Case Report

Recurrent infective endocarditis due to Aggregatibacter actinomycetemcomitans: reinfection or relapse?

Anais Potron,1,2 Jean-Luc Mainardi,2,3,4 Isabelle Podglajen,2,3,4 Fabienne Meunier,1 Marie-José Sanson-le Pors1,5 and Béatrice Bercot1,5

Correspondence
Béatrice Bercot
beatrice.bercot@lrb.aphp.fr

Received 13 July 2010
Accepted 17 August 2010

1AP-HP, Hôpital Lariboisière, Service de Bactériologie – Virologie, Paris, France
2AP-HP, Hôpital Européen Georges Pompidou, Service de Microbiologie, Paris, France
3Université Paris Descartes, Faculté de Médecine, Paris, France
4INSERM, UMR S 872 – Équipe 12, Laboratoire de Recherche Moléculaire sur les Antibiotiques, Centre de Recherche Biomédical des Cordeliers, Université Paris Descartes et UPMC, Paris, France
5Université Paris Diderot, Faculté de Médecine, Paris VII, France

Aggregatibacter actinomycetemcomitans is commonly part of the normal microflora of the human upper respiratory tract. It has been implicated in periodontal disease and various infections, particularly endocarditis. We report here what we believe to be the first case of recurrent infective endocarditis due to A. actinomycetemcomitans in a 44-year-old woman occurring 5 years after the initial episode. Genomic analysis proved that the strains were closely related. Despite efficient antibiotic treatment, surgery was necessary for recovery.

Case report

A 44-year-old woman (patient KHA) was admitted to our hospital for persistent fever in February 2005. Her medical history was remarkable for a reconstructive surgery of rheumatic mitral valvulopathy in 1982, followed by mitral valve replacement with a Sorin mechanical prosthesis and tricuspid valvuloplasty in 1993. In February 2000, she presented a first episode of infective endocarditis (IE). Even though no vegetations were evidenced by transparietal and repeated transtoesophageal echocardiograms, the diagnosis of definite endocarditis was secured by the identification of Aggregatibacter actinomycetemcomitans from three blood cultures using the modified Duke’s criteria (Li et al., 2000).

She was successfully treated with a combination of ciprofloxacin 750 mg twice daily and ceftriaxone 2 g once daily for a duration of 6 weeks. In 2003, aortic valve replacement with a mechanical prosthesis was required for calcific aortic stenosis. Microbiological culture of the aortic valve was negative.

In 2005, physical examination yielded a temperature of 38.2 °C, blood pressure of 99/57 mmHg and a pulse of 93 beats min⁻¹. Cardiovascular examination revealed a 3/6 mitral systolic murmur. Laboratory data showed anaemia with a haemoglobin level of 8.2 g dl⁻¹, a white blood cell count of $6.4 \times 10^9$ l⁻¹ and a C-reactive protein level of 147 mg l⁻¹ (normal level <10 mg l⁻¹). Transthoracic echocardiography evidenced a mobile vegetation on the mitral valve ring. Six out of 11 sets of blood cultures were positive and yielded a Gram-negative rod, identified as A. actinomycetemcomitans by phenotypic and genetic methods using rrs gene sequencing (Fihman et al., 2007). The MICs of amoxicillin, ceftriaxone and ciprofloxacin determined by Etest (AB BIODISK) were 1, 0.032 and 0.023 mg l⁻¹, respectively. Antibiotic therapy was initiated by intravenous ceftriaxone 4 g once a day and gentamicin 90 mg twice daily. Aortic and mitral valve replacements were required 3 weeks later because transtoesophageal echocardiography revealed persistence of the mitral vegetation and two aortic abscesses associated with disinsertion of the aortic valve. Under antibiotic treatment, the detection of bacteria in cardiac tissues using the 16S rRNA gene (Podglajen et al., 2003) remained negative. After surgery, the aminoglycoside was switched to oral ciprofloxacin 750 mg twice daily associated with ceftriaxone for 1 month followed by ciprofloxacin alone for 1 month further. Clinical improvement under this regimen was evident within 10 days with apyrexia. C-reactive protein and haemoglobin levels were within normal limits after the 2 month course of antimicrobial therapy.

The genetic patterns of three isolates of A. actinomycetemcomitans from patient KHA [two isolates from 2000...
Fig. 1. PFGE patterns after Xho I restriction of chromosomal DNA from *A. actinomycetemcomitans* isolates. Lanes 1 and 2, strains isolated from blood cultures from patient KHA from the first IE episode in 2000 (lane 1, isolate LRB2000-1; lane 2, isolate LRB2000-2); lane 3, strain isolated from blood cultures from patient KHA from the second IE episode in 2005 (isolate LRB2005-1). Lanes 4–6, other non-linked clinical strains of *A. actinomycetemcomitans*. M, Molecular mass marker.

