Unusual cluster of mild invasive serogroup C meningococcal infection in a university college

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Abstract

The objective of this study was to describe the epidemiology and public health response to an apparent cluster of Neisseria meningitidis serogroup C infection in university students in a residential college. A conventional epidemiological approach was taken, supported by routine and novel diagnostic techniques. Over the two days of 21-22 August 1997, three cases of suspected meningococcal infection were notified from a residential college complex at a university campus in the Sydney metropolitan area. Neisseria meningitidis was grown from throat swabs of all three cases, and was isolated from the blood of one case only. All three isolates were typed as C:2a:P1.5,2. Seroconversion was demonstrated by a novel method in the three cases. Rifampicin was given to all identified contacts. Forty-seven days after the index case, a 19 year old female living in the same complex was diagnosed with bacterial meningitis, and identified contacts given rifampicin. When this isolate was found to be group C, it was decided to vaccinate residents of the college complex. Genotyping and serotyping (C:2a:P1.5) later revealed the fourth isolate to be distinct from isolates from Cases 1-3. In conclusion the authors note that Australia’s increasing capacity to type meningococcal strains is essential to understanding the epidemiology of this disease. Furthermore, typing information is of critical importance when decisions are made regarding mass vaccination. As early antibiotic treatment may inhibit isolation of the organism,
development of novel approaches to diagnosis and typing should be supported. *Commun Dis Intell* 1999;23 261-264.

**Introduction**

The importance of *Neisseria meningitidis* (*N. meningitidis*) serogroup C (NMSC) as a cause of sporadic cases and outbreaks of invasive meningococcal infection in industrialised countries has risen during the past decade. In particular strains of phenotype C:2a:P1.5 and C:2a:P1.5,2 have increasingly caused outbreaks with high case-fatality rates in Canada, the United States of America and Europe. Clusters caused by similar if not identical strains have been identified in Australia since 1996, including a cluster of 11 cases of confirmed invasive C:2a:P1.5 infection linked to a western Sydney nightclub. Over a three-day period in August 1997 three cases of suspected meningococcal infection were notified among students living in a residential college complex at a university in the Sydney metropolitan area. The epidemiology of and public health response to this cluster of cases are described, and both the unusual clinical features and diagnostic techniques used to support the identification of the cluster are highlighted.

**Methods**

**Epidemiological methods**

Cases were those with consistent clinical features in whom NMSC strains were isolated from normally sterile sites or a throat swab. Contact tracing and chemoprophylaxis was carried out in accordance with standard New South Wales (NSW) public health practice and National Health and Medical Research Council (NHMRC) guidelines. Conventional bacteriology with serogroup determination was undertaken at South Eastern Area Laboratory Service, Randwick. In some instances, throat swabs were taken from contacts and these were also subjected to culture for *N. meningitidis*; resulting isolates were typed as described below.

**Phenotyping**

Serotyping and serosubtyping were performed in the Department of Microbiology and Infectious Diseases, South Western Area Pathology Service, Liverpool, NSW, based on the detection of outer membrane protein antigens using a standard set of monoclonal antibodies obtained from Dr J Poolman, National Institute for Public Health, The Netherlands.

**Genotyping**

Strain differences based on genotypic variation were determined by pulsed field gel electrophoresis (PFGE). Four enzymes (Spe1, BglII, Nhe1 and Not1) were used to digest gel plugs containing meningococcal DNA and the digested plugs electrophoresed in a contour-clamped homogeneous electric field apparatus (CHEF DR III, Bio-Rad). Gels were stained with ethidium bromide and photographed under ultraviolet light. Strain relatedness was determined by the criteria of Tenover. Strains examined were the cultures from the students and strains of similar phenotypes from cases which had occurred in western Sydney.

