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Casi clinici

Case reports

Aortic-right atrium fistula complicating Austrian Syndrome: a case report and literature review

Sindrome di Austrian complicata da fistola tra aorta ed atrio destro: caso clinico e revisione della letteratura

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INTRODUCTION

The finding of *Streptococcus pneumoniae* endocarditis along with pneumonia and meningitis in an alcoholic patient is a severe disease which was firstly described by Osler in 1881 but it is also called Austrian syndrome. This entity including the rupture of the aortic valve was found to be 'uncommon but not rare' in the 1950s since the presence of endocarditis might be anticipated in approximately 20% of patients with pneumococcal meningitis [1]. According to more recent reports, 0.6-2.2% of patients with pneumococcal bacteremia have endocarditis [2-4]. On the other hand, most patients with pneumococcemia (80%) have pneumonia, and fewer patients (8%) have meningitis [2]. Since the introduction of penicillin, the prevalence of pneumococcal endocarditis appears to have significantly declined from ~15% to 1-3% of all cases of native valve endocarditis in adults. Nevertheless, pneumococcal endocarditis still occurs, and is associated with severe valve damage and poor outcome [5-7]. The Austrian syndrome is an uncommon entity in the antibiotic era, although its frequency is not clearly defined. We report a case of Austrian syndrome causing aortic-right atrium fistula in a patient who had undergone splenectomy for Hodgkin's lymphoma. Moreover, we review the literature concerning epidemiology and diagnostic pathways of pneumococcal endocarditis and Austrian syndrome in adults.

CASE REPORT

A 39-year-old woman was admitted to our hospital with a two-week history of fever and non-productive cough which were unresponsive to treatment with ciprofloxacin. In addition, she was complaining with headache and vomiting for 24 hours prior to admission. Her past medical history was remarkable for rheumatic fever in childhood, and Hodgkin's lymphoma treated with chemotherapy, radiotherapy and splenectomy 12 years earlier. She had received two doses of the 23-valent polysaccharide pneumococcal vaccine, respectively prior to splenectomy and five years later. On hospital admission, her temperature was 38.6 °C, heart rate 112 beats/min, blood pressure 100/60 mm Hg, and oxygen saturation 94% on air. Physical examination showed confusion, nuchal rigidity and other signs of meningism, and crepitations in the thoracic low-zones. A chest radiograph showed bilateral lower-lobe infiltrates and small pleural effusions. Cranial computed tomography findings were within normal limits. Laboratory testing revealed the following abnormalities: haemoglobin 9.6 g/dl, white cell count 22,900 cells/mm^3 (94% neutrophils), platelet count 104,000 cells/mm^3, peripheral blood glucose 147 mg/dl, C-reactive protein 18.1 mg/dl (normal value: <0.5 mg/dl). Cerebrospinal fluid (CSF) tests yielded glucose 14 mg/dl, protein 259 mg/dl, and white cell count 1680/mm^3 (85% neutrophils). CSF examination revealed pleocytosis and Gram-positive diplo-

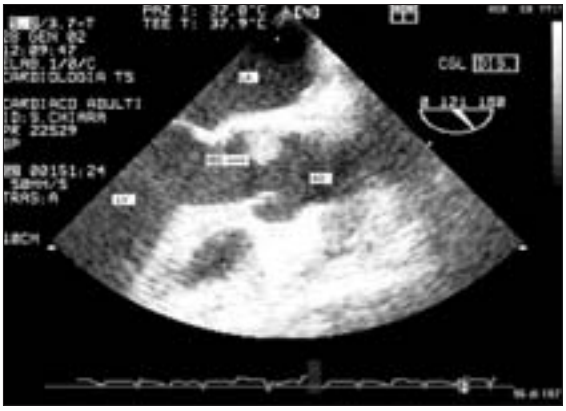

Figure 1 - Transesophageal echocardiography showing an irregular echogenic mass at the posterior non coronaric aortic cusp. Legend: VEG, arrowheads, irregular echogenic mass; LA, left atrium; LV, left ventricle; AO, ascending aorta.

cocci. The patient was started on intravenous cefotaxime and ampicillin, which were replaced by penicillin G as soon as cultures of CSF, blood, and sputum showed penicillin-susceptible *Streptococcus pneumoniae* (MIC, ≤0.06 µg/mL). All pneumococcal strains were typed as serogroup 23 and serosubtype B. Five days after admission, the patient's condition worsened with development of dyspnea, hypotension, tachycardia, and a diastolic murmur. A chest radiograph showed increasing pleural effusions, and an electrocardiogram showed a second-degree heart block. On transesophageal echocardiography (TEE), an irregular echogenic mass was seen at the posterior non coronaric aortic cusp (Figure 1). In addition, a large echogenic mass was present in the right atrium, protruding from the aortic annulus. At colour-Doppler study (systolic frame), a high velocity "mosaic" jet was found in the right atrium originating from the left ventricular outflow (Figure 2). These findings were consistent with an aortic-right atrial fistula complicating aortic valve endocarditis. At that time, the patient underwent urgent valve replacement and aortic root reconstruction. Operative findings confirmed that the non coronary aortic cusp was destroyed by large vegetations which were obstructing the left ventricular outflow tract. In addition, an acquired fistula with a protruding septic thromb was found in the right atrium extending into the aortic root. The patient completed an 8-week course of penicillin G and fully recovered.

