Pneumococcal Endocarditis of Subacute Evolution

Laercio Uemura, Newton César Grassi, Luciane Cazarin

Londrina, PR - Brazil

With the development of penicillin, Streptococcus pneumoniae has become an uncommon cause of bacterial endocarditis in adults. Subacute manifestation of pneumococcal endocarditis has been reported a few times in the literature, but most reports define the disease as acute, severe, and having a high mortality rate.

We report the case of a 58-year-old male with subacute bacterial endocarditis due to Streptococcus pneumoniae. We stress the low frequency of this agent as a cause of endocarditis and the atypical evolution of this case. The pathophysiology, clinical manifestations and evolution, and the therapeutical options for this type of infection are also discussed.

Pneumococcal endocarditis has become a rare disease since the appearance of penicillin in the beginning of the '40s, and it has accounted for 1% to 3% of all cases of endocarditis in native valves. In recent years, however, a greater number of cases have been reported because of the appearance of strains of *Streptococcus pneumoniae* resistant to penicillin.

The disease is usually acute and severe and may be accompanied by purulent meningitis, rapid destruction of the valve, heart failure, and high mortality, even with the introduction of penicillin.

We discuss an uncommon form of pneumococcal endocarditis, only reported a few times in the literature.

Case report

A 58-year-old white married male sought medical assistance complaining of daily fever (38.5 °C), asthenia, myalgia, polyarthralgia, and loss of 12 kg in the last 4 months. Concomitantly, his family reported changes in his personality, such as sadness, easy crying, and suicidal ideation. They denied, however, confusion, disorientation, and agitation. They also denied any psychiatric antecedent. On the 20th day of hospitalization, severe cephalea appeared involving the entire cranium, not associated with nausea or vomiting, which did not subside with common analgesics, such as paracetamol and dipyrone. The patient did not seek medical attention immediately and continued using only antipyretics and analgesics. The patient denied any surgical or dental procedure prior to the symptoms, and also denied the use of tobacco, alcohol, injected drugs, and sexual promiscuity. He reported a left nephrectomy 4 years earlier and that he was hypertensive and under irregular use of antihypertensive medication.

On physical examination, the patient was oriented in regard to time and space, pale (+/4), febrile (38.4 °C). His heart rate was 90bpm, his respiration rate was 20 rpm, and his blood pressure was 130/90mmHg. Clinical signs evidenced meningism. On heart auscultation, a systolic murmur (+/4) was heard in the mitral area and a diastolic murmur (+/4) was heard in the aortic area. The remaining clinical examination was within the normal range, including the fundus of the eye.

Puncture of the cerebrospinal fluid revealed lymphomonocytic meningitis [red blood cells = 126; leukocytes = 69 (lymphocytes = 97%; neutrophils = 3%); glucose = 47; proteins = 41; chloride = 728] without diagnostic confirmation (bacterioscopy, latex, and the cultures and search for Koch's bacillus, fungi and *Cryptococcus neoformans* were all negative). The values of the tests for inflammatory activity were all increased as follows: sedimentation rate = 55; alpha1-acid glycoprotein = 2.69; C-reactive protein =1/16 (104). The hemogram showed microcytic hypochromic anemia, and leukocytosis (leukocytes = 16,200/mm^3). Urinalysis revealed urinary sediment with red blood cells (156,000) and normal leukocytes. The urine culture was negative. Urea, creatinine, glycemia, platelets, and electrolytes were within the normal range. Serologies for HIV and syphilis were negative. The chest X-ray showed a mild enlargement of the cardiac silhouette. The electrocardiogram showed a sinus rhythm and hypertrophy of the left atrium and ventricle.

The transthoracic echocardiogram confirmed the suspicion of infectious endocarditis by evidencing a vegetation of 2.0 x 1.1cm in the aortic valve (fig. 1). Other echocardiographic findings included mild aortic and mitral insuffici-

Hospital Universitário Regional do Norte do Paraná - Universidade Estadual de Londrina
Mailing address: Laercio Uemura – Rua Senador Souza Naves, 1456 – 86015-430 – Londrina, PR, Brazil
English version by Stela Maris C. Gandour

