

Increasing methicillin resistance of *Staphylococcus lugdunensis* in a tertiary care community hospital in Japan

Takahiro Ichikawa¹, Fumihiko Kodama², Atsushi Nagasaka²

¹Kenwakai Otemachi Hospital, Fukuoka, Japan, ²Sapporo City General Hospital, Sapporo, Japan

Contact Information

Takahiro Ichikawa M.D.
Kenwakai Otemachi Hospital
15-1 Otemachi, Kokurakita-ku,
Kitakyusyu-shi, Fukuoka
Telephone : +81 80 6801 4236
E-mail : i3.tichikawa@gmail.com

Abstract

Background: *Staphylococcus lugdunensis* has virulence and pathogenicity similar to that of *Staphylococcus aureus*. Methicillin resistance and presence of *mecA* gene are not common in *S. lugdunensis* in many parts of the world. Recently, higher prevalence of methicillin-resistant *S. lugdunensis* is reported from Taiwan and Japan. We describe the change in methicillin resistance of *S. lugdunensis* in a tertiary care community hospital in Sapporo, Japan.

Methods: We performed a retrospective study of *S. lugdunensis*, isolated from inpatients and outpatients at our hospital from 2008 to 2017. Rate of methicillin resistance of the first 5 years from 2008 to 2012, and that of the second 5 years from 2013 to 2017 were compared. Risk factors of methicillin resistance were also evaluated. Phenotypic detection of methicillin resistance was identified using broth microdilution by VITEK 2 system (bioMérieux).

Results: A total of 369 cases of *S. lugdunensis* were detected during the study period. Of all cases, 228 (61.8%) were men, and 177 (48.0%) were hospitalized. Twenty-one isolates (5.7%) were positive in blood culture, 216 (58.5%) were positive in cultures of skin and soft tissue. Methicillin-resistant strains were found in 43 (31.6%) of 136 isolates from 2008 to 2012, and in 108 (46.4%) of 233 from 2013 to 2017 (OR 1.87; 95%CI 1.20-2.91; $P = 0.006$). Of patients with methicillin-resistant *S. lugdunensis*, 105 cases (69.5%) were hospitalized ($P < 0.001$).

Conclusion: In our hospital, methicillin-resistant *S. lugdunensis* is increasing over the 10 years. Further research is needed to assess trend of methicillin resistance of *S. lugdunensis* in other healthcare facilities and countries.

Background

- Staphylococcus lugdunensis*, a coagulase-negative staphylococci, is a normal skin flora in human, but has high virulence and pathogenicity similar to that of *Staphylococcus aureus*.
- Methicillin resistance of *S. lugdunensis* was 20-30% in some studies in East Asia, while that was reported as 0-3% in the world.
- In Japan, there is a report that oxacillin resistance in children of *S. lugdunensis* bacteremia was 75% (6/8 cases).
- To evaluate the increasing of methicillin-resistant strains, we describe the change in methicillin resistance of *S. lugdunensis* in a tertiary care community hospital in Sapporo, Japan.

Method

- We performed a retrospective study of methicillin resistance *S. lugdunensis*, isolated from inpatients and outpatients at our hospital from 2008 to 2017.
- We confirmed that the methicillin sensitivity determined by VITEK 2 system (bioMérieux) and Microscan series (Beckman Coulter) correspond with positivity of *mecA* gene, for 37 of *S. lugdunensis* isolates from August 2016 to August 2017.
- Primary endpoint**
We compared rate of methicillin resistance of the first 5 years from 2008 to 2012, and that of the second 5 years from 2013 to 2017.
- Secondary endpoint**
We analyzed the risk of methicillin-resistance for each factor: age, gender, disposition (inpatient or outpatient), underlying disease.
- We also compared rate of other antibiotics resistance of the first 5 years and that of the second 5 years.
- We performed Chi-squared test to compare the rate of methicillin resistance among each factor: sex, age, disposition, and underlying disease.

