CASE REPORT

Catheter related recurrent blood stream infection caused by linezolid-resistant, methicillin resistant *Staphylococcus haemolyticus*; an emerging super bug

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Abstract

A 61 year male, admitted in Combined Military Hospital Rawlpindi on 12th March 2017, operated for diverticulitis became colonized with *Staphylococcus haemolyticus*. Patient suffered repeated septic episodes caused by the same organism during his stay in hospital. The strain was identified as methicillin resistant *Staphylococcus haemolyticus* (MRSH) also resistant to Linezolid by analytical profile index for *Staphylococcus* (API Staph) and VITEK 2 Gram positive cocci panel. The isolate was cultured from blood cultures, Central Venous Catheter (CVC) tip and skin swabs. Patient was successfully treated with injectable vancomycin and skin decolonization was acheived with chlorhexidine bath after which no episode of MRSH infection occurred. Patient had an uneventful recovery and was discharged on 21st June. His follow up visit showed clinical improvement.

Keywords: Coagulase negative *Staphylococcus* (CNS), Methicillin resistant S.hemolyticus (MRSH), Linezolid (LNZ) resistant, intensive care unit (ICU), Sepsis.

Introduction

Coagulase negative *Staphylococcus* (CNS) is often underestimated as the etiological factor of human infections. One important specie in this group is *S. haemolyticus*. After *Staphylococcus epidermidis, S. haemolyticus* is the second most frequently isolated coagulase-negative *staphylococcus* from clinical cases, primarily from blood infections.[1] Even though the virulence of S. haemolyticus is lesser than S. aureus, which means that it's potential to cause severe infections is lower, yet it has the ability to acquire resistance against multiple antimicrobial agents.[2] Taking into consideration its adaptability and the ability to survive in the hospital environment, especially on medical devices, S. haemolyticus becomes one of the major agent in nosocomial infections caused by multi drug resistant Staphylococci.[3]

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The case presented here highlights the impact that prolonged hospitalization, invasive procedures and exposure to multiple antibiotics can result in alteration of normal skin/mucous microbiota which leads to a highly adaptable linezolid (LNZ) resistant MRSH. This hospital strain of LNZ resistant MRSH was responsible for catheter-related infections and recurrent episodes of sepsis which was managed by chlorhexidine bath and targeted antimicrobial therapy following which skin cultures turned negative and no further episode of infection by S.haemolyticus occurred.

Case Report

A 61 years old male resident of Rawalpindi, was admitted to Combined Military Hospital Rawalpindi on 12th March 2017 with history of diverticulitis. He underwent hemicolectomy and colorectal anastomosis on 21st March 2017.Post operation, the recovery was uneventful and he was put on parentral nutrition and on combination of meropenem 1gTDS and metronidazole 500 mg, TDS. However, due to fluid collection and purulent discharge from the wound, re-exploratory laparotomy was done on 13 April 2017. Fluid culture yielded growth of MRSA and Enterococcus faecium. Patient remained in intensive care unit for post-op management of wound and antibiotic therapy was changed to linezolid 600mg I/V B.D and Meropenem 1g I/V TDS. On 5th post op-day that is on 18th April 2017 the patient started having fever bouts with temperature rising as high as 102°Fwith increasing levels of C-reactive protein(CRP)and total leucocytes count (TLC). Using blood culture system (bio Mérieux BacT/ ALERT 3D) Gram-positive cocci in clusters were isolated from set of the patient's blood cultures (bio Mérieux BacT/ALERT FA aerobic culture bottles and BacT/ALERT FN anaerobic culture bottles). On subculture, beige to white β haemolytic colonies, about 2-4 mm in diameter, grew on 5% sheep blood agar after 18hours incubation in air at 35±2°C (Figure 1). The organism was catalase positive with negative coagulase reaction (slide as well as tube coagulase) and showed haemolysis on blood agar.

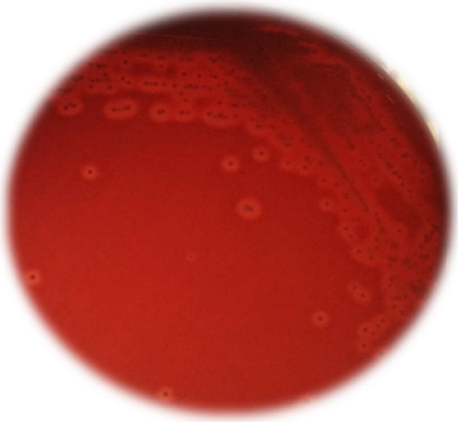

Figure-1: β Haemolytic colonies of S. haemolyticus on sheep blood agar.

The isolate showed positive reactions for maltose, lactose, trehalose and sucrose and negative reactions for oxidase, nitrate reduction, ornithine decarboxylase and urease on API ID 32 Staph (bio Mérieux).

