

## Case report

## Meningococcal meningitis and COVID-19 co-infection

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**SUMMARY**

Bacterial co-infection in the ongoing pandemic of COVID-19 is associated with poor outcomes but remains little understood. A 22-year-old woman presented with a 3-week history of fever, headache, neck stiffness, rigours and confusion. She was noted to have a purpuric rash over her hands and feet. Cerebrospinal fluid bacterial PCR was positive for *Neisseria meningitidis*. A concurrent nasopharyngeal RT-PCR was positive for SARS-CoV-2, the causative virus of COVID-19. She was treated with antibiotics for bacterial meningitis and made a complete recovery. Bacterial infection from nasopharyngeal organisms has followed previous pandemic viral upper respiratory illnesses and the risk of bacterial co-infection in COVID-19 remains unclear. Research characterising COVID-19 should specify the frequency, species and outcome of bacterial co-infection. Management of bacterial co-infection in COVID-19 presents major challenges for antimicrobial stewardship and clinical management. Judicious use of local antibiotic guidelines and early liaison with infection specialists is key.

**BACKGROUND**

In December 2019, a viral pneumonia was identified in Wuhan, China. The cause was determined to be a newly recognised betacoronavirus of likely zoonotic origin, subsequently designated SARS-CoV-2. The clinical illness was termed COVID-19 in February 2020 by WHO.

SARS-CoV-2 demonstrates efficient person-to-person droplet spread with an average estimated basic reproductive value (R0) of 3.28.<sup>1</sup>

The clinical illness is variable with a spectrum from asymptomatic infection to critical illness most typically characterised by an acute respiratory distress syndrome resulting in hypoxic respiratory failure.<sup>2</sup>

Infection with SARS-CoV-2 results in viral replication in the nasopharynx and viral detection is possible there, as well as in sputum, faeces, urine and blood.<sup>3</sup> COVID-19 results in significant morbidity and mortality in all populations with particular severity among the elderly and comorbid.<sup>4</sup> Although antibiotic prescribing in the context of severe COVID-19 is widespread,<sup>4 5</sup> the role of bacterial co-infection is poorly understood.<sup>6 7</sup>

The Gram-negative diplococcus, *Neisseria meningitidis*, is the causative organism of meningococcal meningitis and is exclusively found in the human nasopharynx. Six of the 13 recognised serotypes are pathogenic and between 80% and 90% of invasive disease in the UK is attributed to the serogroup

B.<sup>8</sup> Carriage varies by age and geography, with the highest level of carriage in European countries peaking at approximately 23.7% in 19-year-olds.<sup>9</sup> In the UK, meningococcal vaccination forms part of the routine immunisation schedule and the rates of meningococcal meningitis are resultantly low from a global perspective.<sup>8</sup>

Spread is via droplets within approximately 1 m and invasive disease among close and household contacts is well recognised.

Guidelines for the investigation of suspected cases of invasive meningococcal disease include blood and cerebrospinal fluid (CSF) culture and bacterial PCR as well as nasopharyngeal bacterial culture to maximise yield of microbiological diagnosis.<sup>10</sup>

Triggers for development of invasive meningococcal disease in otherwise well carriers of potentially pathogenic serotypes of *N. meningitidis* are not clear.<sup>11</sup> However, temporal associations between *N. meningitidis* and influenza A and B, and *Mycoplasma pneumoniae* infection, have been noted in at-risk groups, as well as following epidemic and pandemic outbreaks. Typically, development of invasive meningococcal disease trails a preceding infection by around 2 weeks.<sup>12</sup>

Here, we present a case of *N. meningitidis* meningitis co-infection with SARS-CoV-2.

**CASE PRESENTATION**

A normally fit and well 22-year-old woman with no medical history presented to the emergency department of a large inner city teaching hospital complaining of a 3-week history of headache, neck stiffness, rigours, confusion, and a new purpuric rash over her hands and feet. She had no recent travel history, exposure to unwell contacts or any significant family history. Her only regular medication was the combined contraceptive pill. She did not smoke and normally worked full time in a supermarket.