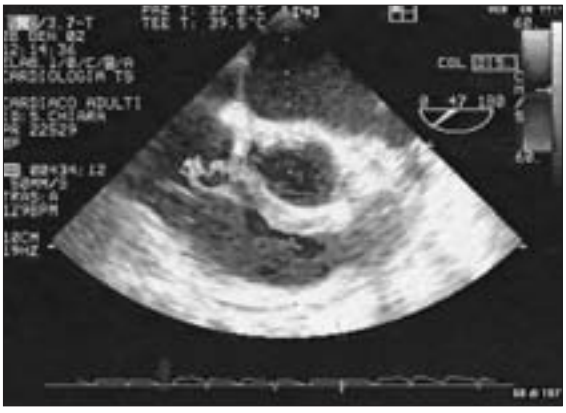

Figure 2 - Transesophageal echocardiography (colour-Doppler) showing a high velocity 'mosaic' jet in the right atrium from the left ventricular outflow. Legend: RA, right atrium; RV, right ventricle; LA, left atrium; LVOT, left ventricular outflow.

DISCUSSION

A computerized Medline search from 1966 to 2006 shows a total of 49 cases of Austrian syndrome. Of them, 36 cases are part of four pneumococcal endocarditis series which are shown in Table 1. In a review that included about two-thirds of these cases [5], pneumococcal meningitis was a common complication of endocarditis, and Austrian syndrome was found in 42% of patients with meningitis. The outcome was poor in 63% of these patients. However, that series included cases of endocarditis occurring during a long period, exactly from 1966 to 1996. Echocardiography was performed in only 19% of cases, and most of them did not undergo TEE. Echocardiography plays an important role both in confirming the diagnosis and assessing valve status to determine the need for surgical intervention in infective endocarditis. Indeed, in that series a combined medical-surgical approach, employing a prolonged course of antibiotics plus early valve replacement, appeared to result in a lower rate of mortality compared with that obtained with antibiotics alone [5]. In a nationwide retrospective survey in France (1991-1998) of *S. pneumoniae* endocarditis, concomitant meningitis was noted in as many as 40% of patients, and Austrian syndrome resulted to be rare among patients with endocarditis [6]. The mortality rate was much lower (24%) compared with that of the previously reported series [5]. The majority of the patients underwent TEE in the French series, and then

Table 1 - Brief overview of pneumococcal endocarditis series in literature.

N.° cases	*Study period*	*Mortality %*	*Meningitis %*	*Pneumonia %*	*Austrian syndrome %*	*Reference*
197	1966-1966	63	59.5a	60.4b	42c	[5]
16	1986-1997	19	31.2	62.5	18.7	[8]
30	1991-1996	24	40.0	36.7	6.6	[6]
63	1978-1998	35	28.5	34.9	3.1	[3]

Legend: a 59.5%: 69/116 patients evaluated for meningitis; b 60.4%: 61/101 patients evaluated for pneumonia; c 42%: 29/69 patients with meningitis had Austrian syndrome

about two-thirds of them received a combined medical-surgical treatment. TEE demonstrated the tendency of pneumococcal endocarditis to cause major valve damage and might have contributed to orienting treatment towards early surgery. Similarly, in a retrospective analysis of pneumococcal endocarditis diagnosed in Denmark (1986-1997) the relatively low fatality rate (19%) supported the view that a course of parenteral antibiotic therapy, combined with early valve replacement if necessary, can improve the outcome of the disease [8]. In fact, about one-half of Danish patients underwent combined medical-surgical treatment. Concomitant meningitis and Austrian syndrome were found respectively in 31% and 19% of patients in that series. More recently, a prospective Spanish study evaluated the effect of penicillin resistance of *S. pneumoniae* on the presentation, treatment, and outcome of pneumococcal endocarditis in 63 patients during a 21-year period (1978-1998) [3]. In that series, 38% and 10% patients had pneumococcal isolates resistant to penicillin and cefotaxime, respectively. Pneumococcal meningitis was found in 28% patients with endocarditis, and Austrian syndrome was quite rare. Similarly, about one-half of patients underwent valve replacement, and the overall mortality rate was 35%. Moreover, left-side heart failure, but not penicillin resistance, was associated with a higher risk of death. Interestingly, the diagnosis of endocarditis was not initially suspected in 25% of patients of the Spanish series, at a median of 8 days after admission, since physicians were often misled by other concomitant pneumococcal diseases including meningitis and pneumonia. The median delay in diagnosis of endocarditis after hospitalization ranged between 7 and 16 days in the other series [5, 6, 8]. This finding underlines the need to consider early the possible diagnosis of endocarditis in every patients with pneumococcal meningitis or bacteremia, particularly in alcoholics and immunocompromised patients. Indeed, we confirm this assumption by presenting a case of Austrian syndrome in whom the diagnosis of endocarditis was made late, at 5 days after hospital admission. Endocarditis involving the aortic valve with aortic-right atrial fistula was finally recognized through development of left-side heart failure and detection of new diastolic murmur. Indeed, *S. pneumoniae* endocarditis causes severe valve damage with high rate of local and systemic complications. Thus, the aggressive nature of invasive pneumococcal infection makes early diagnosis and appropriate medical or combined medical surgical approach crucial.

