Correspondence

Human Metapneumovirus Infection as an Emerging Pathogen Causing Acute Respiratory Distress Syndrome

To the Editor—Viral respiratory infections represent a frequent cause of intensive care unit (ICU) admissions in children and impose a considerable burden worldwide [1]. The main pathogens are respiratory syncytial virus (RSV) and seasonal influenza. Human metapneumovirus (hMPV) is an emerging pathogen of the Paramyxoviridae family causing acute bronchiolitis-like respiratory illness in children [2]. Williams et al [2] have recently reported an annual rate of hMPV-associated hospitalizations of 1.2 per 1000 hospitalized children <5 years of age in the United States, confirming that hMPV contributes significantly to respiratory morbidity with a similar impact as influenza. In their study, most hMPV-infected children had a relatively mild course, with only 1 participant (3%) requiring ICU admission. We would like to comment on severe hMPV infections and to present the case of a child with fatal acute respiratory distress syndrome (ARDS) due to infection with hMPV.

The 20-month-old boy initially presented with a bronchiolitis-like pattern, with rhinitis, cough, and increasing respiratory distress. The child's history was unremarkable except for moderate neurodevelopmental delay of unknown etiology. Because of impending respiratory failure (capillary pH, 7.17; partial carbon dioxide pressure, 86 mm Hg; saturation 83% with 100% oxygen), he was intubated. The oxygenation index was 0.32 and the PaO_2/FiO_2 ratio resulted 68 (55 mm Hg/0.8). On the basis of radiological findings of bilateral diffuse pulmonary infiltrates, the diagnosis of ARDS was made. Echocardiography demonstrated good biventricular function and no evidence for pulmonary hypertension. The patient was placed on high-frequency oscillatory ventilation (Sensormedics 3100A), with a mean airway pressure of up to 30 cm water. Tests for RSV and H1N1 influenza virus were negative. Results of repeated bacterial blood and tracheal fluid cultures were negative. Therefore, an expanded panel of respiratory viruses (adenovirus, picornaviruses, influenzavirus A/B, parainfluenzaviruses 1–3, RSV, and hMPV) was assessed using direct immunofluorescence. The patient tested positive for hMPV. Viral testing was repeated several times and confirmed only infection with hMPV. Because of the high risk of bacterial superinfection, empirical treatment with cefuroxime and vancomycin was initiated.

The patient subsequently developed multi-organ failure, with catecholamine-dependent arterial hypotension, renal failure requiring continuous renal replacement, coagulopathy, thrombocytopenia, leukopenia, and hepatitis. Because oxygenation further deteriorated (oxygenation index, .45), venoarterial extracorporal membrane oxygenation (ECMO) was initiated. After repeated failed attempts to wean from ECMO, the decision to limit treatment was made on day 18 after admission. The patient died after cessation of ECMO. The parents declined an autopsy.

To date, lethal hMPV infections have been primarily described in immunosuppressed adults [3]. hMPV was first reported in the Netherlands in 2001, and several studies have shown that the clinical course of hMPV closely resembles RSV infection with bronchiolitis, pneumonia, and asthma exacerbation as the main manifestations [2]. In contrast, the proportion of children with severe hMPV infection requiring ICU admission or respiratory support is small [2, 4]. However, infants with RSV and hMPV coinfection had a 10-fold increased risk of requiring mechanical ventilation when compared with infants with isolated RSV infection [4]. Although ARDS is known to occur in patients with RSV bronchiolitis [5], hMPV-associated pediatric ARDS is very rare. An extensive literature search resulted in only 4 pediatric patients with isolated hMPV infection who developed severe ARDS: a 17-month-old girl receiving chemotherapy for acute leukemia died after a prolonged period of mechanical ventilation [6]. Two other children, both with underlying diseases (prematurity with chronic lung disease in one, transplant-related immunosuppression in the other), required ECMO but ultimately recovered [7, 8]. The fourth reported case concerns a 2 year-old, previously healthy girl without any known immunodeficiency who died of pulmonary hemorrhage soon after admission [9]. It has been suggested that deficiencies in innate immunity pathways, such as Toll-like receptor 4, lead to an increased risk of severe RSV infection [10], but the role of innate immunity in hMPV infections has not been studied thus far. The underlying neurodevelopmental delay may represent a clinical risk factor for severe respiratory disease in the presented case [2].

In conclusion, the summarized cases illustrate that hMPV infection may cause severe ARDS in susceptible children. Considering that testing for hMPV is not routinely performed, it is likely that hMPV-related ARDS is underreported.

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The mortality of pediatric ARDS remains high and early identification of the causative agent is crucial. We, therefore, suggest early testing for hMPV in patients with presumptive viral ARDS where no other agent can be identified. Additional studies investigating the role of hMPV in severe respiratory infections are needed to improve early and appropriate treatment of high-risk patients.

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