

## **Infective endocarditis due to *Haemophilus aphrophilus*: a case report**

**Ricardo M. Pereira,<sup>1</sup> Fabio Bucarechi,<sup>2</sup> Antonia T. Tresoldi<sup>3</sup>**

### **Abstract**

**Objective:** To report the case of a child with infective endocarditis caused by *Haemophilus aphrophilus*.

**Description:** Boy with 20 days of fever and chills. On admission, he was febrile, pale and with no signs of hemodynamic instability; on cardiac auscultation, a mitral-related holosystolic murmur was observed. Laboratory examination identified anemia (hemoglobin = 9.14 g/dL), total leukocytes of 11,920 mm<sup>3</sup>, platelets of 250,000 mm<sup>3</sup>, elevated sedimentation velocity of red cells and elevated C-reactive protein. The echocardiogram revealed image on mitral valve, resembling vegetation. Considering endocarditis, antibiotic therapy was started with crystalline penicillin (200,000 UI/kg/day) in association with gentamicin (4 mg/kg/day). On the third day of treatment, *Haemophilus aphrophilus* was identified in the blood cultures and the antibiotic scheme was replaced with ceftriaxone (100 mg/kg/day). On the 20th day of evolution, the patient was pale but with no fever or other complaints. Examinations showed hemoglobin = 7.0 g/dL, leukocytes = 2,190 mm<sup>3</sup>, platelets = 98,000 mm<sup>3</sup>, international normalized ratio = 1.95 and R = 1.89. Considering the hypothesis of adverse reaction to ceftriaxone, a 6-week replacement treatment with ciprofloxacin (20 mg/kg/day) was started. Examination results normalized after 72 hours of the replacement therapy. During ambulatory follow-up, patient presented with severe mitral regurgitation, undergoing a valve replacement with a metallic prosthetic valve 9 months after acute event. Patient has done well throughout the 3-year ambulatory follow-up.

**Comments:** Identification of agents of the HACEK group (*Haemophilus ssp*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens* and *Kingella kingae*) in children with infective endocarditis is rare. This case report, with no HACEK agent-related risk factors, reinforces the need for identification of the etiological agent of endocarditis to ensure adequate treatment.

*J Pediatr (Rio J)*. 2008;84(2):178-180: *H. aphrophilus*, endocarditis, ceftriaxone, ciprofloxacin, leukopenia, thrombocytopenia, hypoprothrombinemia.

### **Introduction**

The incidence of infective endocarditis (IE) has increased over the past years as survival rates of patients with congenital heart disease improve.<sup>1</sup> Main agents of IE are: (i) Viridans group *Streptococci* (*S. milleri*, *S. mitior*, *S. salivarius*, *S. mutans* and *S. sanguis*), mainly on patients with congenital heart disease; (ii) *Staphylococcus aureus*, generally associated with placement of central venous catheter and use of injecting drugs; (iii) *Staphylococcus epidermidis*, usually affecting patients following cardiac surgery and catheterized

premature newborns.<sup>1</sup> On the other hand, the HACEK group of bacteria (*Haemophilus ssp*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens* and *Kingella kingae*) is responsible for 3% of IE in adults.<sup>1-3</sup> The objective of this study is to report a case of rare occurrence of IE caused by *Haemophilus aphrophilus* in a child.

### **Report of case**

The patient was a 12-year-old boy with a 20-day history of fever accompanied by chills and weight loss of 1 kg. On

1. Doutor. Médico assistente, Enfermaria de Pediatria, Hospital de Clínicas, Universidade de Campinas (UNICAMP), Campinas, SP, Brazil.
2. Doutor. Professor assistente, Departamento de Pediatria, Faculdade de Ciências Médicas (FCM), UNICAMP, Campinas, SP, Brazil.
3. Professor associado, Departamento de Pediatria, FCM, UNICAMP, Campinas, SP, Brazil.

