Application of nanotechnology antibacterial spray in the treatment of Methicillin-Resistant Staphylococcus Aureus infections: a case report

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Abstract

Background: Methicillin-resistant Staphylococcus aureus (MRSA) infections are prevalent among orthopaedic patients after implant surgery. However, the available treatments for MRSA are currently extremely limited.

Case presentation: A 70-year-old patient developed wound infections after undergoing a bipolar hemiarthroplasty operation, which were subsequently identified as MRSA infections through bacterial culture. After 8 weeks of vancomycin treatment, the infection symptoms and bacterial culture showed no improvement. However, the introduction of a physical antimicrobial spray dressing (JUC) resulted in noticeable effects after just one day of treatment. Within a week, the wound secretion significantly reduced, and complete healing was achieved after three weeks of treatment..

Conclusions: In this case, the application of a nanotechnology antibacterial spray (JUC) proved to be significantly effective in treating MRSA infections.

Keywords: Methicillin-resistant Staphylococcus aureus, nanotechnology antibacterial spray, bacterial resistance, physical antimicrobial method, case report

Background

According to 2015 U.S. National action plan for combating antibiotic-resistant bacteria [1], antibiotics have been instrumental in saving millions of lives since their discovery. However, the emergence of bacterial resistance has rendered some bacterial infections resistant to treatment. Drug-resistant strains cause 2 million illnesses and approximately 23,000 deaths each year in the United States alone. The primary goal of

this action plan is to reduce the incidence of emergencies and serious threats concerning infections of three drug-resistant strains, including methicillin-resistant Staphylococcus aureus (MRSA). A prior research reported that MRSA accounts for 50% to 78% of all Staphylococcus aureus infections [2]. At present, vancomycin is the only effective clinical treatment for MRSA, but there have been reports on the MRSA resistance to vancomycin [3]. Therefore, it is of great significance to find another effective method to treat MRSA. Here, we present a case of MRSA infection that was refractory to vancomycin alone for 8 weeks, but was completely cured after 3 weeks of combined use with a nanotechnology antibacterial spray (JUC).

Case presentation

On March 15, 2014, a 70-year-old man was admitted to the hospital due to a left femoral neck fracture. The patient underwent bioplar hemiarthroplasty operation on March 20, 2014. The detailed parameters for artificial femoral head were as follows: double cup, size 48; size of femoral head 28 mm; stem: 10 (manufacturer: B.Braun Melsungen AG). The patient had no history of MRSA infections. After surgery, the patient received ceftriaxone (trade name: ceftriaxone sodium, 1g, 2 times/d) for 7 days to prevent infection. From March 21 to March 24, the patient's body temperature was normal, and his surgical wound was cleaned with hydrogen peroxide solution and 3% boric acid solution everyday. The wound was kept dry, and sterile dressing was used for coverage.

The patient complained of wound pain since March 25. On March 26, the patient's body temperature rose to 38.5℃. Based on the symptoms, signs and laboratory results (CRP 4.38mg/dl; blood WBC 6,540/mm^3) on March 26, the patient was diagnosed with bipolar hemiarthroplasty infection, and ceftriaxone was replaced by levofloxacin (trade name: lectacin) 0.5g, 2 times/day. At the same time, for precise treatment, 80ml pus was extracted on March 27 for bacterial culture and drug sensitivity test. However, after 4 days of treatment, there were no signs of improvement in the infection. After discussions with the patient and his family members, we removed the implant on March 31 and performed debridement to control the infection. After the implant was removed, the body temperature turned to normal. The bacterial culture results on April 1 showed MRSA positive (Table 1).

From April 2, according to the standard, the patient was treated for 8 weeks with intravenous injection of vancomycin (serum trough concentration 7 md/L, peak concentration 38md/L), for MRSA eradication therapy. During the entire treatment of MRSA infection, the patient was arranged in single room. However, this still didn′t solve the surgical site infection in the patient (Figure 1-1).