**Serological assays**

An enzyme-linked immunosorbent assay (ELISA) was developed to quantitate anti-meningococcal IgG and IgM serum antibodies. The antigens were purified outer membrane proteins from *Neisseria meningitidis* serogroup B, serotypes/serosubtypes 4:P1.15 and 15:P1.7, 16, and serogroup C, serotype/serosubtype 2a:P1.2 (strains supplied by Manchester Public Health Laboratory Service, UK). The antigens were purified using the method described by Gutormsen and coworkers. Class specific antibodies were detected using phosphatase labelled goat anti-human IgG or IgM as conjugate. The optimal dilutions of serum, antigen and conjugate were determined using positive and negative sera identified by checkerboard titrations. The cut-off value for each immunoglobulin class was established by testing 100 sera collected from blood donors. The cut off was taken as the mean plus three standard deviations of the optical density readings obtained from these sera. When possible, acute and convalescent sera were collected from cases and assayed.

**Results**

**Case 1**

On 21 August a notification was received of growth of NMSC on a throat swab taken on 15 August from an 18 year old male hospitalised with a provisional diagnosis of glomerulonephritis. He had given a history of fever, sore throat, arthralgia, and when seen had a purpuric rash and microscopic haematuria. Blood cultures, taken after initiation of antibiotics, were negative. He was treated with IV penicillin and discharged, well, after four days. He was a resident of one of the colleges within a college complex.

**Case 2**

On the same afternoon a presumptive case was notified by the University Health Service in a 19 year old female resident of the same college as Case 1. She had presented that day with a 1-day history of fever, sore throat, headache, myalgia, arthralgia (especially in ankles, wrists and shoulders); a mild purpuric rash was visible on the feet and arms. Blood cultures and a throat swab both later grew NMSC. She remained in hospital for 3 days.

**Case 3**

On 22 August, a further presumptive case was notified by the University Health Service in a 20 year old female student from a different college in the same college complex. She had complained of sore throat, fever, arthralgia and a rash with onset on 18 August. Blood cultures were sterile but a throat swab later grew NMSC. She was hospitalised for 5 days.

**Public health response to the three cases**

Cases were interviewed to determine any links between them and to identify at-risk contacts. It was revealed that Case 2 had cared for Case 1 when he first became ill. No clear link was found between these cases and Case 3, although the affected colleges shared a common dining hall. Rifampicin prophylaxis was provided to contacts by university, emergency department and public health staff.
All college residents and relevant university staff were advised by letter and e-mail of the outbreak, mechanisms of transmission of infection, and restrictions placed on congregating within the college complex. In particular, due to the possible link of the shared dining hall, residents were given take-away meals for two weeks.

The annual college ball planned for 23 August, which would have attracted alumni and friends from around NSW, was cancelled on the advice of the Chief Health Officer. On 22 August, NSW Health issued a media release to alert those potentially at risk. Primary care physicians in the vicinity of the university were informed of the possible cluster and asked to contact the Public Health Unit regarding suspected cases.

On 26 August, a teleconference of experts was convened to discuss further public health action, including the possibility of vaccination of college residents. At the time there were still only three cases in the cluster, of which one was a secondary case, and only one case had been confirmed by blood culture. As these three cases did not satisfy the criteria for an outbreak, it was decided not to initiate a mass vaccination program.

**Case 4**

On 7 October, 47 days after the index case was notified, a 19 year old female living in the same complex was diagnosed with meningitis, and identified contacts given rifampicin. When this isolate was found to be serogroup C, a decision was made to vaccinate residents of the college complex. Prior to this, a highly publicised vaccination program had been undertaken in a boarding school in south western Sydney in response to a cluster of NMSC. In the period 13-21 October, 440 (91%) college residents of the complex were vaccinated by Public Health Unit and University Health Service staff.

**Typing of isolates**

Isolates from Cases 1, 2 and 3 were all serotyped as C:2a:P1.5,2, whilst Case 4 was typed as C:2a:P1.5. Isolates from Cases 1-3 were shown by PFGE to be indistinguishable from each other and distinct from the Case 4 isolate. However, the latter isolate was indistinguishable, by serotyping and PFGE, from strains obtained from recent western Sydney cases.

