

COVID-19 in a Down Syndrome Newborn

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Abstract

A 36-week premature newborn with trisomy 21, had a fever, runny nose and mild dyspnea at 27 days old. Parents had flu-like symptoms. He was admitted to intensive care unit (ICU), in isolation with support therapy. His reverse transcription-polymerase chain reaction (RT-PCR) test for coronavirus disease 2019 (COVID-19) was positive. He had leukopenia and lymphopenia and increased C-reactive protein (CRP) levels, associated with mixed and interstitial opacities on chest radiography. Antibiotic therapy was performed with ampicillin and gentamicin for 10 days. He had improvement of symptoms, with worsening of CRP levels. On the 11th day of hospitalization antibiotic therapy was replaced by clarithromycin, which was performed for 5 days, with laboratory improvement after introduction. Chest computed tomography (CT) showed bilateral ground-glass lesions. He had a good recovery and was discharged from hospital with 17 days of hospitalization.

Keywords: Down syndrome; Coronavirus infections; Neonatology

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Introduction

The new coronavirus, known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a ribonucleic acid (RNA) virus and is responsible for causing coronavirus disease 2019 (COVID-19). In children, including newborns, the disease has been presenting as mild or even asymptomatic, probably due to immune system immaturity [1, 2]. Transmission occurs horizontally, by aspiration of droplets or aerosols [3], the possibility of transplacental transmission has been raised [4, 5].

Complications of the new coronavirus are associated with an immune response exacerbation, known as “cytokine storm”, leading to acute respiratory distress syndrome, thromboembolism and multiple organ failure [6, 7]. Systemic inflammatory response syndrome secondary to COVID-19 may also occur in healthy children [8].

Down syndrome or trisomy 21 is a genetic disorder that has been associated with an overactivation of interferon, increased levels of inflammatory cytokines and chronic immune dysregulation, so it could lead to development of a more exacerbated condition when associated with COVID-19 involving a prolonged and intense cytokine storm [9]. Therefore, the objective of the study is to report a case study in a newborn patient with Down syndrome who acquired COVID-19.

Information contained in this work was obtained by reviewing medical records (evolution of health professionals, laboratory results and imaging tests) of a newborn admitted to intensive care unit (ICU) at the end of April 2020, in the city of Belem, Amazon region of Brazil.

Case Report

Birth information

The newborn of this study was 36-week premature and male. He was the fourth pregnancy of 42-year-old mother and 45-year-old father, who had two previous abortions and performed prenatal care without complications. Parents were not related. First trimester morphological ultrasound record showed increased nuchal translucency. He was born by ce-

Table 1. Laboratory Findings

Day of hospitalization	1	4	11	13	16
White blood cells (cells/mm ³)	3,630	5,920	16,030	8,560	8,100
Lymphocytes (cells/mm ³)	1,235	3,196	6,412	4,314	5,589
Neutrophils (cells/mm ³)	2,390	1,885	8,287	3,578	2,025
Platelets (cells/mm ³)	271,000	397,000	576,000	510,000	450,000
C-reactive protein (mg/dL)	19.7	5.6	59.5	12.8	0.9
Urea (mg/dL)				12	12
Creatinine (mg/dL)				0.39	0.35
Aspartate transaminase (mg/dL)				27	26
Alanine aminotransferase (mg/dL)				18	13
D-dimer (ng/dL)				806	552
Bacteria blood culture	Negative		Negative		
Bacteria urine culture	Negative				

sarean section and was premature due to fetal centralization, cried at birth, Apgar score was 8 at 2 min and 9 at 5 min. His head circumference was 33.5 cm, the height was 45.5 cm, and the weight was 2,950 g. On physical examination, he had heart murmur and the following phenotypic characteristics of trisomy 21: small nose with a flattened bridge, a single line across the palm of the hand, epicanthal folds, up-slanting palpebral fissures, short neck and loose joints.

Echocardiogram performed 2 days after birth showed a patent foramen ovale and inter-atrial communication, both without systemic repercussions. Blood typing was A positive. He was discharged at 48 h of life, on the sixth day of life, he developed jaundice (total bilirubin 16.5 mg/dL; high intermediate risk zone) and needed to be readmitted to perform simple phototherapy for 48 h, with improvement of the condition. He was discharged after that. He got confirmation of Down syndrome by karyotype exam when he was 2 months old.

ICU admission data

According to the parents' report, at 26 days old, he presented runny nose and sneezing. His parents also had those symptoms. The newborn has breastfed. At 27 days old, the parents noticed signs of mild respiratory distress and noticed an episode of fever (38.3 °C), which prompted them to take him to the maternity hospital for medical assistance, where he was hospitalized for 17 days. On physical examination, he was dyspneic with subcostal retraction, respiratory rate of 50 breaths per min, heart rate of 170 beats per min, oxygen saturation level of 99% and fever of 38.7 °C. The hypothesis of late neonatal sepsis with pulmonary focus and COVID-19 infection were raised.

