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COVID-19 IN CHILDREN WITH DOWN SYNDROME- CASE SERIES

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Abstract

Down syndrome (DS) is the most common genetic disease and presents with cognitive impairment, cardiac and gastrointestinal abnormalities, increased risk of hematological malignancy and several autoimmune conditions in addition to other miscellaneous clinical conditions

The aim is to show if the comorbidities that children with Down Sy have, were risk factors for more severe form of COVID-19.

We present three cases of children with Down Sy and COVID-19, with different clinical features. All of them had good clinical outcome, only the first child had more severe form of Covid 19 with need for oxygen support, longer hospitalization but with good clinical improvement and withdrawal of the X-ray changes.

Children with Down Sy are always a high-risk group for more severe and prolonged course of disease, which are partially attributed to defects of the immune system.

Keywords: children, Covid- 19, Down syndrome.

Introduction

Down syndrome (DS) is the most common genetic disease and presents with cognitive impairment, cardiac and gastrointestinal abnormalities, increased risk of hematological malignancy and several autoimmune conditions in addition to other miscellaneous clinical conditions **[**1].

It occurs in 1 in 700 births in the USA, and 1 in 546 birthsin Ireland, which is the highest rate in Europe [2, 3].

They usually have a higher prevalence of respiratory tract infections, immune dysfunction and co-morbidities, leading to poorer clinical outcomes Autoimmune conditions such as hypothyroidism, coeliac disease, arthropathy and type 1 Diabetes mellitus are more prevalent in DS. These chronic inflammatory conditions are as aresult of unchecked and persistent inflammation which can have significant long-term health complications [4].

Children with DS are at increased risk for more severe presentations of COVID-19 because of that efforts should be made to ensure the comprehensive and early detection of COVID-19 in this population.

Chromosome 21 contains multiple genes involved in immune responses, especially four interferons(IFN) receptors; overexpression of these genes may induce an overactive immune system. Another study has found down-expression of *NF-kB1* in cells from DS patients compared to normal subjects [5, 6].

The comorbidities that these children have, including cardiovascular anomalies, obesity, and/or obstructive sleep apnoea [7, 8], are proven to be risk factors for more severe forms of diseases.

The aim is to show if the comorbidities that children with Down Sy have, were risk factors for severe clinical forms of COVID-19.

Case number 1:

In September 2021, a 14year old girl with Down Sy was admitted to our hospital due to fever, cough, myalgia and shortness of breath with likely exposure to a COVID-19 contact. She was tested positive for SARS-CoV-2 on Antigen Rapid Test.

From the anamnesis data Foramen ovale apertum after birth with spontaneous closure, with recurrent respiratory infections. She has regular checkups with endocrinologist because of hypothyroidismon on regular therapy with tab eutirox, with overweight and obstructive sleep apnea (OSA). At admission she was afebrile, pale, with frequent productive cough, dyspneic with low Oxygen saturation 86-89%, tachycardic auscultatory on the lungs with bilateral pneumonic finding.

From Diagnostic findings: with slightly elevated inflammatory markers and liver enzymes, in the blood count leucopenia with neutrophilia , the other biochemical analysis proteinogram, Urea, Creatinin, LDH, Fibrinogen , Troponin CK MB ,CK, IL6, were with normal values.

Haemostasis: Activated Partial Thromboplastin Time (aPTT) and D dimer were elevated.

Chest X-ray: bilateral pericardial areas of consolidation (multifocal opacities) in peripheral and in the lower lobes (figure 1).

Therapy: The patient was treated with carbapenem and oxazolidinone antibiotics, inhaled bronchodilator ,corticosteroids, Remdesivir antiviral medication,Oxygen therapy with facemask,Low Molecular Weight Heparin (LMWH)and intravenous diuretics.

During the hospital stay she was oxygen depended for fourteen days , with difficulties to maintain the facial mask all the time. In the treatment pediatricians and infectiologist were involved. There was slow withdrawal of the the auscultatory lung finding. The control chest Xray showed near complete resolution of the chest x-ray findings which was reached at day 20 from symptom onset(figure 2).She was discharged from hospital after 21 day with corticosteroid , gastroprotective therapy , LMWH, probiotic and vitamins.

