

A particular case of SARS-CoV-2 infection in twins

Andreea Florentina Stoenescu^{1,2}, Geta Vancea^{1,2}, Dana Ispas¹,
Nicoleta Voicu-Parvu¹, Nicoleta Tudor¹, Gabriela Scurtu¹, Raluca Popescu¹,
Claudia Chirila¹, Elena Sandu¹, Emanoil Ceausu^{1,2,3}, Simin-Aysel Florescu^{1,2}

¹„Dr. Victor Babes” Clinical Hospital of Infectious and Tropical Diseases, Bucharest, Romania

²„Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

³Academy of Medical Sciences, Romania

ABSTRACT

Introduction. Although SARS-CoV-2 infection is more common in adults, many cases have been reported in the pediatric population.

Case presentation. An 8-month-old infant from twin pregnancy, confirmed with COVID-19, is hospitalized with nasal obstruction, serous rhinorrhea, rare cough and watery stools. The epidemiological link is known, both the parents and the maternal grandparents of the infant being confirmed with COVID-19. Biologically, he presented with thrombocytosis and discrete inflammatory syndrome, and the lung radiograph did not show any lesions. At the same time, the twin sister was hospitalized, who presented a similar symptomatology, with a negative SARS-CoV-2 PCR test, but the lung radiograph showed specific lesions of COVID-19. During hospitalization, 2 more SARS-CoV-2 PCR tests were performed, but with negative results. The evolution of the twins was favorable under symptomatic treatment, respectively antibiotic and symptomatic treatment.

Conclusion. SARS-CoV-2 infection may be asymptomatic, especially in infants and newborns, and has a lower prevalence.

Keywords: SARS-CoV-2, infants, twins

Abbreviations

COVID-19 = coronavirus disease 2019

SARS-Cov-2 = severe acute respiratory syndrome coronavirus

Rt-PCR = real time polymerase chain reaction

WHO = World Health Organisation

Hb = hemoglobin

URTI = upper respiratory tract infections

HIB = Haemophilus influenzae type B

INTRODUCTION

At the end of 2019, a number of cases of pneumonia of unknown etiology were registered in the Wuhan region, China. Subsequently, the etiological agent was identified, a new beta coronavirus called severe acute respiratory syndrome coronavirus (SARS-CoV-2), and the disease called Coronavirus Disease 2019 (COVID-19). The number of cases

continued to grow, expanding globally, and on March 11th, 2020, the COVID-19 pandemic was declared by the World Health Organisation (WHO) (1). In Romania, the first case was registered at the end of February 2020. During the following months, the cases of COVID-19 followed an ascending slope, affecting all age groups, in various clinical forms.

Children, including infants, are less affected than adults by SARS-CoV-2 infection (2). They usually

Corresponding author:

Andreea Florentina Stoenescu

E-mail: andreeastoenescu0193@gmail.com

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have mild forms of the disease or are asymptomatic. A small percentage of them can develop severe forms with unfavorable evolution and, in some cases, death.

AIM

By presenting this case, we want to highlight the clinical and paraclinical aspects of COVID-19 in infants and the possibility of a lower transmission rate. The informed consent of the patient's legal representatives was obtained.

CASE PRESENTATION

Presenting concerns

We present the case of an 8-month-old male infant from twin pregnancy, confirmed with COVID-19 through SARS-CoV-2 PCR, hospitalized in the "Dr. Victor Babes" Clinical Hospital of Infectious and Tropical Diseases in July 2020. The symptomatology started with nasal obstruction, serous rhinorrhea, rare cough and watery stools, 5 days before hospital admission.

The epidemiological link is known, both the parents and the maternal grandparents of the infant being confirmed with COVID-19. It should be mentioned that the twin sister had a negative SARS-CoV-2 PCR test. From the personal antecedents mentioned, we retained that it is an infant from the twin pregnancy, born prematurely, at 32 weeks having a weight of 1,800 g, artificially fed by gavage from birth for 2 weeks then mixed; he was diagnosed with respiratory distress and hospitalized in the intensive care unit for 2 weeks.

Clinical findings

Clinical examination at hospital revealed a patient with mild general condition, afebrile ($T = 36.7$ degrees), $G = 8,400$ g, with pale skin, intangible superficial ganglion system, discrete hyperemic diffuse pharynx, cardio-respiratory balanced, $SpO_2 = 98\%$ in atmospheric air, mobile abdomen with breathing, intestinal transit present, watery stools, liver and spleen at the costal rib, diuresis present, anterior fontanelle normotensive, no signs of meningeal irritation.

Diagnostic focus and assessment

Biological investigations performed at hospitalization revealed thrombocytosis ($527,000/mm^3$), in-

creased AST (53 IU/dl), discrete biological inflammatory syndrome ($CRP 0.43$ mg/dl). Coprocytological examination was performed, the result of which was within normal limits, and coprocultures were also performed, but with a negative result.

Cardiopulmonary radiography performed at hospitalization did not show the presence of lung lesions.

Therapeutic focus and assessment

The patient received treatment with symptomatic medication (Tasectan) with a favorable evolution, with the improvement of the general condition, remission of watery stools and inflammatory syndrome. On the 8th day of hospitalization, he performed SARS-CoV-2 PCR, from the nasopharyngeal exudate, with a positive result. He was discharged in good general condition after 10 days of hospitalization, cardio-respiratory and digestive balanced.

Presenting concerns of the second patient

Simultaneously with the patient, his twin sister was hospitalized. She presented a fever remitted later under symptomatic treatment, serous rhinorrhea, rare cough and watery stools started 5 days before hospital admission. She performed SARS-CoV-2 PCR, but the result was negative.

