An unusual agent for an unusual localization of infective endocarditis

Jens Litmathe,1 Rene Fussen,2 Alexander Heinzel,3 Marguerite Müller,4 Christoph Sucker,5 Lachmandath Tewarie6 and Manuel Dafotakis1

Abstract
We report on a 32-year-old male patient with acute left-hemispheric stroke caused by embolism due to infective endocarditis affected from the HACEK group. Additionally, atypical findings from the transesophageal echocardiography (TEE) which showed fluttering structures belonging to the papillary muscle could be proven as infectious agents with the help of a glucose positron emission tomography (PET) scan. TEE controls showed increasing vegetation involving the mitral valve so that surgery became necessary. The current work reflects, in detail, the emergent clinical course of this young patient, suffering from both an unusual localization and an infrequent cause of endocarditis and focuses on an actual view to the literature.

Keywords
stroke; mural endocarditis; papillary muscle; HACEK organisms

Introduction
Infective endocarditis (IE) is still associated with a high mortality and one prominent trigger for cerebral embolism.1 Despite clearly defined criteria for diagnosis, the Duke-criteria,2 atypical courses can impede confirming the clinical presumption.

HACEK organisms (Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Klebsiella) are rare causative agents for an IE and occur in only 1–3% of all clinical cases.3,4 Additionally, atypical localizations, e. g. in cases of mural endocarditis, may complicate the accuracy of the diagnosis.

We report on a 32-year-old male patient presenting himself with multiple and recurrent cerebral embolism on the basis of an IE with Haemophilus parainfluenzae. Initial findings from transesophageal echocardiography (TEE) revealed atypical structures at the papillary muscle of the left ventricle, which, however, were confirmed to be of infectious origin with the help of a glucose PET scan. With this background in mind, we discuss the current literature on this topic.

Case report
The 32-year-old male patient was primarily admitted to a local hospital with the symptoms of fatigue, weight loss and sub-febrile temperature for the previous four weeks. Although clinically highly suspicious for endocarditis, TEE imaging, however, did not show pathology in the heart, although blood culture sampling showed Haemophilus parainfluenzae which was treated with cefotaxime. During his hospital stay, the patient developed an acute hemiparesis of the right side of the body, a non-fluent aphasia accompanied by a hemihypaesthesia on the left side. He was subsequently admitted to our An unusual agent for an unusual localization of infective endocarditis

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neurological emergency department and, after computerized tomography (CT) angiography, which showed occlusion of a main branch of the sinistral medial cerebral artery and further multiple embolic lesions, he underwent immediate angiographic embolectomy (Figure 1). The observation was continued at the Neurological Critical Care Department and the stroke symptoms were fluently regressing at first. The septic clinical picture, however, persisted, with a body temperature up to 38.5°C, procalcitonin (PCT) 2.1 ng/ml, C-reactive protein (CRP) 88.6 mg/l and leukocytes 13,200/µl. The TEE control showed new findings of flut-tering structures belonging to the papillary muscle by the posterior mitral leaflet, but certainly without contact to the mitral valve itself (Figures 2 and 3). Besides that, neither mitral insufficiency nor any abscess formations were present at this time. Because of this atypical localization of the endocarditis, an F-18 fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) with 200 MBq was carried out and proved the infectious tissue at the cardiac base to be consistent with the additional structures identified on the control TEE (Figure 4).

