Invasive pneumococcal disease in the post-COVID era

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Physicians caring for children must remain vigilant regarding the multitude of invasive pneumococcal disease (IPD) cases despite the availability of a national immunisation programme designed to provide coverage for pneumococcal infections. In Hong Kong, serotype 3 has remained the most prevalent serotype regardless of presumed coverage by the 13-valent pneumococcal conjugate vaccine (PCV-13) introduced in 2011. During the coronavirus disease 2019 (COVID-19) pandemic, common respiratory pathogens were nearly absent for 2 years due to the implementation of mandatory mask-wearing and home isolation. In the latter half of 2022, during the post-COVID era, a substantial resurgence of all common respiratory pathogens—including *Streptococcus pneumoniae*—was observed. Invasive pneumococcal disease continues to cause substantial morbidity and mortality among children in Hong Kong; serotype 3 remains the most prevalent serotype despite PCV-13 immunisation.[1,2] We reviewed consecutive cases of IPD managed in the paediatric intensive care unit (PICU) of our hospital from late 2022 onwards to assess immunisation status, serotypes, and complications of IPD cases. We reviewed the serotypes, prior immunisation status, and complications of anonymised consecutive IPD cases managed in the PICU between June 2022 and March 2024 (Ref No.: IRB HKCH-REC-2019-009).

Six consecutive cases of IPD from 2023 to 2024 (four female and two male; aged 32 months to 14 years) were reviewed (online supplementary Table). No cases of IPD were reported during the COVID-19 period from 2019 to 2021. All six patients had been fully immunised with PCV-13. Serotype 3 was identified in five of the six cases, whereas serotype 19A was detected in one case. Acute respiratory distress syndrome and acute kidney injury were clinically significant complications. Coinfections were present in all cases, and viral co-infections occurred in all but one case. One patient developed pericarditis and experienced cardiac arrest warranting pericardial drainage; *Streptococcus pneumoniae* serotype 19A was isolated from pericardial fluid, blood culture, and tracheal aspirate. Another patient developed respiratory symptoms before departing for a family vacation to Japan. She became critically ill and was airlifted to a PICU in Hong Kong for further management. All pneumococcal isolates were susceptible to penicillin. No fatalities occurred in this series of IPD cases.

Immunisation status

All patients with IPD in this PICU series had been fully immunised with PCV-13. Serotype 3 was the predominant serotype in five of the six cases (serotype 19A was detected in one case), despite presumed coverage by PCV-13, which has been included in the Hong Kong Childhood Immunisation Programme since 2011.[3] This pattern differs from observations in most developed nations, including the United States, where non-PCV-13 serotypes have become predominant.[4] Trends in serotype 3 incidence rates substantially vary across countries that have incorporated either the 10-valent PCV vaccine, which does not include serotype 3, or PCV-13 in their paediatric immunisation programmes.[5] At the population level, PCV-13 appears to provide some direct and indirect protection against serotype 3. However, researchers in Hong Kong have reported a consistent increase in serotype 3 IPD incidence among local children since the introduction of PCV-13.[2,6,7] Despite the implementation of an immunisation programme and availability of effective treatment, serotype 3 IPD has paradoxically become the predominant serotype. The proposed explanation is that serotype 3 produces protective mucoid colonies which resist opsonising antibodies.[8-11] Additionally, the opsonising antibody response is relatively ineffective in providing protection against serotype 3.

Among patients admitted to PICUs, the serotypes detected were predominantly vaccine serotypes. A Spanish study revealed that the serotype distribution was serotype 19A (23%), serotype 14 (20%), serotype 3 (17%), and serotype 1 (12.5%).[12] In contrast, a Chinese study showed that serotype 19A was the most common overall (54%), whereas serotype 19F was most frequently identified in cases of meningitis.[13]

History of immunisation against invasive pneumococcal disease in Hong Kong

A 7-valent PCV was introduced into the Hong Kong Childhood Immunisation Programme in September 2009, followed by a rapid transition to a 10-valent PCV in 2010 and subsequently to PCV-13 in December 2011.[3] A decrease in pneumococcal disease incidence was observed. However, severe IPD due to serotype 3 has become increasingly prevalent, particularly in PICU settings, despite its presumed coverage by PCV-13.[6] Serotype 3 predominance has also been reported in several other nations.[14]

With the relaxation of public health measures in late 2022, pneumococcal infections and respiratory viruses resurged. Since 2017, serotype 3 cases have been identified in Hong Kong despite widespread PCV-13 immunisation. All six children in our series with pneumococcal disease had been fully immunised with PCV-13, highlighting that fully immunised children remain susceptible to vaccine-covered serotypes, particularly serotype 3.