On May 20, 2014, due to vancomycin expiration, it was replaced by levofloxacin. Two weeks later, on June 3, 2014, vancomycin was resumed as no other medication was available. Meanwhile, the bacterial culture on June 2 and 19 showed that there was still MRSA infection (Figure 1-2). As a last resort, after debridement of the surgical site, we sprayed nanotechnology physical antimicrobial dressing (trade name: JUC, manufacturer: NMS Technologies Co., Ltd.) 2 times a day from June 25. On June 28, the amount, odor, color, and viscosity of the wound exudates were obviously improved, the wound began to shrink (Figure 1-3). On July 1, the odor of discharge disappeared completely. On July 3, the results of bacterial culture of wound secretions were negative (Table 1). Throughout the entire period of using JUC, the patient had no skin itching, rash and other

reactions, and the patient complained of feeling good.

Vancomycin was used for the second time from June 3 to July 11, 2014. JUC was used from June 25 to July 15, 2014. The wound healed completely on July 15. During the subsequent eight-week follow-up, the wound did not become reinfected.

Discussion and conclusion

MRSA is a multi-drug resistant (MDR) bacteria. As MRSA is resistant to a variety of antibiotics, such as methicillin, amoxicillin, penicillin, etc., the drugs that can effectively treat MRSA infection are extremely limited. In 2011, a Clinical Practice Guidelines prepared by Infectious Diseases Society of America (IDSA) shows that the most common method for treating MRSA is the systemic treatment of vancomycin, followed by linezolid, Daptomycin, telavancin, etc. For topical treatment, mupirocin ointment is often used for auxiliary removal of MRSA colonization [4]. Moreover, other literature also have confirmed vancomycin as the preferred MRSA treatment method [5,6]. However, some experiments have shown that a few Staphylococcus aureus are not susceptible to vancomycin, and that long-term use of vancomycin can also lead to vancomycin-resistant Staphylococcus aureus (VRSA) [7,8]. Additionally, Deeny et al. reported a 21.3% drug resistance rate of MRSA to mupirocin [9].

In this case, after the diagnosis of MRSA infection, the patient was treated with vancomycin for 8 weeks (April 2 to May 20), but the MRSA infection did not improve. Subsequently, after switching to levofloxacin ineffective, vancomycin was continued for 8 weeks (June 3 to July 11). From June 25, we started spraying JUC, a product of 'nanotechnology physical antibacterial method', on the surgical sites. Three days later, the wound infection showed improvement, and a week later, the results of the bacterial culture turned negative. These results suggest that JUC has a good inhibitory and killing effect on MRSA. Importantly, previous findings also confirmed this conclusion. Ruttonjee& Tang Shiu Kin Hospital in Hong Kong had used JUC alone for MRSA infection on scalp injury, and had proved its efficacy in killing MRSA [10]. JUC Spray Dressing is a patented product under the 'nanotechnology physical antimicrobial method', which is composed of 2% organosilicone diquaternary ammonium salt and 98% deionized water. The main mechanism is that, when sprayed on body surface, it forms positively-charged film (antimicrobial nano-film) to adsorb negatively-charged microorganisms and causes their cell membrane rupture and die, thus achieves physical antimicrobial purposes [11-16].

The patients and their families expressed profound gratitude for the treatment they received. They fully acknowledged the limited alternatives available in the instance of vancomycin proving ineffective, and understood that these alternatives offered minimal therapeutic benefit. As for the JUC topical spray treatment, it was perceived as easy to administer, comfortable, and reassuring. The efficacy of JUC surpassed their expectations remarkably.

In summary, the use of a nanotechnology antibacterial spray (JUC) has demonstrated significant effectiveness in the treatment of MRSA in current medical practice. Further validation of this treatment method, through individualized treatment plans and extensive, multicenter clinical trials, is both necessary and holds great potential significance.

Abbreviations

MRSA: Methicillin-resistant Staphylococcus aureus; CRP: C-reactive protein; WBC:

White blood cell; MDR: Multi-drug resistant.

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Authors' contributions

KY and IJ made substantial contributions to conception and design. KY made substantial contributions to data collection, and data analysis. IJ was involved in drafting the manuscript, and both authors gave final approval of the version to be published.

