UDC 616.98:578.834:616.379-008.64]-036.1-07-08

R.V. Tkachuk, O.K. Koloskova, M.N. Garas, T.M. Bilous, L.I. Romanchuk

Combined course of acute respiratory coronavirus disease in a child with type 1 diabetes: a clinical case

Bukovinian State Medical University, Chernivtsi, Ukraine

Modern Pediatrics. Ukraine. (2022). 6(126): 88-91. doi 10.15574/SP.2022.126.88

For citation: Tkachuk RV, Koloskova OK, Garas MN, Bilous TM, Romanchuk LI. (2022). Combined course of acute respiratory coronavirus disease in a child with type 1 diabetes: a clinical case.
Modern Pediatrics. Ukraine. 6(126): 88-91. doi 10.15574/SP.2022.126.88.

The clinical course of coronavirus disease (COVID-19) in children in combination with diabetes mellitus is characterized by a more pronounced intensity of clinical manifestations and more frequent complications compared to patients without this premorbid condition. For unknown reasons, the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) may trigger new-onset diabetes. Over the last decade, the incidence of type 1 diabetes mellitus has increased and the peak age for being diagnosed with type 1 diabetes mellitus is getting younger.
This article presents a **clinical case** of an adolescent female patient with new-onset type 1 diabetes mellitus diagnosed during hospitalization for symptomatic COVID-19 (SARS-CoV-2 was confirmed by polymerase chain reaction of naso/oropharyngeal swabs). The patient felt ill suddenly, her condition was rapidly worsening. She was hospitalized with severe acute respiratory tract infection. The blood work of the patient revealed hyperglycemia, hyperstenuria, glycosuria, ketonuria, hypertransferasemia, elevated levels of glycated hemoglobin and decreased levels of C-peptide. The patient has been receiving fluid replacement treatment intravenously, short-acting insulin to correct hyperglycemia followed by symptomatic treatment therapy. The patient responded well to the treatment plan and was discharged from the hospital after 8 days continuing treatment from home.
Conclusions. The presented article describes a clinical case of COVID-19 in adolescent female patient with new-onset type 1 diabetes mellitus. The patient's severe condition was caused mainly by dehydration and COVID-19 precipitated ketoacidosis despite having light respiratory symptoms. At the moment, it is not enough data to conclude whether type 1 diabetes mellitus in pediatric population can cause serious complications from COVID-19. More studies are required to reach a definitive conclusion.
The study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from the patient's parents before the study.
No conflict of interests was declared by the authors.
Keywords: children, type 1 diabetes mellitus, coronavirus disease COVID-19, respiratory pathology.

Поєднаний перебіг гострої респіраторної коронавірусної хвороби в дитини з цукровим діабетом 1-го типу: клінічний випадок

Р.В. Ткачук, О.К. Колоскова, М.Н. Гарас, Т.М. Білоус, Л.І. Романчук
Буковинський державний медичний університет, м. Чернівці, Україна

