CASE REPORT

Fulminant invasive meningococcal disease due to serogroup Y infection: a highly unusual case reflecting worrying increases in carriage and incidence

Akash Maniam,¹ Sriram Ravichandran²

¹ITU and Anaesthetics, Barnet Hospital, London, UK
²Haematology, Barnet Hospital, London, UK

Correspondence to

Dr Akash Maniam, ITU and Anaesthetics, Barnet Hospital, London EN5 3DJ, UK; akash.maniam@nhs.net

Accepted 16 March 2017

SUMMARY

A young man presented to accident and emergency with a short history of diarrhoea and vomiting, with no medical history. He deteriorated rapidly during triage and never regained consciousness. He was pronounced dead after hours of attempted resuscitation. He was found to have organisms suggestive of diplococci on his blood film and subsequently had MenY found via PCR testing. This case illustrates a highly unusual presentation of invasive meningococcal disease caused by MenY which is quietly and dangerously increasing in incidence in the UK, particularly in young healthy patients. All clinicians are reminded to be vigilant in order to diagnose and treat this often fatal disease as well as to promote uptake of the quadrivalent MenACWY vaccine.

BACKGROUND

In the past two decades, the carriage frequency of serogroup Y *Neisseria meningitidis* has increased in Europe, and this has resulted in increased rates of invasive meningococcal disease (IMD), especially in the young. It commonly presents atypically and unless there is a high index of suspicion, it is often missed, unfortunately with fatal outcomes. This case illustrates a rare but clinically important cause of sepsis with an often fulminant course and high mortality. Additionally, it serves to remind us of the importance of being vigilant and acting decisively when faced with such patients, treating promptly and sending PCR samples urgently.

CASE PRESENTATION

A previously fit and well 22-year-old man self-presented to accident and emergency (A+E), with a 3-day history of diarrhoea and vomiting and a 1-day history of headache and bilateral leg pain. He was entirely afebrile during this time and had no evidence of photophobia, rash or nuchal rigidity. Furthermore, he had no contact with anyone with similar symptoms, nor did he have any recent travel history.

While in triage, he had one further episode of vomiting, then collapsed to the floor, whereupon he began actively convulsing. He was entirely unresponsive with an unrecordable blood pressure and absence of pulse. Advanced life support was initiated immediately, and his initial trace showed asystole. He was rapidly intubated, and cardiopulmonary resuscitation (CPR) was maintained throughout.

During resuscitation, he began to exhibit spontaneous profuse bleeding from his cannula site and the endotracheal tube. He was given 2 g of intravenous ceftriaxone immediately and was administered packed red blood cells and fresh frozen plasma.

He then had a brief return of spontaneous circulation, followed by pulseless electrical activity. After 2 hours of CPR, he was declared dead.

INVESTIGATIONS

His initial bloods, taken during resuscitation, showed a haemoglobin of 15.9 g/dL, a white cell count of $7.8 \times 10^9/L$ and a platelet count of $27 \times 10^9/L$. Additionally, his coagulation studies showed a grossly elevated prothrombin time greater than 165 s with an international normalised ratio of more than 8.0. His biochemical analysis revealed a urea of 8 mmol/L, creatinine of 274 $\mu\text{mol/L}$, a C-reactive protein of 104 mg/L.

His liver function tests and bone profile showed a mild hyperbilirubinaemia (42 $\mu\text{mol/L}$) and severe hyperphosphataemia (4.07 mmol/L). These results were entirely in keeping with a dehydrated patient, with disseminated intravascular coagulopathy of an unknown, likely septic, origin.

This patient then had a blood film made and examined. The blood film showed organisms that were suggestive of diplococci within and outside of the neutrophils (figures 1 and 2). Meningococcal PCR testing confirmed the presence of serotype Y *N meningitidis*.

OUTCOME AND FOLLOW-UP

Not applicable—patient is deceased.

