

1 **Application of nanotechnology antibacterial spray in the treatment of Meth**
2 **icillin-Resistant Staphylococcus Aureus infections: a case report**

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14 **Abstract**

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

21 **Case presentation:** A 70-year-old patient
22 developed wound infections after undergoing
23 a bipolar hemiarthroplasty operation, which
24 were subsequently identified as MRSA
25 infections through bacterial culture. After 8
26 weeks of vancomycin treatment, the infection
27 symptoms and bacterial culture showed no
28 improvement. However, the introduction of a
29 physical antimicrobial spray dressing (JUC)
30 resulted in noticeable effects after just one day
31 of treatment. Within a week, the wound
32 secretion significantly reduced, and complete
33 healing was achieved after three weeks of
34 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

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

74

75 **Case presentation**

76 On March 15, 2014, a 70-year-old man was
77 admitted to the hospital due to a left femoral
78 neck fracture. The patient underwent bioplar
79 hemiarthroplasty operation on March 20, 2014.
80 The detailed parameters for artificial femoral
81 head were as follows: double cup, size 48; size
82 of femoral head 28 mm; stem: 10
83 (manufacturer: B.Braun Melsungen AG). The
84 patient had no history of MRSA infections.
85 After surgery, the patient received ceftriaxone
86 (trade name: ceftriaxone sodium, 1g, 2 times/d)
87 for 7 days to prevent infection. From March
88 21 to March 24, the patient's body
89 temperature was normal, and his surgical
90 wound was cleaned with hydrogen peroxide
91 solution and 3% boric acid solution everyday.
92 The wound was kept dry, and sterile dressing
93 was used for coverage.

94 The patient complained of wound pain
95 since March 25. On March 26, the patient's
96 body temperature rose to 38.5°C. Based on the
97 symptoms, signs and laboratory results (CRP
98 4.38mg/dl; blood WBC 6,540/mm³) on March
99 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

144 reactions, and the patient complained of
145 feeling good.

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

152 **Discussion and conclusion**

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

178 In this case, after the diagnosis of MRSA
179 infection, the patient was treated with
180 vancomycin for 8 weeks (April 2 to May 20),
181 but the MRSA infection did not improve.
182 Subsequently, after switching to levofloxacin
183 ineffective, vancomycin was continued for 8
184 weeks (June 3 to July 11). From June 25, we
185 started spraying JUC, a product of
186 'nanotechnology physical antibacterial
187 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 diquatery
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:

232 White blood cell; MDR: Multi-drug resista
233 nt.

234

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241 KY and IJ made substantial contributions to
242 conception and design. KY made substantial
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251 **Availability of data and materials**

252 The authors declare that data supporting th
253 e findings of this study are available withi
254 n the article.

255

256 **Declarations**

257 **Ethics approval and consent to participa
258 te**

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

266

267 **Consent for publication**

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

271

272 **Competing interests**

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

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401 Figure 1



402

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 hemiarthroplasty operation ceftriaxone (trade name: ceftriaxone sodium 1g; time: 2 /d)	
2014/3/21 -2014/3/25	Normal body temperature	ceftriaxone (trade name: ceftriaxone sodium 1g; time: 2 /d) Surgical wound was cleaned with hydrogen peroxide solution and 3% boric acid solution	
2014/3/26	Body temperature: 38.5°C CRP 4.38mg/dl; WBC 6,540/mm ³ ESR 0 mm/hr	levofloxacin (trade name: lectacin) 0.5g, time: 2 times/day	
2014/3/27 -2014/3/30	Body temperature: 38.0~39.0°C	levofloxacin (trade name: lectacin) 0.5g, 2 times/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: MR SA 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: MR SA positive	levofloxacin (trade name: lectacin) 0.5g, 2 times/day	
2014/6/3-2014/6/24	Discharge bacterial culture: MR SA positive	vancomycin 2g, time: 2 times/day	Still a lot of pus on the wound(See Figure 2)

American Journal of Therapeutics

2014/6/25 -2014/7/1 1	2014/7/3 , Discharge bacterial c ulture: MRSA negative	vancomycin 2g, time: 2 times/day Spray JUC, time: 2 ti mes/day	2014/6/28, Significa ntly improved in te rms of discharge a mount, odor, color, viscosity, and the wound start to shri nk(See Figure 3)
2014/7/12 -2014/7/1 5	2014/7/15 Wound healed	Spray JUC, time: 2 ti mes/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°C。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病房。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



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°C 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	

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