Клінічний перебіг коронавірусної хвороби (COVID-19) у дітей у поєднанні з цукровим діабетом характеризується виразнішою інтенсивністю клінічних проявів і частішими ускладненнями порівняно з хворими без такого преморбідного стану. Перебіг гострої респіраторної вірусної інфекції, викликаної SARS-CoV-2, за невідомих причин, може бути ймовірним тригером дебюту цукрового діабету. За останнє десятиліття захворюваність на цукровий діабет 1-го типу зросла, а дебют захворювання в рази помолодшав. Тому аналіз клінічно-параклінічних особливостей перебігу коронавірусної хвороби COVID-19 у хворих із дебютом цукрового діабету 1-го типу дасть змогу накопичувати дані та вивчати потенційні шляхи, за допомогою яких вірус SARS-CoV-2 порушує метаболізм глюкози, що є важливим для розуміння правильної діагностики, моніторингу та подальшої терапії.
У статті наведено власне **клінічне спостереження** перебігу коронавірусної інфекції COVID-19 (лабораторно підтверджений випадок — виявлена РНК вірусу SARS-CoV-2 методом ПЛР у назо/орофарингеальному мазку) у поєднанні з дебютом цукрового діабету 1-го типу в дівчинки переддошкільного віку. Хвороба розпочалася раптово, напередодні дитина поскаржилася на погіршення самопочуття, що прогресивно наростало, з приводу чого була госпіталізована в тяжкому стані з ознаками запального ураження дихальних шляхів. Лабораторні зміни свідчили про виразну гіперглікемію, гіперстенурію, глюкозурію, кетонурію, гіпертрансфераземію, зростання рівня гліколізованого гемоглобіну та зниження С-пептиду в сироватці крові. Лікування включало протекцію гідробалансу оральним та інфузійним шляхом, коригування рівня гіперглікемії інсуліном короткої дії, а також симптоматичну терапію. Стан дівчинки прогресивно поліпшувався, на 8-му добу була виписана зі стаціонару для продовження лікування амбулаторно.
Висновки. Наведений клінічний випадок наочно відображає перебіг COVID-19 у вигляді інфекції верхніх і нижніх дихальних шляхів у дівчинки переддошкільного віку на тлі дебюту цукрового діабету 1-го типу. Тяжкість стану дитини насамперед зумовлена проявами кетоацидозу та дегідратації на тлі невиразних респіраторних симптомів. З'ясування обтяжувальної ролі цукрового діабету 1-го типу в педіатричній практиці щодо тяжкості перебігу COVID-19 наразі обмежене незначною кількістю спостережень і потребує подальшого накопичення даних.
Дослідження виконано відповідно до принципів Гельсінської декларації. На проведення досліджень отримано інформовану згоду батьків дитини.
Автори заявляють про відсутність конфлікту інтересів.
Ключові слова: діти, цукровий діабет 1-го типу, коронавірусна хвороба, COVID-19, респіраторна патологія.

Introduction

Patients with coronavirus disease (COVID-19) experience a variety of clinical presentations ranging from no symptoms or mild illness to critical illness with multi-organ failure even death [3]. Survival decreases, and more complications tend to develop in advanced age populations and patients with underlying comorbidities. This has raised concerns about those suffering chronic conditions like type 1 diabetes mellitus [2,5].

Overburdened healthcare systems during the COVID-19 pandemic led to suboptimal chronic disease management, including that of pediatric type 1 diabetes mellitus. The pandemic also caused delayed detection of new-onset diabetes in children; this increased the risk and severity of diabetic ketoacidosis [1,9]. The prevalence of type 1 diabetes mellitus in patients with COVID-19

ranged from 0.15% to 28.98%. The most common presentation of COVID-19 in patients with type 1 diabetes mellitus included fever, dry cough, nausea and vomiting, elevated blood glucose and diabetic ketoacidosis [7].

During the COVID-19 pandemic, the number of cases of type 1 diabetes mellitus in youth spiked, with evidence suggesting an association between both conditions. During the COVID pandemic, a surge in pediatric type 1 diabetes mellitus cases appears to be occurring, potentially due to the presence of autoantibody-induced immune dysregulation triggered by COVID-19 [8].

Also SARS-CoV-2 (which causes COVID-19 enters human cells via the envelope spike glycoprotein), which is also responsible for host-to-host transmission. This glycoprotein, which is found on the surface of the virus, binds to the ectoenzyme angiotensin-converting enzyme 2 (located on human cells) to gain entry into the cell. As the human endocrine pancreas expresses angiotensin-converting enzyme 2, the coronavirus might enter islets and cause acute β-cell dysfunction, leading to acute hyperglycaemia [10].

