/dl C-reactive protein (CRP) level, an erythrocyte

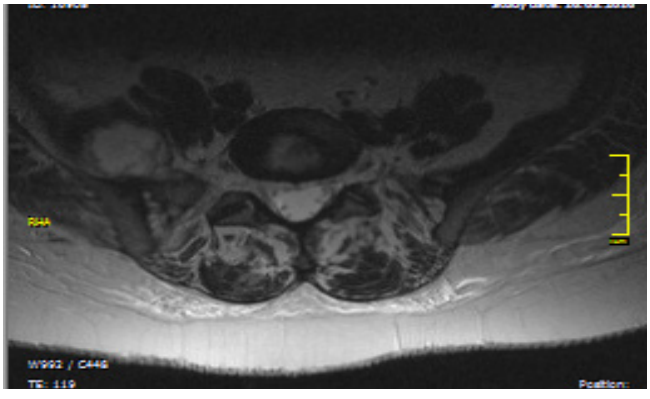

Fig. 1. The MRI examination of the pelvis performed during the previous hospitalisation highlights an apparently well-defined focal image with fine internal septum located adjacent to the right iliac wing, the sacral wing, and the lateral contour of the right sacroiliac joint in contact with the psoas muscle with a demarcation plane against it, apparently without bone invasion.

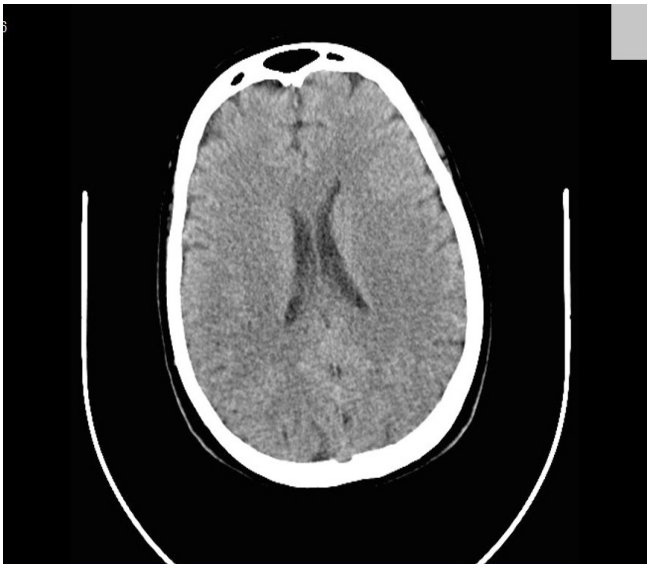

Fig. 2. The CT scan of the brain (narrowing of the intergyral fronto-occipital bilateral sulci)

sedimentation rate (ESR) of 68 mm/h, a creatinine level of 1.12 mg/dl, and a blood sugar level of 158 mg/dL. Opalescent cerebrospinal fluid (CSF) was obtained by lumbar puncture undertaken in the county hospital of Alba Iulia. It showed 213 cells/mm^3, a predominance of polymorphonuclear leukocytes, 80% neutrophils and 20% lymphocytes. CSF glucose was 0.5 mg/dL and CSF protein 568.6 mg/dL. Both the CSF and blood cultures were negative. The radiological examination of the thorax was indicative of bronchopneumonia. The computer tomography (CT) scan of the brain showed no pathological changes, except for the narrowing of the intergyral fronto-occipital bilateral sulci (Fig. 2). The diagnosis was acute bacterial meningoencephalitis, and severe, comatose bronchopneumonia. Antibiotic treatment was initiated with vancomycin 1g IV bid and cefotaxime 3g IV qid, together with dexamethasone 8 mg IV bid, mannitol 20% 130 ml IV bid, and the proton pump inhibitor, pantoprazole 40 mg IV.

Over 48 hours there was a return to a normal state of consciousness and cooperation, but respiratory function remained unstable with persistent respiratory insufficiency, the SaO2 being 88-95%. Oxygen therapy was initiated. The patient had impaired glucose metabolism with a blood glucose of 282 mg/dL. Hypoglycemic therapy with both long-acting and pre-mixed insulin was commenced with Lantus® (Sanofi, Paris, France), 14 UI subcutaneous, once a day, and Humulin R® (Eli Lilly, Indianapolis, USA) three time a day in 4-8-8 UI subcutaneous.

Three days after admission to the hospital, the patient developed mitral and systolic tricuspid murmurs, and on the fourth day accentuated respiratory failure. Oxygen saturation decreased to 87 %, in spite of the patient being on oxygen therapy. She also showed signs of dyspnoea, tachycardia and palpitations. Due to deterioration of the subjective and general clinical condition, the patient was transferred to the Intensive Care Unit on the 5th day after admission. Transthoracic ultrasound revealed aortic valve endocarditis with severe aortic insufficiency.

