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Case Report

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First Report of Vancomycin Intermediate *Staphylococcus Aureus* in Infected Subclavian Stent

Ali Sabateen[1*], Dina Nasser[1], Randa Kattan[2], Hammam Rjoup[1], Tahreer Taha[1], Caroline Hajal[1], Ghada Safi[1], Ihab Helou[1], Nasser Qutineh[1], Ismail Ashhab[1], Khoulod Ashhab[1], Nidal Saifi[1], Ashraf Husseini[1], Musa Hindiyeh[1,2,3,4]

[1]*Augusta Victoria Hospital, Jerusalem*

[2]*Caritas Baby Hospital, Bethlehem, Palestine*

[3]*Bethlehem University, Bethlehem, Palestine*

[4]*Palestine Forum for Medical Research, Ramallah, Palestine*

[*]**Corresponding author:** Ali Sabateen, Department of Infectious Disease, Augusta Victoria Hospital, Jerusalem, Palestine Email: asabateen@avh.org

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Abstract

We report the presentation and management of a patient that developed vancomycin intermediate Staphylococcus aureus while on vancomycin therapy. Positron Emission Tomography Computed Tomography Scanning showed increased uptake in the left proximal subclavian stent compatible with the origin of the bacteremia.

Keywords: Vancomycin Intermediate Staphylococcus aureus; PET/CT; Subclavian

Introduction

Health care providers are continuously challenged with the emergence of antibiotic resistant bacteria. This exerts tremendous pressure on the infection control unit to prevent the spread of such resistant organisms' in the healthcare setting. One of the important emerging pathogens is vancomycin intermediate Staphylococcus aureus (VISA) [**1-2**]. Management of VISA infected patients is extremely problematic and may be difficult to eradicate, especially for patients with infected devices or foreign bodies [**1**][3-5].

Worldwide, the first report of S. aureus with decreased susceptibility to vancomycin was described in Japan in 1997 [**6**]. Since then, several countries have reported the detection of VISA [**7-11**]. Fundamental characteristics of the VISA phenotype includes increased cell wall thickness, caused by differentially regulated cell wall biosynthesis and stimulatory pathway. On the molecular level, it is not well understood what contributes to the VISA phenotype.

Patients at high risk to develop infections due to VISA characteristically have prolonged hospitalization, persistent infections due to a poorly managed infected source, prolonged vancomycin treatment and MRSA treatment failure. What complicates patient management is the narrow range of active antibiotics against VISA. In general, invasive VISA infections are treated with daptomycin and linezolid, two antimicrobial agents that are not readily available in developing countries [**1**][12].

Here we report the first isolation of VISA in the blood culture of a hospitalized dialysis patient at Augusta Victoria Hospital, East Jerusalem, Palestine.

The Study

An 80 year old male patient was admitted to the Augusta Victoria Hospital on June 4th2013 to the Skilled Nursing Facility for long term health care. The patient's past medical history includes ischemic heart disease, status post coronary artery bypass graft (CABG) in 2010, chronic kidney disease on regular hemodialysis (three times weekly through arterial fistula), diabetes mellitus types II and hyperlipidemia, prostate hypertrophy and chronic obstructive pulmonary disease (COPD).

On November 23rd 2017, the patient developed hypotension and disorientation during his hemodialysis session without any other complaints. Detailed physical examination did not reveal an obvious source of infection, and hypoglycemia was ruled out. His laboratory workup results were as follows, C-reactive protein (CRP) 39 mg/L, creatinine 3 mg/dL, Blood Urea Nitrogen (BUN) 42 mg/dL, aspartate amino transferase (AST) 29 U/L, alanine amino transferase (GPT) 6 U/L and alkaline phosphatase 73 U/L. The patient's complete blood count (CBC) showed leukocytosis 12x103/uL of which 94% were neutrophils. One set of aerobic and anaerobic blood cultures, aerobic and anaerobic bottles, were collected from the patient's peripheral blood and incubated in the VersaTREK®instrument (Thermo Fisher, USA). The patient was started empirically on vancomycin 750 mg and gentamicin 80 mg after each hemodialysis session. Subsequent antibiotic doses were adjusted according to the therapeutic antibiotic levels.

Blood cultures were inoculated on the appropriate culture medium according to the American Society of Microbiology Clinical Microbiology Manual [**13**]. All bottles grew Gram positive bacteria in clusters that were both 3% catalase and coagulase positive. Confirmation that the isolate was S. aureus was done on the Vitek® 2 instrument (bioMérieux, France) and by matrix-assisted laser desorption/ionization (MALDI) (Bruker Daltonics Inc, USA).

Antibiotic susceptibility testing (AST) was performed according to the Clinical and Laboratory Standards Institute (CLSI) [14] using Kirby Bauer disk diffusion and the E-test (bioMérieux, France) to determine the minimum inhibitory concentration (MIC) of vancomycin and daptomycin. AST revealed that the Staphylococcus aureus isolate was methicillin-resistant (MRSA) based on the cefoxitin disk screen. It was susceptible to gentamicin, tetracycline, linezolid, rifampin and co-trimoxazole, and resistantto ciprofloxacin, erythromycin, clindamycin and levofloxacin (Table 1). Both vancomycin and daptomycin MIC's by E-test were 1.0µg/mL (Table 1).