Patients with type 1 diabetes mellitus / prediabetes who receive corticosteroids for COVID-19 infection experience acute rise in blood glucose levels, which are difficult to control and need high doses of insulin. In addition, the psycho-socio-economic effects of the pandemic have resulted in altered glucose metabolism manifesting as worsening of glycemic control in people with pre-existing diabetes and in new onset diabetes. Hyperglycemia following pancreatitis associated with COVID-19 infection (presumably due to direct effect of SARS-CoV-19 virus on pancreatic beta cells) has been described. Hyperglycemia has emerged as one of the risk factors for adverse outcomes and mortality of SARS-CoV-2 virus infection (COVID-19). Further, bidirectional relationship of hyperglycemia and COVID-19 has been well recognised. It must be realised that any magnitude of hyperglycemia is associated with poor prognosis in COVID-19. However, the timing and extent of hyperglycemia varies according to several factors: pre-existing diabetes or pre-diabetes, age, presence of obesity, other co-morbidities and stress, severity of infection, type of treatment given, and beta cells capacity during times of COVID-19 infection. These effects are because of the cytokine storm, steroids used in treatment and possibly the direct beta cell injury by virus. Importantly, association of altered glucose metabolism and severe COVID-19, as shown in many studies, indicate that SARS-CoV-2 infection involves interplay with glucose metabolism [6].

Exploration of heterogenous pathways by which SARS-CoV-2 dysregulates glucose metabolism is important for understanding proper diagnosis, monitoring and therapy. Considering the above, we consider it expedient to describe a clinical case of a combined course of the COVID-19 coronavirus disease with the onset of type 1 diabetes in a child of preschool age in order to draw the attention of doctors to clinically significant pathology.

Clinical case

The 4 years old female patient presented to the department of infectious diseases of anesthesiology and intensive care of the Regional Municipal Non-Profit Facility «Chernivtsi Regional Children's Clinical Hospital» in weak condition. She has had a dry cough, followed by a history of fewer (37.8°C) and an increase in urinary frequency for 3 days. The patient's medical history records that the young patient is the first child that was delivered vaginally at full term. No complications occurred during neonatal period or within first year of life. No allergies detected. However, there is a maternal history of diabetes that runs in the family (mother's sister has type 2 diabetes). Girl was vaccinated in accordance with the National Vaccination Calendar of Ukraine. The patient was admitted to the diagnostic department of the Regional Municipal Non-Profit Facility «Chernivtsi Regional Children's Clinical Hospital». Before an admission to the hospital she was tested with a rapid test for Ag SARS-CoV-2 which came out inconclusive and rapid glucose test result was 31.0 mmol/L.

Upon admission, the patient's health condition evaluation confirmed the severe neurological symptoms — sopor caused by ketoacidosis, dehydration, as well as respiratory infection. The patient was lethargic, hypodynamic, accessible to verbal contact, but with delayed responses.

Body temperature was of 37.2°C, pupils D=S, symmetrical, responsive to light. The patient did not show any meningeal symptoms. The skin was pale, clean, mucous membranes were dry, pharynx was hyperemic, and tongue was covered in white coating. Tissue turgor was poor. Extremities were cold to touch. Physical examination further demonstrated increased pulse rate, tachycardia but the heart rhythm was regular, heart rate — 128 bpm, blood pressure — 100/60 mm Hg. Breath was coarse, lung sounds were clear

throughout most of the lung field, respiration rate is 26/min and oxygen saturation of 93%. Abdomen was soft upon palpation. A size of the liver and spleen was normal. Urinary was frequency, urine volume was increased, no bowel movements. Physical examination and lab tests suggested new-onset type 1 diabetes and ketoacidosis, acute bronchitis and possible COVID-19 infection.

Further diagnostic strategy and therapy management was determined according to the national and international treatment protocols at the time. Urine test result showed increase of gravity — 1029 units, glycosuria — 8.3 mg/ml, ketone acids were positive, biochemistry blood test showed hyperglycemia — 17.9 mmol/l, increase of alanine aminotransferase (ALT) — 1.8 mmol/h/ml and aspartate aminotransferase (AST) — 1.6 mmol/h/ml enzymes, hyperkalemia — 6.5 mmol/l. Blood test results revealed decreased levels of C-peptide (0.289 ng/mL, reference range 0.9–7.1 ng/mL) and elevated levels of glycated hemoglobin (14.44%, reference range <6.5%). Naso/oropharyngeal swab polymerase chain reaction (PCR) was confirmed positive for SARS-CoV-2. Chest X-Ray images showed bronchitis. The patient was also diagnosed with acute nasopharyngitis. Echocardiographic examination and abdominal ultrasound detected no abnormalities.

