

Familial Transmission of *emm12* Group A *Streptococcus*

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Incidence and severity of invasive group A *Streptococcus* infections are of increasing concern in France and worldwide. The risk for secondary infection of close contacts is known but rarely described. We report a case of intrafamilial and life-threatening transmission of *emm12* group A *Streptococcus*.

In recent years, incidence and severity of invasive group A *Streptococcus* infections (iGAS) has increased in Europe and worldwide (1). The Centers for Disease Control and Prevention surveillance reports attest to this increase in the United States (2). In northern France, an increase in *emm1* iGAS was reported (3). *Streptococcus pyogenes* can spread from infected persons to close contacts, especially if >24 hours is spent with an infected person (4). However, transmission of life-threatening infections remains a relatively rare event. We report a case of intrafamilial transmission of iGAS.

On August 17, 2016, a 67-year-old woman was admitted to the Centre Hospitalier de Roubaix (Roubaix, France) for knee pain and necrotic zones on her thigh. Her medical history consisted of treated hypertension. At admission, her temperature was 36.3°C, blood pressure 110/80 mm Hg, pulse rate 74 beats/min, blood leukocyte count 8,530 cells/ μ L (89.9% polymorphonuclear), C-reactive protein 281 mg/L, and procalcitonin 32.5 ng/mL. She had acute renal failure (creatinine 35 mg/L) and abnormal clotting test results. We collected a set of blood specimens for culture. She had a recent history of erysipelas and was given non-steroidal antiinflammatory drugs (NSAIDs) the day before her hospital admission. We diagnosed necrotizing fasciitis of the leg. She received intravenous antimicrobial drug therapy with amoxicillin/clavulanic acid, gentamicin, and clindamycin and underwent debridement surgery on the same day.

Her health condition quickly deteriorated; she had disseminated intravascular coagulation and blood pressure of 70/40 mm Hg, despite appropriate hemodynamic care. She experienced toxic shock and multiorgan system failure. A revision surgery was necessary but not possible because of heavy bleeding, hemodynamic instability, metabolic acidosis, acute renal failure, and hyperkalemia. She died on August 18. Cultures of necrotized tissues and blood samples yielded *S. pyogenes*.

On August 21, the index case-patient's husband, who was 66 years of age, was admitted to Centre Hospitalier Régional Universitaire de Lille (Lille, France) with a 2-day history of bursitis of the right elbow. He had been treated during the 2 days by his family's physician with intravenous amoxicillin/clavulanic acid (1 g 3 \times /d), pristinamycin (1 g 3 \times /d), and NSAIDs. At hospital admission, his temperature was 36.5°C, blood pressure 95/55 mm Hg, and pulse rate 95 beats/min, blood leukocyte count 22,300 cells/ μ L (89% polymorphonuclear), and C-reactive protein 511 mg/L. Mobilization of the elbow was possible but limited by major edema to the axilla; severe blistering of the elbow was visible. We drained his forearm surgically to treat extensive cellulitis and diagnosed superinfected bursitis. We stopped pristinamycin and NSAIDs, increased the intravenous amoxicillin/clavulanic acid dose (to 2 g 3 \times /d), added linezolid for antitoxinic action (600 mg 2 \times in 24 h), and provided 14 hyperbaric oxygen therapy sessions. On August 23, the wound condition improved and C-reactive protein decreased (211 mg/L), but a wide erythema was still visible. Clinical outcome was favorable, and we discharged the patient on September 5. Culture of the deep tissue samples yielded *S. pyogenes*. The strain was susceptible to amoxicillin, so we continued it (2 g 3 \times /d) until September 11.

Strains isolated from both patients were the same strain of *S. pyogenes emm12* (online Technical Appendix Tables 1, 2, <https://wwwnc.cdc.gov/EID/article/23/10/17-0343-Techapp1.pdf>). The couple were caregivers for their granddaughter, and they met their 2 adult children and son-in-law several days each week, so we evaluated these close contacts. The son and daughter had had a sore throat 9 days before onset of illness in the mother and were treated empirically by their general practitioner with amoxicillin/clavulanic acid (1 g 2 \times /d for 6 d). We prescribed cefuroxime axetil (250 mg 2 \times /d for 10 d). Buccal swabs cultured remained negative.

The risk for iGAS infection in close contacts of patients was reviewed in 2016 (5): the evidence was based on 13 instances of transmission published in 4 separate studies covering 5,858 household contacts. The annual risk among close contacts was 151 times greater than the risk for sporadic disease and comparable to that estimated for meningococcal disease. However, the benefit from

antimicrobial drug prophylaxis is not known (5), and guidelines vary among countries. In the United Kingdom, prophylaxis is recommended for exposed mothers or babies during the neonatal period, for symptomatic close contacts, or for the entire household if there is >1 case (6). In Canada, prophylaxis is recommended for persons who had close contact with a person with a confirmed severe case during a specified period (7); in France and the United States, prophylaxis is recommended for close contacts with risk factors for invasive infections (8,9). In the cases we report here, the second case-patient did not receive prophylaxis because of the short period between the 2 cases.

