

Staphylococcus haemolyticus: An emerging threat in cancer patient

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ABSTRACT

Staphylococcus haemolyticus, a coagulase-negative *Staphylococcus*, is an opportunistic bacterial pathogen that colonizes human skin and is known for its high antibiotic resistance. After *Staphylococcus epidermidis*, the second most frequently isolated coagulase-negative *Staphylococcus* is *S. haemolyticus*. Increasing clinical significance of *S. haemolyticus* could be due to the great adaptability and the ability of the organism to survive in the hospital environment, especially on indwelling catheters, and the ability to acquire multidrug resistance against available antimicrobial agents. We report a case of a 40-year-old female diagnosed with mixed-lineage leukemia-positive pre-B acute lymphoblastic leukemia. The patient had undergone myeloablative T-replete haploidentical allogeneic stem cell transplantation. Later on, she developed skin graft versus host disease on day 83 and *S. haemolyticus* was isolated from the skin cultures. The patient was successfully managed with injection teicoplanin and skin care, but subsequently, she succumbed to multidrug-resistant *Klebsiella pneumoniae* infection.

Key words: Multiresistance, Nosocomial infection, *Staphylococcus haemolyticus*

Coagulase-negative staphylococci (CoNS) are part of the normal flora of the human skin. *Staphylococcus haemolyticus* is the second most frequently isolated CoNS, after *Staphylococcus epidermidis*, from clinical cases, particularly from bloodstream infections, including sepsis [1]. Most of *S. haemolyticus* strains lack the important virulence factors; however, studies have shown that the presence of various enzymes cytolysins and surface substances affects the virulence of *S. haemolyticus* [2,3].

Infections are often associated with indwelling medical devices [4-6]. Several case reports of nosocomial urinary tract infections [7], bloodstream infections [8], and soft-tissue infections [9] have been documented in the literature. Many reports suggest *S. haemolyticus* to be overriding *S. epidermidis* [10-12]. Here, we report the case of *S. haemolyticus* isolated from a 40-year-old female.

CASE REPORT

A 40-year-old female with no comorbidities was diagnosed with mixed-lineage leukemia (MLL)-positive pre-B acute lymphoblastic leukemia in May 2018. The patient was inducted with the German Multicenter ALL protocol. She attained remission and minimal residual disease (MRD) was <0.01% post-induction. As she was having high risk due to MLL gene positivity, the patient and family members were counseled about the need for allogeneic stem cell transplantation. She had only

haplomatches in the family and matched unrelated donor search showed <8/10 matches worldwide.

She was taken for myeloablative T-replete haploidentical allogeneic stem cell transplantation in September 2018 (pre-transplant MRD was <0.01%). Post-transplant cyclophosphamide 50 mg/kg on days 3 and 4, tacrolimus 1.5 mg twice a day from day 5, and mycophenolate mofetil total 2 g in three divided doses were used as graft-versus-host disease (GVHD) prophylaxis. She developed a veno-occlusive disorder on day 18, which was low grade and was managed conservatively. Subsequently, on day 30, there was cytomegalovirus reactivation which was managed with ganciclovir 5 mg/kg twice a day for 21 days. On day 83, she developed skin GVHD which was Grade 3 and immunosuppression with methylprednisolone 1 mg/kg was started.

Cultures taken from the skin were sent to the microbiology laboratory. Gram staining showed Gram-positive cocci and cultures after 24 h of incubation yielded non-pigmented beta-hemolytic colonies on a blood agar plate which was catalase positive and coagulase negative. Colonies were identified as *S. haemolyticus* by the bioMerieux automated VITEK 2 compact system and were sensitive to novobiocin. Susceptibilities were determined by the fully automated VITEK 2 and Kirby-Bauer disk diffusion method as per the Clinical and Laboratory Standards Institute guidelines. The isolate was found to be susceptible only to vancomycin (minimum inhibitory concentration 1 µg/ml), teicoplanin, and linezolid. The patient was managed with teicoplanin 400 mg twice a day for 2 days