The treatment plan of the patient included external oxygen supply via nasal cannulas, fluid replacement treatment intravenously 100 ml/kg per day, short-acting insulin 0.1 units/kg/hr to correct hyperglycemia followed by short-acting insulin infusion therapy 0.05 units/kg/hr for 2 days.

The patient responded well to the treatment plan, her dehydration and hyperglycemia improved gradually the following day (up to 10.2 mmol/L).

Since the patient's RT-PCR was confirmed positive for SARS-CoV-2 and her positive response to the treatment, she was transferred to the children's ward of infectious diseases department on the 5th day of her admission to the hospital.

On the 8th day of patient's admission the hospital she was retested with PCR for COVID-19 and result was negative. Given negative test result and that the patient's condition has been improving progressively and having her glycaemia under control, she was discharged from the hospital to continue further treatment recommended by endocrinologist at home.

Discussion

Patients with COVID-19 experience a variety of clinical presentations ranging from no symptoms or mild illness to critical illness with multi-organ failure even death. Among hospitalized children aged <2 years, chronic lung disease, neurologic disorders, cardiovascular disease, prematurity, and airway abnormality were associated with severe COVID-19. Among hospitalized children aged 2 to 17 years, feeding tube dependence, diabetes mellitus and obesity were associated with severe COVID-19 [11]. During the COVID-19 pandemic was found a significant increase in diabetic ketoacidosis and severe ketoacidosis at diabetes diagnosis in children and adolescents. Underlying causes may be multifactorial and reflect reduced medical services, fear of approaching the health care system, and more complex psychosocial factors [4]. Nowadays it is not enough data to conclude whether type 1 diabetes mellitus in pediatric population can cause serious complications from COVID-19. More studies are required to reach a definitive conclusion. Further sufficient epidemiologic data collection required.

Conclusions

This article describes a clinical case of COVID-19 in a preschool patient with a new onset type 1 diabetes mellitus.

Despite subtle respiratory symptoms, the patient presented with severe dehydration and ketoacidosis. This case highlights the need for clinical awareness of acute respiratory presentations of confirmed COVID-19 as they may result in ketoacidosis. It is advised to test glucose levels during acute stage of infection.

However, we do believe that in this particular case, COVID-19 triggered new onset type 1 diabetes mellitus in this young patient who had not had any symptoms of type 1 diabetes mellitus before COVID-19.

The authors declare that this article is original, has not been published before and is not currently being considered for publication elsewhere.

No conflict of interests was declared by the authors.