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Availability of data and materials

The authors declare that data supporting the findings of this study are available within the article.

Declarations

Ethics approval and consent to participate

Medical Ethics Committee of Chonggu Seongsim Hospital has approved the research. The patient agreed to participate in this study. Informed consent was obtained from the patient prior to the study. All procedures were conducted according to the Declaration of Helsinki.

Consent for publication

Written informed consent has been obtained from the patient for publication of this case report and any accompanying images.

Competing interests

All authors certify that they have no competing interests to declare that are relevant to the content of this article.

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401 Figure 1

1-1 1-2 1-3

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403 **Figure Legends:**

404 Figure 1. Changes of surgical site infections. 1-1, Surgical site infection on May 14, 20
405 14, 8 weeks after treatment with vancomycin. 1-2, Surgical site infection on June 23, 201
406 4. 1-3, Surgical site infection on June 28, 2014, 3 days after using JUC.

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408 Table 1: Patient Treatment Record Table

Time	Inspection Result	Treatment	Wound Recovery
2014/3/15		Admission	
2014/3/20	Normal body temperature	Operation: bioplar he miarthroplasty operatio n ceftriaxone (trade nam e: ceftriaxone sodium 1g; time: 2 /d)	
2014/3/21 -2014/3/2 5	Normal body temperature	ceftriaxone (trade nam e: ceftriaxone sodium 1g; time: 2 /d) Surgical wound was c leaned with hydrogen peroxide solution and 3% boric acid solutio n	
2014/3/26	Body temperature: 38.5℃ CRP 4.38mg/dl; WBC 6,540/mm^3 ESR 0 mm/hr	levofloxacin (trade na me: lectacin) 0.5g, ti me: 2 times/day	
2014/3/27 -2014/3/3 0	Body temperature: 38.0~39.0℃	levofloxacin (trade na me: lectacin) 0.5g, 2 t imes/day	

2014/3/31	Normal body temperature	Bipolar artificial femoral head replacement were removed levofloxacin (trade name: lectacin) 0.5g, 2 times/day	
2014/4/1	Discharge bacterial culture: MRSA positive Drug sensitivity test results: a. Penicillin G: R b. Ciprofloxacin: R c. Clindamycine: R d. Erythromycin: R e. Fusidic Acid: R f. Gentamicin: R g. Habekacin: S h. Linezolid: S i. Mupirocin: S j. Oxacillin: R k. Quinupristin / Dalfopristin: S l. Rifampicin: S m. Teicoplanin: S n. Telithromycin: R o. Tetracyclin: R p. Tigecycline: S q. Trimethoprim / Sulfamethoxazole: S r. Vancomycin: S	levofloxacin (trade name: lectacin) 0.5g, 2 times/day	
2014/4/2-2014/5/19		vancomycin 2g, time: 2 times/day meropenem (April 3-23) 3g,time: 3 times/day, for pneumonia.	Much bleeding with the color of red blood, with large amount of pus(See Figure 1)
2014/5/20-2014/6/2	Discharge bacterial culture: MRSA positive	levofloxacin (trade name: lectacin) 0.5g, 2 times/day	
2014/6/3-2014/6/24	Discharge bacterial culture: MRSA positive	vancomycin 2g, time: 2 times/day	Still a lot of puson the wound(See Figure 2)

2014/6/25 -2014/7/11	2014/7/3 , Discharge bacterial culture: MRSA negative	vancomycin 2g, time: 2 times/day Spray JUC, time: 2 times/day	2014/6/28, Significantly improved in terms of discharge amount, odor, color, viscosity, and the wound start to shrink(See Figure 3)
2014/7/12 -2014/7/15	2014/7/15 Wound healed	Spray JUC, time: 2 times/day	

