

30%–50% of immunosuppressed patients with coccidioidomycosis (3). Disseminated coccidioidomycosis typically involves the skin, meninges, or bone (3); however, intraocular involvement has also been described (1). A review of the literature shows 25 reported cases of intraocular coccidioidomycosis. When present, intraocular involvement is associated with serious consequences, frequently leading to eye enucleation; 1 case series described eventual enucleation in 50% of reported patients who did not die from disseminated coccidioidal infection (2).

For the patient in our report, in the setting of reported trauma and negative metastatic work-up results, it is unclear whether ocular disease resulted independently as an exogenous infection or from endogenous lymphatic and/or hematogenous spread from the patient's lung. Diagnosis of coccidioidal endophthalmitis can be difficult, often relying on serum or nonocular tissue evaluation (4). Intraocular coccidioidal involvement usually occurs with widespread infection (5). Thus, even with apparent isolated ocular findings, evaluation for disseminated disease is warranted, including a careful history and physical examination, CT chest scan, bone scan, intracranial imaging, and lumbar puncture. Evaluation for immunosuppression, including HIV status, is warranted.

The optimal systemic antifungal therapy for intraocular coccidioidal infection is unclear, although fluconazole is the drug of choice for extrapulmonary coccidioidomycosis, including meningitis (3). Fluconazole has good ocular penetration; however, voriconazole also achieves excellent intraocular levels (6) at lower 90% minimum inhibitory concentration levels (7). Furthermore, Gabrielian and Hariprasad (8) described an immunocompetent patient with treated and stable nonocular

disseminated coccidioidomycosis who showed development of new vitritis and choroiditis 8 weeks into high-dose fluconazole therapy; his intraocular disease resolved within 2–4 weeks of transition to voriconazole.

The patient in our report received systemic voriconazole for 4 weeks plus repeated intravitreal voriconazole injections on follow-up. It is possible that this initial therapy had an effect on his positive outcome and the avoidance of eye enucleation. The optimal length of therapy is unclear; however, this patient will receive prolonged treatment (≥ 1 year) with high-dose fluconazole, followed by a slow taper guided by serologic testing and regular ophthalmologic examination. Future research should evaluate which antifungal therapy is superior and the appropriate duration of treatment.

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References

- Cutler JE, Binder PS, Paul TO, Beamis JF. Metastatic coccidioidal endophthalmitis. *Arch Ophthalmol*. 1978;96:689–91. <http://dx.doi.org/10.1001/archophth.1978.03910050379016>
- Rodenbiker HT, Ganley JP. Ocular coccidioidomycosis. *Surv Ophthalmol*. 1980;24:263–90. [http://dx.doi.org/10.1016/0039-6257\(80\)90056-9](http://dx.doi.org/10.1016/0039-6257(80)90056-9)
- Galgiani JN, Ampel NM, Blair JE, Catanzaro A, Johnson RH, Stevens DA, et al. Infectious Diseases Society of America. Coccidioidomycosis. *Clin Infect Dis*. 2005;41:1217–23. <http://dx.doi.org/10.1086/496991>
- Cunningham ET, Seiff SR, Berger TG, Lizotte PE, Howes EL, Horton JC. Intraocular coccidioidomycosis diagnosed by skin biopsy. *Arch Ophthalmol*. 1998;116:674–7.
- Moorthy RS, Rao NA, Sidikaro Y, Foos RY. Coccidioidomycosis iridocyclitis. *Ophthalmology*. 1994;101:1923–8.
- Riddell J IV, Comer GM, Kauffman CA. Treatment of endogenous fungal endophthalmitis: focus on new antifungal agents. *Clin Infect Dis*. 2011;52:648–53. <http://dx.doi.org/10.1093/cid/ciq204>
- Blumenkranz MS, Stevens DA. Therapy of endogenous fungal endophthalmitis: miconazole or amphotericin B for coccidioidal and candidal infection. *Arch Ophthalmol*. 1980;98:1216–20. <http://dx.doi.org/10.1001/archophth.1980.01020040068006>
- Gabrielian A, Hariprasad SM. New onset of bilateral multifocal coccidioidomycosis choroiditis in a patient on oral fluconazole. *Can J Ophthalmol*. 2010;45:419–20. <http://dx.doi.org/10.3129/i09-270>

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Human MRSA Isolates with Novel Genetic Homolog, Germany

To the Editor: Methicillin-resistant *Staphylococcus aureus* (MRSA) represents a major cause of hospital-, community- and livestock-acquired infections that are increasingly difficult to manage (1–3). Detection and identification of MRSA by culture and nucleic acid-based methods is challenged by heterogeneous penicillin-binding protein 2a (PBP2a) expression and variability of the staphylococcal cassette chromosome (*SCCmec*) elements. Recently, a new *SCCmec* element (XI) carried in bovine and human isolates was described (4,5). This *SCCmec* element contains a novel *mecA* homolog, designated *mecA*_{LGA251}, that is not detectable by usual *mecA*-specific PCR approaches and PBP2a agglutination tests. García-Álvarez et al. reported this novel *mecA* homolog exhibited 70%

identity at DNA level to the *mecA* gene, and suggested these strains were transmitted from livestock to humans (4).