Antibiotics

The treatment of IPD requires prompt antibiotic administration, intensive care support, and renal replacement therapy in cases of haemolytic uraemic syndrome and acute kidney injury.[13,15] Penicillin-resistant serotypes have been reported; these serotypes warrant the use of more potent antibiotics, such as third-generation cephalosporins and vancomycin. All pneumococcal isolates in our series were sensitive to penicillin. For severe community-acquired pneumonia in children, the Centre for Health Protection recommends intravenous or intramuscular ceftriaxone at 50 to 100 mg/kg/day in divided doses every 12 or 24 hours for 7 to 10 days.[16] This antimicrobial regimen is also supported by the recommendations of Lui et al.[17] Certain prevalent non-vaccine serotypes may be associated with distinctive lineages in different countries, where they exhibit various antibiotic resistance profiles. Among isolates displaying non-vaccine serotypes, significant increases in resistance to penicillin and erythromycin have been detected in the PCV-13 period compared with the pre-PCV era.[4]

Complications

In PICU settings, IPD is associated with cardiopulmonary failure, septic shock, and pleural effusions.[7] Extracorporeal membrane oxygenation support or extracorporeal blood purification therapy may be required in critically ill cases.[18] Renal complications associated with IPD include haemolytic uraemic syndrome and acute kidney injury.[13] Pneumococcal-associated haemolytic uraemic syndrome is a recognised complication of serotype 3 and, less frequently, other serotypes of IPD.[13,14] Chronic renal failure may rarely develop, leading to a need for kidney transplantation.[19-22] A case of kidney transplantation due to chronic renal failure associated with serotype 3 IPD in childhood was reported in Hong Kong.[19] Long-term sequelae of severe pneumococcal pneumonia include bronchiectasis, which requires ongoing surveillance.[23]

Microbial isolations

Co-infections and secondary bacterial infections, particularly with respiratory viruses, were present in five of the six cases in our series. Influenza is notable because antiviral treatment with oseltamivir is available. Also, a fatal case involving pneumococcus, *Mycoplasma pneumoniae*, and metapneumovirus has been reported in Hong Kong.[24] A macrolide or doxycycline would be indicated for *Mycoplasma* infection. Generally, bacterial and viral co-infections are common among critically ill patients.[25] In the present series, microbial isolates were identified in all patients.

Prognosis

Although IPD prognosis in PICU settings is often poor, all patients in our series survived. Prompt antibiotic administration, treatment of co-infections, and intensive care support may contribute to favourable outcomes.[15] However, long-term complications, such as bronchiectasis, resection of necrotic lung tissue, chronic kidney injury and sequelae of meningitis, may occur.

Newer vaccines

Serotype selection was observed in Hong Kong shortly after the introduction of PCV-13 in 2011. This vaccine has also been used to prevent IPD among renal transplant recipients.[26] Considering the availability of newer vaccines for IPD, ongoing surveillance of serotype prevalence and vaccine efficacy remains essential for guiding future vaccine development.[27-29] It has not been established whether newer PCVs, such as 15-valent and 20-valent pneumococcal conjugate vaccines, are effective against serotype 3. Stronger targeted adult vaccination may also be necessary to reduce the disease burden.[30] As of late 2023, Hong Kong has begun replacing PCV-13 with the 15-valent vaccine. A 20-valent vaccine has also become available since 2023. Continued surveillance for the emergence of vaccine and non-vaccine serotypes is crucial when seeking to develop novel vaccines for IPD.

Author contributions

All authors contributed to the concept or design, acquisition of data, analysis or interpretation of data, drafting of the manuscript and critical revision of the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an editor of the journal, KL Hon was not involved in the peer review process. KL Hon presented at meetings organised by MSD and Pfizer but has not received any honorarium from either company. Other authors disclosed no conflicts of interest.

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Supplementary material

The supplementary material was provided by the authors, and some information may not have been peer reviewed. Accepted supplementary material will be published as submitted by the authors, without any editing or formatting. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by the Hong Kong Academy of Medicine and the Hong Kong Medical Association. The Hong Kong Academy of Medicine and the Hong Kong Medical Association disclaim all liability and responsibility arising from any reliance placed on the content. To view the file, please visit the journal online (https://doi.org/10.12809/hkmj2411759).

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