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一种非药物治疗耐甲氧西林金黄色葡萄球菌感染的方法

一名 70 岁人工股骨头置换术后出现耐甲氧西林金黄色葡萄球菌感染患者，采用万古霉素治疗 8 周无法控制，加用物理抗微生物喷雾敷料治疗三周后完全愈合。

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关键词：耐甲氧西林金黄色葡萄球菌感染，JUC 物理抗微生物喷雾敷料，多重耐药菌，细菌耐药性，非药物治疗，抗微生物的物理方法

总结

一名 70 岁患者在人工股骨头置换术后出现创面感染，细菌培养为耐甲氧西林金黄色葡萄球菌（MRSA）感染。采用万古霉素治疗 8 周后，感染症状和细菌培养情况并没有改变。加用物理抗微生物喷雾敷料治疗 1 天后起效，一周后创面分泌物明显减少，三周后完全愈合。

引言

根据 2015 年美国国家对抗抗生素抗药性行动计划［1］：自发现抗生素工具拯救数百万人生命奇迹以来，然而，今天，细菌耐药性的出现，有些细菌已不存在药物治疗方法。耐药菌每年仅在美国就会造成二百万 人生病，约 23000 人死亡。这一行动计划主要目标是至 2020 年，降低包括耐甲氧西林金黄色葡萄球菌（MRSA）的三种耐药菌感染的紧急和严重威胁事件发生。David 研究美国相关感染，每年在所用金黄色葡萄球菌感染患者中有 50~78%为 MRSA[2]。目前临床治疗 MRSA 唯一有效的是万古霉素，但是，已有 MRSA 对万古霉素耐药的报道[3]。本文病例就是针对万古霉素治疗 8 周后感染并没有改变的 MRSA 患者，加用物理抗微生物喷雾敷料治疗三周后完全愈合，这一种非药物治疗新型方法报道。

病例叙述

2014 年 3 月 15 日，一名 70 岁老年男性因左股骨颈骨折被收治入院。病人于 2014 年 3 月 20 日接受双极人工股骨头置换术，人工股骨头详细参数如下：双杯，大小 48 号；直径 10 码；股骨头大小 28 毫米（生产厂家：贝朗医疗）。患者过往无 MRSA 感染史。手术后，患者持续 7 天使用头孢曲松（商品名：头孢曲松钠 1g；时间：2 次/d）预防感染。在 3 月 21 日-24 日间，患者体温正常，手术创面每天采用过氧化氢溶液和 3%硼酸溶液清洁，创面保持干燥，采用无菌敷料覆盖。

患者从 3 月 25 日开始主诉有手术创面胀痛，并且患者在 26 日体温上升至 38.5℃。根据 26 日同一天的症状、体征和实验室结果（CRP 4.38mg/dl；血 WBC 6,540/mm3），患者被诊断为双极人工股骨头置换术感染，并将头孢曲松替换为左氧氟沙星（商品名：lectacin）0.5g，时间：2 次/d 治疗。同时，为了针对性治疗，于 3 月 27 日抽取 80ml 脓液进行细菌培养及药敏试验。但是，治疗 4 天后，感染并没有好转的迹象。与患者及其家属商讨后，我们在 3 月 31 日移除了植入物并进行清创来控制感染，植入物移除后体温转向正常。4 月 1 日细菌培养结果显示：MRSA 阳性（表 1 ）。

从 4 月 2 日起，按照标准患者接受了为期 8 周的万古霉素静脉注射（期间万古霉素血药谷浓度为 7md/L，峰浓度为 38md/L），来进行耐甲氧西林金黄色葡萄球菌根除治疗。在耐甲氧西林金黄色葡萄球菌感染的整个治疗过程中，患者被安排在单独的一个单人间。然而，这仍然未能解决患者的手术部位感染（figure 1-1）。

2014 年 5 月 20 日，由于万古霉素已到使用期限，被替换使用左氧氟沙星。两周后，2014 年 6 月 3 日恢复使用万古霉素，同时在 6 月 2 日、19 日进行细菌培养，仍然有 MRSA 感染（figure 1-2）。而从 6 月 25 日开始，对手术部位清创后增加喷洒物理抗微生物敷料（商品名：JUC，生产厂家：南京神奇科技开发有限公司）每天 2 次，到了 6 月 28 日，创面分泌物排出量、臭味、颜色、粘稠度明显改善，创面开始缩小（figure 1-3）；7 月 1 日分泌物的臭味完全消失；7 月 3 日创面分泌物细菌培养时，结果显示无微生物（表 1）。