Meanwhile, new control blood culture sampling again showed *Haemophilus parainfluenzae*. According to the antibiogram, an antibiotic treatment with 2 x 2 g ceftriaxone i. v. was started. Two days after admission, the patient once again developed a hemiparesis on the right side due to a renewed embolic occlusion of the left medial cerebral artery. Immediate angiographic embolectomy was performed for a second time and the patient recovered well, now with the help of intensive physiotherapy, ergotherapy and speech training. Poor dentistry, with root abscesses of two right upper molars as the most suggestive access for endocarditis, was corrected during hospitalization. After six weeks of antibiogram-analog antibiotic therapy, the patient recovered falteringly and a new TEE control showed a persisting and even growing
fluttering subvalvular structure at the papillary muscle and chordae tendinae group now, with contact to the P-3-segment of the mitral valve and severe mitral regurgitation (Figure 5). Thus, the patient was sent to surgery and underwent mitral valve reconstruction with a 32 mm Carpentier© ring, as well as repair of the affected chordae tendinae group. After this, he recovered completely and was admitted to rehabilitation.

Discussion

Left-sided endocarditis is still associated with tremendous morbidity and mortality, especially in situations of increasing antibiotic resistance. Most of the patients fulfill at least one criterion for surgery once a neurological complication has occurred. A particularly perilous situation is represented by prosthetic valve endocarditis, which is associated with an increased risk of redo-surgery and the need for ongoing anticoagulation despite often multiple or even territorially large embolic cerebral lesions.1

The HACEK group consists of Haemophilus, Aggregatibacter (formerly Actinobacillus), Cardiobacterium hominis, Eikenella corrodens and Klingella and is a heterogenous group of fastidious gram negative bacteria frequently found in the oropharynx.7 Recent publications have addressed HACEK organisms as causing infection for infective endocarditis in below 6% of patients.8-10 approximately congruent to the findings of other study groups.3,4

In 2013, Chambers and colleagues presented outcomes of HACEK endocarditis from a large multinational cohort, enrolling 5591 endocarditis patients from 64 hospitals in 28 countries. In these cases, HACEK endocarditis had a prevalence of 1.4% and was associated with younger age, vascular manifestations and stroke. Stroke, however, was strongly associated with mitral valve vegetation (p<0.01, OR 3.6). Haemophilus parainfluenzae was the most common agent found within the HACEK group (28/77). The overall mortality (3%) of HACEK cases was comparably low.3 These findings are principally congruent to our case presented here and Chambers found, in only four HACEK cases, echocardiographic characteristics other than valvular vegetation.

Mural endocarditis is correspondently a rare diagnosis: some authors have recently presented singular cases or smaller case series of infective endocarditis, presenting in such a way: Mak et al. reported, in 2011, a multivalvular endocarditis, with mural vegetation of the right atrium and ventricle in a 39-year-old man, due to Streptococcus anginosus bacteremia and sepsis. The vegetation also involved both the mitral and aortic valves so that double valve replacement became necessary.11 Furthermore, an involvement of the papillary muscle with subsequent rupture was seen in an 82-year-old man, as published by Maruo and colleagues in 2014.12 Due to severe mitral insufficiency, the patient was sent to surgery and a complete valve replacement was performed. Adel and colleagues, in 2014, reported a small series of three patients with Staphylococcus-triggered mural endocarditis, however, without valvular involvement.13

The overlap between mural endocarditis and HACEK bacteria is, to the best of our knowledge, reported in only one case throughout the literature: Girugea and Lahey have recently presented a case of a Haemophilus parainfluenzae mural endocarditis, involving the anterior papillary muscle and anterior mitral leaflet as well as the chordal system. The 62-year-old female immunocompetent patient with preceding neurological deficits developed severe mitral insufficiency under treatment with ceftriaxone. Valvular as well as subvalvular reconstruction was carried out, similar to our presented patient. All in all, both cases are, indeed, very comparable.14

Our currently presented case reflects, therefore, the second case worldwide comprising a Haemophilus parainfluenzae as a typical representative of the HACEK group causing a mural endocarditis. The clinical course of this uncommon kind of endocarditis caused by an unusual agent underlines, nevertheless impressively, the clinical impact of valvular as well as embolic, i.e., neurological, complications in such rare instances.

Conclusion

Every single case of IE may be very special. Only effective and sustained diagnostics, with all and even rare appearances in mind, can finally lead to successful therapy.
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