She had completed her full primary childhood course of vaccination. This included vaccination against *N. meningitidis* serogroup C in childhood and against serogroups A, C, W and Y in adolescence. She had not received vaccination against *N. meningitidis* serogroup B which only became routinely available for infants in 2015.

On presentation, she was noted to have a fever of 38.0°C and heart rate of 108 beats per minute. She was normotensive and alert. A mild purpuric rash was evident on her hands and feet. Moderate neck stiffness on flexion was noted. There were no other neurological signs and examination was otherwise unremarkable.



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A presumptive diagnosis of meningo-encephalitis was made and intravenous ceftriaxone was commenced.

### INVESTIGATIONS

Initial blood testing revealed a raised C reactive protein of 214 mg/L (reference range 0–10), a white cell count of  $26.4 \times 10^9$  (reference range 4–10) with a neutrophilia of  $22.6 \times 10^9$  (reference range 2.0–7.0) and lymphocyte count of  $2.5 \times 10^9$  (reference range 1.1–5.0). Liver function tests, and urea and electrolyte testing were unremarkable. A venous blood gas revealed a venous lactate of 2.1 mmol/L (reference range 0.6–2.2). A CT head scan without intravenous contrast was performed and was normal.

Blood and urine cultures were negative. Lumbar puncture revealed an opening pressure of 45 cmH<sub>2</sub>O with cloudy CSF obtained. The CSF white cell count was 760 mm<sup>3</sup> (50% neutrophils and 50% lymphocytes). Red cell count was 10 mm<sup>3</sup>. Direct Gram stain of the CSF and CSF culture were both negative. CSF viral PCR test was negative for *Herpes simplex 1 & 2*, *Vari-cella zoster*, *Enterovirus* and *Parechovirus*. CSF bacterial PCR was positive for *N. meningitidis* (crtA gene) and negative for *Haemophilus influenzae* and *Streptococcus pneumoniae*.

A nasopharyngeal swab was taken for reverse transcriptase PCR (RT-PCR) testing for SARS-CoV-2 in accordance with local and national guidance for the diagnosis of COVID-19 in secondary care settings. This detected SARS-CoV-2 at a low level.

### DIFFERENTIAL DIAGNOSIS

The diagnosis of meningococcal meningitis was established by the CSF bacterial PCR, CSF white cell count and the typical clinical picture. The detection of SARS-CoV-2 was unexpected and led to the postulation that the proven invasive meningococcal disease may be related to the presence of nasopharyngeal viral infection.

Subsequent reference laboratory DNA PCR and multilocus sequence typing confirm the *N. meningitidis* to be a member of serogroup B. All investigations were carried out in accordance with guidelines<sup>10</sup> expected for a nasopharyngeal bacterial culture throat swab which was not carried out.

### TREATMENT

The patient was treated with 5 days of intravenous ceftriaxone, and following rapid improvement in hospital, she was discharged to complete treatment via the local outpatient parenteral antibiotic service.

### OUTCOME AND FOLLOW-UP

The patient was left with no neurological deficit and she was advised of the need to self-isolate in view of her diagnosis of COVID-19. Contact tracing for *N. meningitidis* was carried out by the local public health protection team. A repeat nasopharyngeal throat swab was taken on completion of antibiotic therapy and was negative for SARS-CoV-2.

### DISCUSSION

We report a case of meningococcal meningitis and SARS-CoV-2 coinfection. While symptoms were typical of bacterial meningitis, the prolonged period of illness prior to presentation was not. We hypothesise that primary infection with SARS-CoV-2 accounted for the early symptoms and potentially predisposed to invasive meningococcal disease. This would account for the timeline of her symptoms and the low level of virus detected

on her nasopharyngeal throat swab towards the presumed end of her viral illness.<sup>13</sup>

Bacterial–viral co-infection is well recognised but poorly understood. Multiple mechanisms for susceptibility to bacterial infection have been suggested.<sup>14</sup> In established and better understood viral infections, such as influenza A, increased risk of bacterial and fungal infections is well described and associated with significantly poorer outcomes.<sup>15 16</sup>

