Acute renal failure due to severe rhabdomyolysis provoked by a mild covid-19 infection in patient with LCHAD deficency- a case report

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Abstract:

Introduction: LCHAD (long-chain 3-hydroxy-acyl-CoA dehydrogenase) deficiency is an inherited fatty acid oxidation disorder in which the body is unable to break down certain fats resulting in hypoketotic hypoglycemia, myopathy, episodic rhabdomyolysis and neuropathy. Metabolic decompensation is often precipitated by infection or fasting.

Case report: A 26-year-old patient was admitted to the emergency department because of generalized myalgias. This is a patient with known congenital deficiency of long-chain 3- hydroxy-acyl- CoA dehydrogenase (LCHAD). He was diagnosed at the age of 3 years and regularly undergoes check-ups in specialized metabolic department. 10 days prior to the symptoms he had milder form of covid-19 infection with a persistent dry cough. Previously, he was vaccinated with two doses of the mRNA SARS-COV 2 vaccine. Initially laboratory findings at emergency department showed elevated levels of creatine kinase (46000 U/L) with normal renal function (egfr: 105 ml/min/1.73m2). Chest X-ray excluded pneumonia. Abundant hydration with intravenous infusions (0.9% NaCl, 5% glucose) was started, but during the observation the patient developed oliguria with urine output <10 ml/hour. Further laboratory findings showed acute kidney injury with worsening rhabdomyolysis (CK>80,000 U/L, egfr: 19 ml/min/1.73m2, creatinine: 369 umol/L). Due to the need for hemodialysis, he was hospitalized in the intensive care unit where dialysis procedures (CVVHD, CVVHDF) were continuously performed for 7 days until gradual decrease in creatinine and CK levels. In continuation he was carefully hydrated with infusions of 10% glucose and received a specially adapted diet to ensure sufficient caloric intake and to prevent catabolism. In total, he was 12 days on continuous hemodialysis and the renal function completely recovered after 3 weeks with the normalization of creatinine and CK values. Beside mild SARS-CoV-2 infection, we haven't founded any other cause of patient's metabolic decompensation.

Conclusion: Patients with LCHAD should be educated and controlled more often in the covid-19 pandemic, as even the mild form of SARS-CoV-2 infection can lead to a rapid metabolic decompensation and a possible fatal outcome.

Keywords: LCHAD deficiency, rhabdomyolysis, SARS-CoV-2, acute kidney failure

Sažetak:

HRV NASLOV

Uvod: Nedostatak LCHAD (dugolančana 3-hidroksi-acil-CoA dehidrogenaza) je nasljedni poremećaj oksidacije masnih kiselina u kojem tijelo ne može razgraditi određene masti što rezul-

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tira hipoketotičkom hipoglikemijom, miopatijom, ponavljajućom rabdomiolizom i neuropatijom. Metabolička dekompenzacija često je uzrokovana prolongiranim gladovanjem ili infekcijom.
Prikaz slučaja: 26-godišnji pacijent javlja se u hitni prijem zbog generaliziranih mialgija. Riječ je o pacijentu s poznatim kongenitalnim nedostatkom LCHAD kojemu je dijagnoza postavljena u dobi od 3 godine. Redovito provodi kontrole kod vodećeg specijalista u Zavodu za bolesti metabolizma. Pacijent je 10-ak dana prije mialgija prebolio blaži oblik covid-19 infekcije s ostatnim suhim kašljem. Redovito je cijepljen s mRNA SARS-COV 2 cjepivom. Obradom u hitnoj službi verificirane su povišene razine kreatin kinaze (46000 U/L) uz urednu bubrežnu funkciju (npr. 105 ml/min/1,73 m2). RTG prsnog koša isključio je upalu pluća. Započeta je obilna hidracija intravenskim infuzijama (0,9% NaCl, 5% glukoza), no u kontrolnom intervalu pacijent razvija oliguriju s diurezom <10 ml/sat. Daljnji laboratorijski nalazi pokazali su akutnu ozljedu bubrega s pogoršanjem rabdomiolize (CK>80 000 U/L, egfr: 19 ml/min/1,73m2, kreatinin: 369 umol/L). Zbog potrebe za hemodijalizom hospitaliziran je u jedinici intenzivnog liječenja gdje je kontinuirano provođen postupak dijalize (CVVHD, CVVHDF) do postupnog pada vrijednosti kreatinina i CK. U nastavku je pažljivo hidriran infuzijama 10% glukoze uz prehranu posebno prilagođenom dijetom kako bi se osigurao dovoljan kalorijski unos i spriječio katabolizam. Pacijent je sveukupno proveo 12 dana kontinuirane dijalize, a do potpunog oporavka bubrežne funkcije došlo je za 3 tjedna. Osim blage SARS-CoV-2 infekcije, nismo pronašli nijedan drugi uzrok metaboličke dekompenzacije.
Zaključak: Bolesnike s LCHAD-om treba češće educirati i kontrolirati u pandemiji covid-19 infekcije jer i blaži oblik infekcije može dovesti do brze metaboličke dekompenzacije i mogućeg smrtnog ishoda.

