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A clinical case of sepsis due to *Staphylococcus pettenkoferi*

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SUMMARY

Coagulase-negative staphylococci are part of the human skin flora but are frequently responsible for bloodstream infection, especially in the presence of intravascular devices or immunosuppressive conditions. Antibiotic resistance in such bacteria is common, with more than 80% of isolates resistant to methicillin. Among this genus *Staphylococcus pettenkoferi* is a recently identified organism, reported to be responsible for a growing number of infections. Here we describe a case of sepsis due to methicillin-resistant *S. pettenkoferi*.

Keywords: *Staphylococcus pettenkoferi*, sepsis, emerging infections, antimicrobial resistance, coagulase-negative staphylococci.

INTRODUCTION

Coagulase-negative staphylococci (CoNS) are among the most important bacteria responsible for bloodstream infections, osteomyelitis, nosocomial infections, infections in preterm newborns and infections of implanted-devices such as prosthesis, central venous lines, pacemakers, cerebrospinal fluid drainages or artificial heart valves. Most of the affected patients are old adults with different comorbidities, such as cerebral vascular accidents, tuberculosis, hematologic malignancies, diabetes mellitus and high blood pressure [1, 2].
Furthermore, antibiotic resistance is a constantly growing problem for coagulase negative Staphylococci, with some hospitals showing that almost 90% of their CoNS isolates are methicillin-resistant, posing several problems to antibiotic stewardship and infection control programs [3].

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Among CoNS, *Staphylococcus pettenkoferi* is a recently described species with specific metabolic features and responsible for human diseases [4]. It was first reported in 2002, and so far, worldwide, only few cases of *S. pettenkoferi* infections have been described [5].
In this case report we describe the first documented case reported in our tertiary care hospital (Fondazione IRCCS Policlinico San Matteo, Pavia - Italy), the third case in Italy of sepsis caused by methicillin-resistant *S. pettenkoferi* and its clinical implications regarding antimicrobial therapy and infection control [6,7].

CASE REPORT

A 88 years old woman living in her house was taken to the ER department after a fall to the ground. At the arrival she appeared severely dyspneic, she had high grade fever (39.2°C) and altered mental status. Her past medical history included acute myocardial infarction treated with coronary bypass and biventricular pacemaker implanted 5 years before, Alzheimer dementia and chronic obstructive pulmonary disease.

At the arrival her heart rate was 62 beats per minute, respiratory rate was to 40 per minute, blood pressure 123/76 mmHg and peripheral SpO_2 100% with oxygen administered via Venturi mask, 8 Lt per minute 35%. She was comatose and responsive only to pain. The qSOFA score was equal to 2, hence the likely diagnosis was sepsis, with a 6% chance of bad outcome (8). Chest X-ray excluded pleuro-parenchimal abnormalities and laboratory analysis included white blood cell (WBC) count of 21.470/microliter (neutrophils=89%), C reactive protein (CRP) of 33.42 mg/dL, procalcitonin 17.10 ng/mL, serum creatinine of 2.05 mg/dL and serum creatininekinase 586 mU/mL, with prerenal acute kidney injury and oliguria. The patient was admitted to our ward where two sets of blood cultures and a urine culture were collected and volume repletion with saline solution and dopamine at renal dosage were initiated. Blood samples for cultures were collected from different venipuncture sites in BD BACTEC™ aerobic/anaerobic culture vials and incubated into BACTEC™ automated blood culture system (Becton, Dickinson and Company, Franklin Lakes, NJ, USA), according to the manufacturer's instructions.

Positive broths were subjected to Gram-staining and sub-cultured into aerobic sheep blood agar plates, chocolate agar plates, selective plates and into Schaedleer agar + 5% sheep blood plates (bioMérieux SA, Marcy-l'Étoile, France) anaerobically and incubated at 37°C overnight: the organisms were identified by Matrix-Assisted Laser Desorption Ionization time-of-flight (MALDI-TOF) (Bruker Daltonics GmbH, Bremen, Germany) with a turnaround time of 1 hour. The isolate was tested for antimicrobial susceptibility using Phoenix 100™ (BD) automated system according to European Committee on Antimicrobial Susceptibility Testing clinical breakpoints (version 6.0).

Empiric antibiotic therapy was selected on the hypothesis of a urinary tract infection and it consisted of piperacillin/tazobactam adjusted to the glomerular filtration rate. On day 2 of hospitalization *S. pettenkoferi* was identified from 3 out of 4 blood cultures and the antimicrobial therapy was consequently tailored according to the antibiogram shown in Table 1, discontinuing piperacillin/tazobactam and introducing tigecycline and

Table 1 - *Staphylococcus pettenkoferi* antibiogram. Breakpoint are based on EUCAST (European Committee on Antimicrobial Susceptibility Testing) tables v 6.0

Antimicrobial agent	*R-S-I*	*MIC (mcg/mL)*	*Clinical breakpoint (mcg/mL)*
Fusidic Acid	S	1	<=1
Ampicillin	R		
Ciprofloxacin	R	>4	
Clindamycin	R	>1	<=0.25
Oxacillin	R	0.5	
Daptomycin	S	1	<=1
Erithromycin	R	>2	<=1
Fosfomycin	R	>64	<=32
Gentamycin	R	>4	
Linezolid	S	2	<=4
Moxifloxacin	R	>1	<=0.25
Penicilin G	R		
Rifampicin		<=0.25	
Teicoplanin	S	2	<=2
Tetracycline	S	<=0.5	<=1
Tigecycline	S	<=0.25	
Trimethoprim/Sulfametoxazole	S	2/38	<=2
Vancomycin	S	1	<=2

