Introduction

*Staphylococcus caprae* belongs to the broad family of coagulase-negative *Staphylococcus* (conS), and is a potential colonizer of human skin. Initially isolated from goat milk, its has been sufficiently characterized from a bacteriological point of view since the year 1995 [1-11], although some unexpected features like the possible production of *S. aureus*-like enterotoxins deserve further studies [7,12,13]. Although showing a mild virulence potential, its biofilm (slime) production and its unpredictable antimicrobial susceptibility profile [2,4,5] make it a rare, but challenging pathogen especially in nosocomial settings [11,14-16] or when prosthetic devices are of concern, with bone and joints as the most frequently reported localizations [1,6,10,17-22].

CASE SERIES

Invasive Diseases Due to Fatal *Staphylococcus caprae* Infection: A Case Series and Literature Review

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Abstract

We report a case series of fatal invasive diseases due to *Staphylococcus caprae*. We describe the first cases of *S. caprae* sepsis in two Italian patients. In the first patient there was also evidence of the fourth case reported in the English language literature of mitral endocarditis. We also discuss the main features of differential diagnosis on the basis of a literature review.

Keywords

*Staphylococcus caprae*, Coagulase-negative *Staphylococcus*, Infective endocarditis, *Staphylococcal* sepsis, Fatal brain thromboembolism, Native valve endocarditis

Although sporadic episodes of otitis, mastoiditis, meningitis, endophthalmitis, urinary tract infection, pneumonia, and peritonitis have been described, usually after surgery or interventional procedures, as well as very infrequent cases of sepsis or bacteremia remain very rarely reported ([Table 1] [23,24]). Reports of endocarditis are even more rare [24,25], and are usually related to prosthetic valves or implanted electronic devices (IED). The only report of *S. caprae* native valve mitral endocarditis is that described by Kwok, et al. [25].

Cases

A 68-year-old male suffering from a compensated type 2 diabetes mellitus and multiple comorbidities (COPD, diabetes-related nephropathy and a previous CNS vascular disease with severe neurological remnants including hemiplegia and claudication), accessed the Emergency Room of our Hospital due to altered mentation, low back pain, and an overwhelming acute heart failure with pleural-pericardial effusion. A transesophageal chest ultrasonography disclosed an endocarditis with 1.5 cm diameter vegetation on a trilobated valve, conditioning a severe left atrial-ventricular dysfunction (ejection index 40%). A CNS scan did not show further abnormalities, when compared with the previous one obtained 7 months before. Routine laboratory examinations addressed a moderate leukocytosis with neutrophilia, and increased serum C-reactive and procalcitonin levels (65.9 mg/dL and 0.97 ng/mL respectively). Multiple consecutive...
blood cultures allowed the growth of *Staphylococcus caprae*, while urine cultures tested negative. The microbial strain proved phenotypically susceptible to clindamycin, daptomycin, rifampicin, tetracycline, glycopeptides, linezolid, tigecycline and cotrimoxazole, and resistant to oxacillin, gentamycin, erythromycin, and levofloxacin. A diagnosis of defined aortic endocarditis was therefore posed, according to the modified Duke criteria. A SARS-CoV-2 disease was excluded, and the surveillance nasal and rectal swabs proved negative for colonizations. Combined i.v daptomycin (at 350 mg day), plus tigecyclin at 100 mg/day after a 100 mg loading dose), were started plus supportive therapy. A concurrent spondilodiscitis was excluded by a MRI examination of the spine, while a brain MRI scan did not show signs of metastatic infectious foci. Both ophthalmologic and odonto-stomatologic consultancies were recommended, together with the appropriate instrumental assessments. After the 6-week attack antibiotic therapy, a de-escalation schedule based on oral rifampicin-tetracycline therapy was suggested, but our patient did not survive an acute-on chronic heart ischemic attack, when still hospitalized at the intensive Cardiology Unit of our Hospital.

A 54-year-old male already suffering from a macrocephaly due to an Arnold-Chiary syndrome and a permanent ventriculo-peritoneal shunt, experienced an acute subarachnoidal hemorrhage after a head trauma occurred at home. Through the Emergency Room he was hospitalized at the Neurosurgical Department of our Hospital, where he received neurosurgical decompression of a large right temporal subdural hematoma, confirmed by a brain CT scan, which also allowed a correct positioning of a cranial drainage. Laboratory assessment obtained upon admission did not show relevant abnormalities save a moderate increase of serum creatinkinase level (404 U/L), related to the recent trauma. Oral, nasal, and rectal surveillance swabs tested negative for all searchable microorganisms, while blood culture repeatedly yielded *S. caprae*, which proved susceptible to all tested antibiotic compounds. Intravenous dexamethasone, mannitol, furosemide therapy was immediately started to contain brain edema, together with phenobarbital-levetiracetam to prevent seizures. The standard preoperatory antibiotic prophylaxis with cefazolin was followed by co-amoxiclavulanate, and subsequently switched to linezolid at 600 mg/d, which guarantees an excellent brain penetration. Despite neurosurgery and the intensive management, our patient went to death after 5 sole days since hospitalization.

