CASE REPORT

Haemophilus parainfluenzae endocarditis with systemic embolisation following maxillary sinusitisMargarida Barreto Cortes,¹ Vitor Teixeira,² Samuel Raimundo Fernandes,³ Fernanda Rego¹¹Serviço de Medicina Interna, Hospital de Santa Maria, Lisbon, Portugal²Serviço de Reumatologia e Doenças ósseas metabólicas, Hospital de Santa Maria, Lisbon, Portugal³Serviço de Gastrenterologia e Hepatologia, Hospital de Santa Maria, Lisbon, Portugal**Correspondence to**Dr Samuel Raimundo Fernandes,
Samuelrfernandes@gmail.com

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SUMMARY

The authors present a case of a man with *Haemophilus parainfluenzae* endocarditis complicated with embolisation to the central nervous system. The patient had no evidence of endocarditis by transoesophageal and transthoracic echocardiograms at baseline, but shortly after developed large mitral valve vegetations with valve rupture. The case highlights how rapidly structural valve damage can ensue despite good clinical and laboratorial antibiotic response.

BACKGROUND

Infective endocarditis (IE) is defined as an infection of the inner tissues of the heart which may include the heart valves, the endocardium or a septal defect. IE usually occurs in people older than 50 years and is generally fatal if left untreated.¹ We present an uncommon case of IE in a young man with normal echocardiogram at baseline and rapid clinical development despite adequate antibiotic treatment. We highlight the clinical suspicion previous to the evidence of vegetations on the transoesophageal echocardiogram.

CASE PRESENTATION

We present a 36-year-old man born in the West coast of USA (San Francisco), currently in Portugal on vacation. His medical history was relevant for spinal fractures due to a car accident, and occasional consumption of drugs such as ecstasy, ketamine and cocaine. He denied intravenous drugs consumption and did not participate in any vaccination programme in his country. The patient was admitted following a 2-week symptom of seromucous nasal discharge, productive cough, fatigue, myalgia and fever (maximum 39°C). He underwent a course of azithromycin prescribed by a primary healthcare professional, without significant improvement. His physical examination revealed mild grade fever (37.9°C), normal vital signs and no evidence of other findings including heart murmurs, hepatosplenomegaly or lymphadenopathies. Blood tests on admission showed elevated erythrocyte sedimentation rate (30 mm/hour, normal range <10 mm/hour), C reactive protein (8 mg/dL, normal range <0.5 mg/dL), alanine aminotransferase (135.5 IU/L, normal range <49.0 IU/L), aspartate aminotransferase (83 IU/L, normal range <34 IU/L), amylase (273 U/L, normal range <53 U/L), lipase (117 U/L, normal range <60 U/L), lactate dehydrogenase (390 U/L, normal range <378 U/L) and troponin I (0.31 ng/mL,

normal range <0.07 ng/mL). Haemoglobin, leucocytes, γ -glutamyltranspeptidase, total bilirubin and creatinine were within normal range. His ECG, chest X-ray and abdominal ultrasound scan were normal. The patient was admitted for further investigation and was started on empirical amoxicillin clavulanate. Serologies for HIV, hepatitis B and C, cytomegalovirus, Epstein-Barr virus, Q fever, Legionella and Syphilis were negative.

INVESTIGATIONS

On the third day of hospitalisation, the patient developed severe holocranial headaches that worsened with Valsalva manoeuvres, and were accompanied by photophobia and diplopia. Urgent CTscan of the head revealed a focal hypodensity in the head and body of the left caudate nucleus, and left maxillary sinusitis. Cerebrospinal fluid puncture was performed showing elevated lymphocytes (18 cells/ μ L, normal range <5/ μ L) with no other abnormal findings, effectively excluding meningitis. Head MRI (HMRI) revealed multiple small hyperintense foci in the parietal cortex, right frontal lobe and left caudate nucleus (figure 1), compatible with an ischaemic event. On the fourth day of hospitalisation, *Haemophilus parainfluenzae* was isolated in two separate blood cultures. Taking these findings into account, the patient was immediately started on anti-aggregation with aspirin and intravenous ceftriaxone 2 g/day. Transthoracic and transoesophageal

Figure 1 Head CT scan showing a large area of infarction in the left caudate nucleus (arrow).

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Figure 2 Transoesophageal echocardiogram showing normal mitral valve leaflets.

echocardiographs depicted only a mild thickening of the mitral valve, excluding overt endocarditis (figure 2). Carotid ultrasound scan was unremarkable. By the 12th day of hospitalisation, despite 7 days of systemic antibiotics, a holosystolic, grade III/VI heart murmur, not previously present, was detected on physical examination. A second transoesophageal echocardiography revealed a dilated left atria and a prolapse of the anterior leaflet of the mitral valve due to secondary rupture of the tendinous cord with severe eccentric mitral regurgitation. A 7 mm vegetation was found attached to the mitral valve (figure 3).