DISCUSSION

N meningitidis commensally inhabits the nasopharyngeal mucosa of 16.7% of British teenagers and young adults.¹ Its carriage frequency is increased independently by frequent attendance at pubs/clubs, intimate kissing and cigarette smoking. Given the prevalence of the above risk factors among adolescents and young adults, it follows logically that this dangerous pathogen is being carried with great frequency in these groups.

N meningitidis itself is a complex species. It is a Gram-negative B-proteobacterium that boasts no fewer than 13 serogroups,² which have different immunogenicity and pathogenicity profiles. Clinically, six of these are significant in causing IMD, viz.

To cite: Maniam A, Ravichandran S. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-219510

Figure 1 This figure shows diplococci in the peripheral blood smear.

serogroups A, B, C, X, W135 and Y. The advent of the conjugate MenC vaccine has seen its incidence decline markedly, from causing approximately 30% of IMD to <2%. The relative and absolute incidences of W135 and Y have increased profoundly, but this is inadequately explained by the successful vaccination programme and, crucially, they do not correspond with MenC vaccine uptake, thereby rendering the idea of serogroup replacement highly improbable.

Serogroup Y disease classically was described in Racoosin's work of 1998,³ in which he showed that Y disease is significantly associated with older, Afro-Caribbean patients with immunosuppression, underlying diseases or medications, particularly diabetes, systemic lupus erythematosus and chronic lung disease. Importantly, he noted that IMD due to serogroup Y was commonly associated with pneumonia, especially in the elderly. This was corroborated by Winstead's review 2 years later,⁴ in which he found that the median age of those affected with meningococcal pneumonia was 57.5 with a bimodal peak but sharing similar comorbidities. Of the 52 patients serogrouped in his seminal work, 44% of those cases were due to Y disease.

This contrasts widely with the modern trend in Europe. In France, the average age of patients with MenY changed from 76.1 in 2005 to 20.8 in 2010, which coincided with the overall rise in MenY cases.⁵ Of particular concern, a study in 2009 by the European Monitoring Group on Meningococci showed that

Figure 2 This figure shows diplococci being phagocytosed by a neutrophil on the same smear.

in England and Wales, only 13% of children under the age of 5 had protective antibody titres against MenY.⁶ This shows that it is highly unlikely that there is widespread environmental exposure to it, and this therefore limits greatly the opportunity to produce natural immunity.

Furthermore, although teenagers, who represent a primary carriage subgroup, display a peak in protective titres to most serogroups of *N meningitidis*, this did not apply to MenW or MenY. Consequently, this leads to a scenario in which those at greatest risk have no greater means of defending themselves against IMD from MenY. Naturally, the risk is further enhanced in those with congenital or acquired immunodeficiency states, such as in properdin, factor H, factor D or terminal complement pathway deficiencies as well as in asplenic and HIV-positive patients.

Moreover, serogroups W and Y are associated with atypical manifestations, such as septic arthritis, pneumonia, epiglottitis and endocarditis. Recently, a study by Campbell *et al* in the UK showed that MenW IMD caused rapidly fatal disease, requiring aggressive resuscitation shortly after presentation, and tended to present in adolescents with short histories of diarrhoea and vomiting, leading commonly to fulminant sepsis and high mortality rates.⁷

Complicating matters further, many of these cases were initially misdiagnosed as gastroenteritis, with catastrophic outcomes. This was a landmark study, for two reasons, as it linked a hitherto obscure clinical presentation of IMD to a particularly virulent serogroup of MenW (ST-11) as well as it emphasised the disconcerting rise in frequency among the adolescent and young adult populace. It also underlined that a high index of clinical suspicion is required in order to act urgently and save such patients, as as out of the three patients (total 15) who were suspected to have IMD, two survived. Thus, early recognition and management are essential.

