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Consequences of uncontrolled diabetes – hemichorea-hemiballismus syndrome

Skutki niekontrolowanej cukrzycy – zespół hemichorea-hemiballismus

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Abstract

Introduction*: Long-standing uncontrolled diabetes mellitus (DM) may lead to non-ketotic hyperglycemia (NKH). It manifests with the hemichorea-hemiballismus syndrome (HCHB) characterized by ballistic movements, hyperglycemia, and basal ganglia lesions seen in radiological imaging. Prevalence is estimated at 1/100 000 people.* **Case presentation***: An 81-year-old woman with a history of long-standing DMT2 was admitted to the emergency department due to increasing movement disorders and disturbance of consciousness. An initial physical examination revealed unilateral left limbs ballistic movements. In laboratory analysis presented an elevated level of glycemia - 529mg/dl, glycated hemoglobin HbA_{1c} – 14.7%, but no features of acidosis. Computer tomography (CT) showed hyperdensity in the right basal nuclei. HCHB associated with NKH was suspected. An intravenous insulin therapy and fluids were applied to restore electrolyte balance resulting in resolve neurological symptoms.* **Conclusions***: Awareness of HCHB as complication of uncontrolled DM2 enable to correctly diagnose and successfully treat upon restoring normal glycemic and electrolyte levels. (Gerontol Pol 2022; 30; 201-204) doi: 10.53139/GP.20223025*

Keywords: *diabetic complications, non-ketotic hyperglycemia, ballism*

Streszczenie

Wstęp*: Długotrwała i niekontrolowana cukrzyca może prowadzić to powikłań w postaci nieketotycznej hiperglikemii (NKH). Ujawnia się ona jako zespół hemichorea-hemiballismus (HCHB), charakteryzujący się występowaniem ruchów balicznych, hiperglikemią oraz zmianami w obrębie jąder podstawy widocznymi w badaniach obrazowych. Częstość tego zespołu określa się na 1/100 000 osób.* **Opis przypadku***: 81-letnia kobieta zmagająca się z wieloletnią cukrzycą typu 2 (DM2) została przyjęta na izbę przyjęć z zaburzeniami świadomości oraz narastającymi wyrzucającymi ruchami kończyn lewych. Badanie przy przyjęciu ujawniło lewostronny hemibalizm. Badania laboratoryjne wykazały podwyższony poziom glikemii – 529mg/dl oraz hemoglobiny glikowanej HbA_{1c} – 14.7%, bez cech kwasicy. Tomografia komputerowa (TK) wykazała hiperdensyjne zmiany obejmujące prawe jądra podstawy. Wysunięto podejrzenie HCHB związanego z NKH. Ustąpienie objawów po zastosowaniu insulinoterapii dożylnej i wyrównaniu równowagi wodno-elektrolitowej potwierdziło diagnozę.* **Wnioski***: Świadomość na temat występowania HCHB jako rzadkiego powikłania niekontrolowanej cukrzycy, umożliwia szybkie postawienie właściwej diagnozy oraz skuteczne leczenie poprzez wyrównanie glikemii i równowagi wodno-elektrolitowej. (Gerontol Pol 2022; 30; 201-204) doi: 10.53139/GP.20223025*

Słowa klucze: *powikłania cukrzycy, nieketotyczna hiperglikemia, balizm*

Introduction

Diabetes mellitus (DM) and its complications pose a major global treatment challenge. The International Diabetes Federation (IDF) reports that today 537 million adults aged 20-79 years are living with diabetes and this number is predicted to rise to 643 million by 2030 [1].

