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CASE REPORT

A Pediatric Case of Serogroup Y Meningococcal Meningitis in a 12-Year-Old Boy Combined with Respiratory Infection of Three Species of Viruses in China

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Background: Serogroup Y (MenY) invasive meningococcal disease (IMD) is uncommon in China, and MenY IMD cases combined with respiratory infections caused by several viruses are rare worldwide.

Case Presentation: A 12-year-old boy was admitted by ambulance to a secondary hospital in Yunnan on January 9, 2025, due to sore throat for three days, fever, headache, and vomiting for six hours. *Neisseria meningitidis* (Nm) was cultured from the cerebrospinal fluid, whereas influenza A virus, adenovirus, and rhinovirus were detected in throat swab by PCR. After treatment with ceftriaxone and oseltamivir, the patient's condition improved and was discharged. Whole-genome sequence analysis of the Nm isolate (Nm534) showed a molecular type of Y: P1.5–1,10-1: F4-1: ST-1655(CC23) without antimicrobial resistance-associated mutations. Phylogenetic analysis indicated that Nm534 was assigned to Clade II and was closely related to isolates from Guangdong and Guangxi, which have the potential to be the infection source of this IMD case.

Conclusion: A rare case of MenY meningococcal meningitis combined with respiratory infection caused by three species of viruses was reported in China. It is recommended that school-aged children and adolescents be immunized with meningococcal polysaccharide conjugate vaccine ACYW.

Keywords: *Neisseria meningitidis*, serogroup Y, invasive meningococcal disease, virus infection, whole genome sequencing

Introduction

Invasive meningococcal disease (IMD) is caused by *Neisseria meningitidis* (Nm), which is ranked as the first pathogen in the World Health Organization (WHO) roadmap for defeating meningitis by 2030.[1] According to the capsular polysaccharide, Nm can be classified into 12 serogroups, among which A, B, C, W, X, and Y are responsible for most of the cases.[2] Serogroup Y (MenY) IMD cases are uncommon in China,[3] and took up 1.2% of all the IMD cases in China during 2010–2020.[4] MenY IMD cases combined with respiratory infections caused by several viruses are rare worldwide. Here, we report a pediatric case of meningococcal meningitis caused by MenY combined with respiratory infections caused by three species of viruses in China.

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Case Presentation

A 12-year-old boy was admitted to a secondary hospital in Yunnan by ambulance on January 9, 2025, with complaints of sore throat for three days, fever, headache, and vomiting for six hours. The temperature was 39.8 °C, and projectile vomiting occurred for three times, with all being stomach contents.

The patient was diagnosed with arachnoidal cyst on the tempus sinistrum and received conservative treatment in December 2023. He received regular vaccinations, including the MenA and MenC meningococcal vaccines. He had never travelled to other cities or countries, without contacts with IMD patients.

Physical examination on admission revealed temperature of 36.1 °C, heart rate of 100 beats per minute, respiratory rate of 23 breaths per minute, blood pressure of 98/76 mmHg, blood oxygen saturation (SPO_2) of 95%, confusion, and scattered petechiae and ecchymoses on the trunk and limbs. Both pupils were equally round and large, with a sluggish pupillary light reflex. Pharyngeal congestion and mild nuchal rigidity were observed without pathological reflexes.

