

PRIKAZ SLUČAJA – CASE REPORT

Covid 19 Pneumonia and Immunodeficiency in an Adolescent

Adolescentkinja sa COVID19 pneumonijom i imunodeficijencijom

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Summary

Covid 19 infection in children in most cases is asymptomatic or children develop a milder disease. Most evidence suggests that children have a lower incidence of severe acute respiratory syndrome due to coronavirus 2 infections (SARS-CoV-2). We represent a case report of COVID-19 infection in a previously healthy, 17-year-old girl, with pneumonia, fever over 38°C and hypoxia. Obesity was a risk factor for the more severe clinical course in this case. Due to the prolonged elevated temperature, hyposaturation and consequently the long-term need for oxygen support, an additional examination was performed, and hypogammaglobulinemia was diagnosed. This patient had one of the highest CT scores recorded, 19 out of 25. In addition to oxygen supplementation and systemic corticosteroids, the adolescent also received immunoglobulin replacement therapy. The patient recovered and was released from the hospital on the 23rd day in order to continue the treatment of the newly discovered hypogammaglobulinemia in the regional health center.

Key words : Covid 19, pneumonia, adolescent, immunodeficiency.

Sažetak

Covid 19 infekcija kod dece u većini slučajeva je asimptomatska ili deca razviju blažu kliničku sliku. Većina dokaza sugeriše da deca imaju nižu incidencu razvoja teškog akutnog respiratornog sindroma usled infekcija virusom korona 2 (SARS-CoV-2). Ovo je prikaz slučaja težeg oblika COVID-19 infekcije kod ranije zdrave, 17-godišnje devojke, sa upalom pluća, temperaturom preko 38°C i hipoksijom. Gojaznost je bila faktor rizika za teži klinički tok bolesti. S obzirom na produženu povišenu temperaturu, hiposaturaciju i posledično dugotrajnu potrebu sa kiseoničnom potporom, izvršeno je dopunsko ispitivanje, te dijagnostikovana hipogamaglobulinemija. Ova pacijentkinja je imala jedan od najviših CT skorova, 19 od 25. Pored suplementacije kiseonikom, sistemske primene kortikosteroida, kod adolescentkinje je primenjena i supstituciona terapija imunoglobulinima. Pacijentkinja se oporavila i otpuštena je 23. dana iz bolnice radi nastavka lečenja novootkrivene hipogamaglobulinemije u regionalnom zdravstvenom centru.

Ključne reči: Kovid 19, pneumonija, adolescenti, imunodeficijencije

We present a case of 17 years old girl, transferred from the regional General Hospital, with symptoms of lower respiratory tract infection due to Covid19 infection.

The illness began seven days before admission to our hospital, with fever over 38.5°C and mild symptoms of the upper respiratory tract. On the fourth day from the beginning of the disease, she was examined in the pediatric office, the Ag test SARS COV 2 was positive, and the radiography of the lungs done with an undefined finding. On the seventh day of the disease, still febrile up to 38°C and therefore the radiography was repeated with the following finding - emphasized interstitial pattern, reduced basal transparency. Due to the prolonged fever and radiographic findings, the patient is referred to our hospital for further treatment. During the transfer by ambulance, she was stable, normal vital parameters, normal body temperature, without the need for added oxygen and without any other problems. She

states that on one occasion she noticed a small amount of fresh blood when she coughed.

At admission to our hospital, her body weight was 101kg, height 168cm, BMI 35.8. Her clinical presentation was: conscious, afebrile, eupnoic, acyanotic, without signs of respiratory distress, Sat Hb 02-97% on room air, rhythmic heart action, clear tones, no rumbles, SF 96 / min.

Her general condition was good upon arrival, denies weakness, does not sweat, rarely coughs, denies pain when breathing and denies increased nose secretion and nosebleeds. She denies chest pain and fatigue or abdominal pain. Denies urinary problems or painful joints and muscles. She sleeps well, has no headaches, dizziness and fainting, has not lost consciousness, sees well and hears well.