He was then admitted to the ICU, in isolation. Precautionary contact, droplets and aerosol precautions were performed. Empirical treatment with ampicillin (300 mg/kg/day intravenous (IV)) and gentamicin (4 mg/kg/day IV) was performed for 10 days. There was no need for ventilatory support.

Laboratory tests showed leukopenia, lymphopenia and

increased C-reactive protein (CRP) levels (leukocytes $3,630 \times 10^3/\mu\text{L}$; lymphocytes $1,235 \times 10^3/\mu\text{L}$; CRP 19.7 mg/dL; respectively) (Table 1).

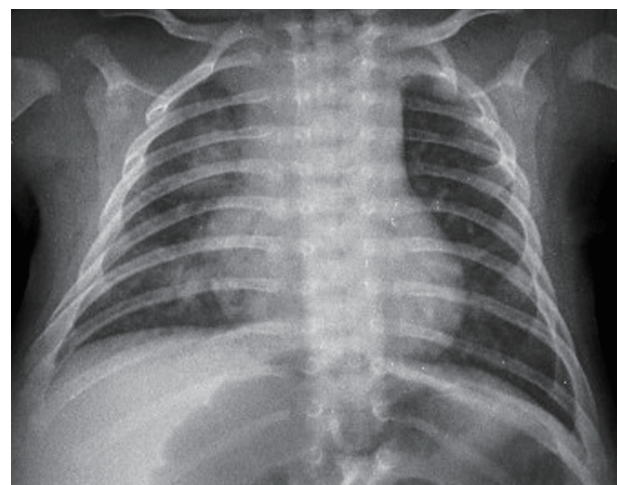
The admission radiological study of chest showed mixed interstitial and alveolar opacities with interstitial aspect scattered throughout the lungs, predominantly in the lower lobe of the right lung (Fig. 1).

He had no bacterial growth in blood culture. Reverse transcription-polymerase chain reaction (RT-PCR) test for COVID-19 in an oropharynx and nasopharynx swab was positive.

Evolution and discharge

He had remission of fever on the fourth day of hospitalization as shown by the thermal curve in Figure 2, as well as remission of respiratory distress. On the fifth day of hospitalization, he had conjunctival injection.

Laboratory controls also showed improvement (the fourth

**Figure 1.** Chest X-ray.

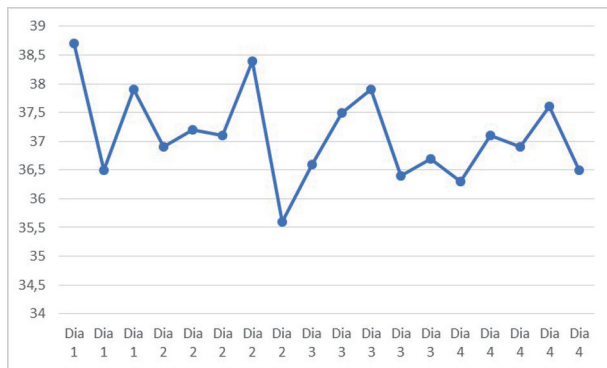


Figure 2. Thermal curve.

day of hospitalization: leukocytes $5,920 \times 10^3/\mu\text{L}$; lymphocytes $3,196 \times 10^3/\mu\text{L}$; CRP 5.6 mg/dL).

On the ninth day of hospitalization, at 38 days old, the infant performed chest computed tomography (CT) which showed diffuse ground glass opacification, superimposed on peribronchovascular and reticular interstitial pulmonary involvement as well as thickening of some interlobular septa. Pulmonary abnormalities were predominantly basal and posterior in distribution, without pleural effusion or mediastinal lymph node enlargement (Fig. 3).

Laboratory controls on the 11th day of hospitalization showed increased result of CRP (59.5 mg/dL), but clinically he was asymptomatic. Antibiotic therapy was then replaced for clarithromycin (15 mg/kg/day IV, for 5 days), with decrease of CRP levels after 5 days (0.9 mg/dL). D-dimer levels were 806 ng/dL and 552 ng/dL on the 13th and 16th day of hospitalization, respectively.

A new blood culture collected on the 11th day of hospitalization was negative and had no bacterial growth again. The therapy with clarithromycin was then suspended on the fifth day of antibiotic. A new echocardiogram was done on the 15th day of hospitalization, with same changes previously described, maintaining normal coronary artery diameter. He was discharged on the 17th day of hospitalization and he has been followed up.