Ključne riječi: nedostatak LCHAD, rabdomioliza, SARS-CoV-2, akutno zatajenje bubrega

Introduction

LCHAD (long-chain 3-hydroxyacyl-CoA dehydrogenase) deficiency belongs to the group of fatty acid oxidation disorders in which the body in unable to break down certain fats. They are categorized based upon the length of the fatty acid chain. Like most of metabolic diseased LCHADD (LCHAD deficiency) is inherited in an autosomal recessive way with a prevalence of 1:150 000(1). It is caused by a genetic variant in the HADHA gene that encodes alpha and beta subunits of mitochondrial trifunctional protein. Majority of cases is caused by p.(Glu510Gln) variant in *HADHA*, but genetic testing revealed novel variant c.1108G > A, p.(Gly370Arg) associated with late onset, moderate disease (2,3) . Severe neonatal form of the disease presents with recurrent hypoketotic hypoglycaemia, episodic rhabdomyolysis, myopathy and rapidly progressive cardiomyopathy. Surviving patients with LCHADD may develop slowly progressing peripheral neuropathy, pigmentary retinopathy and during illness recurrent rhabdomyolysis (1). Metabolic decompensation is often precipitated by infection or prolonged fasting. Treatment of LCHADD involves dietary fat restriction and MCT (middle-chain triglycerides) or triheptanoin supplementation in order to decrease plasma hydroxyacylcarnitine. Given the low proportion of fat in the diet, it is necessary to supplement essential fatty acids and fat-soluble vitamins in patients with LCHADD (4).

Case report

A 26-year-old patient was admitted to the emergency department because of generalized myalgias. This is a patient with known congenital deficiency of long-chain 3-hydroxy-acyl- CoA dehydrogenase (LCHAD). The disease was diagnosed at the age of three due to hypoketotic hypoglycaemia and elevated levels of creatine kinase (CK). He regularly undergoes check-ups in specialized metabolic department. Ten days prior to the symptoms he had milder form of covid-19 infection (low-grade fever) with a persistent dry cough. Previously, he was vaccinated with two doses of the mRNA SARS-COV 2 vaccine. Initially laboratory findings at emergency department showed elevated levels of CK (46000 U/L), ALT (305 U/L) with normal renal function (egfr: 105 ml/min/1.73m2). Chest X-ray excluded pneumonia. Abundant hydration with intravenous infusions (0.9% NaCl, 5% glucose) was started at the emergency department. During observation, in a time interval of 12 hours, the patient developed oliguria with urine output <10 ml/hour. Further laboratory findings showed acute kidney injury with worsening rhabdomyolysis (CK>80,000 U/L, egfr: 19 ml/min/1.73m2, creatinine: 369 umol/L). Due to the need for hemodialysis, he was hospitalized in the intensive care unit where dialysis procedures (CVVHD, CVVHDF) were continuously performed for 12 days until gradual decrease in creatinine and CK levels. In order to prevent

further catabolism, a detailed diet plan was organised in cooperation with nutritionist. He was carefully hydrated with infusions of 20% glucose and received a specially adapted carbohydrate rich diet with only 10% fats from long-chain triglycerides. Beside mild SARS-CoV-2 infection, we haven't founded any other cause of patient's metabolic decompensation.