Personal history reported no diseases of importance. There are few data on the earlier treatment of anemia. In telephone contact with the mother, it was stated that she had been receiving cephalosporin for two weeks before this

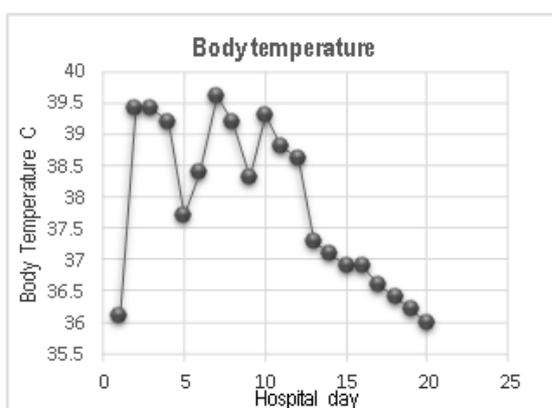
disease due to tooth swelling. On the tenth day during that therapy, she had a rash on her body. She continued on the oral antibiotic and had no new side effects.

The family history is in order with no important diseases. The parents did not state possible contact with a covid 19 positive person.

Sociological and epidemiological anamnesis were in order. The first four days the patient was febrile with a body temperature over 38C, then the fifth day subfebrile and further until the 10th day of hospitalization febrile over 38C, the 11th and 12th day subfebrile and the other days until discharge afebrile.

Graph 1. Dynamics of the body temperature

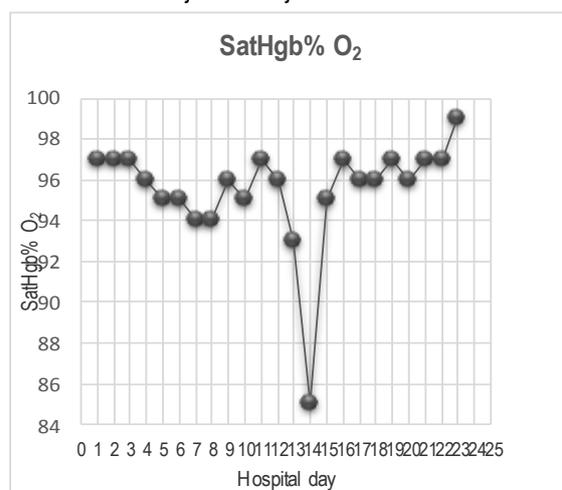
Grafikon 1. Kretanje povišene temperature



From the fourth day of hospitalization, a decrease in saturation begins, and from the fifth day, oxygen was introduced, through nasal cannulas and / or masks, starting from two liters to a maximum of 8 l / min. She maintained on oxygen therapy until the 20th day of hospitalization.

Graph 2. Dynamics of oxygen saturation.

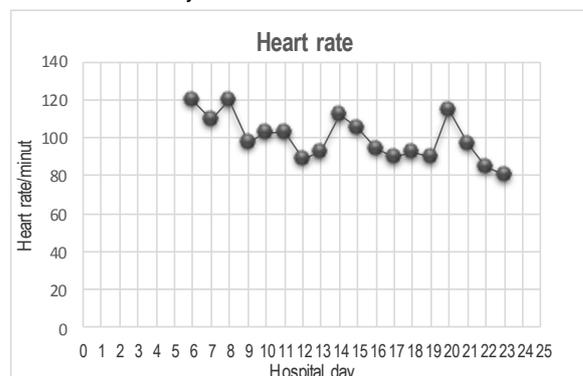
Grafikon 2. Kretanje saturacije Hb kiseonikom



Heart rate and respiration rate are shown on graphs 3 and 4.

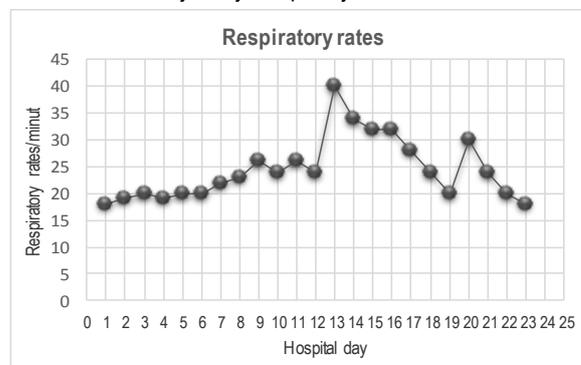
Graph 3. Dynamics of the heart rate.

Grafikon 3. Kretanje srčane frekvence



Graph 4. Dynamics of respiratory rate.