Result

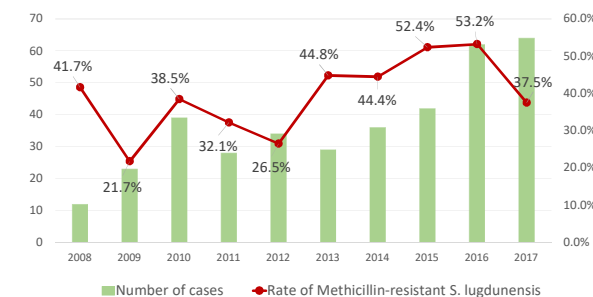
Table1 : Factor of Methicillin-resistant *Staphylococcus lugdunensis*

	N(%)		P	OR	95% CI
	Susceptible	Resistant			
	218	151			
2008/1/1~2012/12/31	93(73.8)	43(26.2)			
2013/1/1~2017/12/31	125(53.6)	108(46.4)	0.006	1.87	1.17-2.99
Age≥65	94(57.7)	69(42.3)	0.67	1.11	0.72-1.72
Inpatients	75(41.2)	107(58.8)	<0.001	4.62	2.89-7.46
Female	88(62.9)	52(37.1)	0.28	1.29	0.82-2.03
Underlying disease	149(57.5)	110(42.5)	0.42	1.24	0.77-2.02
Cardiovascular disease	57(55.3)	46(44.7)	0.41	1.24	0.76-2.01
Respiratory disease	12(46.2)	14(53.8)	0.21	1.75	0.73-4.26
Liver disease	5(45.4)	6(54.6)	0.37	1.76	0.44-7.44
Hemodialysis	22(45.8)	26(54.2)	0.06	1.85	0.96-3.59
Diabetes	77(63.6)	44(36.4)	0.26	0.75	0.47-1.20
Malignancy	40(58.0)	29(42.0)	0.89	1.05	0.60-1.86
Endocrine disease	7(38.9)	11(61.1)	0.09	2.36	0.81-7.37
Hematologic disease	5(62.5)	3(37.5)	1.00	0.86	0.13-4.51
Autoimmune disease	17(60.7)	11(39.3)	1.00	0.92	0.38-2.18
Neurological disorder	29(58.0)	21(42.0)	0.87	1.05	0.54-2.01

Table2 : Oxacillin and other antibiotics resistance of *Staphylococcus lugdunensis*

	2018/1/1- 2012/12/31	2013/1/1- 2017/12/31	P	OR	95% CI
Oxacillin	43(28.4)	108(71.6)	0.006	1.87	1.17-2.99
Penicillin G	95(34.8)	178(65.2)	0.18	1.4	0.84-2.30
Vancomycin	0	0			
Gentamycin	12(12.4)	85(87.6)	<0.001	5.91	3.04-12.45
Levofloxacin	9(23.1)	30(76.9)	0.08	2.08	0.93-5.15
Erythromycin	21(32.3)	44(67.7)	0.48	1.27	0.70-2.38
Minocycline	3(13.0)	20(87.0)	0.013	4.15	1.20-22.23
ST	1(100)	0	0.37	0	0.00-22.76

Figure1 : Rate of Methicillin-resistant *Staphylococcus lugdunensis* by year



Conclusion

- In our hospital, methicillin-resistant *S. lugdunensis* emerged at a higher rate after 2013 compared to before 2012.
- Similar trends were found for gentamicin and minocycline.
- Gender, age, or underlying disease has no association with presence of methicillin-resistance.
- On the other hand, the rate of methicillin-resistant *S. lugdunensis* is higher in hospitalized cases.
- There are reports suggesting the relationship between medical-related infection and high rate of methicillin-resistant *S. lugdunensis*, and we consider the possibility that nosocomial transmission is one factor to increase.
- S. lugdunensis* has pathogenicity as high as *S. aureus*, infection control such as contact isolation could be considered as MRSA.

References:
1) Kleiner E. Clinical Infectious Disease. 2010;51(7):801-803.
2) Boucher S. Journal of Clinical Microbiology. 2009;47(9):946-950.
3) Choi SH. Journal of Clinical Microbiology. 2010;48(7):3346-3349.
4) Lin J. Journal of Microbiology, Immunology and Infection. 2015; 48: 406-412.
5) Yen T. Journal of Microbiology, Immunology and Infection. 2016; 49: 885-891.
6) Sato K. J Infect Chemother. 2016 May; 22(5): 298-302.