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SARS-CoV-2 attacks the weakest point - COVID-19 course in a pediatric patient with Friedreich's ataxia

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ABSTRACT

COVID-19 pandemic is the biggest epidemiologic problem of the 21st century. A severe course of SARS-CoV-2 infection in children is rare. Sometimes, especially in patients with chronic disease, COVID-19 may be insidious and life-threatening. This article presents the course of COVID-19 in a 17-year-old boy with Friedreich's ataxia-induced hypertrophic cardiomyopathy. Although, the main symptoms of COVID-19 (i.e., fever, cough) were moderate at the beginning of the illness, the patient's condition deteriorated rapidly due to cardiac problems, atrial fibrillation, and heart failure. The patient required antiarrhythmic treatment and pharmacological and electrical cardioversion. Moreover, because of pneumonia requiring supplemental oxygen, remdesivir and convalescent plasma therapy was given to the patient., The administration of the antiviral treatment was crucial to the patient's recovery.

Introduction

The most common symptoms of SARS-CoV-2 infection in children are fever, cough, and pharyngitis (Mania et al., 2021). The severe course of COVID-19 infection in children (4–5%) (Cui et al., 2021) mainly affects patients with chronic diseases (Gallo et al., 2021), especially cardiovascular, respiratory, and neurologic disorders (Tsabouri et al., 2021). The virus entry point into the cell is angiotensin-converting enzyme 2 (ACE2). The tissues with the highest expression of the receptor may be more susceptible to damage (Muus C et al., 2021). The infection may lead to the progression of neurodegenerative changes and dysfunction of the heart muscle (Zareef et al., 2020). The current treatment of COVID-19 includes, among other medications, remdesivir (Shi et al., 2020) and convalescent plasma therapy (Małecki et al., 2021). Friedreich's ataxia (FA), an autosomal recessive neurodegenerative disease, is the most commonly inherited ataxia. In 98% of the cases, the disease is caused by a dynamic mutation in the frataxin gene. Lowering the concentration of this protein leads to iron accumulation in the mitochondria, and consequently, to cell damage. Typically, symptoms appear between the ages of 8 and 15 years. In the course of the disease, degeneration occurs within the spinal-cerebellar tracts, posterior cords of the spinal cord, and the pyramidal pathways and cerebellum. The most common symptoms are ataxia and dysarthria. Limb weakness progresses, resulting in paresis and, subsequently, paralysis. Approximately 90% of the patients develop cardiomyopathy (most often hypertrophic). The causal treatment is unknown (Pandolfo, 2008).

Case report

The case presented is a 17-year-old boy with hypertrophic cardiomyopathy (HCM) due to FA. One year before his admission to the hospital accelerated ventricular rhythm episodes were recorded during the Holter monitoring (Table 1). From then on, the patient was prescribed metoprolol (47.45 mg daily). The patient had other symptoms characteristic of FA: limb ataxia, dysarthria, and paresis of the lower and upper limbs. The patient had gener-

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Table 1
Markers of myocardial damage, electrocardiography, echocardiography, Holter ECG, and treatment in the following periods of hospitalization