Computed tomography (CT) of the head revealed an arachnoid cyst in the temporal sinistrum. Lung CT showed bilateral lower lobe inflammatory lesions and minimal bilateral pleural effusion. Laboratory investigations showed the following: blood routine examination: Day 1, white blood cell (WBC) 21.10×10^9/L, neutrophils 94.0%; platelet (PLT) 92×10^9/L; C-reactive protein (CRP) 145.4 mg/L, procalcitonin (PCT) 30.90 ng/mL, IL-6 1170.00 pg/mL, activated partial thromboplastin time 35.53 s, international normalized ratio 1.76, prothrombin time 20.17s, fibrinogen 4.21 g/L, fibrin degradation products 9.55 μg/mL, D-dimers 3.95 μg/mL, and antithrombin III 98%; Day 11, WBC 10.53×10^9/L, neutrophils 70.3%; PLT 382×10^9/L; CRP 9.3 mg/L, PCT 0.142 ng/mL, and IL-6 4.51 pg/mL. CSF analysis, on Day 1, showed yellowish-white, turbid, protein qualitative test positive, WBC 12,000/mm^3, segmented neutrophils 92.0%, glucose 1.58 mmol/L, and chlorine 119.9 mmol/L; on Day 4, showed colorless, clear and transparent, turbid, protein qualitative test negative, WBC 18/mm^3, segmented neutrophils none, glucose 5.42 mmol/L and chlorine 127.0 mmol/L. Targeted next-generation sequencing (tNGS) of the CSF revealed that Nm nucleotides were 47,084 copies/mL. On Day 3, Nm isolate (Nm534) was cultured from CSF and validated using matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF-MS; bioMérieux, France). The minimum inhibitory concentrations (MICs) of 12 antimicrobial agents were determined using the broth microdilution method and interpreted followed the 2025 guidelines of the Clinical and Laboratory Standards Institute (CLSI).[4] Except being intermediate to trimethoprim-sulfamethoxazole (MIC, 0.25/4.75 μg/mL), the isolate was susceptible to other 11 antimicrobial agents, including penicillin, ceftriaxone, and ciprofloxacin (Table S1). Throat swab was tested using real-time polymerase chain reaction kit (Sansure Biotech, China) targeting six respiratory pathogens, and was positive for influenza A virus, adenovirus, and human rhinovirus.

After admission, the patient was empirically treated with ceftriaxone (2 g) twice daily, oseltamivir, and symptomatic medication, and the results of antimicrobial resistance test on Day 5 also supported the choice of ceftriaxone. The patient was cured and discharged on January 20 (the 11th day after admission) and was diagnosed with meningococcal meningitis, secondary thrombocytopenia, influenza A, infection with adenovirus, infection with human rhinovirus, and arachnoid cyst.

Isolate Nm534 was identified as MenY using monoclonal antiserum (Remel Europe Ltd.) and sequenced on an Illumina HiSeq platform (Illumina, CA, USA). The assembled genome sequence was submitted to the PubMLST *Neisseria* Database (ID: 169416). The fine type of Nm534 was Y: P1.5–1,10-1: F4-1: ST-1655(CC23). The alleles of the antimicrobial resistance genes were *gyrA*-1, *penA*-22, and *rpoB*-34 without mutations. To put Nm534 into the context of global ST-1655 isolates, we performed phylogenetic analysis involving Nm534 and 1,457 ST-1655 genomes deposited in the PubMLST *Neisseria* Database from 25 countries (Table S2), including 27 isolates from China (Table S3), using core genome single nucleotide polymorphism (SNP) in Parsnp (v1.2). Two clades were identified (Figure 1). Accounting for 15.9% (231/1,452), Clade I was mainly composed of European isolates (92.2%, 213/231), with almost identical PorA_VR1 (P1.5–1) and FetA (F4-1) variants and diverse PorA_VR2 variants. Including all Chinese isolates, Clade II accounted for 84.1% (1221/1,452), with the similar PorA_VR1, PorA_VR2, and FetA variants as P1.5–1,10-1: F4-1. Nm534 was closely related to the isolates from Guangdong and Guangxi. Analysis of quinolone resistance mutations showed that 0.9% (13/1,452) of global ST-1655 isolates possessed GyrA mutations, which were only discovered in China