**Meningococcal serology**

Cases 1-3 demonstrated IgG seroconversion and IgM positivity, which was not found with contacts (Table 1).

**Discussion**

This cluster of invasive serogroup C meningococcal infection which involved three young adults residing in a university college was suspected clinically and epidemiologically, and confirmed by phenotyping and genotyping of isolates. The cluster had a number of unusual features: all three illnesses were relatively mild, necessitating only brief hospitalisations, and were characterised by fever, sore throat, joint pain and transient purpuric rash. Bacteraemia could only be established in one case, but strains of indistinguishable phenotype and genotype were isolated from the throats of all three cases. The diagnosis of invasive disease in all three cases was suggested by the constellation of systemic symptoms and by the use of a novel serological assay which demonstrated the appearance of meningococcus-specific IgM as well as IgG seroconversion.

During the last decade, an increase has been observed in the prevalence of C:2a strains (attributed to the ET37 complex) in Canada, the United States and Europe. Outbreaks have particularly affected adolescents and young adults, and have been characterised by a large proportion of cases of fulminant meningococcaemia and high case-fatality rates. Serogroup C outbreaks have been recorded in Australia in recent years, including five clusters in north Queensland during 1990-1994, and an outbreak of severe disease caused by a C:2a:P1.5 strain in western Sydney in 1996. The strain causing the UNSW cluster was associated with much milder disease and seems to have appeared only transiently in Sydney, as no other C:2a:P1.5,2 strains were detected in NSW during 1997.

The first three cases in the cluster did not conform to the definition of an outbreak for the purposes of a mass vaccination program. Following identification of the fourth case a vaccination program was introduced, partly as a response to public concerns related to cases at the university and in other Sydney schools and colleges at the same time. What was thought to be a fourth case in the cluster was later shown by phenotyping and genotyping to be distinct. This illustrates the difficulty that may occur in balancing public concerns with the recommendations outlined in the NHMRC guidelines and the importance of rapid serotyping/subtyping of isolates during an apparent cluster. A labour intensive, expensive and disruptive mass vaccination campaign would have been avoided if the decision to vaccinate had awaited the serotyping results. This highlights the need for continuing support of facilities for the rapid serotyping/subtyping of isolates during the investigation of an apparent cluster. A decision regarding vaccination should not be made without this typing information.

In addition, increased support is required for the use of novel approaches to the diagnosis of invasive meningococcal disease, including the polymerase chain reaction technique. These approaches will be of increasing importance as more cases of suspected disease are treated with parenteral antibiotics prior to hospitalisation. It is recommended that a throat swab collected at the time of presentation be sent for meningococcal culture in all suspected cases of invasive disease and that any meningococcal isolates obtained be stored for typing. Further work is underway investigating the place of serological testing in the diagnosis of invasive meningococcal infection.

**Acknowledgements**

We wish to thank the Chief Executive, residents and staff of the College complex at the university, for their prompt response to our recommendations, and staff of St Vincent’s Microbiology Department and Prince of Wales Hospital for reporting suspected cases.

**References**


Table 1. Results of throat swab culture and serology for Cases 1-3 and selected contacts

<table>
<thead>
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<th>Case or contact</th>
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<th>Acute serology</th>
<th>Convalescent serology</th>
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<td>NMSC</td>
<td>M (+) G (-)</td>
<td>M (+) G (+)</td>
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<tr>
<td>Case 2</td>
<td>2</td>
<td>NMSC</td>
<td>M (-) G (-)</td>
<td>M (+) G (+)</td>
</tr>
<tr>
<td>Case 3</td>
<td>3</td>
<td>NMSC</td>
<td>M (-) G (-)</td>
<td>M (+) G (+)</td>
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<tr>
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<td>-</td>
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<td>M (-) G (-)</td>
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<td>M (-) G (+)</td>
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<tr>
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NMSC = Neisseria meningitidis serogroup C
NM = Neisseria meningitidis
M = IgM
G = IgG