Time	Troponin I* BNP**	ECG or Holter ECG	Echo	Treatment
1 year before admission	troponin I <9 ng/l BNP 119 pg/ml	ECG: sinus rhythm, HR 86 bpm, normal axis; Holter ECG: 2% of single VPBs	massive LVH, IVS 1.4 cm, LVPW 1.6 cm, no LVOTO, LVEF 75%,	metoprolol (47.5 mg q.d.)
1st day	troponin I 926.9 ng/l BNP 184.9 pg/ml	ECG: sinus rhythm, HR 105 bpm, normal axis PQ 110 ms, QRS 80 ms, QTc 393 ms, LVH, repolarization abnormalities (negative T waves in leads I, II, III, aVF, V4-V6, positive T in aVR)	massive LVH, IVS 1.4 cm, LVPW 1.6 cm, LVEF 50%, minimal fluid in the pericardial sac	as above and: ceftriaxone (2000 mg q.d.) dexamethasone (3 mg t.i.d.) enoxaparin (20 mg q.d.)
2nd day	troponin I 1184.3 ng/l BNP not done	ECG: sinus rhythm, HR 120 bpm, LVH, repolarization abnormalities	not done	as above
4th day	troponin I 322.7 ng/l BNP 583.9 pg/ml	ECG: atrial fibrillation, HR 140-190 bpm	massive LVH, LVEF 40%, minimal fluid in the pericardial sac	as above and: metoprolol (71.25 mg q.d.) amiodarone (200 mg b.i.d.) electrical cardioversion- 2 trials
5th day	troponin I 801.4 ng/l BNP 643.1 pg/ml	ECG: short-term episode of atrial fibrillation which resolved spontaneously	as above	as above and: remdesivir – 200 mg q.d. (100 mg q.d. in 4 consecutive days) convalescent plasma -1unit 200 ml
17th day	troponin I 37.6 ng/l BNP 63.7 pg/ml	ECG: sinus rhythm, HR 75 bpm, normal axis, PQ 140 ms, QRS 90 ms, QTc 450-460 ms, negative T waves in inferolateral leads; Holter ECG: 3/24h VPBs, 18/24h SVPBs	IVS 1.4 cm, LVPW 1.7 cm LVESD 2.4 cm, LVEDD 3.6 cm, LVEF 75%	as above and: amiodarone dose reduction (200 mg q.d.)

Abbreviations: b.i.d. (lat. bis in die) – twice a day; BNP – brain natriuretic peptide; bpm-beats per minute; ECG – electrocardiography; Echo – echocardiography; HR – heart rate; IVS – intraventricular septum; LVEDD – left ventricular end-diastolic diameter; LVEF – left ventricular ejection fraction; LVESD – left ventricular end-systolic diameter; LVH – left ventricular hypertrophy; LVOTO – Left Ventricular Outflow Tract Obstruction; LVPW – left ventricle posterior wall; q.d. (lat. quaque die) – once a day; SVPBs – supraventricular premature beats; t.i.d. (lat. ter in die) – 3 times a day; VPBs – ventricular premature beats.

* Troponin I – the reference range <9 ng/l;

** BNP - the reference range <100 ng/l.

alized muscle atrophy, was underweight (body mass index [BMI] 15.4, z-score - 3.3), visible scoliosis, and contractures of the lower limbs. The first symptoms of infection in this patient were dry cough and fever (38.5°C). The patient received azithromycin and supportive treatment. SARS-CoV-2 infection was confirmed by a PCR test. Because of progressive weakness, the patient was referred to the hospital. The fever and intensive cough were resolved by the time of admission to the hospital. The patient's oxygen saturation (SpO_2) was above 96%, whereas the heart rate remained at the level of 70–100/min. The alveolar murmur over the lung fields was muffled, with no additional sounds. The patient's heart rate was stable. His capillary refill time was extended to 3 seconds, but his other vital parameters were normal (blood pressure [BP] 103/67 mmHg; heart rate [HR] 90/min; SpO_2 96–97%). Laboratory tests found erythrocytosis ($6.57 \times 10^6/\mu l$; reference range: $4.5\text{-}5.5 \times 10^6/\mu l$), thrombocytopenia ($119 \times 10^3/\mu l$; reference range: $150\text{–}400 \times 10^3/\mu l$), elevated levels of troponin I (926.9 ng/l; upper limit of normal (ULN): <9 ng/l), and brain natriuretic peptide (BNP) 184.9 pg/ml; ULN:<100 ng/l). Inflammatory, gasometric analysis, coagulation and other biochemical parameters, and electrolyte concentrations, remained in the reference range. The patient's chest x-ray did not show consolidation or pneumonic infiltrates. The electrocardiography (ECG) revealed left ventricular (LV) hypertrophy with secondary repolarization abnormalities (Table 1). Massive LV hypertrophy was confirmed by echocardiography; LV ejection fraction was 50%. We started administering ceftriaxone, dexamethasone, and enoxaparin (Table 1). On the third day of hospitalization, oxygen therapy was started (4 l/min) because of the decrease in SpO_2 to 92%. The next day, during the oxygen withdrawal test, the saturation was 85%. Chest computed tomography (CT) revealed bilateral ground-glass opacification with the parenchymal densities consistent with viral pneumonia. The patient developed tachycardia: HR 180/min (BP 80/50 mmHg). ECG showed atrial fibrillation (AF). An attempt at pharmacological cardioversion (amiodarone 200 mg iv) and 2 attempts at electrical cardioversion were unsuccessful. The metoprolol dose was increased by 25 mg. Shortly after drug administration the rhythm became moderate (HR 135/min; BP 107/76 mmHg). On day 5, there was a short episode of AF with hypotension (BP 88/42 mmHg). The episode was resolved by itself. The parameters of myocardial damage were still significantly elevated (troponin I 801.4 ng/l and BNP 643.1 pg/ml). Because of the severe course of the infection, pneumonia, and decreased SpO_2, the patient received remdesivir (200 mg) and convalescent plasma (anti-SARS-CoV-2 titer 1:600; 1 unit-200 ml). The patient clinical condition improved during the subsequent days, and his muscular strength returned to the pre-infection state. Treatment with remdesivir was continued for the next 4 days (100 mg daily). No further cardiac episodes were observed. Myocardial injury parameters normalized. Lung ultrasound showed a reduction in the severity of inflammatory lesions. During the patient's hospitalization, no negative results of the SARS-CoV-2 PCR test were obtained. The patient was discharged home on day 17 of hospitalization. The echocardiogram performed 1 month later did not reveal any intensification of cardiomyopathy after SARS-CoV-2 infection. We did not observe any apparent psychological and cognitive sequelae of the COVID-19 in the patient.