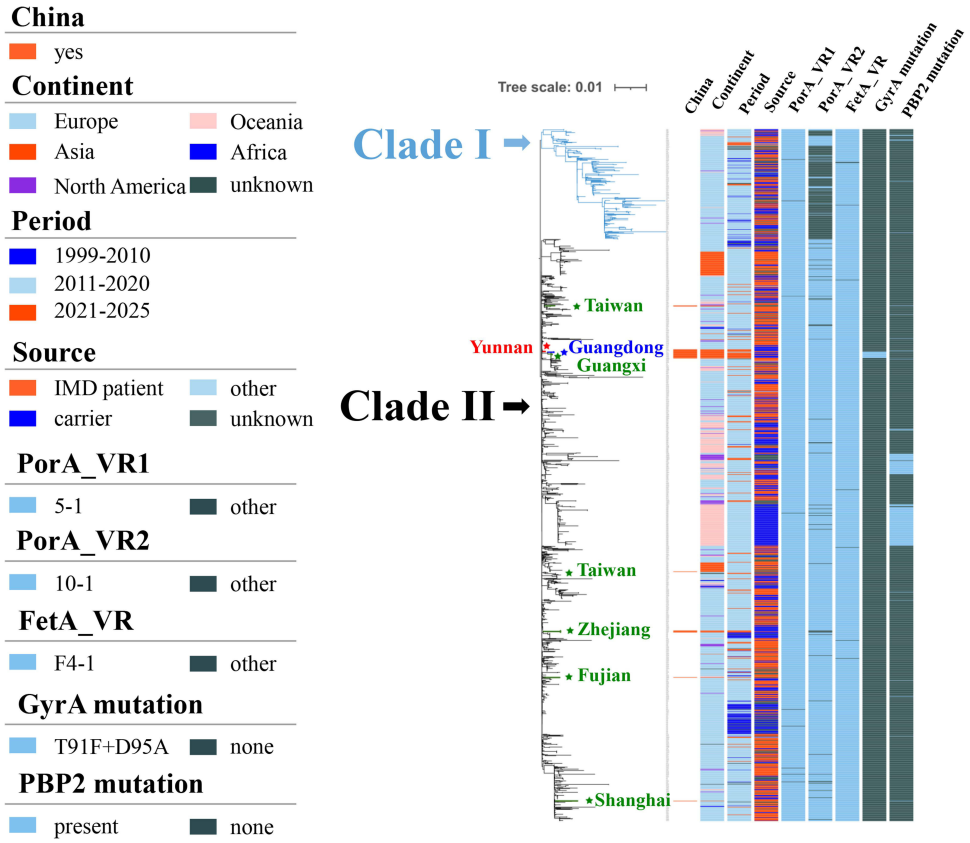

Figure 1 Single nucleotide polymorphism (SNP)-based phylogenetic analysis of global serogroup Y ST-1655 isolates. Isolates from different provinces of China are labeled using stars with different colors.
Abbreviation: IMD, invasive meningococcal disease.

(Figure 1 and Table S2), mainly in isolates from Guangdong and Guangxi (T91F and D95A; Table S3). Analysis of penicillin resistance mutations showed that the frequency of the five typical mutations (F504L, A510V, I515V, H541N, and I566V) was 10.1% (147/1,452), which were found in three isolates from China (one each from Shanghai, Hebei, and Taiwan).

Discussion

In China, IMD cases were mainly caused by MenA (>90%) before 2000, MenC (60%) and MenW (24%) between 2003 and 2014, and MenB (52%) from 2015 to 2020.[5,6] There are no reports of MenY IMD combined with infections caused by other pathogens. We searched for reports of Chinese MenY IMD cases in English and Chinese, and found only 18 cases (Table S4).

The 18 Chinese MenY patients were all male from 10 provinces or municipalities, with ages ranging from 28 days to 65 years, most of whom were students (72.2%, 13/18), with case fatality rates (CFRs) of 11.1% (2/18) and 72.2% (13/18) occurring after 2020. These features were different from IMD cases in China during 2015–2019 of MenA (3 provinces, ~67% from ≥15 years old, CFR of 7.1%), MenB (19 provinces, ~61% from 0–4 years old, CFR of 15.0%), MenC (17 provinces, ~51% from 10–14 years old and ~30% from ≥15 years old, CFR of 11.8%), and MenW (4 provinces, ~67% from ≥15 years old, CFR of 22.2%).[7] Meningococcal polysaccharide vaccines (MPV) A and A+C are included in the National Expanded Program on Immunization (EPI), but meningococcal polysaccharide conjugate vaccine (MPCV)-ACYW, the only vaccine covering MenY cases in China, is self-paid. None of the 18 patients received vaccines covering MenY. Based on the increasing trends of MenY cases in China after 2020, we recommend that school-age children and

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adolescents should be immunized with MPCV-ACYW. We discovered that none of the 18 cases was combined with infection by other pathogens.