第二次万古霉素从 2014 年 6 月 3 日使用至 7 月 11 日，而 JUC 从 2014 年 6 月 25 日使用至 7 月 15 日，创面于 7 月 15 日完全愈合。之后 8 周随访

中，伤口没有出现感染。

讨论

MRSA 是一种多重耐药菌种，由于 MRSA 对β-内酰胺类抗生素耐药，用于治疗 MRSA 感染的药物相对较少，2011 年美国感染性疾病学会（IDSA）制定的 MRSA 临床实践指南指出，目前最常见的是采用万古霉素全身治疗，其次是利奈唑胺、达托霉素、替拉万星等，局部常用莫匹罗星软膏辅助去除 MRSA 定植[4]；其他往期文献也证实万古霉素为首选治疗 MRSA 方法[5,6]。但国外有实验证明少部分金黄色葡萄球菌对万古霉素不敏感，长期使用万古霉素亦诱导耐万古霉素金黄色葡萄球菌（VRSA）产生[7,8]；另一方面，据 Deeny 等发现，MRSA 对于莫匹罗星也存在 21.3%的耐药率[9]。

本例患者在诊断为MRSA 感染后，采用万古霉素治疗了 8 周（从 4 月 2 日至 5 月 20 日），MRSA 感染情况并没有好转。随后再次恢复采用万古霉素治疗了 8 周（从 6 月 3 日至 7 月 11 日），从 6 月 25 日开始在原有治疗方法上加用“物理抗微生物方法”产品 JUC 喷洒手术部位，3 天后创面感染情况就有所改善，一周后创面已无微生物感染，显示 JUC 在抑制和杀灭 MRSA 上有良好的疗效。香港律敦治及邓肇坚医院曾单独应用 JUC 解决一例头皮外伤 MRSA 感染，已证明 JUC 可以杀灭 MRSA，本研究与该文献报道在治疗作用方向上是一致的［10］。JUC 喷雾敷料是“抗微生物的物理方法”专利技术产品，成分是 2%有机硅双长链双季铵盐和 98％的去离子水，其主要机理是喷洒体表形成正电荷膜（纳米抗微生物膜）吸附带负电荷的微生物并使其细胞膜破裂死亡，达到物理抗微生物的目的［11-16］。

结论

该病例的治疗过程，我们发现了一种 MRSA 物理非药物治疗新方法，但仍需进行单独治疗临床研究和大样本多中心临床研究，来进一步证实这一治疗方法的有效性，以发现多重耐药菌感染抗生素的替代治疗方案。