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An adequate treatment focused on effective glycemic control is crucial for the prevention of diabetic complications. Nowadays, these issues are even more challenging, since the COVID-19 pandemic has caused severe disruption of diabetic care services. The World Health Organization (WHO) survey conducted in mid-2020 reported that services for diabetes and diabetes-related complications had been partially or completely disrupted in around half of the countries surveyed [2]. Uncontrolled glycemia may lead to many acute and chronic complications as well. Chronic complications of diabetes arise as a result of vascular damage and are divided into microvascular, such as retinopathy, nephropathy and neuropathy (associated with dysfunction of the retina, kidneys, and peripheral nervous system), and macrovascular, which lead to cardiovascular disease. Acute conditions, caused by uncontrolled DM include hypoglycemia, hyperosmolar-hyperglycemic state (HHS), lactic acidosis, ketotic acidosis, and non-ketotic hyperglycemia (NKH), are thought to be life-threatening complications [3,4]. Not widely known is the fact that NKH may be related to neurological symptoms called hemichorea--hemiballismus syndrome (HCHB) or diabetic striatopathy (DS). The prevalence of this rare complication is approximately 1/100 000 people, but it is thought the numbers are underestimated. It mostly affects elderly women suffering from DM type 2 (DMT2), with poorly controlled glycemia. The ratio of men to women is estimated as 1:1,3-1,8, and HCHB mainly concerns the Asian population. In the Caucasians, it is a rare condition. [4] HCHB is characterized by the triad: involuntary throwing ballistic movements, hyperglycemia, and basal ganglia lesions seen in radiological imaging including computer tomography (CT) and magnetic resonance (MR). The main locations of these abnormalities involve not only striatum (especially putamen), but also caudate nucleus and globus pallidus [5]. The exact mechanism of the ballistic and chorea symptoms appearing in HCHB is unclear, but several hypotheses have been considered. The theory of interruption of gamma-aminobutyric acid (GABA) suggests that in NKH the shift to anaerobic metabolism causes the brain to utilize GABA as an alternate energy substrate, which causes the rapid depletion of GABA, and ultimately interrupts its transmission in the basal ganglia [6]. Another hypothesis is that hyperglycemia may directly induce alterations in dopaminergic activity by the upregulation of dopamine receptors and decreased dopamine catabolism in the striatum [7]. In addition, it has been considered that the mechanism relating to increasing viscosity in the blood may lead to hyperperfusion of the basal ganglia area [4,8]. Nevertheless, all proposed pathomechanisms result in non-inhibition of the thalamus, leading to increased excitatory action in the cortex, causing chorea or throwing ballistic movements observed in the patients with HCHB associated with NKH [4,6-8].

Case presentation

An 81-year-old woman living alone was admitted to the emergency department due to increasing movement disorders and disturbance of consciousness. She had a medical history of hypertension, hypothyroidism, and long-standing DMT2 treated with metformin and a medication from the group of sulfonylureas, glimepiride. Other medications used by the patient included levothyroxine, atorvastatin, candesartan, amlodipine, and metoprolol. On an initial physical examination, the patient's cardiovascular and respiratory conditions were stable. However, she presented some features of dehydration. Her blood pressure was 117/56 mmHg and heart rate was 105/min. The neurological examination revealed preserved awareness, and autopsychic and allopsychic orientation. The pupils were symmetrical and reactive to the light. There were no meningeal symptoms and no abnormalities on the examination of cranial nerves. Muscle strength and reflexes were proper and symmetrical. The patient presented unilateral ballistic movements of the left limbs without paresis or pathological reflexes. Abnormalities on the sensory and coherence examination were not observed. Romberg's test was negative. The gait was proper.

In laboratory analysis, the patient presented signs of decompensated diabetes: an elevated level of glycemia – 529 mg/dl (laboratory reference range (LRR) 70-99 mg/dl), glycated hemoglobin, HbA_{1c} – 14.7% (LRR 4.8-5.9%), but no features of acidosis, with pH – 7.44 (LRR 7.35-7.45). Computer tomography (CT) presented a characteristic hyperdensity in the area of right basal nuclei.

Based on the clinical picture and results of the diagnostic workup, HCHB associated with NKH was suspected. Intravenous insulin therapy and intravenous fluids were applied to restore electrolyte balance. ACE inhibitors and Beta-adrenolytics have been applied as well. Two days after the treatment, the described neurological symptoms were resolved, which confirmed the diagnosis of HCHB, associated with NKH. Symptomatic treatment was not required. Hospitalization was prolonged due to the cholecystitis that was diagnosed based on the ultrasound examination, and high inflammatory markers (CRP >100 mg/dl; LRR 0-5.0 mg/dl, leucocytes 16.1×10^3/µl). The patient received empirical antibiotic therapy including cyprofloxacin 2×400 mg daily and

metronidazol 3×500 mg daily for 7 days. During this infection period, a worse glycemic control was observed, but no involuntary movements were observed. As a result of the therapy, the patient's clinical condition improved, and on the 12th day of hospitalization, she was discharged home. After her discharge, the patient did not experience any of the described neurological symptoms again, and her glycemic control was improved.

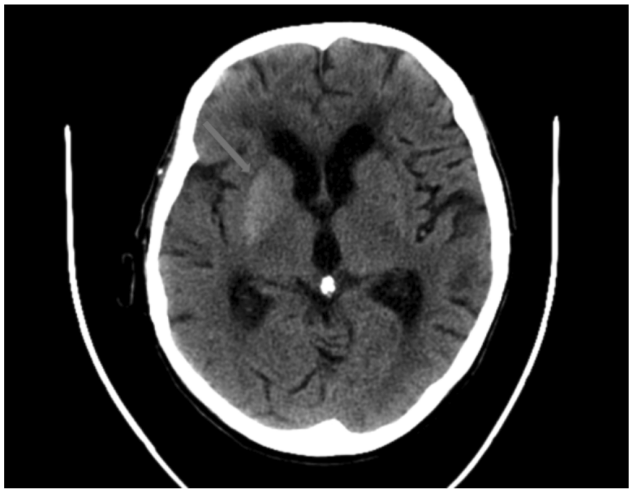

Figure 1. CT scan of the brain of an 81-year-old woman with decompensated diabetes mellitus type 2 and nonketotic hyperglycemia shows hyperdense signals in the right basal nucleus comprising the lentiform nucleus.