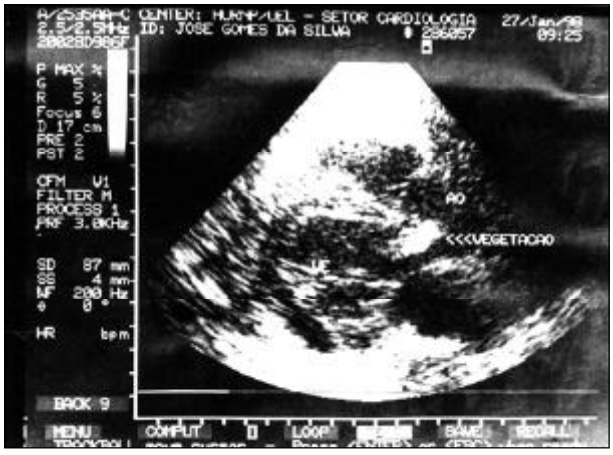

Fig. 1 - Vegetation in the aortic valve. Echocardiography evidenced a vegetation of 2.0 x 1.1 cm in the aortic valve.

ency, moderate enlargement of the left atrium (5.2cm), and moderate concentric hypertrophy of the left ventricle with normal ventricular function. *Streptococcus pneumoniae* was isolated from the blood culture of 3 samples collected in different puncture sites, but with no time interval.

On the 4th day of hospitalization, the patient experienced a sudden and short episode of mental confusion that resolved spontaneously. Tomography of the cranium confirmed the suspicion of embolism to the central nervous system, showing a nodular area of 2.0cm located in the cortical region of the right frontal lobe. This area had an increased internal density and perilesional edema, and did not change after injection of the contrast medium (fig. 2). The hypothesis of a possible mycotic aneurysm was not confirmed by conventional arteriography.

Despite isolation of *Streptococcus pneumoniae* in the serum, it was initially questioned as the causative agent of infectious endocarditis because of the subacute evolution of the disease. Penicillin and gentamicin were introduced to cover enterococcus and *Streptococcus viridans*.

On the 8th day of treatment, a sudden reduction in the consciousness level (Glasgow 13) occurred, accompanied by left paresis (grade I muscle strength), dysarthria, and right facial paralysis. A new cerebrospinal fluid examination revealed a xanthochromic appearance, a mixed pattern of cellularity, and absence of an infectious agent. With the hypothesis of cerebral abscess due to clinical worsening, and as no new tomographic study was immediately performed, we chose to widen the antimicrobial scheme, replacing the former by vancomycin, ceftazidime, amikacin, and metronidazole. A control cranial tomography showed an extensive hemorrhagic area with a slight deviation of the middle line in the area of the previous embolism. Nevertheless, the new therapeutical scheme was maintained until the 28th day (fig. 3).

The patient remained afebrile until the end of the treatment with a progressive normalization of the tests of inflammatory activity. A control echocardiography showed a vegetation (1.3 x 2.2cm), calcification of the leaflets, and a functioning aortic valve. On hospital discharge, the patient had only a left motor deficit, but the muscle strength was preserved.

In a further literature review, we found reports of subacute forms of endocarditis caused by *Streptococcus pneumoniae* and a high positive predictive value for pneumococcus in the blood. Then, the possibility of the pneumococcus being the causative agent in our case of infectious endocarditis was reconsidered and accepted.

Discussion

The incidence of pneumococcal endocarditis is not entirely known because the literature available comprises only reports of cases and series with a small number of patients. In the preantibiotic era, the *Streptococcus pneumoniae* accounted for approximately 15% of the cases of infectious endocarditis [1]. With the appearance of penicillin, a reduction has occurred and the current incidence ranges from

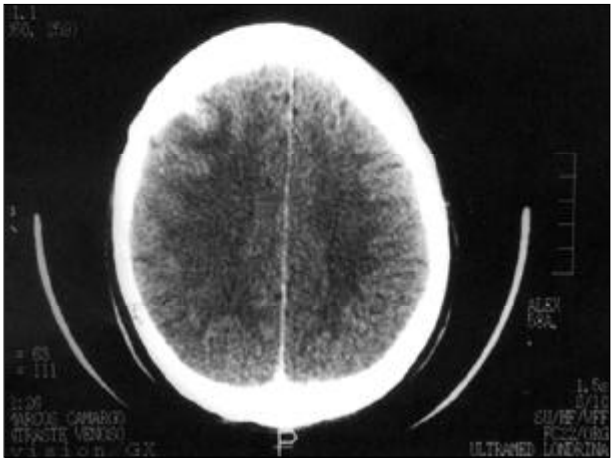

Fig. 2 - Embolism to the central nervous system. Computed tomography of the skull depicts a nodular ischemic area of 2.0 cm in the cortical region of the right frontal lobe.