Table 1: Reported cases of *Staphylococcus haemolyticus* infection

No.	Study	Year	Sample	Clinical indications	Pathogenic role
1.	Degener <i>et al.</i> [19]	1999	Blood	Chronic myelogenous leukemia	Pathogenic
2.	Sato <i>et al.</i> [20]	2010	Blood	Acute leukemia	Pathogenic
3.	Hitzenbichler <i>et al.</i> [21]	2017	Blood	Bloodstream infection due to foreign body device	Pathogenic
4.	Vijayan <i>et al.</i> [22]	2019	Cerebrospinal fluid	Pituitary macro adenoma	Pathogenic

followed by 400 mg once a day for 2 weeks and skin care and discharged with Hickman's *in situ*.

The patient was readmitted in January 2019 on day 99 with fever, right-sided pleural effusion, and lower lobe consolidation. Blood cultures and pleural fluid cultures grew *S. haemolyticus* with similar sensitivity. The patient was started on teicoplanin, and subsequently, she developed paraparesis. Imaging showed spinal cord medullary infarcts. Cerebrospinal fluid culture also grew *S. haemolyticus*. Echocardiography was done to rule out infective endocarditis which was found negative. As the patient was not fit for the procedure, a transesophageal echocardiogram was not done.

She improved clinically for 1 week, but subsequently, her pneumonia worsened. Serum procalcitonin was 0.4 ng/ml and the test for C-reactive protein was not done. Serum ferritin was markedly elevated to 11,553 ng/ml suggestive of acute inflammation. Repeat cultures of sputum and blood grew *Klebsiella pneumoniae* which was a multidrug-resistant (MDR) strain. The patient subsequently succumbed to her infection.

DISCUSSION

S. haemolyticus is an opportunistic pathogen well known for its antibiotic resistance. The resistance genes for each type of antibiotic can be located on the chromosome (methicillin), on the plasmids (macrolides), or on both chromosomes and plasmids (aminoglycosides). The resistance mechanisms also include the production of beta-lactamases and alteration of penicillin-binding protein by expressing the *mecA* gene [13]. *S. haemolyticus* isolates are saprophytic bacteria with the ability to colonize human skin and mucosal membranes. *S. haemolyticus* is second to *S. epidermidis* among CoNS isolates and the third most common organism among clinical isolates of methicillin-resistant staphylococci [14].

S. haemolyticus, an emerging cause of nosocomial infection, plays an important role in causing opportunistic infections related to implanted medical devices [15]. The ability to form a biofilm is considered as the most important virulence factor in CoNS foreign device-associated infections [16]. *S. haemolyticus* easily migrates from the skin to the external surface of the device. The severity of these infections depends on the 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 [1,15]. In this case, colonization of the skin was the major reservoir for the organism and central venous catheter served as the foreign source for transmission of isolate into the bloodstream.

The isolate was resistant to methicillin but sensitive to linezolid. In contrast, Gupta *et al.* reported the first case of linezolid-resistant *S. haemolyticus* from India in 2012 [17] and Rajan *et al.*, in 2017, reported the occurrence of linezolid-resistant *S. haemolyticus* in two tertiary care hospitals of South India [18]. The reported cases of *S. haemolyticus* are shown in Table 1.

In the present case study, the patient was treated with teicoplanin as the isolate was susceptible. Although the patient was responding well to teicoplanin, due to immunosuppression and other associated comorbidities, the patient ultimately died of sepsis, which was due to an MDR strain of *K. pneumoniae*.

CONCLUSION

S. haemolyticus is considered a less important pathogen, but due to its multidrug resistance, more effective strategies are required to detect and combat this emergent opportunistic pathogen. *S. haemolyticus* might be the reservoir of resistance genes for other staphylococci (including *staphylococcus aureus*). Due to the great adaptability and ability to survive in the hospital environment, including on medical devices, *S. haemolyticus* may be considered a crucial factor in hospital-acquired infections caused by multiresistant staphylococci.

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