Case Report

Kocuria kristinae endocarditis related to diabetic foot infection

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We report an unusual case of endocarditis occurring in a 74-year-old man with a history of systemic hypertension, diabetes mellitus and minor amputation for left forefoot ulcer. The patient was hospitalized for vacuum-assisted closure therapy to aid in wound healing. After the first treatment session, the patient reported abdominal pain with haematemesis and fever (40°C). Owing to persistent fever, three blood cultures were performed, all positive for Kocuria kristinae. The identification was based on biochemical tests and automated systems. The speciation of the micro-organism was achieved with MALDI-TOF and then confirmed by 16S rRNA gene sequencing. Transthoracic echocardiographic examination showed the presence of a large vegetation (38×20 mm) on the posterior mitral leaflet and moderate mitral regurgitation. Since there are no current guidelines for the treatment of K. kristinae endocarditis, empiric antibiotic therapy with intravenous sulbactam/ampicillin (1.5 g twice daily) and gentamicin (6 mg kg⁻¹ per day) was started. After 7 days of hospitalization, the patient’s condition suddenly worsened because of the occurrence of haemorrhagic stroke. Despite inotropic support and rifampicin infusion, the haemodynamic status progressively deteriorated. After an initial improvement, he worsened again, becoming stuporous, hypotensive and dyspnoeic. In the following days, the patient developed compartment syndrome resulting in right foot ischaemia. Unfortunately, 25 days after hospitalization, the patient died of multiple organ failure from overwhelming sepsis. To the best of our knowledge, this is the first case of K. kristinae endocarditis on a native valve that is not related to a central venous catheter but associated with diabetic foot infection.

Introduction

The genus Kocuria belongs to the family Micrococcaceae. These micro-organisms are ubiquitous in the environment as well as in a wide variety of animals. In humans, they may colonize the skin, mucosa and oropharynx, but rarely they can be opportunistic pathogens; in particular, K. kristinae is the species most frequently isolated from immunocompromised patients (Stackebrandt et al., 1995). Only a few cases of infections by K. kristinae have been reported so far in the literature and most of them are catheter-related bacteraemia (Basaglia et al., 2002; Carlini et al. 2011; Dunn et al., 2011; Oncel et al., 2012; Lai et al., 2011; Ma et al., 2005; Martinaud et al., 2008).

We report an unusual case of K. kristinae endocarditis on a native valve that was not related to a central venous catheter but associated with diabetic foot infection. Similar cases reported in the literature are discussed.

Case report

A 74-year-old man with a history of systemic hypertension, diabetes mellitus and minor amputation for left forefoot ulcer was hospitalized in an outside hospital in April 2012 for vacuum-assisted closure therapy to aid in wound healing. After the first treatment session, the patient reported abdominal pain with haematemesis and fever (40°C). Owing to persistent fever, the patient was referred to our department for suspected endocarditis (within 9 days of fever onset). Chest examination revealed decreased breath sounds bilaterally, with no crackles or wheezes. Heart sounds were muffled, without murmurs or gallops. His abdomen was globular, soft, non-tender and non-distended. Laboratory tests revealed leukocytosis, slightly reduced after antibiotic therapy with intravenous ceftriaxone (2 g twice daily) and metronidazole (500 mg three times daily), anaemia and mild renal failure. The electrocardiogram showed atrial flutter. Transthoracic echocardiographic examination showed normal left
ventricular systolic function and the presence of a large vegetation (38 × 20 mm) on the posterior mitral leaflet, with atrial excursion during systole and partial obstruction of the left ventricular outflow tract. Moderate mitral regurgitation was also noted. Pulmonary artery systolic pressure was slightly elevated. Three blood cultures were performed, all positive for *K. kristinae*. The identification was based on biochemical tests and automated systems (Vitek-2; bioMérieux). For more precise identification of this unusual pathogen, the isolate was sent to a reference laboratory where identification was achieved using protein ‘fingerprints’ measured by MALDI-TOF MS. The diagnosis was confirmed later by 16S rRNA gene sequencing, performed at our molecular biology laboratory. Since there are no current guidelines for the treatment of *K. kristinae* endocarditis, empiric antibiotic therapy with intravenous sulbactam/ampicillin (1.5 g twice daily) and gentamicin (6 mg kg⁻¹ per day) was started. On admission, we preferred not to give rifampicin because the patient reported a previous adverse cutaneous reaction to a similar drug, with itching and macular rash. Moreover, 2 days after admission, surgical debridement of leg ulcers was performed. After 7 days of hospitalization, the patient’s condition suddenly worsened because of the occurrence of haemorrhagic stroke. Physical examination revealed a state of stupor, pulmonary rales, hypotension, bradycardia and oliguria. Mitral valve replacement as well as foot surgery were planned and delayed because of the high operative risk. The benefit of early surgery is significant in reducing the risk of systemic embolism. However, when eligibility for mitral valve replacement was considered, our patient had already experienced a major embolic event (likely related to a ruptured mycotic aneurysm). In the following days, a radiological examination revealed pneumonia.

