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Intra-familial transmission of life-threatening group A streptococcal infection

R. A. RECCO*, M. M. ZAMAN[1], H. CORTES[2], J. COLUCCI[2], G. POOMKUDY[2] AND E. L. KAPLAN[3]

[1] *Division of Infectious Diseases, Department of Medicine, Coney Island Hospital and State Univeristy of New York Health Science Center at Brooklyn, Brooklyn, New York, USA*
[2] *Department of Medicine, Methodist Hospital, Brooklyn, New York, USA*
[3] *World Health Organization Collaborating Center for Reference and Research on Streptococci, Department of Pediatrics, University of Minnesota Medical School, Minneapolis, MN, USA*

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SUMMARY

Invasive group A streptococcal (GAS) infections have been of increasing concern worldwide during the past 15 years. Spread of group A streptococci to contacts with resulting invasive infection has been reported in families, in residential nursing homes, and even from patients to health care workers. We report an instance of temporally related life-threatening group A streptococcal infection in a husband and 2 weeks later in his wife. This example further emphasizes the need for careful observation among family members and other close contacts of patients with invasive group A streptococcal infection. Although at present there are no universal recommendations for monitoring or for antibiotic prophylaxis of close contacts of persons with invasive GAS infection, when added to existing literature, this report suggests additional consideration is required.

INTRODUCTION

During the past 2 decades there has been an apparent increase of invasive Group A streptococcal (GAS) infections in many parts of the world [1, 2]. As a part of this, person-to-person spread of invasive GAS infection has been reported. Reports of family clusters, nursing home outbreaks and even spread of infection from a patient to a health care worker have been described [3–7]. However, secondary transmission of life-threatening invasive GAS infection remains a relatively rare event, even though an increased risk has been described in families where there has been invasive disease [5]. We wish to report the occurrence of life-threatening GAS infection in a husband and then 2 weeks later in his wife. The apparent transmission of the infection should stimulate additional thought about management of close contacts of patients with invasive group A infection.

* Author for correspondence: Department of Medicine, Coney Island Hospital, 2601 Ocean Parkway, Brooklyn, NY 11235, USA.

CASE REPORTS

Case 1

A 77-year-old Caucasian male was admitted to the hospital after complaining of pain in his left knee, chills and 'flu-like' symptoms for 4 days prior to admission. The knee pain had progressed until the patient was unable to bend his knee. He had appeared weak and confused, causing his family to call for assistance from emergency services. When they arrived, the patient was pale, diaphoretic and cyanotic but alert and orientated. Blood pressure was 60 mm Hg by palpation, the pulse was 100 per min

and respirations 18 per min. He was stabilized and then transported to a nearby hospital.

His past medical history included hypertension, hyper-cholesterolemia and degenerative joint disease, for which he had been taking metoprolol, atorvastatin and celecoxib. He had been working as a livery driver and lived in a two family house with his wife; his adult children, and two grandchildren lived in the other part of the house.

Physical examination at the hospital found him to be diaphoretic and hypotensive (80/50). The temperature was 98·6 °F and respirations were 20/min. His left knee was swollen, warm and tender. There was no rash.

Admitting laboratory studies included a white blood cell count of 25200 per ml with 41% bands, a haematocrit of 46·9%, and the platelet count was 220000/ml. The creatinine was 2·5 mg/dl. The total bilirubin was 2·2 mg/dl, SGOT 99 U/l, and SGPT 56 U/l. Creatinine kinase was 1592 U/l with an index of 0·4.

Fluid was aspirated from his knee joint. The joint fluid was cloudy with an red cell count of 270000 per ml, a white cell count of 228000 per ml, a protein 3·9 g/dl and glucose of 241 mg/dl. Gram-positive cocci in chains were seen on Gram stain of the joint fluid. Blood cultures were done. A chest X-ray was negative for infiltrates. A spinal fluid examination was negative.

Supportive therapy for hypotension and diabetic ketoacidosis was instituted. He was initially treated with gentamicin, ceftriaxone and clindamycin, but changed to ampicillin, clindamycin and gamma globulin when Gram-positive cocci grew from both blood and joint fluid; both organisms were identified as group A beta-hemolytic streptococci. Despite this treatment, his condition did not significantly improve. He subsequently developed adult respiratory distress syndrome, and died 14 days after admission. Although prophylactic antibiotic administration to family members and close contacts was considered and discussed, none was recommended or given after consulting available guidelines [8].