Discussion

As was mentioned, HCHB is mostly caused by NKH. In fact, this type of striatopathy could be induced by some acute complications of uncontrolled hyperglycemia, such as the hyperosmolar state [9]. Statistically, it is very rare, but there are some cases, which describe this syndrome in patients with ketotic hyperglycemia or patients with type 1 diabetes [4,6,10].

Diabetic striatopathy may appear not only as a complication of NKH, but also as a result of many severe conditions, including inflammation and infection of the central nervous system (CNS), cerebrovascular or metabolic states, neurodegenerative disorders, growing tumors, or drug side effects [7,11]. Hyperkinetic movements are noted as complications of treatment by substances that modify dopaminergic transmission. Anticonvulsants, noradrenergic stimulators, opioids, steroids, antihistamine drugs, and other agents are also potential causes of these symptoms [12]. It is commonly known that polypragmasia, which is one of the greatest problems in the medical care of elderly patients, raises the risk of side effects and drug interactions. It is possible that this multidrug effect contributes to difficulties with effective glycemic control in the older population, and could be one of the factors responsible for the increased prevalence of HCHB in this voulnerable group of patients.

The sudden onset of ballistic movements is always suggestive of severe neurological life-threatening conditions, like intracranial hemorrhage or ischemic stroke, which were mainly considered in the differential diagnosis of other described cases [8,9,13]. In suspicion of these serious conditions, it is obligatory to get radiological imaging of CNS with CT scan as the most available radiology method in the emergency department. In neuroimaging, both HCHB and recent hemorrhage may manifest with hyperdense changes. Important features to differentiate a hemorrhage include the absence of any mass effect, edema, or volume loss in the CT. Although ischemia is a common cause of ballistic movements, it is mostly presented as CT hypodense changes otherwise than HCHB. Nevertheless, in questionable cases MRI may be performed. As mentioned, HCHB is also related to a very high level of glycemia and glycated hemoglobin which may support our diagnosis [4,9]. Basal ganglia lesions may be seen in radiological imaging like CT or MR of the head. In a few cases of HCHB, described in the available literature, in the diagnostic process both proposed methods were performed, but only the MR demonstrated striatal anomalies [5].

In our case, only the CT was performed. Despite its lower accuracy, CT has greater availability, lower cost, and shorter time of performing, which is essential for patients having uncontrolled ballistic movements and being unable to stop moving (especially when an ischemic or hemorrhagic stroke is considered as a possible cause of these symptoms). It should be highlighted that HCHB may be diagnosed using the radiological method that is faster and more accessible in the emergency ward. Due to very high levels of glycemia and characteristic symptoms of our patient, the CT results, presenting characteristic hyperdense changes in basal ganglia, could have confirmed our diagnosis of HCHB, which required a rapid implementation of the effective treatment. On the other hand, the MR is more specific in HCHB. According to the analysis of research described by Chua et al. [5], in more than half of patients, who presented negative findings on CT, the MR scans demonstrated striatal changes. Therefore, MR can be useful to verify or confirm some uncertain diagnostic situations, what was not necessary in that case [9,13].

The treatment of HCHB associated with NKH is simple and effective. It mainly includes the normalization of glycemia, resulting in significant improvement of hemichorea. In case of prolonged and intensified extra-

pyramidal symptoms, symptomatic medical treatment with neuroleptics, benzodiazepines, drugs reducing dopaminergic transmission, or selective serotonin reuptake inhibitors, may be used [4,14]. In the analysis assessing 126 patients receiving anti-chorea medications, the most commonly used single anti-chorea medication was haloperidol, and of the all combined regimens the most common was a combination of haloperidol and diazepam. In some cases, deep brain stimulation (DBS) or neurosurgical methods, such as pallidotomy or ventrolateral thalamotomy could be used. However, these instances were very rare, especially since the anti-chorea medications' efficiency was assessed as 76.2% [5].

Conclusions

In summary, the findings of our case study demonstrate that HCHB, a severe neurological condition, is a very rare complication of poorly controlled DMT2. However, if physicians are aware of that, it is possible to correctly diagnose (based on typical radiological findings correlated with laboratory blood tests) and successfully treat HCHB and NKH, which are reversible upon restoring normal glycemic and electrolyte levels.

Conflict of interest
none

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