To search for isolates possessing the novel *mecA*_{LGA251}, we screened *S. aureus* databases for those entries describing oxacillin/cefoxitin-resistant phenotypes that were negative for *mecA* by PCR (6) or harbored *S. aureus* protein A gene (*spa*) types known to be associated with the occurrence of *mecA*_{LGA251} (4,5). The databases of the University Hospital Münster contain *S. aureus spa* typing results of *S. aureus* isolates obtained from hospital admission screenings and specimens from patients treated at University Hospital Münster. Moreover, they include isolates derived from human and animal subjects, respectively, of 2 cross-border projects between the Netherlands and Germany: MRSA-net EUREGIO Twente/Münsterland and SafeGuard MRSA vet-net (2,7).

The presence of *mecA*_{LGA251} was verified by using a specific PCR that applied newly designed primers: *mecAL1* (5'-AGC TGG CCA TCC CTT TAT TT-3') and *mecAL2* (5'-CTG GCA TAT GGA GAA GAA GAAA-3'), derived from the sequence

of *S. aureus* LGA251 provided by M. Holden (Wellcome Trust Sanger Institute, Hinxton, UK; accession no. FR821779). The sensitivities and specificities of primers were checked by applying *S. aureus* and other staphylococcal isolates of different clonal backgrounds (8,9). Positive PCR products were sequenced to confirm identification of *mecA*_{LGA251}; the isolates were then characterized by typing the SCC*mec* region with specific primers for *mecR1*, *mecI*, *blaZ*, *ccrA*, and *ccrB* related to type XI SCC*mec* as described by García-Álvarez et al. (4). Identified isolates were tested for PBP2a by using a latex agglutination assay (Oxoid Deutschland GmbH, Wesel, Germany). We used Etest (bioMérieux SA, Marcy-l'Étoile, France) for antibacterial agent susceptibility testing of β -lactams and other antibacterial agents.

We report on 16 (clinically derived, n = 14; ovine origin, n = 2) oxacillin/cefoxitin-resistant *S. aureus* isolates possessing the recently described *mecA*_{LGA251} isolate, but lacking the classical *mecA* gene currently defining classic MRSA (Table). The isolates belong to *spa* types t843, t978, t1535, t1773, and t7189. Concurring with the

findings in the United Kingdom and Denmark, we found t843 to be the most prevalent *spa* type. Results of the PBP2a latex agglutination assay were negative for all isolates except for 1 (no. 14), which was indeterminable. García-Álvarez et al. described negative results for all tested isolates (4); Shore et al. reported inconsistent results with this test (5).

According to the Clinical and Laboratory Standards Institute MIC interpretative standards for staphylococci (10), antibacterial agent susceptibility testing revealed resistance to benzylpenicillin and oxacillin/cefoxitin for all isolates. All isolates were shown to produce β -lactamases. Apart from the general categorization of oxacillin/cefoxitin-resistant isolates as resistant to all β -lactams, the MICs of drugs for all isolates included were read as susceptible for imipenem (MIC for 90% of strains tested 0.5 μ g/mL) as well as for the anti-MRSA cephalosporin ceftobiprole (MIC for 90% of strains tested 1 μ g/mL applying provisional breakpoint \leq 4 μ g/mL). A large range of MICs were observed for classic cephalosporins, ranging from those isolates categorized as susceptible

Table. Description of *mecA*_{LGA251}-positive isolates regarding their *spa* type, ability to grow on selective MRSA media, PBP2a agglutination, *mec* gene possession, and SCC*mec*-type*

Isolate no. and origin	Year of isolation	Specimen	<i>spa</i> type	Characteristics				
				Growth on selective MRSA medium†	PBP2a agglutination	Presence of		
						<i>mecA</i>	<i>mecA</i> _{LGA251}	SCC <i>mecXI</i>
Human								
1	2010	Nasal swab	t843	+	-	-	+	+
2	2010	Wound	t843	+	-	-	+	+
3	2010	Wound	t843	+	-	-	+	+
4	2010	Nasal swab	t843	+	-	-	+	+
5	2011	Nasal swab	t843	+	-	-	+	+
6	2004	Sputum	t843	+	-	-	+	+
7	2010	Nasal swab	t843	+	-	-	+	+
8	2007	Mouth swab	t843	+	-	-	+	+
9	2010	Nasal swab	t843	+	-	-	+	+
10	2011	Nasal swab	t843	+	-	-	+	+
11	2011	Joint aspirate	t843	+	-	-	+	+
12	2007	Nasal swab	t978	+	-	-	+	+
13	2010	Nasal swab	t7189	+	-	-	+	+
14	2009	Nasal swab	t1773	+	ND	-	+	+
Sheep								
15	2010	Unknown	t1535	+	-	-	+	+
16	2010	Unknown	t1535	+	-	-	+	+

**spa*, *Staphylococcus aureus* protein A; MRSA, methicillin-resistant *S. aureus*; PBP2a, penicillin-binding protein 2a; SCC, staphylococcal cassette chromosome; +, positive; -, negative; ND, not done.