### Table 1. *Kocuria kristinae* infections in humans

<table>
<thead>
<tr>
<th>Patient sex, age</th>
<th>Site of isolation</th>
<th>Underlying disease or condition*</th>
<th>Antimicrobial therapy</th>
<th>Outcome/date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, 89</td>
<td>Blood, endocarditis</td>
<td>Ischaemic bowel status post-resection, short bowel syndrome, CVC for TPN (removed)</td>
<td>Vancomycin → Teicoplanin → Oxacillin</td>
<td>Good/NA</td>
</tr>
<tr>
<td>Male, 2</td>
<td>Blood</td>
<td>Congenital short bowel syndrome, hypogammaglobulinaemia, Port A catheter, TPN use (removed)</td>
<td>Oxacillin + vancomycin</td>
<td>Good/NA</td>
</tr>
<tr>
<td>Female, 37</td>
<td>Blood</td>
<td>Gastric cancer, CVC for TPN (removed)</td>
<td>Piperacillin + tazobactam → Ciprofloxacin</td>
<td>Good/NA</td>
</tr>
<tr>
<td>Female, 68</td>
<td>Blood</td>
<td>Gastric cancer, CVC for TPN (removed)</td>
<td>Oxacillin</td>
<td>Good/NA</td>
</tr>
<tr>
<td>Female, 29</td>
<td>Blood</td>
<td>Pregnancy, hyperemesis gravidarum, CVC for TPN (removed)</td>
<td>Vancomycin + clindamycin</td>
<td>Good/6 weeks post-discharge</td>
</tr>
<tr>
<td>Female, 51</td>
<td>Blood</td>
<td>Ovarian cancer undergoing chemotherapy, permanent CVC (removed)</td>
<td>Ciprofloxacin + clindamycin</td>
<td>Good/after 6 months</td>
</tr>
<tr>
<td>Male, 68</td>
<td>Blood</td>
<td>MDS, acute myelogenous leukaemia, tuberculosis CVC for chemotherapy (removed)</td>
<td>Ceftriaxone + ofloxacin</td>
<td>Death/after 16 days of hospitalization</td>
</tr>
<tr>
<td>Male, 78</td>
<td>Peritoneal fluid</td>
<td>End-stage renal disease on chronic ambulatory peritoneal dialysis (catheter not removed)</td>
<td>Cefotaxime + tazobactam → ciprofloxacin + teicoplanin + amoxicillin/ clavulanic acid</td>
<td>Good/after 1 month</td>
</tr>
<tr>
<td>Male, 69</td>
<td>Peritoneal fluid</td>
<td>End-stage renal disease on chronic ambulatory peritoneal dialysis (catheter not removed)</td>
<td>Intraperitoneal cefazolin + cefepime</td>
<td>Good/after 2 weeks of antibiotic therapy</td>
</tr>
<tr>
<td>Male, 56</td>
<td>Biliary fluid</td>
<td>Gallstones</td>
<td>Levofloxacin</td>
<td>Good/after 2 weeks of antibiotic therapy</td>
</tr>
<tr>
<td>Female, 4 months</td>
<td>Blood</td>
<td>Fever, prolonged diarrhoea, black tongue</td>
<td>Ceftriaxone + vancomycin</td>
<td>Good/after 1 week of antibiotic therapy</td>
</tr>
</tbody>
</table>

NA, Not available.

*CVC, Central venous catheter; MDS, myelodysplastic syndrome; TPN, total parenteral nutrition.*

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After 7 days of antibiotic therapy, blood cultures were performed in a BacT/Alert FA/FAN bottle. No growth was observed. Despite inotropic support and rifampicin infusion, the haemodynamic status progressively deteriorated.

Eleven days after hospitalization, the patient received a blood transfusion due to anaemia. After an initial improvement, he worsened again, becoming stuporous, hypotensive and dyspnoeic. A radiological examination performed 17 days after admission showed progression of pneumonia. In the following days, the patient developed compartment syndrome resulting in right foot ischaemia. Urgent arteriography of the lower limbs was planned, but it was not performed because of the severe clinical condition. Unfortunately, 25 days after hospitalization, the patient died of multiple organ failure from overwhelming sepsis.

Discussion

K. kristinae is a facultatively anaerobic Gram-positive bacterium that is catalase-positive, coagulase-negative, non-motile, nitrite reduction-negative and aesculin hydrolysis-positive (Stackebrandt et al., 1995). Although diverse automated microbial identification systems using phenotypic methods are currently available, they may provide unreliable results for coagulase-negative species, in particular Staphylococcus epidermidis, leading to misidentification of Kocuria species. Thus the correct identification of Kocuria species requires confirmation by molecular techniques, such as MALDI-TOF (Ben-Ami et al., 2005).

K. kristinae is aetiologically associated with catheter-related bacteraemia, probably because Kocuria species are common inhabitants of the skin.

After careful review of the literature, we found only 11 cases of K. kristinae infections in humans: 7 cases of systemic infection (one with endocarditis) in patients with central venous catheters (Lai et al., 2011; Dunn et al., 2011; Basaglia et al., 2002; Martinaud et al., 2008), 2 cases of peritoneal dialysis-related peritonitis (Carlini et al., 2011; Cheung et al., 2011), 1 case of acute cholecystitis (Ma et al., 2005) and 1 case of black tongue in a child (Oncel et al., 2012) (Table 1). However, only one case reported the development of infective endocarditis in an immunocompromised patient with a central venous catheter receiving parenteral nutrition (Lai et al., 2011).

The peculiarity of our case resides in the fact that (i) it represents the second case of K. kristinae endocarditis reported so far in the literature, (ii) we believe it to be the first case of K. kristinae endocarditis associated with diabetic foot infection and not related to a central venous catheter, and (iii) the patient died from multiple organ failure despite adequate antibiotic and supportive therapy.

Acknowledgements

We are indebted to Dr C. Senatore for his assistance in 16S rRNA gene sequencing.

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Discussion

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