DIFFERENTIAL DIAGNOSIS

In our case, the age of the patient, the history of drug consumption and the central nervous system lesions made the diagnosis of endocarditis very likely. Other differentials should include vasculitis (the negative autoantibodies and the positive microbiological result made this an unlikely diagnosis), cardiac myxomas, mycotic aneurisms and connective tissue diseases.

TREATMENT

After 21 days of intravenous ceftriaxone, the patient showed no significant clinical improvement. After discussion in a multidisciplinary group, the patient was submitted to a minimally invasive cardiac surgery for valve repair.

OUTCOME AND FOLLOW-UP

The patient's clinical condition improved considerably after surgery. Follow-up HMRI showed improvement of the ischaemic cerebral lesions. Phase reactants markers, hepatic enzymes and troponins normalised and blood cultures became negative.

Figure 3 Follow-up transoesophageal echocardiogram showing (A) a mass attached to the posterior leaflet of the mitral valve (arrow) (B) causing mitral regurgitation. LA, left atrium; LV, left ventricle; MV, mitral valve; RV, right ventricle.

The patient was discharged after a 6-week course of intravenous ceftriaxone.

DISCUSSION

H. parainfluenzae is a Gram-negative bacterium that belongs to the HACEK group (*H. aphrophilus*, *Actinobacillus actinomyces*, *Cardiobacterium hominis*, *Eikenella corrodens* and *Kingella kingae*). *H. parainfluenzae* is an indigenous agent of the oropharynx and nasopharynx, present on 5–25% of healthy individuals. Nevertheless, endocarditis caused by *H. parainfluenzae* has seldom been reported in the literature.² In our case, this was the first case of endocarditis by this agent in our tertiary centre in over 30 years of existence. Infection usually develops after dental or cardiac procedures, in patients with heart defects or tongue piercings, and following an oropharyngeal infection. Our patient reported of sore throat and nasal discharge, suggesting that the latter might have been responsible for the bacteraemia. Regarding our case, a clinical diagnosis of endocarditis was considered after suggestive clinical (persistent fever), imaging (signs of cerebral embolisation) and microbiological (isolation of the bacteria in several separate blood cultures) findings and before the echocardiographic identification of cardiac vegetations. As stated in the modified Duke criteria, the diagnosis of endocarditis is possible even in the absence of detectable valve vegetations, as in our case.³ The presence of bacteraemia by this agent should always warrant a transoesophageal echocardiogram to rule out endocarditis, as some studies have reported this condition in half of all *H. parainfluenzae* infections.⁴ Unfortunately, HACEK microorganisms are known for their fastidious growth and long culture time and, in the case of *H. parainfluenzae* endocarditis, incubation may take longer than 20 days to render a positive result.⁵ It is not known if the time of culture translates into severity of the infection. If a high clinical suspicion persists, longer incubation periods should be requested. Current guidelines, recommended first-line treatment with ceftriaxone 2 g/day for 4 (native-valve) to 6 (prosthetic-valve) weeks.^{6 7} Other options include ampicillin plus gentamicin in non- β -lactamase producing bacteria or ciprofloxacin. Most cases of *H. parainfluenzae* endocarditis present an indolent course, but surgery may be required in selected cases. Surgical treatment is required in almost half of the patients with IE because of severe complications. The main indications for surgery in IE include heart failure, uncontrolled infection and prevention of embolic events. In heart failure the time for surgery should be considered depending on patient's tolerance and severity of the valve lesion. Persistent infection is usually defined as fever and positive blood cultures for more than 7 days despite an appropriate antibiotic regimen. The best timing for surgery is still unclear, but a recent study suggests that surgery should be considered when blood cultures remain positive after 3 days of antibiotic therapy, as this has been

shown to be an independent risk factor for hospital mortality.⁸ Embolic events are a frequent (in 20–50%) and life-threatening complication of IE. The risk of embolism is highest during the first 2 weeks of antibiotic therapy but falls to 6–21% after initiation of antibiotic therapy. The decision to operate early to prevent embolism is dependent on several factors including the size and mobility of the vegetation, previous embolism, type of microorganism and duration of antibiotic therapy.⁹ In our case, surgery was considered necessary due to the rapid clinical deterioration following mitral valve rupture and the evidence of systemic embolisation, despite adequate antibiotic coverage. In conclusion, IE should be considered in the differential of persistent fever of unknown origin, especially in patients with abnormal heart examination and positive blood cultures. We highlight the absolute need of careful daily cardiac auscultation as in our case it was decisive to warrant a new transoesophageal echocardiogram.

Learning points

- ▶ Persistent fever, a new regurgitant heart murmur and positive blood cultures should raise the suspicion of infective endocarditis.
- ▶ Despite adequate antibiotics, surgery may be required in complicated cases of infective endocarditis.
- ▶ Daily clinical assessment including careful heart auscultation may improve early detection of endocarditis.
- ▶ Transthoracic and even transoesophageal echocardiogram cannot exclude endocarditis with 100% certainty, and in case of worsening progression they should be repeated after a few days.

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