†ChromID MRSA-Plates (bioMérieux, Marcy-l'Étoile, France).

(cephalothin, n = 15; cefuroxime, n = 10; ceftriaxone, n = 2; cefepime, n = 9) to those classified as resistant.

We observed relatively low oxacillin/cefoxitin MICs for some of the *mecA*_{LAG251}-positive isolates (MIC 3 µg/mL, n = 1; MIC 4 µg/mL, n = 1; MIC 8 µg/mL, n = 3) compared with the MRSA reference strain ATCC 43300 (MIC 32 µg/mL). All isolates tested were susceptible to all non-β-lactam antibacterial agents, comprising glycopeptides, lipopeptides, fluoroquinolones, macrolides, lincosamides, oxazolidinones, rifampins, streptogramins, glycyclines, folate pathway inhibitors, aminoglycosides, and fosfomycin.

Until *mecA*_{LAG251} is included as a diagnostic target in molecular MRSA detection tests, oxacillin/cefoxitin-resistant isolates determined to be methicillin-susceptible by traditional, culture-based susceptibility testing methods should not be disregarded, even if *mecA* and/or PBP2a tests fail to detect their targets. Susceptibility patterns of *mecA*_{LAG251}-positive *S. aureus* isolates revealed low MICs of oxacillin compared with those for MRSA of the classical *mecA* type. We presume this indicates an altered affinity of β-lactam antibacterial agents to the putative *mecA*_{LAG251} gene product or a divergent expression of the gene. The choice and the dosage of antibacterial agents applicable for *S. aureus* infections should be reconsidered in light of this novel *mecA* homolog in molecular screening and identification tests. Studies are warranted to investigate the prevalence of this novel MRSA entity in and outside of hospitals in the human population and in livestock, its clinical effects, and its response to antibacterial agent therapy.

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References

- Grundmann H, Aanensen DM, van den Wijngaard CC, Spratt BG, Harmsen D, Friedrich AW. Geographic distribution of *Staphylococcus aureus* causing invasive infections in Europe: a molecular-epidemiological analysis. *PLoS Med.* 2010;7:e1000215. <http://dx.doi.org/10.1371/journal.pmed.1000215>
- Köck R, Harlizius J, Bressan N, Laerberg R, Wieler LH, Witte W, et al. Prevalence and molecular characteristics of methicillin-resistant *Staphylococcus aureus* (MRSA) among pigs on German farms and import of livestock-related MRSA into hospitals. *Eur J Clin Microbiol Infect Dis.* 2009;28:1375–82. <http://dx.doi.org/10.1007/s10096-009-0795-4>
- Klein E, Smith DL, Laxminarayan R. Community-associated methicillin-resistant *Staphylococcus aureus* in outpatients, United States, 1999–2006. *Emerg Infect Dis.* 2009;15:1925–30. <http://dx.doi.org/10.3201/eid1512.081341>
- García-Álvarez L, Holden MT, Lindsay H, Webb CR, Brown DF, Curran MD, et al. Methicillin-resistant *Staphylococcus aureus* with a novel *mecA* homologue in human and bovine populations in the UK and Denmark: a descriptive study. *Lancet Infect Dis.* 2011;11:595–603. [http://dx.doi.org/10.1016/S1473-3099\(11\)70126-8](http://dx.doi.org/10.1016/S1473-3099(11)70126-8)
- Shore AC, Deasy EC, Slickers P, Brennan G, O'Connell B, Monecke S, et al. Detection of staphylococcal cassette chromosome *mec* type XI encoding highly divergent *mecA*, *mecI*, *mecR1*, *blaZ* and *ccr* genes in human clinical clonal complex 130 methicillin-resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother.* 2011;55:3765–73. <http://dx.doi.org/10.1128/AAC.00187-11>
- Murakami K, Minamide W, Wada K, Nakamura E, Teraoka H, Watanabe S. Identification of methicillin-resistant strains of staphylococci by polymerase chain reaction. *J Clin Microbiol.* 1991;29:2240–4.
- Friedrich AW, Daniels-Haardt I, Köck R, Verhoeven F, Mellmann A, Harmsen D, et al. EUREGIO MRSA-net Twente/Münsterland—a Dutch-German cross-border network for the prevention and control of infections caused by methicillin-resistant *Staphylococcus aureus*. *Euro Surveill.* 2008;13 [cited 2012 Mar 30]. <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=18965>.
- von Eiff C, Becker K, Machka K, Stamm H, Peters G. Nasal carriage as a source of *Staphylococcus aureus* bacteremia. *N Engl J Med.* 2001;344:11–6. <http://dx.doi.org/10.1056/NEJM200101043440102>
- Becker K, Harmsen D, Mellmann A, Meier C, Schumann P, Peters G, et al. Development and evaluation of a quality-controlled ribosomal sequence database for 16S ribosomal DNA-based identification of *Staphylococcus* species. *J Clin Microbiol.* 2004;42:4988–95. <http://dx.doi.org/10.1128/JCM.42.11.4988-4995.2004>
- Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing: twenty-first informational supplement (M100–S21). Wayne (PA): The Institute; 2011.

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