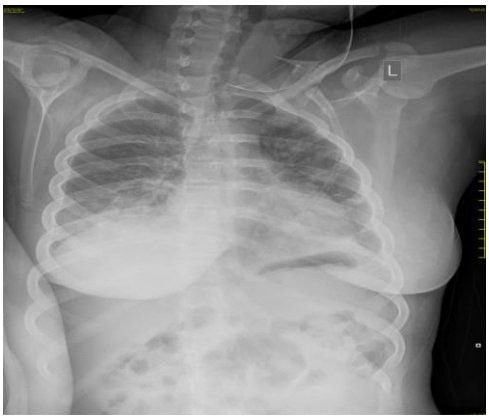

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Figure 1. Chest X-ray, bilateral pericardial areas of consolidation (multifocal opacities) in peripheral and in the lower lobes

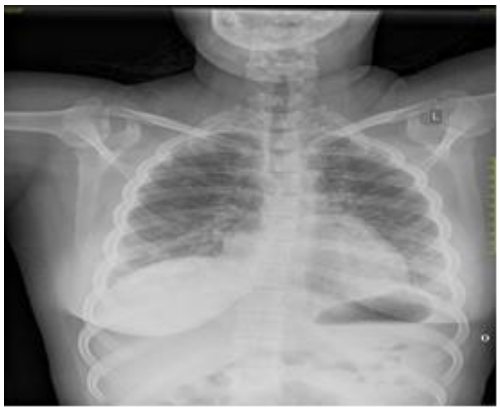

Figure 2. Control Chest X-ray: improvement of the finding.

Case number 2:

In March 2022, a 5 year old boy with Down Sy was admitted to our hospital due to fever, rhinorrhea, vomiting , dehydratation, cough,tested positive for SARS-CoV-2 on Antigen Rapid Test.

From the anamnestic data, child with Down Syndrome, with amaurosis,congenital glaucoma treated with surgery at age of two , hospitalisation in University Clinic for Infectious Diseases and Febrile Conditions with varicella at two years of age, with reccurent respiratory infections

At admission he was subfebrile, pale with moderate dehydration, dry buccal mucous membranes, tachycardia, sunken eyes, hypotonic auscultatory on the lungs with pneumonic finding Palpation revealed that abdomen was soft and painless in all areas.

Diagnostic findings: with slightly elevated inflammatory markers, in the blood count leucopenia with neutrophilia , blood gases (ABG) was suggestive of metabolic acidosis at admission the other biochemical analysis liver enzymes proteinogram, Urea, Creatinin, LDH , Ferritin , were with normal values. **Blood Culture**s were negative. **Hemostasis** showed activated Partial Thromboplastin Time(aPTT) slightly elevated and D dimer= 618.

Chest X-ray finding : patchy areas of consolidation in right pericardial area (figure 3).

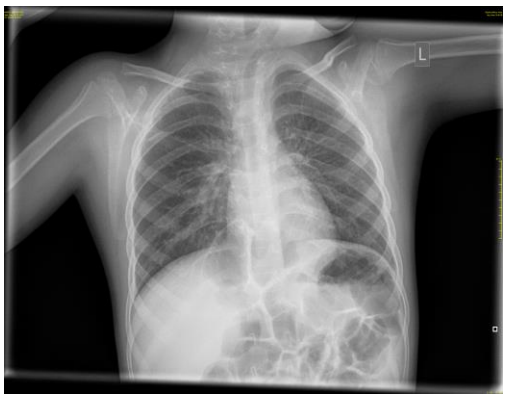

Figure 3. Chest X-ray, patchy areas of consolidation in right pericardial area

Therapy: Treatment was started with intravenous (IV)fluid, antibiotics (cefotaxime and azithromycin) and inhaled bronchodilator. There was withdrawal of the auscultatory lung finding during the10 days of hospital stay.