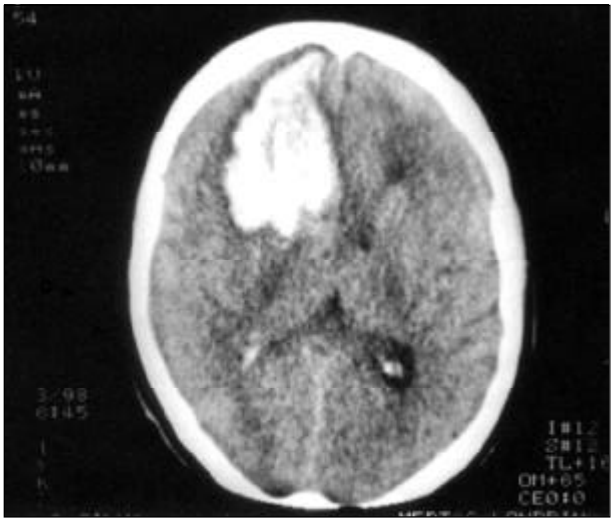

Fig. 3 - Hemorrhagic transformation of the ischemic cerebral infarction. The computed tomography of the skull shows an extensive hemorrhagic area in the cortical region of the right frontal lobe in the same site of the previous ischemic area caused by embolism.

1% to 3% [2]. This decline results from a better control and prevention of bacteremia [3-5]. Aronin et al [3], in a published review, reported 197 cases of pneumococcal endocarditis after the introduction of penicillin.

Most cases reported occur in elder and alcoholic males. Alcohol is by itself the major risk factor for pneumococcal endocarditis [1-5]. Its role, however, has not yet been defined, and we do not know whether alcohol has a direct action on the immunologic system or whether its influence derives from clinical conditions associated with the alcoholic patient, such as malnutrition and predisposition to bronchoaspiration [3].

Infection of lower airways is the major condition favoring the development of endocarditis due to *Streptococcus pneumoniae*. In addition to pulmonary and cardiac involvements, the meninges are often also involved in the pneumococcal infection [1,3-5]. The association of pneumonia, endocarditis, and meningitis was initially reported by Heschl in 1862, and later by Osler in 1881, the year the *Streptococcus pneumoniae* was discovered. This association is known as the Osler triad, and it is a relatively common finding in patients with pneumococcal endocarditis [3,5].

The most common clinical presentation of pneumococcal endocarditis is the acute form with a rapid and aggressive evolution associated with high morbidity and mortality rates. Peripheral signs and symptoms of endocarditis are not usually found in pneumococcal endocarditis, delaying the diagnosis and treatment of the infection. In addition, cardiac and noncardiac complications are common, particularly hemodynamic instability, formation of abscesses, and systemic embolism [1-5].

Streptococcus pneumoniae affects preferably the aortic valve, which, compared with the other valves, relates to a higher frequency of local complications. We do not know, however, whether the rapid tissular destruction that leads to rupture of the leaflets and heart failure results only from the direct action of the pneumococcus or whether it is associated with factors inherent in the host organism itself. The presence of large vegetations is a frequent finding in pneumococcal infection and increases the risks of embolism [1,3,5].

Uncommon forms have been reported, such as the subacute form with only 4 cases reported in the literature [4].

The clinical findings of our patient were not completely uncharacteristic, as in the case of the 2 female patients reported by Gelfand and Threlked [4], in which both patients, in addition to not being alcoholic and not having fever, pneumonia, or meningitis, had impairment of the mitral valve. In our patient, the findings of impairment of the aortic valve with formation of a large vegetation and embolic complications for the central nervous system stand out, as does the association with meningitis, even though not purulent [1,3,5]. No focus of bacteremia was identified.

The diagnosis of infectious endocarditis meets the new criteria proposed by Scheld and Sande [2] and Durack et al [6]. Visualization of a vegetation in the aortic valve, even in the transthoracic echocardiogram, was the only major criterion accepted. Isolation of the *Streptococcus pneumoniae*, even in 3 samples, was considered a minor criterion for the diagnosis. No doubt in regard to the pneumococcus as the causative agent existed, because specificity in the blood culture for pneumococcus is almost 100% [2,6].