The role of bacterial co-infection with SARS-CoV-2 remains speculative and poorly characterised<sup>6</sup> although presumptive treatment of suspected bacterial infection is commonplace and antibiotic use is widespread.<sup>4 17</sup>

While the published experience to date suggests a predominantly benign course for SARS-CoV-2 in children and young adults, the possibility of *N. meningitidis* co-infection is of particular concern among this group in view of the higher rates of meningococcal carriage. Invasive meningococcal disease carries around a 10% mortality rate and significant rates of neurological sequelae.<sup>11</sup> To our knowledge, there is currently no signal suggesting increase in invasive meningococcal disease in association with the SARS-CoV-2 pandemic either in Europe or elsewhere. Surveillance systems should be alert to any change in disease notification.

During the 1919 influenza pandemic, infections, with *S. pneumoniae*, followed around 2 weeks after the initial viral

### Patient's perspective

Following a 3 week period of being severely ill with viral meningitis, I ended up in hospital with bacterial meningitis. The speed the NHS staff within the A&E department worked to support me was amazing. Within a few hours I had a brain scan, chest scan and was admitted into a ward.

Throughout the week I was in hospital all the staff were kind and supportive and I am so grateful to them that they allowed my mum to stay with me during this horrific painful period.

It was the scariest experience I have ever faced, especially when I discovered that along with the meningitis I also had COVID-19.

It is frightening how a healthy young individual can go to sleep and a few hours later wake up with horrific symptoms leading to meningitis, hallucinations and COVID-19. Unfortunately, it has made me very apprehensive in case this illness reoccurs, however my specialist did reassure me and my family that it was a positive outcome and I am better.

I am grateful to all the NHS staff who helped me through this time and to my specialist.

### Learning points

- ▶ A case of *Neisseria meningitidis* and SARS-CoV-2 co-infection is presented.
- ▶ Viral predisposition to respiratory tract bacterial co-infection remains poorly explained but of real significance in the development of invasive bacterial infections.
- ▶ Although antibiotic prescribing is high in hospitalised patients with COVID-19, the role of bacterial co-infection is poorly understood. This has important implications for antimicrobial stewardship and future antimicrobial resistance.
- ▶ Surveillance for invasive bacterial infection is important to characterise and to help protect against bacterial co-infection in the context of the ongoing COVID-19 pandemic.

infection.<sup>13</sup> It is possible that we have observed a similar timeframe in this case in association with *N. meningitidis*. While we remain in the uncertain early days of managing the COVID-19 pandemic, consideration should be given to the possibility of a coming wave of invasive bacterial infections as a result of increased susceptibility following COVID-19 infection.<sup>18</sup> Meningococcal meningitis remains a largely vaccine-preventable disease. Therefore, any change to the incidence or geographical clustering of new cases should prompt consideration of expanded vaccination targeted to those at risk. This is particularly true with vaccination against *N. meningitidis* serogroup B where routine infant vaccination has only been routinely available since 2015.<sup>11</sup>

The management of suspected bacterial co-infection in the context of COVID-19 is a challenging area of practice. Very high rates of empirical antibiotic use in suspected COVID-19 and low rates of documented bacterial infection have important implications for antibiotic stewardship. There is an urgent need to better understand and identify bacterial co-infection as unchecked, unnecessary use of antibiotics will further fuel antimicrobial resistance and other antibiotic-related adverse events.

This case demonstrates a number of the uncertainties that surround the diagnosis and management of the bacterial complications of COVID-19. The publication of more detailed analysis of the number and species of bacterial co-infection in those with COVID-19 will be helpful, as well as further dissemination of the existing advice on antibiotic use from relevant antimicrobial prescribing bodies.<sup>19</sup>

Ongoing surveillance for the association of meningococcal and other invasive bacterial infection of upper respiratory tract origin will be important as the pandemic progresses.

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