Discussion

Our patient presented typical symptoms during the first phase of COVID-19 infection, which were fever and cough. Apart from elevated troponin I and BNP levels, we found minor deviations in laboratory tests with no common abnormalities like leukopenia. CT revealed bilateral ground-glass opacification with the parenchymal densities consistent with viral pneumonia. The presented case, except for significantly increased myocardial damage parameters and

ECG changes, could appear like a typical course of COVID-19 (Cui X et al., 2021). The patient with FA belonged to the risk group of severe courses of COVID-19 because of the cardiomyopathy with the history of arrhythmia episodes. During the COVID-19 infection, the patient's initially stable general condition collapsed sharply. Atrial fibrillation (AF) is a commonly reported complication of HCM (Olivotto et al., 2001) and myocarditis (Canter CE et al., 2014). Arrhythmias, associated with an increase in mortality, are a common occurrence in COVID-19 infections also in patients with no such previous episodes (Coromilas et al., 2021). AF is significantly associated with an increased risk of unfavorable outcomes among patients with COVID-19 (Yang H et al., 2021). The findings of our patient were similar to that described in the case report of fatal SARS-CoV-2 infection in an 18-year-old girl with type 2 diabetes, metabolic syndrome, and hypertrophic cardiomyopathy (Simpson et al., 2020). Rapid deterioration of health in both young patients could be related to the increased ACE2 expression in the heart muscle that occurs in patients with hypertrophic cardiomyopathy. This mechanism may increase viral replication (Bos et al., 2020) and myocardial damage. The role of iron deposits in the mitochondria present in FA (Pandolfo, 2008) and consequently the intensification of oxidative stress remains an open question. During the COVID-19 infection in our patient, pharmacological and electrical cardioversion did not result in immediate rhythm control. The administration of available antiviral drugs: remdesivir, and convalescent plasma, had a significant effect on stabilizing the patient's condition. It is possible that controlling viral replication may be crucial to the functioning of the heart.

Conclusion

During SARS-CoV-2 infection, the organs affected by the chronic disease process are most susceptible to damage. COVID-19 in children with FA-induced hypertrophic cardiomyopathy can induce AF and heart failure. Rapid administration of available anti-SARS-CoV-2 agents: remdesivir and convalescent plasma therapy are essential for a good prognosis in COVID-19 cases.

The authors declare no conflict of interests.

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