**Discussion**

The first described case is extremely challenging due to: its clinical differential diagnosis with arterial coronary disease [22] and spondylodiscitis [18], both rare but already described occurrences in the setting of *S. caprae* infection. Both complications have been expected by us, but were carefully ruled out in our patient with appropriate clinical and instrumental examinations. The neurological signs and symptoms

<table>
<thead>
<tr>
<th>References, Patient sex/year</th>
<th>Patient, sex, year</th>
<th>Underlying condition</th>
<th>Antibiotic susceptibility</th>
<th>Disease</th>
<th>Complications</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vandenesch, et al. [1]</td>
<td>A 46-year-old man</td>
<td>None</td>
<td>R to PEN, AMP; S to: OXA, CEF, ERY, OFL, VAN</td>
<td>MV IE</td>
<td>None</td>
<td>Cardiac surgery + 2 weeks of vancomycin</td>
<td>Recovery</td>
</tr>
<tr>
<td>Spellerberg, et al. [27]</td>
<td>A 2-day-old neonate</td>
<td>Congenital heart disease</td>
<td>None</td>
<td>Sepsis</td>
<td>None</td>
<td>Cardiac surgery + antibiotic therapy: 14 days of cefotiam</td>
<td>Recovery</td>
</tr>
<tr>
<td>Kini, et al. [23]</td>
<td>A 30-year-old African American woman</td>
<td>None</td>
<td>R to PEN, AMP; S to: AMPS, CLI, CEP, ERY, GEN, IMI, OXA, RIF</td>
<td>Nosocomial sepsis</td>
<td>None</td>
<td>Antibiotic therapy: vancomycin—CFZ</td>
<td>Recovery</td>
</tr>
<tr>
<td>Kwork, et al. [25]</td>
<td>A 76-year-old man</td>
<td>None</td>
<td>MV IE</td>
<td>A subacute small vessel infarct</td>
<td>Antibiotic therapy: 6 weeks of FLU.</td>
<td>Recovery</td>
<td></td>
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following the thromboembolism from the ascertained aortic endocarditis were more difficult to be recognized timely, due to the concurrent, severe remnants of our patient who already had a very high risk of ischemic heart-cerebral disease. They were hindered by the sequelae of a previous stroke documented by appropriate imaging techniques.

Moreover, both the potential nosocomial source and bacterial colonization, both frequent underlying conditions in other studies [4,5,8,9,11,15,16,24,25], and the resort to invasive procedures as frequent proxies for _S. caprae_ disseminated human disease, were excluded or absent in our setting, respectively.

Other interesting aspects which deserve further investigation are those related to colonization and intra species competition of _S. caprae_ with other Staphylococci on the human skin, especially in hospital settings [4,5,8,9,16,26], an those related to the _in vivo_ antibiotic effectiveness [1,4,5,8], which could not be addressed in our patient, because of his death due to an acute-on chronic heart failure. It is conceivable that our second patient described for a severe and fatal _S. caprae_ sepsis contracted the staphylococcal infection during his hospitalization, as this bacterium has been implicated in several nosocomial infections [23]. Together with the case described here, three of four isolations of _S. caprae_ from blood cultures were associated with cardiac malformations or endocarditis [1,24,25]. In a Indian study performed to speciate coagulase-negative staphylococci (CoNS) and their antibiotic susceptibility pattern isolated from clinical samples, among the 120 consecutive CoNS strains isolated from various clinical samples, _S. caprae_ accounted for 5% (6 isolates) of all isolates (4, 66.6%, from blood). All _S. caprae_ isolates from this study were susceptible to doxycycline, linezolid, and teicoplanin, and methicillin resistant was in _S. lugdunensis_ (64.71%), _S. epidermidis_ (66.67%), _S. caprae_ (67.5%). The highest resistance percentage to ciprofloxacin, gentamycin and cotrimoxazole was 33.33%. The highest resistance was in _S. caprae_ (66.67%), _S. epidermidis_ (64.71%), _S. lugdunensis_ (57.1%) [28].

In one other study evaluating the ability of automated ribotyping to identify isolates of CoNS species obtained from the blood of hospitalized patients during a 4-year period, among 177 CoNS isolates, the collection of clinical isolates comprised 3 isolates of _S. caprae_ [29].

In conclusion, we briefly report and discuss a unique case of native valve aortic endocarditis due to _S. caprae_, the only complicated by a lethal cerebral thromboembolism, in absence of colonization and resort to surgery or invasive procedures. Also _S. caprae_ should be considered in the setting of severe, complicated, and potentially lethal endocarditis, and prevention measures like colonization screening promoted in hospital settings.

**Author Contributions**

All the authors contributed to the clinical evaluation of the cases and to the drafting of the manuscript.

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None.

**Conflicts of Interest**

None.

**Patient’s Consent**

A signed informed consent for publication was obtained, and the manuscript is in accordance with the institution’s ethics committee.

**References**