R: resistant, I: intermediate, S: susceptible

rifampin. We did not chose to use daptomycin since one of main side effects of this drug is myopathy and the patient already had elevated level of creatinine kinase at the biochemistry.
The isolate was identified as *S. pettenkoferi* with a score of 2.098 using the MALDI BioTyper automation 2.3 software (Bruker Corporation, USA). Also Phoenix 100™ (BD) automated system, used for susceptibility testing, identified it as *S. pettenkoferi* with a 98% certainty.
After 12 days of antibiotics the patient was afebrile, the blood cultures negative, inflammatory biomarkers significantly decreased and renal function completely normalized. A transthoracic echocardiogram showed no evidence of cardiac pacemaker wires involvement or endocarditis.

Table 2 - Literature review, modified and updated from [11].

Study	*No. of patients*	*Age (median) sex (M/F)*	*Comorbidities*	*Presentation*	*Nosocomial*	*Cultures*	*Treatment scheme*	*Clinical outcome (No. of patients)*
Mihaila L. et al.	9	(57), (8/1)	Acute hepatitis, cholangiocarcinoma, HCV cirrhosis, liver transplantation, hepatectomy, HIV, liver and renal transplantation, alcoholic cirrhosis	N.A.	N.A.	Blood cultures	N.A.	N.A.
Hashi A.A. et al.	1	75, F	Hypertension, type 2 diabetes mellitus, psoriasis, dyslipidemia, seizure disorder, right knee arthroplasty	Vertigo, skin rash, fever	No	Blood cultures	Vancomycin (1gr q12h, then Cloxacillin 2gr q6h)	Survived
Sholhui P. et al.	6	(70), (3/3)	Chronic alcoholic, hypertension, diabetes mellitus, cerebral vascular accident, pulmonary tuberculosis, acute myelomonocytic leukemia, major depressive disorder, benign prostate hyperplasia, peripheral T-cell lymphoma, intracerebral and intraventricular hemorrhage	Septic shock (1 patient), skin contaminants or catheter colonizers (5 patients)	N.A.	Blood coltures	Ceftriaxone Cefpiran, Metronidazole Teicoplanin, Voriconazole, Vancomycin Ceftriaxone, Vancomycin, Metronidazole Cefepime, Teicoplanin Colistimethate	Transferred (1), Stable (3), Expired (1), Recovered (1)
Saader HS. et al.	10	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Savini V. et al.	1	86, M	Ruptured abdominal aortic aneurysm	Wound infection	Yes	Blood cultures	ciprofloxacin, metronidazole, meropenem, piperacillin/ tazobactam, clindamycin, colistin, tigecycline and fluconazole	Died
Teeraputon S. et al.	2	N.A	N.A.	N.A.	N.A.	Blood culture	N.A.	N.A.
Mansson E. et al.	16	(68,5)/ (8-6, two patients n.a.)	N.A	N.A	N.A.	Blood cultures	N.A.	N.A.

DISCUSSION

Coagulase-negative Staphylococci represent some of the major nosocomial pathogens at the present day, accounting for serious infections in special populations of patients. ICU patients, preterm newborns, older adults and patients carrying implanted devices or indwelling catheters are some of the patients at highest risk of acquiring such infections. Moreover several methicillin-resistant CoNS (MR-CoNS) have been described in the community, possibly acting as reservoirs of SCCmec IVa gene for community acquired methicillin-resistant *Staphylococcus aureus* [9, 10]. Antibiotic resistance has constantly increased in these strains, making it difficult for clinicians to choose the most appropriate antimicrobial therapy. Only few options are available, among them glycopeptides, linezolid, moxifloxacin, tigecycline, daptomycin and ceftobiprole.

Staphylococcus pettenkoferi is a recent CoNS species, with a small number of confirmed identifications reported in medical literature, probably because of difficult identification process, despite reports suggest that the use of Maldi-TOF for identification of CoNS may improve the diagnosis of blood stream infection by this novel species [11].

As shown in Table 2, *S. pettenkoferi* can be the causative agent of septic shock, bacteraemia, wound infections as well as colonizer of the skin or intravascular devices, as reported in recent medical literature from 2012 until 2017 [7, 11-16].

In the patient that we describe, a clear source of infection or a pathogenetic mechanism was not clearly identified, since we excluded the presence of indwelling catheters, skin or oral lesions, joint prosthesis, heart valves and pacemaker involvement. Probably a minor breach of the skin undetectable at the physical examination was responsible for the entry of bacteria into soft tissues and the resulting bacteremia and sepsis.

Clinicians should be aware of *Staphylococcus pettenkoferi* as a possible yet underdiagnosed cause of infections in both hospitalized and community-residing patients, as they should be aware that they are possible carriers of antibiotic resistance mechanisms. These mechanisms can hinder therapeutic choices and contribute to further spreading of methicillin-resistant *Staphylococcus aureus* (MRSA) in both community and hospital settings.

Conflict of interest
None related to the content of this article.

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