Case 2

Thirteen days after her husband's admission, his 74-year-old spouse developed diarrhoea, nausea, abdominal pain, fever and a yellow vaginal discharge. She had visited her husband daily during his illness. She was seen by her own physician in his office and found to be hypotensive (blood pressure 60/40 mm Hg), febrile (temperature 102·2 °F) and tachycardic (pulse 120 per min). The woman was transported directly to the emergency room of another hospital.

Her past medical history included hypercholesterolaemia, hypothyroidism (partial thyroidectomy), and surgery for a benign ovarian tumor and uterine polyps some 38 years ago. Current medications were thyroxine, alendronate, atorvastatin, and calcium with vitamin D.

Upon arrival at that emergency room, the blood pressure was 95/59 mm Hg, the temperature was 101·3 °F, the pulse 117 per min and respirations were 22 per min. She was admitted to the intensive care unit.

Admission laboratory tests included a white blood cell count of 9600 per ml with 71·3% neutrophils; the haematocrit was 39·6%, and platelets were 146000 per ml. Her creatinine was 1·4 mg/dl. Liver function was within normal limits. Chest X-ray showed only increased bronchovascular markings; CT scans of abdomen and pelvis were negative.

Blood cultures drawn on admission 2 days later yielded group A beta-hemolytic streptococcus. Vaginal cultures which had been obtained on admission to the hospital also grew group A beta-hemolytic streptococci.

Piperacillin-tazobactam and doxycycline were initially started, but later switched to piperacillin-tazobactam and clindamycin when the organism was presumptively identified. After 2 days, the patient improved. Antibiotic treatment was continued for 2 weeks and the patient was discharged without residual problems.

ANALYSIS OF GROUP A STREPTOCOCCAL ISOLATES

Three group A streptococcal isolates were available for characterization; two from the husband (blood and joint fluid) and one from the spouse (blood). The three group A streptococcal isolates were characterized at the World Health Organization Collaborating Center for Reference and Research at the University of Minnesota by serological grouping as well as by T agglutination pattern, M serotyping and/or opacity factor serotyping by previously published methods [9]. All three strains were opacity

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Table 1. *Group A streptococcal characterization*

				Serotyping†		
Patient	Site	Group	SOR*	T	M	OF
1	Blood	A	P	28/11	ND	87 (PT2841)
	Joint fluid	A	P	28	ND	87 (PT2841)
2	Blood	A	P	NT	ND	87 (PT2841)

* SOR, production of streptococcal serum opacity factor: 'P' refers to production.
† T, T agglutination pattern; M, serological M-type; OF, serological type of the serum opacity factor, if produced (OF-type correlates with M-type); ND, not done; PT, provisional type.

factor producers and were characterized as type 87 (Table 1).

After the wife became ill (13 days following the onset of her husband's illness) family members in close association with either or both patients were cultured (throat); all cultures were negative for the presence of group A streptococci.

DISCUSSION

The occurrence of invasive group A streptococcal infection with the same organism (in this case, opacity factor type 87 group A streptococci) in this husband and wife was notable for several reasons. The likelihood of transmission having occurred between the husband and wife was high, especially since the throat cultures of all family members living in this two family structure and all other family contacts (including the grandchildren) did not yield group A streptococci from their upper respiratory tracts. The occurrence of an aggressive GAS infection with the same pathogen in two family members in close temporal relation suggests transmission of a virulent organism from one spouse to the other; although an unidentified common source of exposure cannot be entirely ruled out.

Secondly, although it was considered and discussed, available 1995 recommendations from the Centers for Disease Control did not specifically recommend surveillance among close family contacts and members [8]. Whether or not culturing of the spouse and other members of the family would have yielded the organism at the time the index patient became ill is speculative, but 2 weeks later the other family members had negative cultures without having received antibiotics.

Group A streptococcus may commonly be introduced into households by an infected child. Other family members generally become infected weeks to months later [10, 11]. The time interval between the index patient and the subsequent patient of 2 weeks is consistent with the temporal sequence reported in the literature [4, 10]. The husband and wife lived close to their children and grandchildren, but cultures of these family members were negative 2 weeks later. The index case worked as a livery driver and frequently transported patients from home to hospital, perhaps providing another possible source for the GAS, but there was no evidence to support this possibility.

A very important issue raised by this instance of apparent transmission within a family relates to whether there is a need for surveillance or therapy of close family contacts. Clusters of invasive GAS have been reported in families, nursing homes and health care workers, albeit not often [3–7]. Although the elderly and patients with underlying immunosuppressive disease are at increased risk for invasive GAS [5], these infections have been seen in all age groups and in many patients who do not have predisposing underlying conditions. Invasive infections progress very rapidly, and despite appropriate antibiotic therapy, the mortality with the most severe manifestations, TSS and necrotizing fasciitis, remains high (40–80%) [5, 10].