REFERENCES/ЛІТЕРАТУРА

1. Alaqeel A, Aljuraibah F, Alsuhaibani M, Huneif M et al. (2021, Apr). The Impact of COVID-19 Pandemic Lockdown on the Incidence of New-Onset Type 1 Diabetes and Ketoacidosis Among Saudi Children. Frontiers in Endocrinology. 12: 1-5. https://doi:10.3389/fendo.2021.669302.
2. DiMeglio LA, Albanese–O'Neill A, Muñoz CE, Maahs DM. (2020). COVID-19 and children with diabetes-updates, unknowns, and next steps: first, do No extrapolation. Diabetes Care. 43 (11): 2631-2634.
3. Huang C, Wang Y, Li X et al. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet (London, England). 395 (10223): 497-506. https://doi.org/10.1016/S0140-6736(20)30183-5.
4. Kamrath C, Mönkemöller K, Biester T et al. (2020). Ketoacidosis in Children and Adolescents With Newly Diagnosed Type 1 Diabetes During the COVID-19 Pandemic in Germany. JAMA. 324 (8): 801-804. https://doi:10.1001/jama.2020.13445.
5. Koliaki C, Tentolouris A, Eleftheriadou I, Melidonis A, Dimitriadis G, Tentolouris N. (2020). Clinical management of diabetes mellitus in the era of COVID-19: practical issues, peculiarities and concerns. J Clin Med. 9 (7): 1-25. https://doi.org/10.3390/jcm9072288.
6. Misra A, Ghosh A, Gupta R. (2021). Heterogeneity in presentation of hyperglycaemia during COVID-19 pandemic: A proposed classification. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 15 (1): 403-406. https://doi.org/10.1016/j.dsx.2021.01.018.
7. Nassar M, Nso N, Baraka B, Alfishawy M, Mohamed M, Nyabera A, Sachmechi I. (2021). The association between COVID-19 and type 1 diabetes mellitus: A systematic review. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 15 (1): 447-454. https://doi.org/10.1016/j.dsx.2021.02.009.
8. Nielsen–Saines K, Li E, Olivera AM, Martin–Blais R, Bulut Y. (2021). Case Report: Insulin-Dependent Diabetes Mellitus and Diabetic Keto-Acidosis in a Child With COVID-19. Frontiers in Pediatrics. 9: 1-5. https://doi:10.3389/fped.2021.628810.
9. Okhotnikova OM, Ivanova TP, Oshlyanskaya OA, Ponochevnaya OV et al. (2020). Treatment protocol of coronavirus infection (COVID-19) in children with chronic somatic diseases. Modern Pediatrics. Ukraine. 4(108): 18-32. [Охотнікова ОМ, Іванова ТП, Ошлянська ОА, Поночевна ОВ та інш. (2020). Клінічний протокол медичної допомоги дітям із коронавірусною інфекцією (COVID-19), яка перебігає на фоні хронічних соматичних захворювань. Сучасна педіатрія. Україна. 4(108): 18-32]. doi 10.15574/SP.2020.108.18.
10. Soliman AT, Al-Amri M, Alleethy K, Alaaraj N, Hamed N, De Sanctis V. (2020). Newly-onset type 1 diabetes mellitus precipitated by COVID-19 in an 8-month-old infant. Acta biomedical. 91 (3): e2020046. https://doi.org/10.23750/abm.v91i3.10074.
11. Woodruff C, Campbell AP, Taylor ChA et al. (2022). Risk Factors for Severe COVID-19 in Children. Pediatrics. 149 (1): e2021053418. https://doi.org/10.1542/peds.2021-053418.

Відомості про авторів:

Ткачук Роман Васильович — аспірант каф. педіатрії та дитячих інфекційних хвороб Буковинського ДМУ. Адреса: м. Чернівці, вул. Пл. Театральна, 2; тел. (0372) 55-37-54. https://orcid.org/0000-0002-6753-2365.

Колоскова Олена Костянтинівна — д.мед.н, проф., зав. каф. педіатрії та дитячих інфекційних хвороб Буковинського ДМУ. Адреса: м. Чернівці, вул. Пл. Театральна, 2; тел. (0372) 55-37-54. https://orcid.org/0000-0002-4402-8756.

Гарас Микола Несторович — к.мед.н, доц. каф. педіатрії та дитячих інфекційних хвороб Буковинського ДМУ. Адреса: м. Чернівці, вул. Пл. Театральна, 2; тел. (0372) 55-37-54. https://orcid.org/0000-0001-7304-2090.

Білоус Тетяна Михайлівна — д.мед.н, проф. каф. педіатрії та дитячих інфекційних хвороб Буковинського ДМУ. Адреса: м. Чернівці, вул. Пл. Театральна, 2; тел. (0372) 55-37-54. https://orcid.org/0000-0002-9469-401X.

Романчук Леся Іванівна — асистентка каф. педіатрії та дитячих інфекційних хвороб Буковинського ДМУ. Адреса: м. Чернівці, вул. Пл. Театральна, 2; тел. (0372) 55-37-54. https://orcid.org/0000-0002-0676-3960.

Стаття надійшла до редакції 12.07.2022 р., прийнята до друку 20.10.2022 р.