Both case-patients received NSAIDs during the onset of the disease. The role of these drugs in streptococcal infection outcome is frequently discussed; they seem to cause an increase of severe infection, most probably in children (10).

These cases highlight that different life-threatening transmissible types of *S. pyogenes* are circulating in the same area and that transmission can occur rapidly. Clinician and family education about prophylaxis and symptoms requiring medical care is needed.

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References

1. Meehan M, Murchan S, Bergin S, O'Flanagan D, Cunney R. Increased incidence of invasive group A streptococcal disease in Ireland, 2012 to 2013. *Euro Surveill*. 2013;18:20556. <http://dx.doi.org/10.2807/1560-7917.ES2013.18.33.20556>
2. Centers for Disease Control and Prevention. Active bacterial core surveillance. *Surveillance Reports* [cited 2017 May 10th]. <https://www.cdc.gov/abcs/reports-findings/surv-reports.html>
3. Agence nationale de santé publique. Increase in invasive emm1 group A streptococcal infections in Nord and Pas de Calais departments in 2016 [in French] [cited 2016 Dec 26]. http://www.infectio-lille.com/Fichiers_infectio-lille/Recrudescence-SGA-emm1-NPdc.docx.
4. Weiss K, Laverdière M, Lovgren M, Delorme J, Poirier L, Béliveau C. Group A *Streptococcus* carriage among close contacts of patients with invasive infections. *Am J Epidemiol*. 1999;149:863–8. <http://dx.doi.org/10.1093/oxfordjournals.aje.a009902>
5. Carr JP, Curtis N, Smeesters PR, Steer A. QUESTION 1: Are household contacts of patients with invasive group A streptococcal disease at higher risk of secondary infection? *Arch Dis Child*. 2016; 101:198–201. <http://dx.doi.org/10.1136/archdischild-2015-309788>
6. Health Protection Agency, Group A Streptococcus Working Group. Interim UK guidelines for management of close community contacts of invasive group A streptococcal disease. *Commun Dis Public Health*. 2004;7:354–61.
7. Public Health Agency of Canada. Guidelines for the prevention and control of invasive group A streptococcal disease. October 2006 [cited 2017 April 4th]. <https://portal.mountsinai.ca/Microbiology/protocols/pdf/GAS%20guidelines%202006.pdf>
8. Direction générale de la Santé. Notification from the French High Council for Public Hygiene (Communicable Diseases section) concerning conduct to be taken in cases of one or more invasive group A streptococcal disease of community origin. Session of November 18th, 2005 [in French] [cited 2016 Dec 26]. http://www.hcsp.fr/docspdf/cshpf/a_mt_181105_streptococcus.pdf
9. Prevention of Invasive Group A Streptococcal Infections Workshop Participants. Prevention of invasive group A streptococcal disease among household contacts of case patients and among postpartum and postsurgical patients: recommendations from the Centers for Disease Control and Prevention. *Clin Infect Dis*. 2002;35:950–9. Erratum in: *Clin Infect Dis*. 2003;36. <http://dx.doi.org/10.1086/342692>
10. Bryant AE, Bayer CR, Aldape MJ, Stevens DL. The roles of injury and nonsteroidal anti-inflammatory drugs in the development and outcomes of severe group A streptococcal soft tissue infections. *Curr Opin Infect Dis*. 2015;28:231–9. <http://dx.doi.org/10.1097/QCO.0000000000000160>

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Six-Month Response to Delamanid Treatment in MDR TB Patients

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Technical Appendix

Table 1. Antimicrobial susceptibility test results of *emm12* Group A *Streptococcus pyogenes* spread by familial transmission*†

Antimicrobial drug	Antimicrobial susceptibility testing (disk diffusion method)‡	
	Case-patient 1	Case-patient 2
Penicillin G	S	S
Ampicillin	S	S
Amoxicillin	S	S
Cefotaxime	S	S
Gentamicin	I	I
Tetracycline	S	S
Levofloxacin	S	S
Erythromycin	S	S
Lincomycin	S	S
Pristinamycin	S	S
Linezolid	S	S
Teicoplanin	S	S
Vancomycin	S	S
Nitrofurantoin	S	S
Rifampin	S	S

*S, susceptible; I, intermediate categorization.

†The 2 strains of *Streptococcus pyogenes* were identified by the hospital laboratories and by the Centre National de Référence des Streptocoques using mass spectrometry.

‡Antimicrobial susceptibility testing and genotyping of the 2 strains were performed simultaneously by the Centre National de Référence des Streptocoques.

Table 2. Strain analysis of *emm12* Group A *Streptococcus pyogenes* spread by familial transmission

Specimen*	Toxins and superantigens genotyping	
	Case-patient 1 <i>emm12</i>	Case-patient 2 <i>emm12</i>
<i>SpeA</i>	Negative	Negative
<i>SpeB</i>	Positive	Positive
<i>SpeC</i>	Positive	Positive
<i>SsA</i>	Negative	Negative
<i>Sic</i>	Negative	Negative
<i>Smez</i>	Positive	Positive

*Protein M genotyping (sequencing of the N terminus variable region of the *emm* gene).