Grafikon 4. Kretanje broja respiracija



On the sixth day of hospitalization, chest MSCT was performed, without contrast application:

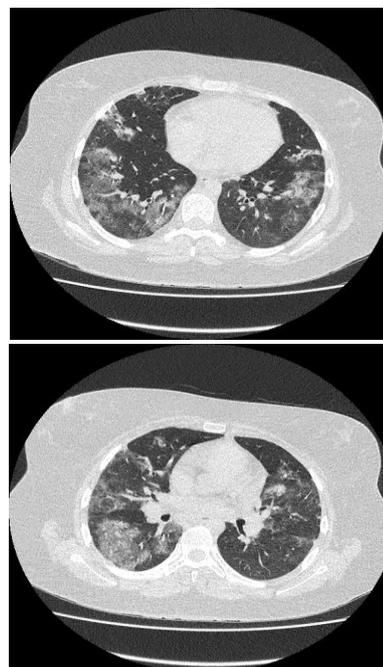


Figure 1 Chest computerised tomography

Slika 1. Kompjuterizovana tomografija grudnog koša

In the lung parenchyma, zones of altered parenchyma, the “ground glass” and “crazy paving” on both sides with some small consolidation zones. There was no significant mediastinal lymphadenopathy or pleural effusions. Conclusion - Bilateral interstitial pneumonia. Total MSCT severity score – was 19 points out of a maximum of 25, MSCT findings first corresponds to the peak with initial regression. (Figure 1)

Bilateral interstitial pneumonia. Total MSCT severity score – was 19 points out of a maximum of 25, MSCT findings first corresponds to the peak with initial regression

On the eighth day of hospitalization, fever was maintained, the need for additional oxygen was increased, the Hb O2 saturation was repeatedly below 90%, and a control X-ray of the lungs and heart was performed - findings shadows of inflammatory genesis are observed on both sides, with slightly reduced transparency in the projection of the left cf sinus - Hilus shadows partially in summation with the described inflammatory changes. Tent adhesions on the right hemidiaphragm, costo-frenic sinuses without X-ray signs for larger pleural effusions. Heart shadow corresponds to age. (Figure 2)



Figure 2. Chest X ray 8th day of hospitalization- Bilateral interstitial pneumonia

Slika 2. Radiografija grudnog koša osmog dana hospitalizacije - bilateralna intersticijalna pneumonija

On the 19th day of hospitalization, a control MSCT of the chest was performed, findings - in the lung parenchyma there are zones of “fibrous bands” at the site of previous consolidations, as well as zones of opacification of residual ground glass findings, but compared to the previous examination inflammatory zones are larger in size, especially apically on both sides, which is in favor of the fact that inflammatory changes occurred in different time periods. Discrete pneumomediastinum. Lymph nodes up to 12 mm was detected in mediastinum. (Figure 3).

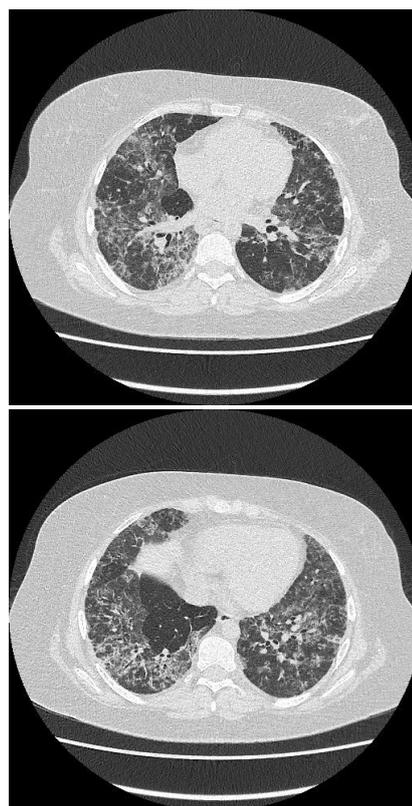


Figure 3. Second MSCT 19th day of hospitalization - chest-zones of “fibrous bands” at the site of previous consolidations, as well as zones of opacification of residual ground glass findings

Slika 3. Ponovljen MSCT 19.dana hospitalizacije – “ground glass” i rezidualne fibrozne trake

Arterial blood pressure was measured and maintained in the upper values of normal, cardiac biomarkers were in normal ranges and the laboratory parameters of the metabolic syndrome were in order.

Table 1. Values of relevant laboratory parameters

Tabela 1. Relevantni laboratorijski parametri

Dani hospitalizacije	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23		
Leukociti ($10^9/L$)	5.8			4		3.8		5.8		6.7		5.4				9.40								11	
Neutrofili (%)	51			62		62		67		72		74				65									69
Limfociti (%)	42			31		30		27		22		19				25									22
Monociti (%)				3.6		6.2		3.7		4.2		4.6				5.3									6.5
C-reaktivan protein (mg/L)	19			49		21		56		46		75				5.6									1.3
Prokalcitonin (ng/ml)						0		0		0		0.1				3.7									
Feritin (ng/ml)						227		431		408		394				215									
IL-6 (pg/ml)						6.5		42		89		9.6				3.7									
D-dimer (mg/L)	0.2					0.7		1.1				2.2				1.4									

Additional laboratory analyzes performed on day 11th showed the following values for immunoglobulins and their subclasses: IgA <0.10 (g/L), IgM 0.21 (g/L), IgG 2.6 (g/L).