Recently, we reported a fulminant MenC meningococcal meningitis case following infection with the influenza A virus in Shanghai in 2019.[8] Infection with the influenza A virus is an important risk factor for IMD because it disrupts the nasopharyngeal mucosal barrier and facilitates invasion of Nm colonized in the nasopharynx.[9] In addition, there are reports of IMD cases with infection by SARS-CoV-2 or *Cryptococcus neoformans* globally.[10–14] By analyzing those six co-infection cases, we found that they were all immunocompetent but with a high fatality (33.3%, 2/6) and the pathogenic *N. meningitidis* isolates can be from different serogroups, including MenB, MenC, and non-groupable. Similar to those co-infection cases, this MenY case showed no signs of immunodeficiency. However, there are no reports of IMD combined with infection by several viruses. In this case, upper respiratory infection symptoms including sore throat occurred in the patient first, and the nucleotide tests suggested that the symptoms were related to the infection with influenza A virus, adenovirus, and human rhinovirus, which might have provided convenience for the invasion of MenY Nm, leading to the symptoms and physical signs of meningococcal meningitis. Among the three viruses, infection of influenza A virus can enhance the adhesion of *N. meningitidis* to human Hec-1-B epithelial cells,[15] while adenovirus and human rhinovirus do not trigger meningococcal disease in children.[16]

MenY IMD cases have raised global concern in recent years. In 2013 and 2020, a penicillin- and ciprofloxacin-resistant MenY ST-3587 (CC23) strain appeared.[17] This strain produces β-lactamase ROB-1 and harbors the quinolone resistance-associated mutation T91I in GyrA, with the fine type P1.5–2,10-2: F4-1: ST-3587(CC23). None of these features were found in the MenY isolates reported in China (Y: P1.5–1,10-1: F4-1: ST-1655[CC23]; Table S4), suggesting that the dual-resistant MenY strain did not appear in China. The increase in MenY IMD cases in China coincided with similar trends in Europe and Australia,[18] but the highest proportions of age groups were different, with 14–18 years old (55.6%) in China, < 1 year old (30%-50%) in Europe, and 15–24, 45–64, and > 65 years old in Australia.

Epidemiological information, including no travel histories to other cities and no recent contacts with IMD patients, could not give a clue to the source of this IMD case. However, we performed a phylogenetic analysis of all the ST-1655 genomes globally, including 27 isolates from China, indicating the close relationship between the isolate from this study and those from Guangdong and Guangxi (Figure 1). Guangdong and Guangxi are nearby Yunnan, with Guangxi neighboring Yunnan. This data suggests the possibility of this IMD case to get infection from the strains from Guangdong and Guangxi.

There are some limitations in this study. We were unable to collect throat samples from the close contacts of the patient; therefore, we had no data of their carriage of *N. meningitidis* for further analysis of the source of this IMD case. On the other hand, findings from this study were from a single case, and we should be careful to generalize the conclusion to a wide scale.

Here, we report a rare pediatric case of meningococcal meningitis caused by MenY Nm combined with respiratory infections caused by three species of viruses in China. This type of multiple infections is very rare, and clinicians need to pay more attention to avoid serious sequelae and complications. It is recommended that school-aged children and adolescents be immunized with MPCV-ACYW.

Ethical Approval

This study and the publishment of the case details were approved by the Ethics Committee of Minhang District Central Hospital (No. 2024-036-01K). The consent for publication has been obtained from the patient's father.

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This study used *Neisseria* genomic data deposited in the *Neisseria* PubMLST Database (https://pubmlst.org/neisseria/) located at the University of Oxford (Jolley & Maiden 2018, Wellcome open research, 3:124); the development of this database was funded by the Wellcome Trust and European Union. This study was supported by the National Natural Science Foundation of China (Grant Numbers 82272381 and 82472322). The funders played no role in the study design, data collection, interpretation, or decision to submit this manuscript for publication.

Disclosure

The authors declare no conflict of interest.

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