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physical examination, he was febrile (40 °C), pale 1+/4+, good peripheral perfusion, heart rate = 112 beats/min, respiratory rate = 24 breaths/min and blood pressure = 100/60 mmHg. During cardiac auscultation, he presented with a mitral-related harsh holosystolic murmur, with radiation throughout the precordium, the spleen was palpable 3 cm below the left costal margin, hard 1+/4+. Dental examination showed a good dental status, with no signs of gingivitis. Complete blood count revealed hemoglobin (Hb) = 9.14 g/dL, hematocrit = 27.56%, total leukocytes = 11,920 mm<sup>3</sup> (9% band, 72% segmented, 7% lymphocytes, 12% monocytes), platelets = 250,000 mm<sup>3</sup>, sedimentation velocity of red cells = 120 mm, C-reactive protein = 15.6 mg/dL (reference value < 0.8 mg/dL) and no alterations in urine I. Chest radiograph was normal, echocardiogram revealed a 3mm image on the anterior surface of the anterior mitral valve leaflet, resembling vegetation. Due to hypothesis of IE, three blood samples were collected and antibiotic therapy was started with crystalline penicillin (200,000 UI/kg/day) in association with gentamicin (4 mg/kg/day). On the third day of treatment, *H. aphrophilus* susceptible to chloramphenicol, ciprofloxacin, and ceftriaxone was detected in the three blood cultures and the antibiotic scheme was replaced with ceftriaxone (100 mg/kg/day). After the eighth day of treatment, the patient remained afebrile. On the 20th day of evolution, the patient was pale but with no fever or other complaints. Screening examinations showed Hb = 7.0 g/dL, leukocytes = 2,190 mm<sup>3</sup>, platelets = 98,000 mm<sup>3</sup>, international normalized ratio = 1.95 and R = 1.89. Since the patient did not show other risk factors (only peripheral venous access was used), the hypothesis of an adverse reaction to ceftriaxone was considered. Ceftriaxone was then replaced with a 6-week treatment with ciprofloxacin (20 mg/kg/day). Leukocyte count, platelet count and coagulation normalized after 72 hours under the new scheme. During hospitalization, echocardiograms performed every 15 days demonstrated a progressive reduction in the vegetation size, with evidence of severe mitral regurgitation on the last echocardiography. At the end of the antibiotic therapy, patient was discharged from hospital to ambulatory follow-up. Due to the severe mitral regurgitation, the patient underwent a valve replacement with a metallic prosthetic valve 9 months after discharge, with no intercurrent events. Patient has done well throughout the 3-year ambulatory follow-up.

The patient's legal guardian signed a free and informed consent form.

## Discussion

The HACEK group bacteria are gram-negative bacilli of the normal oropharyngeal flora. Since these bacteria can be found in the dental plaque and in the gingiva, clinical features of infection, including respiratory tract infections, may follow dental manipulation.<sup>3-5</sup> A case of *H. aphrophilus* endocarditis after tongue piercing in a patient with congenital heart disease was reported.<sup>6</sup>

These bacteria are slow growers that require special culture media for their identification.<sup>7</sup> In a report of 46 cases of IE caused by microorganisms of the HACEK group, the mean time to blood culture positivity was 3,4 days.<sup>7</sup>

Feder et al., in a literature review, found 36 cases of pediatric patients with IE caused by HACEK bacteria (13 *H. parainfluenzae*, 13 *K. kingae*, five *A. actinomycetemcomitans*, four *H. aphrophilus*, one *C. hominis*) and 60% of these cases showed previous cardiac alteration.<sup>2</sup>

The suggested treatment for IE caused by HACEK bacteria is a 4-week administration of third-generation cephalosporin for native valves and a 6-week administration for prosthetic valves.<sup>2,3,8</sup>

The use of fluoroquinolones, especially ciprofloxacin, is an alternative since their pharmacokinetic properties allow eradication of bacteria that adhere to prostheses.<sup>8</sup>

The reported patient did not show the risk factors described for infection by bacteria of the HACEK group, since he did not have previous cardiac alteration, periodontal disease or previous dental manipulation. Despite the absence of known risk factors, *H. aphrophilus* is an oral bacteria and the oral cavity must have provided a port of entry for the bacteria. This fact reinforces the need for accurate identification of the etiological agent of IE to determine adequate treatment.

The probable adverse reaction to ceftriaxone, in particular, is worthy of attention. Severe hematological alterations, including death, have already been associated with the use of ceftriaxone, especially hemolytic anemia, in which presence of ceftriaxone antibodies has already been observed.<sup>9</sup> Thrombocytopenia and hypoprothrombinemia have already been associated with ceftriaxone as well.<sup>9,10</sup> Although in the present case specific antibodies against ceftriaxone were not researched, the complete recovery observed in the patient's examination results after drug withdrawal strongly suggests a possible adverse reaction to ceftriaxone.

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Correspondence:

Ricardo Mendes Pereira  
Rua Dr. Ruy Vicente de Mello, 240  
Cidade Universitária, Barão Geraldo  
CEP 13084-745 – Campinas, SP – Brazil  
E-mail: ricardom.p@uol.com.br