Serum immunoglobulin subclasses:

IgG 1.57 (5.52-16.31), IgG1 1.61 (4.05-10.11), IgG2 0.10 (1.69-7.86), IgG3 0.01 (0.11-0.85), IgG4 0.003 (0.03-2.93), IgM 0.16 (0.33-2.93), IgA < 0.05 (0.65-4.21).

Immunoglobulin values after intravenous immunoglobulins: IgA <0.10 (g/L), IgM 0.22 (g/L), IgG 3.1 (g/L)

Treatment consisted of parenteral antimicrobial therapy (ceftriaxone), peroral antimicrobial therapy (levofloxacin), systemic corticosteroid therapy, gastroprotective therapy (pantoprazole), multivitamin therapy, symptomatic, supportive and physical supportive therapy.

Due to prolonged high fever and deterioration of condition, on the eighth day, the antimicrobial therapy was switched to vancomycin and meropenem for the next 10 days.

On the sixth day of hospitalization, anticoagulant therapy (fraxiparin) was started due to the increase in the value of d-dimer. (Table 2).

Table 2. Treatment during her hospital stay

Tabela 2. Terapija sprovedena tokom hospitalizacije

Dani hospitalizacije	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	
Ceftriakson	*****																							
Levofloksacin	*****																							
Vancomicin								*****																
Meropenem								*****																
Antipiretik	*****																							
Pantoprazol	*****																							
Deksametazon					*****																			
Metilprednizolon					*****																			
Prednizon																								
Budesonid																								
Fraksiparin																								
Imunoglobulini																								
Kiseonik	*****																							

During hospital stay the adolescent was hemodynamically stable, but with pronounced fatigue and malaise. Worsening of the respiratory symptoms with dry cough, dyspnea, increased respiratory rate and hypoxia, demand the additional oxygen therapy up to 8 l / min by facial mask. Girl recovered slowly, the last three days of hospitalization without the need for additional oxygen. After 23 days of hospital treatment patient was sent to the regional health center where she was previously monitored by a hematologist, due to anemia, and for further diagnosis and monitoring of newly detected hypogammaglobulinemia. Risk factors in this adolescent for the development of a more severe clinical course and prolonged course of the disease were severe obesity, metabolic syndrome and immunodeficiency.

Studies show that the prevalence of obesity raised since the 1990s, with the characteristics of an epidemic, both in adults and children. (1) Metabolic syndrome, as defined by the International Diabetes Federation (IDF) (2,3) is a set of factors: obesity, dyslipidemia, hypertension, high blood sugar, a set of elements that lead to development of type 2 diabetes and cardiovascular disease. Patients with metabolic syndrome are thought to have a persistent,

chronic state of inflammation (4) with discretely elevated values of acute inflammatory reactants - levels of c-reactive protein, ferritin and fibrinogen and rise in indicators of endothelial dysfunction, both found in covid19 infection and acute respiratory distress.(5) Increased inflammatory response in patients with metabolic syndrome, is very likely to be further enhanced in the presence of Sars-CoV-2 virus and gives a longer, more severe and more complicated clinical course. (6,7) A more severe clinical course may also occur in obese adolescents, although there is no laboratory evidence or developed comorbidities at this time, but there is certainly a subclinical enhanced inflammatory condition. (8) A study by Denson JL et al. on 5069 patients with COVID19 infection and metabolic syndrome, showed that there is an increased risk of developing acute respiratory distress, severe disease and death in these patients. And, the severity of the clinical course increases with each present criteria for metabolic syndrome. (9)

Since the onset of the pandemic, early studies have indicated that combined and / or individual diabetes, obesity, and hypertension lead to a more severe form of COVID19 disease, from mechanisms that are still poorly understood. (10, 11)

Both risk factors were important in the complicated clinical course and prolonged treatment of the adolescent with COVID19. (12, 13)

The diagnosis of hypogammaglobulinemia is most likely secondary, our patient did not present with recurrent episodes of respiratory infections or any other infections.(14) Extremely low values have not significantly improved after the administration of immunoglobulin substitution therapy, which may be an introduction to a form described as late-onset immunodeficiency.

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