Some insight for management of individual family members is provided by a recent study of household contacts of patients with invasive GAS infection in Ontario, Canada [5]. In that report the risk of subsequent invasive infections among family contacts was increased almost 200-fold. The risk was especially high in the elderly (patients > 75 years) and also in those with underlying medical conditions such as human immunodeficiency virus infection, cancer, diabetes, alcohol abuse and varicella.

There are no universally agreed-to recommendations regarding surveillance and/or chemoprophylaxis

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for household or other close contacts of persons with invasive group A streptococcal infection. Even if one were tempted to take a more aggressive approach, it is not clear whether only symptomatic culture positive contacts should be given antibiotics [4], or whether all close contacts should be investigated. Admittedly, at the present time there are no comprehensive data about the effectiveness of antimicrobial chemoprophylaxis for the prevention of severe invasive GAS infection [8].

A secondary case or a subsequently infected patient with group A streptococci can have devastating consequences from this disease with as high as a 70% mortality. Hence, until there are more definitive data to the contrary, based upon isolated published instances in the literature, including the Canadian report with an increased risk of almost 200-fold, we believe it is appropriate to identify household or other close contacts (including at least upper respiratory tract culturing) and to offer them prophylaxis with one of several theoretically effective antibiotics. Consideration should be given to those antibiotic regimens that effectively eradicate group A streptococci from the respiratory tract, including penicillin, first generation cephalosporins (12), penicillin along with rifampin (13), or clindamycin (14).

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REFERENCES

1. Stevens DL, Tanner MH, Winship J, et al. Severe Group A streptococcal infections associated with a toxic shock-like syndrome and scarlet fever toxin A. N Engl J Med 1989; **321**: 1–7.
2. Gaworzewska ET, Colman G. Changes in the pattern of infection caused by *Streptococcus pyogenes*. Epidemiol Infect 1988; **100**: 257–69.
3. DiPersio JR, File TM Jr, Stevens DL, et al. Spread of serious disease-producing M3 clones of group A streptococcus among family members and health care workers. Clin Infect Dis 1996; **22**: 490–5.
4. Schwartz B, Elliot JA, Butler JC, et al. Clusters of invasive group A streptococcal infections in family, hospital, and nursing home settings. Clin Infec Dis 1992; **15**: 277–84.
5. Davies HD, McGeer A, Schwartz B, et al. Invasive group A streptococcal infections in Ontario, Canada. N Engl J Med 1996; **335**: 547–54.
6. Valenzuela TD, Hoonton TM, Kaplan EL, et al. Transmission of 'Toxic Strep' syndrome from an infected child to a firefighter during CPR. Ann Emerg Med 1991; **20**: 90–2.
7. Gamba MA, Martinelli M, Schaad HJ, et al. Familial transmission of a serious disease-producing group A streptococcus clone: Case reports and review. Clin Infect Dis 1997; **24**: 1118–21.
8. The Working Group on Prevention of Invasive Group A Streptococcal Infections. Prevention of invasive Group A streptococcal disease among household contacts of case-patients. Is prophylaxis warranted? JAMA 1998; **279**: 1206–10.
9. Johnson DR, Kaplan E (World Health Organization Collaborating Center for Reference and Research on Streptococci; Minneapolis, MN, USA) and Sramek J, Motlova J, Bicova R, Havlickova H, Havilcek J, Kritz P (World Health Organization Collaborating Center for Reference and Research on Streptococci; Prague, Czech Republic). Laboratory diagnosis of group A streptococcal infections: A laboratory manual. Geneva, Switzerland: WHO, 1996.
10. Stevens DL. Invasive group A streptococcus infections. Clin Infect Dis 1992; **14**: 2–13.
11. James WES, Badger GF, Dingle JH. A study of illness in a group of Cleveland families. N Engl J Med 1960; **262**: 687–94.
12. Dajani AS, Kessler SL, Mendelson R, et al. Cefpodoxime proxetil vs. penicillin V in pediatric streptococcal pharyngitis/tonsillitis. Pediatr Infect Dis J 1993; **12**: 275–9.
13. Chaudhry S, Bilinsky SA, Hennessy JL, et al. Penicillin v and rifampin for the treatment of group A streptococcal pharyngitis: a randomized trial of 10 days penicillin vs. 10 days penicillin with rifampin during the final 4 days of therapy. J Pediatr 1985; **106**: 481–6.
14. Tanz RR, Poncher JR, Corydon KE, et al. Clindamycin treatment of chronic pharyngeal carriage of group a streptococci. J Pediatr 1991; **119**: 123–8.