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figure 1：手术部位感染治疗情况变化

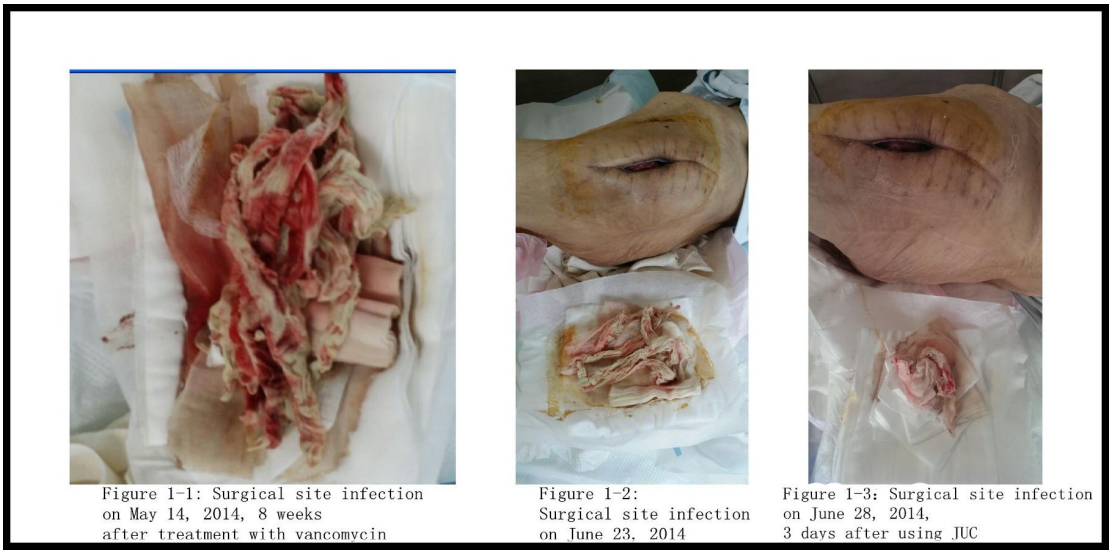

Figure 1-1: Surgical site infection on May 14, 2014, 8 weeks after treatment with vancomycin

Figure 1-2: Surgical site infection on June 23, 2014

Figure 1-3: Surgical site infection on June 28, 2014, 3 days after using JUC

表 1：患者治疗过程记录表

时间	检查结果	治疗	创面愈合情况
2014/3/15		入院	
2014/3/20	体温正常	手术：双极人工股骨头置换术 头孢曲松（商品名：头孢曲松钠 1g；时间：2 次/d）	
2014/3/21-2014/3/25	体温正常	头孢曲松（商品名：头孢曲松钠 1g；时间：2 次/d） 采用过氧化氢溶液和 3%硼酸溶液清洁创面	
2014/3/26	体温：38.5℃ CRP 4.38mg/dl； 血 WBC	左氧氟沙星（商品名：lectacin）0.5g，时间：2 次/d	

	6,540/mm^3 ESR 0 mm/hr		
2014/3/27-2014/3/30	体温：38.0~39.0℃	左氧氟沙星（商品名：lectacin）0.5g，时间：2 次/d	
2014/3/31	体温正常	移除双极人工股骨头 左氧氟沙星（商品名：lectacin）0.5g，时间：2 次/d	
2014/4/1	分泌物细菌培养：MRSA 阳性 药敏试验结果： a. 青霉素 G：耐药 b. 环丙沙星：耐药 c. 克林霉素：耐药 d. 红霉素：耐药 e. 夫西地酸：耐药 f. 庆大霉素：耐药 g. 丁胺二去氧卡那霉素：高度敏感 h. 利奈唑胺：高度敏感 i. 莫匹罗星：高度敏感 j. 苯甲异噁唑青霉素：耐药 k. 奎奴普丁/达福普丁：高度敏感 l. 利福平：高度敏感	左氧氟沙星（商品名：lectacin）0.5g，时间：2 次/d	

	m.替考拉宁：高度敏感 n. 泰利霉素：耐药 o. 盐酸四环素：耐药 p. 替加环素：高度敏感 q. 甲氧苄氨嘧啶/新诺明：高度敏感 r. 万古霉素：高度敏感		
2014/4/2-2014/5/19		万古霉素 2g，时间：2 次/d 美罗培南（4 月 3 日-23 日）3g，时间：3 次/d，用于肺炎	出血量多伴血色鲜红，排脓量大（见图 1）
2014/5/20-2014/6/2	分泌物细菌培养：MRSA 阳性	左氧氟沙星（商品名：lectacin）0.5g，时间：2 次/d	
2014/6/3-2014/6/24	分泌物细菌培养：MRSA 阳性	万古霉素 2g，时间：2 次/d	创面仍存在较多排脓（见图 2）
2014/6/25-2014/7/11	2014/7/3，分泌物细菌培养：MRSA 阴性	万古霉素 2g，时间：2 次/d 喷洒 JUC，时间：2 次/d	2014/6/28，创面分泌物排出量、臭味、颜色、粘稠度明显改善，创面开始缩小（见图 3）
2014/7/12-2014/7/15	2014/7/15 创面愈合	喷洒 JUC，时间：2 次/d	