Discussion

In patients with inborn errors of metabolism, it is important to avoid any factors that could precipitate metabolic crisis. Even a milder form of infection can be life-threatening for patients, as it was in the case of our patient. During the covid-19 pandemic, we encountered a major problem of inadequate treatment of metabolic patients due to large number of infected people. Wongkittichote and al. descripted a case of 23-years old female patient with LCHADD who developed acute respiratory failure and severe cardiomyopathy which progressed to multiple organ failure and death. She presented with nausea, dry cough and chest pain and tested positive for COVID-19. As well as our patient laboratory findings revealed rhabdomyolysis with acute kidney injury. She was relative stabile until day 11 when she suddenly developed respiratory arrest and hypotension due to cardiomyopathy. Despite all modalities of intensive treatment, a fatal outcome occurred (5). One of the most serious complications of LCHADD is cardiomyopathy, which occurs due to deposition of toxic acylcarnitines (6). Carefully monitoring patient's vital signs and ECG during metabolic crisis is necessary in order to avoid this complication. Despite the late recognition of the metabolic crisis, urgent dialysis procedures and sufficient caloric intake prevented further complication and lead to a fully recovery.

Conclusion

Patients with LCHADD should be educated and controlled more often in the covid-19 pandemic, as even the mild form of SARS-CoV-2 infection can lead to a rapid metabolic decompensation and a possible fatal outcome. It is necessary to educate medical doctors in the emergency departments about metabolic diseases and way of preventing catabolism to avoid fatal outcomes of patients with LCHADD.

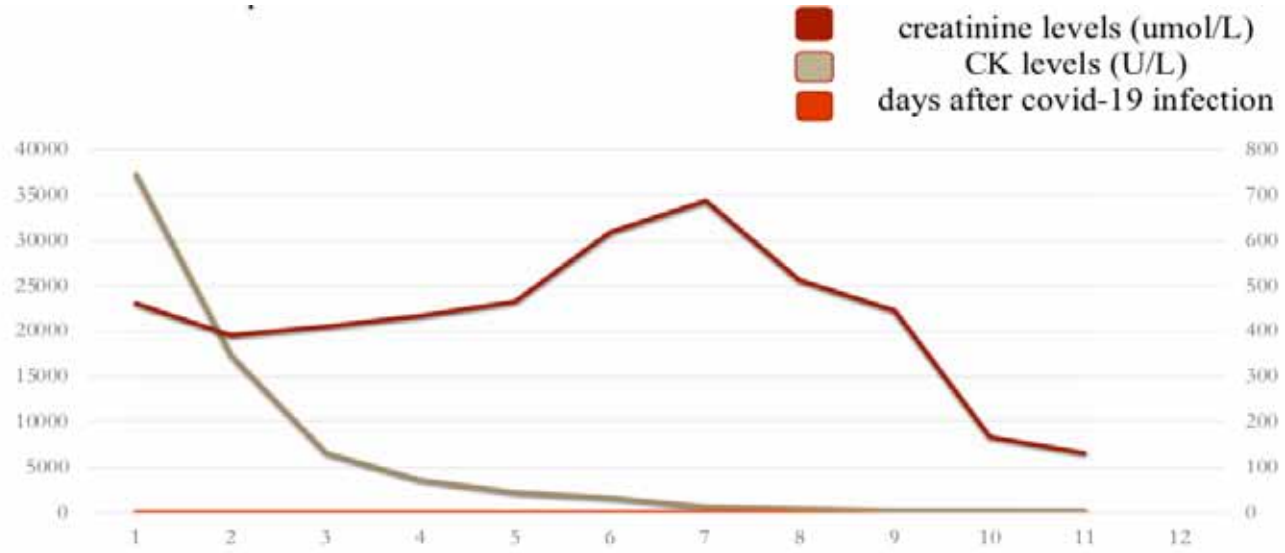

Figure 1. Dynamics of decreasing CK and creatinine levels during hospitalization and dialysis procedures

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