In regard to treatment, the current management is the association of surgery with antibiotic therapy for those patients who evolve with hemodynamic instability [1,3,5]. In the review by Aronin et al [3], this strategy reduced mortality to 32% as compared with 62% for the patients treated only clinically. This did not result from the presence of *Streptococcus pneumoniae* strains resistant to penicillin in the group treated only with antibiotics, because the cases selected by the authors had been reported before resistance to penicillin was reported in the literature [3].

Treatment of infectious endocarditis frequently comprises difficult decisions, such as surgery and the choice of the proper time for it. Surgery should only be indicated for patients who may benefit from it. Literature data show that mortality is extremely high when patients with intracardiac complications evolving with hemodynamic instability are treated only with antibiotics. On the other hand, mortality is reduced when these patients undergo a treatment that combines the use of antibiotics and surgery [5]. It has been well documented that progressive severe heart failure due to the new valvar dysfunction or to worsening of the preexisting valvar dysfunction has a better prognosis with the therapy combining antibiotics and surgery. It is also clear that when maximum antibiotic therapy fails to eradicate infection, surgery improves evolution [5].

Currently, the choice of antibiotics for pneumococcal endocarditis has undergone some changes, not only because of the appearance of resistance to penicillin, but also because of the aggressive evolution of the disease and its association with meningitis. Penicillin is not the first-choice antibiotic for pneumococcal endocarditis, and, even though no formal recommendation exists up to now, the treatment is the same administered for pneumococcal meningitis, ie, the use of a 3rd generation cephalosporin associated or not with vancomycin, depending on the level of resistance to cephalosporin in the region studied [1,3,5].

The natural history of the vegetations during therapy varies [5,7]. Our patient showed a satisfactory response to clinical therapy and, by the end of the treatment, the control echocardiogram depicted persistence of the vegetation in the aortic valve with unaltered size. The study by Vuille et al [7], using serial echocardiography in patients with infectious endocarditis during a favorable response to clinical treatment, showed that out of the 41 initial vegetations, 12 (29.3%) disappeared, 7 (17%) decreased in size, 17 (41.5%) remained unaltered, and 5 (12.2%) increased in size. The evolution of these vegetations has not been related to duration of the antibiotic therapy or to the initial size of the vegetation. In patients who underwent successful clinical treatment, persistence of vegetations was not associated with late complications. Therefore, vegetations persisting after effective therapy should not be erroneously interpreted as recurrence of infectious endocarditis, unless clinical support and microbiologic evidence exist [5,7].

Even though the incidence of pneumococcal endocar-

ditis has decreased with the appearance of penicillin, morbidity and mortality rates remain elevated, which may be attributed to host factors (advanced age, alcoholism, diabetes mellitus, and other associated diseases) and to the infectious agent (tendency to infect and rapidly destroy the valves of the left side of the heart). Therefore, early diagnosis and treatment are crucial to significantly alter the unfavorable evolution of pneumococcal endocarditis.

References

1. Ugolini V, Pacifico A, Smitherman TC, Mackowiak PA. Pneumococcal endocarditis update: analysis of 10 cases diagnosed between 1974 and 1984. Am Heart J 1986: 112: 813-9.
2. Scheld WM, Sande MA. Endocarditis and Intravascular Infections. In: Mandell GL, Bennet JE, Dolin R. Principles and Practice of Infections Diseases. 4ª edição.: Churchill Livingstone, 1995: 740-73.
3. Aronin SI, Mukherjee SK, West JC, Cooney EI. Review of Pneumococcal Endocarditis in Adults in Penicillin Era. Clin Infect Dis 1998: 26: 165-71.
4. Gelfand MS, Threlked MG. Subacute Bacterial Endocarditis Secondary to Streptococcus pneumoniae. Am J Med 1992: 93: 91-3.
5. Karchmer AW. Infective Endocarditis. In: Braunwald E. Heart Disease. A Textbook of Cardiovascular Medicine. 5ª edição. Philadelphia: WB Saunders Company, 1997: 1077-104.
6. Durack DT, Lukes AS, Brigh DK. New criteria for diagnosis of infective endocarditis: utilization of ecocardiographic findings. Am J Med 1994; 96: 200-9.
7. Vuille C, Nidorf M, Weyman AE, Picard MH. Natural history of vegetations during successful medical tretment of endocarditis. Am Heart J 1994; 128: 1200-9.