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CASE REPORT

Gemella sanguinis: endocarditis, hypercoagulability, and stroke. First case report in Italy.

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Abstract

Endocarditis is a severe life-threatening infection. In the last decades *Gemella sanguinis* became a rare new cause of infective endocarditis. We here describe the first case report of endocarditis by *Gemella sanguinis* in Italy with multiple complications including stroke and thromboembolism at multiple sites in the presence of a high resistance to heparin administration. Cardiac surgery, antibiotics and anticoagulation allowed to reverse the clinical complication and to improve the patient outcome. However, antibiotic prophylaxis in the presence of congenital or acquired cardiac risk factors of endocarditis and surgical oral or dental procedures should be strictly provided.

Introduction

Endocarditis is one of the most severe life-threatening infections after pneumonia, sepsis and intraabdominal abscesses. *Staphylococcus aureus* is the most involved pathogen, followed by *Streptococci viridans, Streptococcus bovis* and HACEK group. [1] In the last decades *Gemella sanguinis* became a rare new cause of infective endocarditis. Before rRNA and DNA sequencing in 1988 the *Gemella* species were misrecognised with the *Neisseria* genus or *Streptococcus* genus due to similarities in gram coloration and colonial morphology. [7,22]

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Gemella sanguinis (G. sanguinis) is a catalase-negative, facultative anaerobic, gram-positive coccus. It was first isolated and described in 1998 from six human blood cultures. Until that moment three strains of the same genus were known: *Gemella haemolysans*, *Gemella bergeriae* and *Gemella morbillorum* and other five species besides *Gemella sanguinis* have been recognized so far: *Gemella assacharolytica*, *Gemella taiwanensis*, *Gemella parahaemolysans*, *Gemella palaticanis*, *Gemella cuniculi*. Although being commensals of the oral cavity, gastrointestinal and genitourinary tract, these different strains of *Gemella* were described as the cause of different cases of endocarditis and opportunistic infections in immunocompromised patients, including arthritis, osteomyelitis, meningitis. [3] To our knowledge, from the first case described in 1998 until today fifteen cases of infective endocarditis related to *G. sanguinis* were reported in the literature around the world. [2-16] We describe the first case of endocarditis from *G. sanguinis* ever reported in Italy.

Case report

A 52-year old woman was admitted to the emergency department (ED) of Moriggia Pelascini Hospital in Gravedona (Como) with a right hemiplegic syndrome and aphasia and a history of recurrent episodes of fever treated with antibiotics in the previous days. Past medical history reported appendicectomy and thyroidectomy with subsequent thyroid hormone replacement therapy. Two months before the event the patient underwent multiple dental extractions. At the ED computed tomography revealed a left middle cerebral artery acute ischemic stroke, that was treated with mechanical thrombectomy after the patient tranfer to Sant'Anna Hospital, Como (**Figure 1**).

In the meantime, a transthoracic and transoesophageal echocardiography unveiled a large vegetation (2.4 x 2.4 cm) on the posterior leaflet of the bicuspid aortic valve leading to severe aortic insufficiency (**Figure 2 panel A-B**). Vancomycin, gentamycin, and ceftriaxone were empirically started. Gentamycin was then discontinued after the isolation of *Gemella sanguinis* in the blood culture.

FIGURE 1 - Left cortical-subcortical hypodensity related to a subacute ischemic lesion at the first hospital admission.