Antimicrobial Sensitivity Testing of Patients Staphylococcus aureus Isolates				
Date of Bacterial Detection	23-11-2017	28-12-2017	16-02-2018	21-02-2018
Gentamycin	S	S	S	S

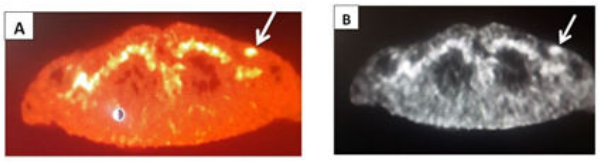
Ciprofloxacin	R	R	R	R
Amickacin	R	R	R	R
Tetracycline	S	S	S	S
Erythromycin	R	R	R	R
Clindamycin	R	R	R	R
Linezolid	S	S	S	S
Rifampin	S	S	S	S
Levofloxacin	R	R	R	R
Cefoxitin	R	R	R	R
Trimethoprim-sulfamethazaole	S	S	S	S
MIC for vancomycin µg/mL	1	2	2	4
MIC for Daptomycin µg/mL	1	1	1	1
MIC for Linezolid µg/mL	ND	ND	1	1

The patient underwent workup for his MRSA bacteremia. Detailed physical examination did not reveal signs of endocarditis, osteomyelitis, infected fistula or soft tissue infections. Transthoracic echocardiogram (TTE) did not show signs of endocarditis. Rheumatoid factor (RF) was negative. Vancomycin treatment was continued for 2 weeks while keeping the trough level between 15 and 20 µg/mL, and gentamicin was stopped after 3 days of therapy. Follow up peripheral blood cultures after 3 and 9 days of antibiotic treatment were negative. The patient's medical condition improved during therapy and he returned back to his base line.

On December 28th, 3 weeks after stopping vancomycin therapy, the patient developed fever (38.7oC), without chills, and no other symptoms. A septic workup was performed which included CBC and drawing two peripheral sets of blood cultures one from each arm. The CBC showed WBC 7.3 x 103 /µl, with 62% neutrophils;both blood culture bottles grew MRSA. The vancomycin MIC by E-Test increased to 2µg/mL (Table 1). The patient was started on vancomycin 750mg and gentamicin 80mg after each hemodialysis session with close vancomycin trough level monitoring around 20 mg/dL. Extensive workup to find the source of the MRSA infection included transesophageal echocardiography (TEE), whole body computerized tomography (CT) scan and RF did not indicate the source of infection. The patient was treated for 6 weeks and allfollow up blood cultures during therapy were negative. During therapy the patient felt well with no complaints and returned back to his base line.

On 16th of February, 6 days after stopping the vancomycin treatment the patient developed hypotension with blood pressure 75/50 without fever or chills, and again with no obvious source of infection. Two sets of peripheral blood cultures were collected which grew MRSA with vancomycin MIC 2µg/mL. The patient was started on daptomycin 6mg/kg after each hemodialysis session, with adding cefazolin 1g once daily [**14**]. While the patient was on daptomycin, a repeated two sets of blood culture on February 21stgrew S. aureus with vancomycin MIC by E-test of 4µg/mL. Per CLSI guidelines the S. aureus is now considered a VISA [**13**].

The patient underwent Positron Emission Tomography Computed Tomography (PET/CT) Scanning to complete the work up and to determine the possible source of the VISA infection. On March 2018, the PET/CT scan showed increase uptake in the left proximal subclavian area, identifying the presence of a stent in the artery, compatible with the source of the bacteremia (Figure 1 A: colored image and B: Black and white).



The presence of the stent was unexpected, and undocumented in the patient's medical records at Augusta Victoria Hospital. Follow up to ascertain the stents presence failed to reveal any new information when re-interviewing the family and the patient. Upon tracing the patient medical records to the referring hospital, a 2012 admission revealed documentation that the patient had a history of a subclavian artery stent insertionperformed due to stenosis at athird hospital.

The patient was continued on daptomycin with high dose of 8 mg/kg in combination with cefazolin 1 gram daily and was referred to a vascular surgeon for possible removal of the stent. At the time of writing this manuscript, the patient was free of relapse for 2 months.

Molecular characterization of the MRSA isolates revealed that the MRSA isolate contained the hospital acquired SCCmecType II cassette and was negative for the PVL gene and was not MRSA USA300 or USA400 strains by PCR [**15**].

Infection control measures included placing the patient with the VISA in a single room under strict contact isolation; hand hygiene adherence was strictly monitored daily. To assess if the bacteria had spread in the department, nasal swabs were collected from all the patients (N=21) in the unit and sent to the laboratory for S. aureus detections. Of the 21 patients 9 had MRSA in the nasal cavity, 4 MRSA strains had vancomycin MIC of 2µg/mL and 5 patients had MRSA with vancomycin MIC less or equal to 1µg/mL. The patient with the MRSA bacteremia was negative for MRSA in the nasal cavity. In order to prevent the spread of the bacteria in the hospital, MRSA nasal decolonization with mupirocinointment, twice daily for 5 days was initiated in addition to 4% chlorhexidine bathing, twice weekly. All patients tested negative for MRSA after the decolonizing step.

Our case emphasizes the importance of finding the source of the infection as prolonged vancomycin therapy can lead to the emergence of VISA. PET/CT scan was very instrumental in determining the source of the patient's bacteremia. These case reports represent the first VISA bacteremia as a result of infected subclavian artery stent.

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