On day 7, the patient developed acute renal failure with a creatinine clearance of 36.34 ml/min, heart failure, acute liver failure with a prothrombin time of 28.9 %, aspartate aminotransferase (ASAT) of 1634U/L, and alanine aminotransferase (ALAT) of 1658U/L. The platelet count was 124000/µl, indicative of thrombocytopenia. The CT scan revealed bronchopneumonia, bilateral pleural effusion (Fig. 3, 4), cerebral oedema, hepatic steatosis, complete resorption of the intra-abdominal process described previously.

Later, she developed severe oedema in the right inferior limb with mottled discolouration of the skin and blisters. Doppler echocardiography excluded pathological changes at the arteriovenous level. Laboratory data revealed progressive worsening with recorded creatinine 3.16 mg/Ll, elevated transaminase level, performed in dynamics (ALAT 1995/2232 U/L, ASAT 1442/1042 U/L), prothrombin time 25%, INR 2.73, fibrinogen 157 mg/dL, creatinine-kinase 24788 mg/dL.

The possibility of multiple organ failure and the occurrence of disseminated intravascular coagulation was taken into account. The patient required inotropic support. Orotracheal intubation and mechanical ven-

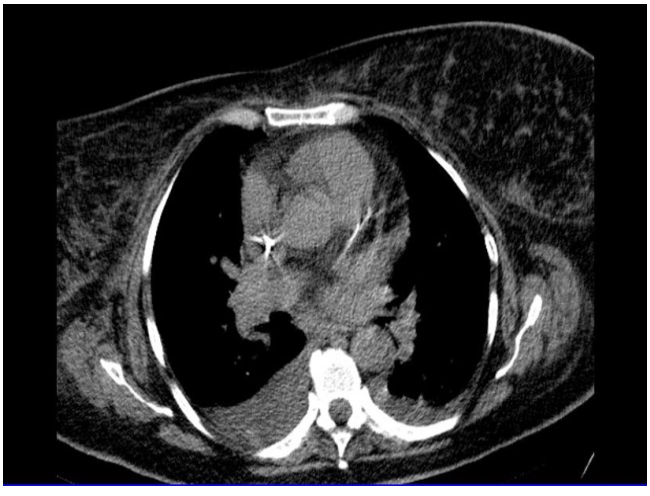

Fig. 3. The CT scan of the chest (multiple foci of opacity disseminated in both lung fields, bilateral pleural effusion)

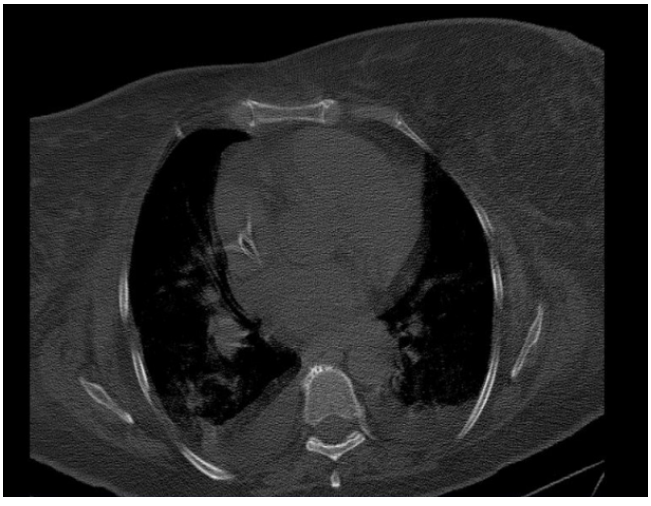

Fig 4. The CT scan of the chest (multiple foci of opacity disseminated in both lung fields)

tilation were performed, using synchronised intermittent mandatory ventilation, with a respiratory rate of 12 breaths/minute, tidal volume of 500 ml/minute, fraction of inspired oxygen (FiO2) of 60%, I:E ratio 1:2.

Vancomycin 1 g IV bid was prescribed in conjunction meropenem 1 g IV bid, with the doses adjusted based on creatinine clearance, and intravenous immunoglobulins.

The patient's general condition worsened, with an increasing severity of multi-organ failure, persistent hypotension (blood pressure of 60/45 mmHg) despite adequate fluid resuscitation and vasopressor support. She went into cardiac arrest and did not respond to cardiopulmonary resuscitation. She died nine days after being admitted to hospital.

Anatomopathological examination

The histopathological examination and necropsy, revealed cerebral oedema, leptomeningeal hyperaemia, bilateral bronchopneumonia, right pleural effusion and multi-organ changes suggestive of septic shock associated with thrombophlebitis of the right inferior limb. The relevant changes including the occurrence of voluminous vegetation attached to the right atrial wall, the tricuspid valve and the aortic valve and the sclerotic changes of the mitral valve, observed at the morphological examination, were suggestive of acute bacterial endocarditis.