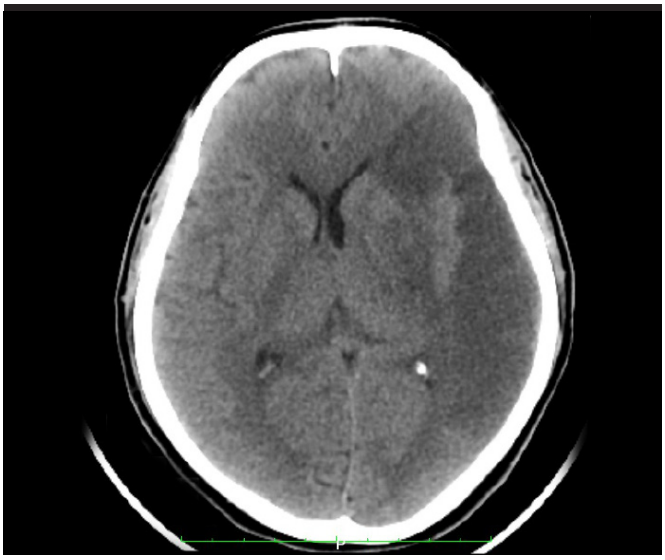
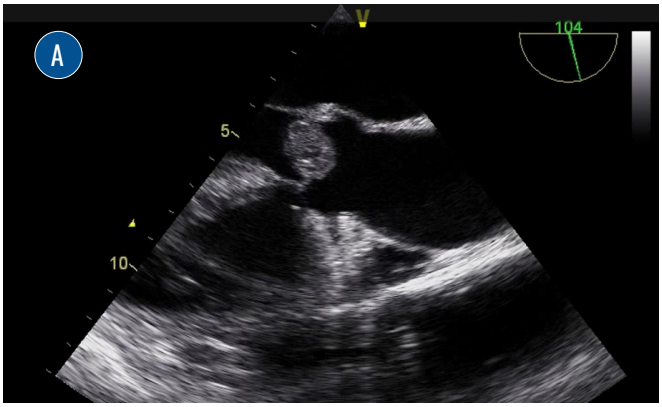
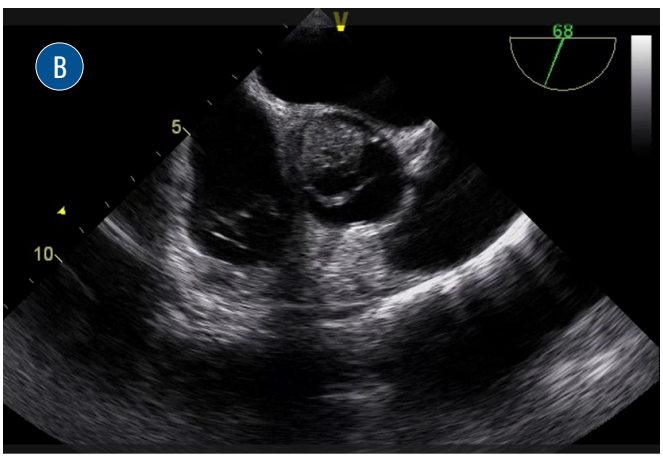


FIGURE 2 - Aortic valve vegetation during transesophageal echocardiogram. Left Panel (A), Mid-Esophageal Transgastric View; Right Panel (B), Mid-Esophageal Aortic Valve Short Axis View.





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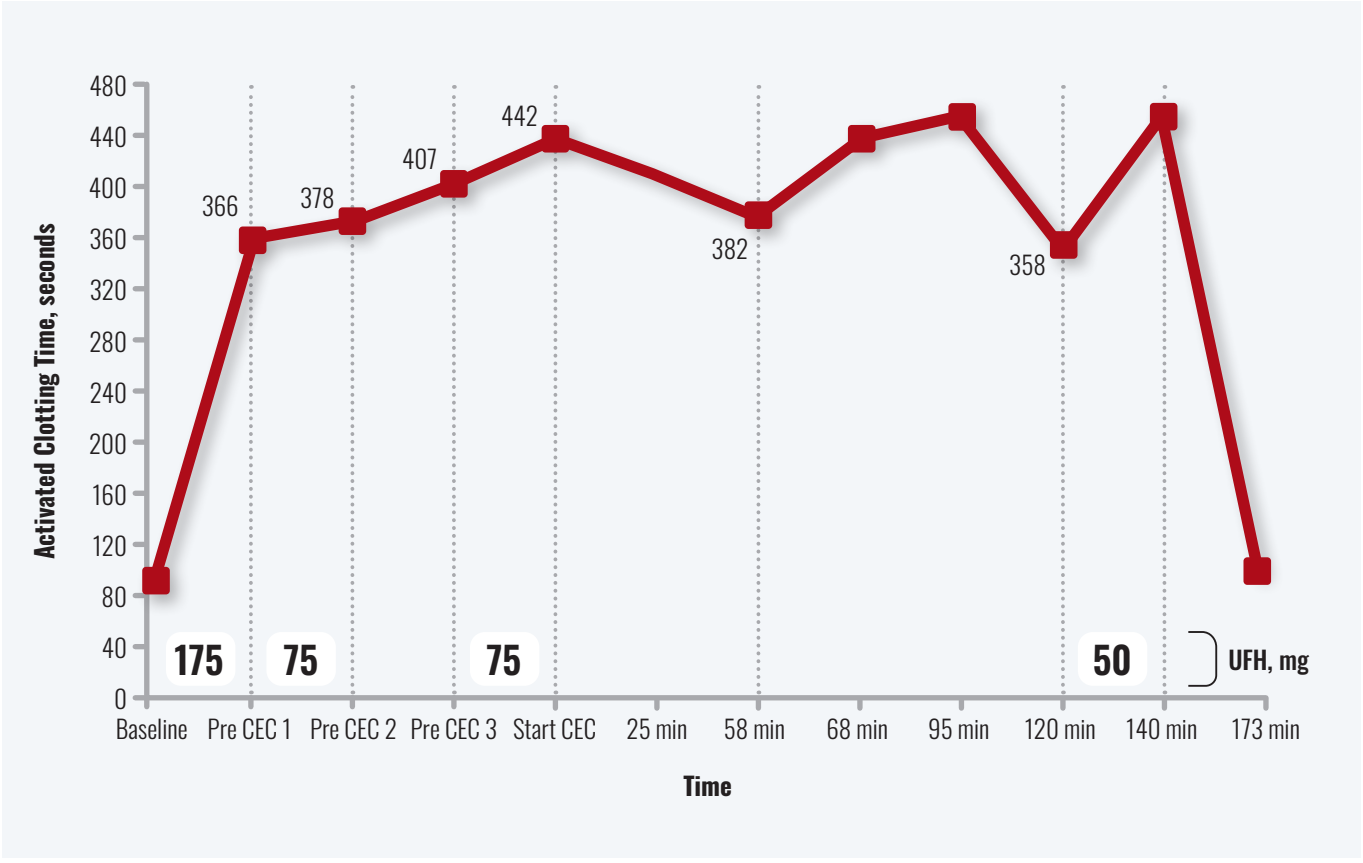
The patient was diagnosed with infective endocarditis according to the positivity of one major Duke's criterion (i.e. evidence of endocardial involvement) and three minor criteria (i.e. positive blood culture, an embolic phenomenon, and a congenital heart condition).
During the hospitalization the patient developed deep venous thrombosis in the left femoral vein, pulmonary thromboembolism, interstitial pneumonia, urinary tract infection and atrial fibrillation. Therefore, therapeutic anticoagulation with low-molecular-weight-heparin and antiarrhythmic therapy with amiodarone were started.