Most *S. pneumoniae* endocarditis has been seen in patients with chronic alcoholism, which has been identified as a risk factors in 28-50% of cases [5, 6]. In a study of pneumococcal endocarditis in indigenous Alaska natives, no patient had known preexisting heart disease and the most common underlying disease was alcoholism [9]. However, other underlying medical diseases including diabetes mellitus, valvular disease, asplenia or acquired spleen dysfunction, and HIV infection have been reported in patients with pneumococcal endocarditis [7]. Our patient underwent splenectomy for Hodgkin's lymphoma, 12 years earlier the present admission. In a surveillance study of overwhelming infections in asplenic patients, nearly 90% of episodes have been reported to be caused by *S. pneumoniae* but only 31% of individuals had received the 23-valent pneumococcal polysaccharide vaccine before infection [10]. Both previous studies, as summarized in a Cochrane analysis and in a more recent case-control analysis, confirm that the 23-valent pneumococcal vaccine does not protect against nonbacteremic pneumonia but provides a moderate protective effect against pneumococcal

bacteremia and invasive disease [11, 12]. Our patient had received two doses of the 23-valent polysaccharide pneumococcal vaccine, respectively prior to splenectomy and five years later, namely seven years before this hospitalization. Nevertheless, she developed invasive pneumococcal disease due to the 23 capsular serotype, which is represented in the vaccine. Although a recent review showed that there are insufficient data on duration of efficacy for 23-valent polysaccharide pneumococcal vaccine, the British Committee for Standards in Haematology currently recommends pneumococcal re-immunisation of asplenic patients every five years or more frequently, particularly if there is an underlying disease causing immunosuppression [13, 14]. In our patient, a probable decreasing titre of antibodies to pneumococcal polysaccharides might explain the development of the invasive pneumococcal disease, as reported in up to 20% of asplenic individuals [15]. Alternatively, another reason for vaccination failure is that certain pneumococcal serotypes including serotype 23 may be poorly immunogenic [10].
The potential of *S. pneumoniae* to cause severe valve damage is confirmed in this report. Our review shows that the prevalence of Austrian syndrome is decreasing from 19% to 3% in patients with pneumococcal endocarditis in recent years. This finding is presumably due to early administration of antibiotic therapy to patients with pneumococcal invasive disease. Our case emphasizes that the diagnosis of endocarditis and Austrian syndrome should be considered as soon as possible in every patient who presents with pneumococcal meningitis or bacteremia, particularly in immunocompromised patients.

Key words: Austrian syndrome, pneumococcal endocarditis, pneumococcal infection

SUMMARY

The triad of pneumonia, meningitis, and endocarditis due to *Streptococcus pneumoniae* is known as Austrian syndrome. We report a case with an aortic-right atrium fistula in a 39-year-old woman who had undergone splenectomy for Hodgkin's lymphoma.
The review of literature shows that the prevalence of Austrian syndrome is decreasing from 19% to 3% of patients with pneumococcal endocarditis in recent years. This case emphasizes that diagnosis of endocarditis should be considered early in every patient with pneumococcal meningitis or bacteremia, particularly in immunocompromised patients.

RIASSUNTO

La triade polmonite, meningite ed endocardite da Streptococcus pneumoniae *è conosciuta come sindrome di Austrian. Si descrive un caso con fistola tra aorta ed atrio destro in una donna sottoposta a splenectomia per linfoma di Hodgkin. La revisione della letteratura dimostra che negli anni recenti la prevalenza della sindrome di Austrian si stà riducendo dal 19% al 3% tra i pazienti con endocardite pneumococcica. Questo caso clinico sottolinea che la diagnosi di endocardite deve essere considerata precocemente in tutti i pazienti con meningite o batteriemia pneumococcica, soprattutto nei soggetti immunocompromessi.*

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