The histological section of samples collected from the affected endocardium, processed and fixed in formaldehyde and stained with haematoxylin and eosin, were examined under the optical microscope. The vegetation adherent to the wall and valve consists of fibrin, extensive bacterial colonies, leukocytes and erythrocytes.

Molecular diagnostic technology

The formalin-fixed paraffin-embedded (FFPE) valvular tissue was sent to the National Institute for Infectious Diseases, Bucharest, Romania, for further microbiological investigations. DNA was extracted from FFPE tissue using a commercial kit (Qiagen, Duesseldorf, Germany). The eluate was then tested using a commercial molecular assay, based on multiplex broad range polymerase chain reaction coupled with electrospray ionisation-mass spectrometry (PCR ESI-MS) (Abbott, Des Plaines, USA) The test identified a high level for *S. pneumoniae*, and a weak level of *Acinetobacter spp*.

Discussion

Diagnosis of pneumococcal endocarditis is sometimes delayed due to the low incidence of the agent causing the cardiac pathology, the absence of classical stigmata of infective endocarditis and the delayed occurrence of cardiac auscultation signs [6]. A review of the literature gives alcoholism as an important risk factor in the development of Austrian syndrome, with a frequency of 10.4-28.1 % [2, 6] [14]. In the presented case, the risk factor for the invasive infection with *S. pneumoniae* was an immunodeficiency caused by splenectomy, a condition which increases the risk of disease with encapsulated bacteria.

The patient's previous history of repeated hospitalisations, the treatment of lumbar discopathy with lumbar steroid injections, the appearance of a suggestive image of intra-abdominal abscess, initially raised the suspicion of *Staphylococcus aureus* infection, which is the primary pathogen responsible for native valve infective endocarditis [15].

In this case, the severe form of meningoencephalitis, the delayed appearance of a heart murmur, and the imposing differential diagnosis problems, together with the absence of a pathological agent following culture based bacteriological investigations and limited access to molecular investigations, delayed the etiologic diagnosis.

Polymerase chain reaction molecular techniques are particularly useful in identifying the aetiology of endocarditis concomitant with negative blood cultures, but these investigations are sometimes inaccessible due to their high costs. In this case, the aetiological diagnosis was obtained using PCR ESI-MS, a molecular method designed to identify DNA from more than 750 different species of bacteria and *Candida*. This can be undertaken from numerous clinical samples, with results produced within six hours.

Several studies have shown that left-sided heart failure is characteristic of Austrian syndrome, especially aortic valve lesions, but in our case the endocardial damage comprised both the aortic valve and the right side of the heart, passing through the tricuspid valve and the right atrium wall, observed during necropsy. *Staphylococcus aureus* is incriminated as the major etiologic agent of multivalvular endocarditis, intravenous drug users or patients with venous catheterisation being at risk [16, 17].

Although empirical treatment with cefotaxime and vancomycin was administered at the time of admission to the Infectious Diseases Clinic, she developed infective endocarditis on the third day after being admitted, with an acute and rapid deterioration in her overall clinical status.

Antimicrobial resistance studies of *Streptococcus pneumoniae* strains show the susceptibility of bacterial isolates to vancomycin. Of the cephalosporins, cefotaxime is classified as the most effective antipneumococcal antibiotic [18, 19].

In accordance with the guidelines for the management of patients with heart valve disease (American Heart Association/American College of Cardiology Guidelines for the Management of Patients with Valvular Heart Disease), the presented case raises questions on surgical indication. Although the presence of severe aortic insufficiency, which predisposes to important haemodynamic complications, could have indicated surgical treatment, the increasing thrombocytopenia, the occurrence of multiple organ failure syndrome and disseminated intravascular coagulation were associated with an increased intraoperative risk [12, 13].

According to the new classification and sepsis definition (SEPSIS-3), our patient fell within the septic shock criteria [21]. She developed cardiac failure, with persisting hypotension, despite adequate fluid resuscitation and she required vasopressor support with noradrenaline. The patient developed cardiac arrest, not responsive to cardiopulmonary resuscitation, with a fatal outcome.

Introduction of the pneumococcal vaccine had a dramatic impact on decreasing the prevalence of disseminated pneumococcal infections in both paediatric and adults patients [21]. In our case, seven years after therapeutic splenectomy, pneumococcal vaccination was not administered. As a result the patient developed an invasive, fatal, pneumococcal infection, thus highlighting the importance of prophylaxis in a susceptible host.

Conclusions

Austrian syndrome is a rare entity which may occur in people with predisposing risk factors. Although PCR ESI-MS is not widely used in Romania, this molecular technique is particularly helpful in identifying the bacterial pathogen in cases of culture-negative endocarditis. Despite a well-managed antibiotic treatment and vital functional support, the patient's progression was unfavourable. The development of extensive valvular destruction and multiple organ insufficiencies led to a fatal outcome.

Conflict of interest

None to declare.

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