She was finally admitted to Niguarda hospital where she underwent aortic valve replacement with a mechanical valve and after the drainage of a perianular abscess. During surgery a significant heparin resistance required the administration of multiple additional boluses of unfractionated heparin besides the initial one until a total dosage > 800 UI/Kg and 500 UI of ATIII to achieve and maintain an ACT ≥ 400 seconds before and during extracorporeal circulation (**Figure 3**). The major cardiac surgery intervention was successful and ten days after the patient was discharged to a cardiac rehabilitation centre.

FIGURE 3 - Trend of measured activated clotting time (ACT) before and after administration of unfractionated heparin (UFH) boluses during extracorporeal circulation.



Discussion

Fifteen cases of infective endocarditis from *Gemella sanguinis* were reported in the literature until today. Most of them involved mainly the aortic valve and to a lesser extent the mitral valve. Only one case affected the tricuspid valve. All the reported endocarditis processes regarded natural valves, except in the case of involvement of two prosthetic valves. Half of patients had previous congenital or acquired cardiac risk

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factors, such as rheumatic heart disease, bicuspid aortic valve, and degenerative valvular disease. One out of two patients had a poor oral hygiene with dental caries, periodontal disease or underwent dental procedures shortly before developing the infection.

The treatment was usually surgical with valve replacement in addition to long term combined antimicrobial therapy with ceftriaxone, penicillin G, vancomycin, daptomycin or gentamycin. [2-16]

Our case report describes the first available evidence of complicated endocarditis by *Gemella sanguinis* in Italy.

According to the AHA recommendation, antibiotic prophylaxis for dental procedures should be strictly considered in patients with a high risk of adverse outcome from endocarditis, such as those with prosthetic cardiac valve, previous or recurrent infective endocarditis, cyanotic congenital heart disease or valvulopathy after cardiac transplantation. [17,18]

Active infective endocarditis was demonstrated to be an independent risk factor for heparin resistance, due to an hyperinflammatory state that causes acute-phase proteins increase with neutralization of heparin's activity and hypercoagulation due to the activation of platelets and reduced ATIII activity. Lower albumin level, preoperative heparin use, and high platelet count have also been associated with reduced heparin responsiveness. [19,20] It has been reported a potentiation of the heparin activity after the administration of 1000 UI of ATIII concentrate in patients with initial failure to obtain therapeutic anticoagulation with the usual dose of heparin before cardiac surgery. [21] Identification and treatment of potential correctable risk factors for heparin resistance could be useful before starting cardiac surgery even in patients with uncomplicated infective endocarditis.

Conclusions

In conclusion, although infective endocarditis by *Gemella sanguinis* has usually a good outcome after combination of surgery and prolonged antimicrobial therapy, clinical consequences of bacteremia by *Gemella sanguinis* can be devastating. Therefore, oral and dental care and treatment should be considered in the presence of congenital or acquired cardiac risk factors and antibiotic prophylaxis during dental extraction should be strictly provided.

Authors' contribution

L.A. interpreted data and wrote the manuscript; T.C. collected and interpreted data and reviewed and edited the manuscript; F.C. collected radiological data and reviewed and edited the manuscript; M.P.G. interpreted data and reviewed and edited the manuscript; F.M. collected and interpreted data, reviewed and edited the manuscript and conceived the case report; E.R. collected, analyzed and interpreted data, wrote the manuscript, conceived and supervised the case report.

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