Automated identification system VITEK-2 (bioMérieux, Marcy l'Etoile, France) confirmed the isolate as S. haemolyticus (ID-GP VITEK-2 card).Antimicrobial susceptibility performed as per Clinical and Laboratory Standards Institute guidelines showed cefoxitin screen positive, Minimum inhibitory concentration (MIC)values suggested that isolate was resistant to penicillin (MIC ≥ 1μg/ml), resistant to gentamicin (MIC ≥ 16μg/ml) , resistant to erythromycin (MIC ≥8μg/ml) and resistant to clindamycin(MIC ≥ 8μg/ml). MICs for linezolid LNZ (MIC ≥08μg/ml) and vancomycin (MIC ≤ 1 μg/ml) demonstrated the strain to be vancomycin sensitive and LNZ resistant. Patient's central venous line (CVL) was removed and tip was sent for culture along with paired blood cultures. The microbiological study of the catheter tip, according to Maki's semi quantitative technique showed more than 15 colonies of S.haemolyticus. Meanwhile the blood cultures were positive for S. haemolyticus growth with similar biochemical test results and antibiogram suggesting a catheter related blood stream infection. Patient was started on intravenous vancomycin 25 mg/kg loading dose followed by 15 mg/kg twice daily. The patient showed improvement with this regimen with settling of fever and inflammatory markers. On 10th day of treatment patient had a spike of temperature again and CRP started to rise. Paired blood sample was sent for culture but this time culture yielded growth of Candida albicans sensitive to fluconazole. Patient was started on intravenous fluconazole 800 mg as loading dose followed by 200 mg twice daily whereas Vancomycin was discontinued on 14th day of treatment. Antifungal therapy was continued for 14 days of the last blood culture negative for Candida. On 6thJune2017, the patient spiked a fever yet again with rising CRP and TLC levels. Paired blood culture yielded growth of S. haemolyticus with similar antibiogram and MICs as was from previous blood culture and CVL tip sample. This time, the flora of the patient's palms, axillae, site of CVC insertion, and nasal mucous membrane were examined for the presence/colonization of S. haemolyticus. Swabs taken form skin surfaces and CVC insertion site yielded growth of S haemolyticus with similar antibiogram and MICs, however swabs taken from nares were negative. Central venous catheter was placed at different site and intravenous vancomycin 15mg/kg body weight was administered to treat invasive blood stream infection and serum trough levels were monitored. Skin decolonization was carried out with chlorhexidine bath for 5 days, peripheral venous catheter was also replaced. Post treatment skin swab cultures showed negative results with no further detection of S. haemolyticus from skin and paired blood cultures (one taken from peripheral line and other from catheter site). Staph haemolyticus isolated from different sites was tested for biofilm production by tube adherence method, loopful of microorganisms from young cultures was inoculated in 10ml Oxoid Brain Heart Infusion Broth (Themo Scientific) and incubated at 35± 25°C for 48 hours, the supernatant was discarded and borosilicate glass tube was stained with 0.1% Safranin solution followed by 3 washings with distilled water, visible slime layer formation was seen Figure 2.

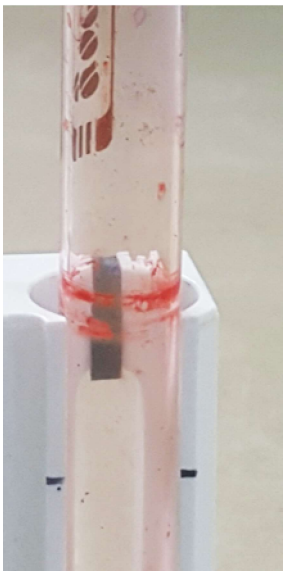

Figure-2: Biofilm detection.

Patient was discharged on 21st June 2017 along with instructions for intensive follow up. On follow up visits he had no active issues and found to have complete clinical recovery.

Discussion

Coagulase negative staphylococci (CNS) are major nosocomial pathogens. *Staphylococcus haemolyticus* is second *S. epidermidis* among CNS isolates and third most common organism among clinical isolates of methicillin-resistant Staphylococci.[4] *Staphylococcus haemolyticus*, an emerging cause of nosocomial infection plays an important role in causing opportunistic infections related to implanted medical devices.[5] The ability to form a biofilm is considered the most important virulence factor in CNS foreign device associated infections.[6] Here we report a case of recurrent catheter related blood stream infection caused by S.haemolyticus. In this case skin colonization that led to CVC line colonization due to the isolate's ability to form biofilm was the likely cause of recurrent infection.

Froggatt et al describe that S. haemolyticus carries the maximum level of antimicrobial resistance amongst all CNS species.[7] In our patient, the isolated organism was methicillin resistant and was also resistant to LNZ leaving glycopeptides as the only available option for treating this multidrug resistant isolate. Gupta et al reported first case of LNZ resistant S haemolyticus from India in 2012[8] and in the present year Rajan V et al reported occurrence of linezolid-resistant *Staphylococcus haemolyticus* in two tertiary care hospitals of South India[9], the present case is the first reported case of a linezolid resistant S. haemolyticus from Pakistan

De Allori MC et al and Karsten Becker et al have stressed that colonization of different parts of the skin and mucous membranes of the host is the key source of catheter associated endogenous infections in ICU patients under prolonged hospitalization. In these conditions, the organism easily migrates from skin to the external surface of the device. Severity of these infections depends on type of catheters, frequency of carriage and virulence factors of the strain involved. Some studies have strongly recommended the removal of external medical devices such as catheters in case of catheter related infections.[5,10] Our case showed that colonization of the skin was the major reservoir for the organism and that CVC served as the foreign source for transmission of isolate into bloodstream.

The present report clearly demonstrated that risk factors like prolonged hospitalization, major abdominal surgical procedures, presence of prosthetic device such as CVC and extended use of antimicrobials resulted in recurrent episodes of infections in such cases.

Conclusion

S. haemolyticus is one of the most important species in the CNS group. Threat posed by S. haemolyticus is due to factors like multi drug resistance and biofilm formation. The burden of BSI due to CNS can decline by implementation of strict surveillance guidelines in ICUs that would not only improve patient care but also decrease the economic burden on health care.

Patients Consent: Authors took permission from the patient before sending this case report for publication.
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