Fatal respiratory distress syndrome due to coronavirus infection in a child with severe combined immunodeficiency

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Introduction

Severe combined immunodeficiency (SCID) is a genetically and clinically heterogeneous group of the most severe primary immunodeficiencies, characterized by the absence of functional T lymphocytes resulting in profound impairment of the cellular and humoral adaptive immunity. Depending on the genetic defect, B lymphocytes and natural killer (NK) cells may be present or absent and this feature constitutes the basis for the classical division into T-B+ SCID and T-B−SCID, with further subdivisions into NK+ and NK− disorders. Respiratory tract infection is a common manifestation in children in question and may be present within the neonatal period or in early infancy. Opportunistic pathogens may lead to rapidly progressive, fatal interstitial pneumonitis accompanied by hyperinflation resulting from small airway obstruction or to persistent bronchiolitic presentation. Apart from pyogenic bacteria, such as Pseudomonas aeruginosa, Stenotrophomonas spp, Burkholderia spp, as well as Mycobacteria and fungi, in particular Pneumocystis jiroveci, respiratory viruses like respiratory syncytial virus (RSV), adenovirus, parainfluenza virus, human metapneumovirus (hMPV) and other viruses – cytomegalovirus (CMV), varicella−zoster virus (VZV), and Epstein−Barr virus (EBV) are associated with severe pneumonia in SCID children. Human coronaviruses (HCoV) HCoV-229E and HCoV-OC43 and related new strains HCoV-NL63 and HCoV-HKU1, identified after the epidemic outbreak of severe acquired respiratory syndrome (SARS) coronavirus, are likely to be common respiratory viruses in otherwise healthy children and were not implicated in severe lung infections in immunocompromised patients thus far. In this report we present the case of a child with delayed-onset SCID and fatal respiratory coronavirus infection.

Case presentation

A 15-month-old girl was referred to the University Hospital due to persistent fever and interstitial pneumonitis for the purposes of diagnosis and treatment.

She was the first child of young, non-consanguineous parents, born from the first pregnancy which was terminated in the 39th week of gestation using Cesarian section surgery because of condylomata acuminata due to human papilloma
Coronavirus infection in a SCID child

Analysis of the available data concerning the effects of non-SARS human coronaviruses (HCoV) in children suggests that their clinical relevance in children is substantial, particularly in the hospital settings, even though the incidence of HCoV airway infections are generally less frequent than with other viruses which have an established role in respiratory disease, such as RSV and influenza.4 However, detailed epidemiological data on the prevalence of HCoV infections in children are discordant, ranging from 2.5% of NL63 strain in young children with bronchiolitis reported by Ebihara et al.5 to 18% in the study by Vabret et al.6 in different age groups of the child population. Moreover, seroconversion with regard to HCoV-229E and above-mentioned HCoV-NL63 in young children was much higher and was estimated to 42.9–50% and 75%, respectively.7 The characteristics of clinical manifestation of coronavirus respiratory tract infection are predominantly reliant on case reports, and in otherwise, healthy children are comparable with bronchitis, bronchiolitis, and pneumonia due to other viral infections. The epidemiological study by Kuypers et al.8 indicated that a considerable proportion of coronavirus-infected children had underlying chronic central nervous system, cardiovascular, pulmonary, allergic, and renal or hepatic conditions and diseases. These authors also paid attention to immunocompromised pediatric patients with acute lymphocytic leukemia and organ transplant recipients as a high-risk group for the development of severe lung dis-
ease. However, it is worth noting that coronavirus respiratory infections have not been described in children with genetically determined immunodeficiencies thus far and this is the first report of a documented HCoV-HKU1-related pneumonia with the RDS in a child with SCID. It is also interesting to note that the preliminary clinical diagnosis in this patient was Kawasaki disease, what is consistent with the hypothesis by Esper et al.\textsuperscript{9} regarding the association between Kawasaki disease with HCoV infection, supported by identification of the ’New Heaven’ coronavirus (HCoV-NH) in 72-7\% of respiratory specimen from affected children.

Concluding remarks

The identification of HCoV-HKU1 provides a novel insight into the epidemiology and clinical implications of coronavirus infections in severely immunocompromised children and indicates for consideration of this pathogen-related etiology of respiratory infection in SCID. Further, epidemiological studies are necessary to define the impact of HCoV on lung disease in children with immunodeficiencies.

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Competing interests

The authors have no competing interests.

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