Discussion

We described a case of a Down syndrome newborn patient who developed flu-like syndrome at 26 days of life, probably transmitted by his parents, who also had the same symptoms. He was admitted to an ICU, where he received supportive care and underwent antibiotic therapy with ampicillin and gentamicin. His clinical condition improved. However, there was laboratory worsening during treatment, and antibiotic therapy was replaced for clarithromycin, with a fall in CRP afterwards. He had positive RT-PCR test for COVID-19 and imaging tests highly suggestive of this disease.

Patients with trisomy 21 could have more severe disease due to dysregulation of the immune response [9]. The patient involved in our study presented mild respiratory symptoms and thermal instability with favorable evolution.

Other cases of COVID-19 in newborns have been de-

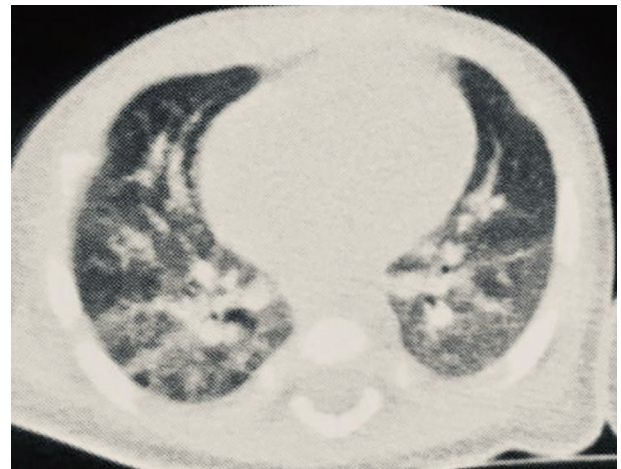


Figure 3. Chest computed tomography.

scribed with often mild presentation. The first case of infection reported was in a 39-week newborn, who was 17 days old when he was admitted to the hospital [10], but no other cases of newborns with Down syndrome were identified in the studied literature. He had sneezing and difficulty breastfeeding a week earlier. His parents had also cough and fever 3 days before admission. The newborn presented fever (37.8 °C), diarrhea and vomiting, without respiratory distress. He had a positive RT-PCR result in anal and oropharyngeal swab.

It was also reported a case of 26-week premature newborn whose mother had flu-like symptoms 1 day after delivery, with confirmation of COVID-19 infection. The newborn had a positive test for this disease at 7 days of life and had leukopenia and lymphopenia. In addition, he had bilateral nonspecific infiltrate in chest radiography performed with 17 days of life [11]. The newborn had no respiratory symptoms or hemodynamic instability because of COVID-19.

In a cohort study with 33 newborns born to mothers with confirmed COVID-19 infection, three of them had the disease, two of which had mild respiratory symptoms and one required non-invasive ventilatory support, but this one also had other risk factors for respiratory distress, such as prematurity and bacterial co-infection [12]. A case report described the clinical course of four newborns infected with COVID-19 whose mothers also had confirmed disease, reported that the main newborn symptoms were fever, respiratory distress and cough, and they needed just support care, without requiring ventilatory support or admission to the ICU [13]. Three of them had increased lung marking in chest CT. Another study involving children of different ages, included three newborns, whose chest CT showed no changes [14].

Chest CT has been used in patients with COVID-19 due to its high sensitivity [15]. Changes in CT tend to be less frequent in children, in addition to have lesser extent compared to adults [16].

We had some research limitation, like not have D-dimer test result at hospital admission and lack of coronavirus test in patient's parents. Further studies are needed to improve understanding of the relationship between COVID-19 infection and Down syndrome.

Conclusions

We reported a case of COVID-19 in a Down syndrome newborn. Transmission occurred horizontally from parents. The symptoms included fever, runny nose and mild dyspnea. He received supportive care associated with antibiotic therapy, without the need of respiratory support. Chest radiography showed mixed interstitial and airspace opacities, and chest CT showed ground glass-opacities. He recovered by the end of this study and was discharged on the 17th day following admission.

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Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

We have obtained informed consent from the patient's guardians of this study.

Author Contributions

ACRL, SMS, DFAS, RSB, BDO, TOCM, AGC, and KCC participated in the management of the patient and gave substantial contributions to this work. AFS contributed to the interpretation of the image results. GCLP wrote the manuscript with support from ACRL, SMS, DFAS, AFS, RSB, BDO and TOCM. AGC and KCC were responsible in supervising the study and all authors revised it critically. Each author has given final approval of the final version of this study.

Data Availability

We declare that any inquiries regarding supporting data availability should be directed to the corresponding author.

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