Against this backdrop, we now have clear insight into the magnitude of the potential impact that this case has. This particular case stands out for three main reasons. First, it emphasises that adolescents are now the prime vulnerable group to MenY IMD, which contrasts sharply with the heretofore 'classical' depiction of MenY infection as causing pneumonia in elderly comorbid patients. Second, it shows that it can run a fulminant and rapidly progressive course, even in those without immunosuppression, and that, without awareness and early recognition, these patients will have extremely high mortality rates. Finally, and perhaps most importantly, it is among the first-ever documented cases of MenY presenting in such a manner, which was ascribed characteristically to the hypervirulent ST-11 MenW serogroup in the aforementioned study.

The magnitude of this last impact can hardly be overstated. This should serve as an important clinical lesson to us all, reminding us to consider the prospect of MenY infection when faced with young patients presenting to A+E with unusual presentations of sepsis or in patients with diarrhoea and deterioration out of proportion to the initial presentation. Moreover, the time taken for a blood culture result to return is prohibitively long in such patients, and therefore, PCR testing should be performed immediately on suspicion to facilitate rapid diagnosis.

PCR testing has a sensitivity of 83%–100% and a specificity of 87%–100%, making it an easily accessible and highly reliable choice. It has the added advantage of giving positive results in culture-negative patients,⁸ which is particularly useful as many patients have negative cultures due to early antibiotic treatment, making culture an unreliable source for excluding IMD.

That being said, the usage of PCR should not replace or supercede blood cultures, which are taken as part of the management of suspected sepsis. It should instead be viewed as a valuable

adjunct, especially when faced with profoundly unwell and rapidly deteriorating septic patients, or when faced with those who remain unwell in the face of clinically suspected sepsis, despite negative blood cultures.

Indeed, PCR testing must occur only in parallel with full sepsis management as per trust protocol, including prompt antibiotic therapy (MenY is sensitive to penicillins, cephalosporins and fluoroquinolones) and fluid resuscitation, which categorically improve outcomes. Even in those in whom the disease runs a fatal course, identification of MenY allows for a database to be built, hence increasing awareness of the disease and allowing for identification of contacts for testing and potential protection.

Finally, from a national perspective, the identification of such cases and recognition of its increasing incidence should prompt discussion regarding the use of the quadrivalent MenACWY vaccine in the UK. This vaccine has been implemented in the UK since August 2015 and was primarily instituted to address the rise of MenW IMD by targeting those in the preadolescent phase, before they approach the maximal carrier risk age.⁹

It is hoped that this case report will serve as an important reminder to all clinicians both to encourage vaccine uptake in these vulnerable groups to promote prevention and awareness as well as to reiterate the hidden danger it poses in the acute setting, with fulminant and often fatal outcomes due to late recognition.

Learning points

- ▶ Invasive disease due to MenY is rising and should be suspected early in young patients with unusual infective presentations and/or rapidly worsening disease.
- ▶ PCR testing offers a highly reliable and fast means of detecting MenY.
- ▶ Prompt recognition and antibiotic therapy save lives.
- ▶ Uptake of the quadrivalent MenACWY vaccine should be encouraged in all at-risk groups.

Contributors I hereby certify that SR and I, AM, collaborated together during our time at Barnet Hospital to produce this manuscript. SR presented me with this case, which I wrote in its entirety, while researching the literature used in this case. SR supervised me during this process and reviewed my draft and edited it to our mutually agreed final version. For this paper, it has been agreed that I shall be the first author and he shall be the second author.

Competing interests None declared.

Patient consent Patient is deceased. After exhaustive attempts, we were unable to contact his next of kin for this. We have anonymised the information contained in this case as much as possible and have ensured that this will not cause harm to the patient's family, to the best of our ability. We take full responsibility for this manuscript and the attempts to contact the deceased patient's family. We strongly believe that it is in the best interests of society to have the awareness from this case, which did not require any sensitive or identifying patient information.

Provenance and peer review Not commissioned; externally peer reviewed.

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