Table 1. Similarity matrix of the sequence types of *A. actinomycetemcomitans* isolates

Nucleotide sequences to a length of 4109 bp of the housekeeping genes *adk* (559 bp), *atpG* (494 bp), *frdB* (506 bp), *hbpA1* (439 bp), *hbpA2* (329 bp), *mdh* (434 bp), *pgi* (521 bp), *recA* (490 bp) and *tbpA* (339 bp) were aligned by using the BioEdit program. The GenBank accession numbers for the *A. actinomycetemcomitans* isolate HK1651 genes are EF142164.1, EF142218.1, EF142336.1, EF142489.1, EF142428.1, EF142568.1, EF142653.1, and those for the KHA isolate LRB2000-1 genes are HM630293, HM630294, HM630295, HM630296, HM630297, HM630298, HM630299, HM630300 and HM630301, respectively.

<table>
<thead>
<tr>
<th>KHA isolate LRB2000-1</th>
<th>KHA isolate LRB2000-1</th>
<th>KHA isolate LRB2005-1</th>
<th>BRE isolate</th>
<th>BOU isolate</th>
<th>MRA isolate</th>
<th>HK1651 isolate</th>
</tr>
</thead>
<tbody>
<tr>
<td>KHA isolate LRB2000-1</td>
<td>1.000</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>KHA isolate LRB2000-1</td>
<td>1.000</td>
<td>1.000</td>
<td>1.000</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>KHA isolate LRB2005-1</td>
<td>1.000</td>
<td>1.000</td>
<td>1.000</td>
<td>1.000</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>BRE isolate</td>
<td>0.976</td>
<td>0.976</td>
<td>0.976</td>
<td>1.000</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>BOU isolate</td>
<td>0.976</td>
<td>0.976</td>
<td>0.976</td>
<td>0.999</td>
<td>1.000</td>
<td>–</td>
</tr>
<tr>
<td>MRA isolate</td>
<td>0.999</td>
<td>0.999</td>
<td>0.999</td>
<td>0.976</td>
<td>1.000</td>
<td>–</td>
</tr>
<tr>
<td>HK1651 isolate</td>
<td>0.975</td>
<td>0.975</td>
<td>0.975</td>
<td>0.998</td>
<td>0.975</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Discussion

*Agregatibacter* (*Actinobacillus*) *actinomycetemcomitans* belongs to the HACEK group of bacteria, along with *Haemophilus* species, *Cardiobacterium hominis*, *Eikenella corrodens* and *Kingella* species (Das et al., 1997). These Gram-negative bacteria are frequently found as colonizers of the oral cavity and grow slowly (Zambon, 1985). They are responsible for 3% of all cases of IE (Das et al., 1997), and, among them, *A. actinomycetemcomitans* is the most frequently involved. Recurrent IE due to the same microorganism is rare (approx. 3% of IE cases). A time-based
clinical criterion, defined as the delay in recurrence of less or more than 6 months, is usually used to distinguish relapse from reinfection (Mansur et al., 2001). To our knowledge, four cases of endocarditis clinically considered as reinfections but classified as relapses using molecular methods have been described. They involved Staphylococcus aureus (Chu et al., 2005), Propionibacterium acnes (Chu et al., 2005), Pseudomonas stutzeri (Grimaldi et al., 2009) and Streptococcus gallolyticus (Mühlemann et al., 1999) and occurred 9, 24, 48 and 96 months after the initial episode, respectively. Here, we report what we believe to be the first case of recurrent IE involving A. actinomycetemcomitans, which occurred after a 5 year period. Using the modified Duke’s criteria of endocarditis (Li et al., 2000), the patient was classified as having definite IE in 2000 (one major and three minor criteria) and in 2005 (two major and two minor criteria). Considering the fact that the genetic methods demonstrated the involvement of identical or closely related isolates in the two IE episodes, this raises the question of how this bacterium has been able to persist for 5 years. We cannot reliably determine whether the patient had a persistent cardiac focus or a persistent unknown abscess, which led to IE on two separate occasions. However, when cardiac surgery was performed in 2003, cultures of the aortic valve were negative after an incubation period of 30 days, and clinical examination of the mitral valve was normal during the surgery. It therefore appears more conceivable that these two episodes of endocarditis could have resulted from a chronic dental focus where the same A. actinomycetemcomitans isolate persisted. This hypothesis is supported by the fact that a periodontal disease was highlighted in the patient’s oropharyngeal flora was not performed. In fact, oropharyngeal samples are never taken in clinical practice in the case of endocarditis due to streptococci or HACEK bacteria. Molecular methods offer advantages for epidemiological investigation and are able to determine identity between clinical strains. Our case report highlights that the identification of two similar isolates can be related to either a relapse from a persistent cardiac focus or a reinfection from a persistent unknown abscess, which must be identified and removed.

References