Case number 3:

In March 2022, a 6 year old boy with Down Sy was admitted to our hospital due to fever, laryngitis with hoarseness, dry cough, dehydratation, tested positive for SARS-CoV-2 on Antigen Rapid Test

From the anamnestic data, child with Down Syndrome, with Type 1 insulin-dependent, diabetes mellitus (Type 1 DM) diagnosed at age of 5. One hospitalisation in Institute for Respiratory Disease in children-Kozle at one year of age with pneumonia, with reccurent respiratory infections

At admission febrile, pale, dehydrated with hoarseness, dry laryngeal cough, tachycardia, auscultatory on the lungs vesicular breathing with bubbly crackles.

Diagnostic findings: complete blood count was with normal values, slightly elevated CRP on admission 15,3mg/l. Blood gases (ABG) were suggestive of compensatory metabolic acidosis, urine with ketonuria and glycosuria, following blood sugar values

Hepatal enzymes, Creatinin,and LDH were normkal, , glucose level was variable from 2,8 to mmol/l. **Haemostasis showed** elevated D dimer – 1029.

Chest X-ray: patchy areas of consolidation in right lower lung zones (figure 4).

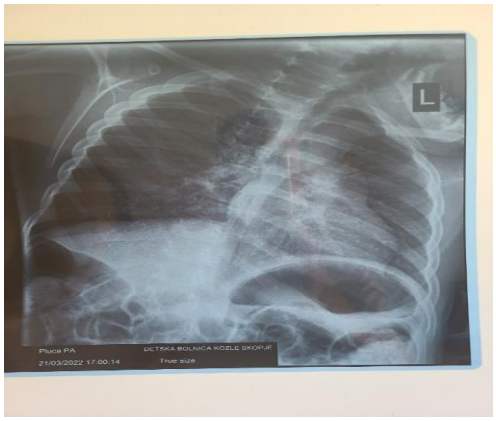

Figure 4. Chest X-ray , patchy areas of consolidation in right lower lung zones

Therapy: Treatment was started with intravenous (IV)fluid, antibiotics (cefotaxime) and topic corticosteroids and the regular insulin therapy with Fiasp (fast-acting insulin) and Tresiba (long-acting insulin). There was withdrawal of the auscultatory lung finding and laryngeal cough during the8 days of hospitalstay.

Discussion

Unlike in the adult population, limited data are available on children with DS and COVID-19. Risk factors for a severe course of COVID-19 are also well-documented for the adult population with [9] and without DS [10,11], but less so for the paediatric population.

In a period from September 2021 until July 2022 in our hospital were admitted over 390 pediatric patients with Covid 19.

During that period we had three children with Down Sy. Each of them had different clinical path of the disease and comorbidities.

The first child with Down Sy was overweight, with hypothyroidism and sleep apnea had the most severe course of disease, while the second child who had diabetes type 1 and the third child which had impared vision and congenital glaucoma, had milder form of Covid 19 infection.

The first child was admitted to our hospital in September 2021 in the period when the Delta variant of SARS Cov2 was dominant variant circulating globally, which was responsible for more severe cases and deaths worldwide. The other two children were admitted in hospital in March 2022 in the period when the Omicron variant dominated and like the other pediatrics patients in that period they had milder course of the disease.

Krishnan et al. reported three patients with Down syndrome, pulmonary hypertension, congenital heart disease, and COVID-19. They were 3, 21, and 25 years old, respectively. Interestingly, two of these patients had a history of repeated viral infections and presented with a mild clinical course of the disease, whereas one patient with no history of common viral infections had a more severe and prolonged course of the infection [12].

From our experience, these three children with Down Sy had good clinical outcome during the Covid 19 pandemics, only the first child had more severe form of Covid 19 with need for oxygen support, longer hospitalization but with good clinical improvement and withdrawal of the X-ray changes.

Conclusion

Children with Down Sy are always a high risk group for more severe and prolonged course of disease, which are partiallyattributed to defects of the immune system. Various medical and anatomical comorbidities commonly associated with Down Sy increase the susceptibility to infections and might also affect the immuneresponses.

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