Clinical findings

Clinical examination at hospital revealed a patient with mild general condition, afebrile ($T = 36.8$ degrees), $G = 7,500$ g, intangible superficial ganglion system, serous rhinorrhea, rare dry cough, cardio-respiratory balanced, $SpO_2 = 98\%$ in atmospheric air, mobile abdomen with breathing, intestinal transit present, watery stools, liver and spleen at the costal rib, diuresis present, anterior fontanelle normotensive, no signs of meningeal irritation.

Diagnostic focus and assessment

Similar to the twin brother, biological investigations performed at hospitalization showed thrombocytosis ($569,000/mm^3$) and increased AST (51 IU/dl).

Coprocytological examination was also performed, the result of which was within normal limits, and coprocultures were also performed with a negative result.

Cardiopulmonary radiography performed at hospitalization showed a tendency to form a right parahilar condensation alveolar focus.

Based on biological and imaging investigations, the diagnosis of acute pneumonia was established.

Therapeutic focus and assessment

The patient received treatment with antibiotic (Azithromycin) for 5 days, symptomatic medication (Tasectan) with a favorable evolution, with the improvement of the general condition, remission of stools. On days 5 and 9 of hospitalization, she performed SARS-CoV-2 PCR, from the nasopharyngeal exudate, with a negative result. She was discharged in good general condition after 10 days of balanced cardio-respiratory and digestive hospitalization. Also, the possibility that the patient may have been infected with SARS-CoV-2 prior to hospital admission should not be ruled out, and thus the multiple negative results of the PCR-SARS-CoV-2 test could be explained.

Follow-up and monitoring

Both of the twins were monitored by their family doctor.

DISCUSSIONS

Common circulating human coronaviruses can cause between 15 and 35% of acute respiratory tract infections. In hospitalized children, they can be isolated in 4-6% of cases. In the last 2 decades, the 4 circulating species of human coronaviruses have been known as etiological agents of acute upper respiratory tract infections (3).

Acute severe lower respiratory tract infections have been associated with recent zoonotic crosses of coronavirus – SARS-CoV, identified in 2002, and MERS-CoV, identified in 2012. A notable feature of the SARS-CoV epidemic was the paucity of infections in the pediatric population. No deaths were reported in children and adolescents. In particular, children under the age of 13 had milder forms of the disease and minimal residual changes in exercise tolerance and lung function 6 months after healing (4). Previous exposure to other respiratory viruses, including human coronaviruses, the inability to generate a mature immune response during the immune disorder phase, and thus fewer organ damage have been associated with reduced mortality and morbidity (5). During the MERS-CoV epidemic, the incidence of the disease in children was 1%. Out of a

total of 858 deaths, 2 deaths were recorded in children, both in patients with comorbidities (infantile nephrotic syndrome and cystic fibrosis) (6).

There are several theories regarding the low prevalence of SARS-CoV-2 infection in infants and newborns:

Angiotensin II conversion enzyme (SARS-CoV-2 receptor)

It is present in large quantities in alveolar epithelial cells and small intestine enterocytes in adults. ACE2 tissue distribution may be different in infants and newborns, and its maturity and function may be lower. If the maturity of ACE2 in children is low, it cannot function properly as a receptor for SARS-CoV2, and the intracellular response induced by ACE2 in children's alveolar epithelial cells is lower than in adults (7,8,9). Both of the patients presented are infants so it is possible that the distribution of the ACE2 to be lower. This could explain the presence of mild forms of the disease.

Fetal hemoglobin

Viral proteins (orf1ab, ORF10, and ORF3a) attack the heme group in the beta1 chain of hemoglobin (Hb) to dissociate iron to form porphyrin (10). Thus, Hb is reduced –hypoxia and the metabolic pathway of heme is inhibited. Newborns have up to 80% fetal Hb, consisting of Alpha and Gamma chains, which could have a protective role (11). This theory, however, does not explain the low incidence of severe forms in older children, where fetal Hb disappears. The waning period of HbF is between 5 and 6 months (12). The twins were 8 months old, and probably the fetal Hb was disappeared at their age.

Cross-immunity with other viral agents

On average, children under the age of 6 may have 8-12 acute upper respiratory tract infections (URTI) episodes/year compared to adolescents and adults with an average of 2-4 URTI/year (13). Immunity acquired from contact with other viruses, including common circulating coronaviruses, may have a protective role in the pediatric population. A study that investigated the presence of cross-immunity acquired from previous viral infections showed that patients confirmed with adenovirus developed immunity against adenovirus, rhinovirus, influenza, coronavi-

rus, enterovirus (14). The lower severity in infants compared to young children could be explained by the initial dependence of humoral immunity on maternal immunoglobulins.

Cytokine storm

The immune system is developing in infants and newborns, not being able to cause a cytokine storm similar to that of adults (15). Observational studies have shown that the number of lymphocytes in the peripheral blood decreases during the inflammatory phase in adults and allows viral proliferation. In children, the number of lymphocytes is generally normal, which may refer to the incomplete development of natural immunity (16). None of the twins had leukopenia.

More efficient T lymphocytes

The young immune system and T lymphocytes could induce a superior response against

SARS-CoV-2. T cell subsets undergo dynamic changes between childhood and adolescence, in particular by decreasing regulatory T cells and increasing the number of memory cells (17).

Also, according to Otto et al., those who received the combined diphtheria-tetanus-pertussis, *Haemophilus influenzae* type B (HIB), and polio vaccine at 3 months of age had a significantly lower number of symptomatic infections compared to the partially or delayed immunized population, probably due to non-specific improvement in immunological activity (via IL2) (18). In our case, both of the twins were vaccinated.

CONCLUSIONS

SARS-CoV-2 infection may be asymptomatic, especially in infants and newborns, but may also be lower in prevalence.

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