Nonketotic Hyperglycemic Hemichorea-hemiballismus in a Pediatric Patient: A case report

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Abstract

Nonketotic hyperglycemic hemichorea-hemiballismus (NHHH) is an infrequent complication of diabetes mellitus, and rarely occurs in children. We present an adolescent boy with recent diagnosis of type 1 diabetes who presented with hemichorea and brain imaging findings consistent with NHHH. His symptoms resolved with euglycemia and valproic acid after few weeks.

Introduction

Type 1 diabetes (T1D) is a common chronic disease in childhood. In 2015, the incidence of T1D in youth in the United States was 22.3 per 100,000[1] and the incidence has been reported to by increasing by 2-3%every year [2]. Most of the patients with T1D present with typical symptoms of hyperglycemia like polyuria and polydipsia, however around 30% present in diabetic ketoacidosis (DKA)[3]. Neurologic complications are relatively rare but can be present at initial diagnosis like lethargy, decreased level of consciousness, and coma. Other rare neurologic presentations that are more commonly seen in adult patients with T1D include cerebellar ataxia, hemiballismus-chorea, peripheral neuropathy, hyperosmolar coma, and stroke at the time of diagnosis; however these tend to be rarely reported in children [4]. Furthermore, the metabolic derangements and dehydration associated with the severity of DKA have been reported to affect brain structure resulting in different neurological sequelae [5, 6]. While nonketotic hyperglycemic hemichoreahemiballismus (NHHH) has been reported in adults as a neurologic complication of uncontrolled type 2 diabetes (T2D), it's rather rarely reported in children where T1D is much more common than T2D. NHHH, also known as diabetic striatopathy, was first described in 1960 [7] and is a movement disorder characterized by a typical triad of involuntary movements, striatal abnormalities on neuroimaging and hyperglycemia in the setting of uncontrolled or newly diagnosed diabetes mellitus[8]. This condition is rare and has been described in the elderly population with T2D with an estimated incidence of less than 1:100.000 [9]. NHHH has only been reported to occur in a few pediatric patients [10]. We describe the case of an adolescent boy who presented to our institution with NHHH after a recent diagnosis of T1D.

Case History:

A 14-year-old boy was transferred to a tertiary children's hospital for evaluation and treatment of abnormal movements and brain imaging findings that were initially concerning for a brain tumor. He complained of progressive involuntary movements of the left upper and lower extremities for the past week. The movements did not involve the right side of the body, resolved during sleep, and were noted to be worsening. He reported that the movements were not painful but were very bothersome and were not associated with any numbness or tingling sensation. Three weeks prior to presentation, he presented to the emergency room of an outside hospital with shortness of breath, weight loss, polyuria, polydipsia, and polyphagia. Evaluation showed severe DKA where he had a pH of 6.89, bicarbonate 4 mmol/L, anion gap 22, and glucose 662 mg/dL (36.8 mmol/L). He was started on an insulin drip and transferred to another outside hospital for admission and

management of new onset T1D, the official records of which were unavailable. However, he reported being admitted for 3 days during which he received subcutaneous insulin injections and he and his mom received diabetes education. After discharge, he reported having poor glycemic control at home. His past medical history was otherwise negative, and he had no previous surgeries. Regarding his birth history, he was born at term via normal vaginal delivery without any perinatal complications. He lived with his mom at home, his biological father was not involved, and he had no siblings. The family received support mainly from maternal relatives. He was in 9th grade and was active in playing basketball which he recently stopped because of the movements. He also complained of some polyuria and polydipsia, otherwise the remainder of his review of systems was negative. His vital signs were within normal ranges with a temperature: 37.1°C, blood pressure: 121/71 mmHg, heart rate: 78 bpm, respiratory rate: 15 br/min, and oxygen saturation of 97%. On physical exam, his weight was 64.9 Kgs (80.74 % ile), his height was 172 cm (67.59 % ile) and his BMI was 23.7 kg/m^2 (87.12 %ile). He was alert and oriented and exam was significant for choreiform movements in the left upper and lower extremities without associated muscle weakness. Otherwise, the remainder of his neurologic and general exam were normal. Laboratory studies were notable for hyperglycemia with glucose 321 mg/dL (17.8 mmol/L), normal electrolytes except for sodium of 132 (135-145 mmole/L) indicating pseudohyponatremia, HbA1c 14.5% (4-5.6%), the presence of elevated levels of glutamic acid decarboxylase antibodies 10.3 (0-5 IU/mL) further confirming type 1 diabetes, and islet cell antibodies <5.4 (0-7.4 Units/mL). His urine analysis was negative for glucose, protein, and ketones for 3 occurrences during his admission. An interpretation of the brain CT scan performed at the outside hospital revealed a hyperintense lesion in the right basal ganglia (Figure 1A and 1B). To further characterize this lesion, a brain MRI was performed at our institution and was significant for T1 hyperintense/T2 hypointense signal within an atrophic right caudate nucleus and lentiform nucleus (Figure 2A, 2B and 2C). Given the history of uncontrolled T1D and the associated imaging findings. he was diagnosed with nonketotic hyperglycemic hemichorea-hemiballismus which is a rare complication of uncontrolled diabetes mellitus.

The patient was hospitalized for 3 days during which his insulin doses were titrated, and he and his parent received 2 days of diabetes education. He was also prescribed valproic acid 500 mg daily per neurology recommendations that was gradually increased during outpatient follow-up to 500 mg in the morning and 750 mg in the evening because his symptoms persisted after discharge. His movements gradually improved until they completely disappeared after 6 weeks from initial presentation. Unfortunately, metabolic and glycemic control of his diabetes were complicated by social determinants of health. He was placed in the foster care system due to not having his needs met and his diabetes remained poorly controlled. Despite his consistently high HbA1c values with follow-up which ranged between 10.3%-14.4%, he had significant weight gain from 52.2 Kgs at initial diagnosis of DKA to 77 Kgs at his last follow-up appointment after one year of diagnosis. His choreiform movements however did not recur despite poor glycemic control.

Discussion

The pathophysiology of NHHH is still not yet completely understood. According to a recent metanalysis[11], the estimated prevalence of 1:100,000 is thought to be underestimated due to the lack of knowledge about this condition. There is a slight predominance in females (male to female ratio of 1:1.7) and Asia contributes to 71.6% of the reported cases followed by Europe (8.5%) and the Americas (4%)[11].

The chorea of NHHH has some pathognomonic characteristics. According to their type and severity, the abnormal involuntary movements can be classified from mild chorea to severe ballism. Ballismus is uncoordinated wild-flinging movements caused by contraction of the proximal limb muscles[12]. Chorea consists of more continuous and random motions restricted to the distal muscles[13]. The movements usually have an acute or subacute onset, can present with different severities, are most commonly unilateral, rarely bilateral, resolve with sleep and are progressive if not treated [8]. They are typically associated with contralateral imaging findings mainly striatal hyperintensity on T1-weighted MR images or high density on CT scans in the basal ganglia, most commonly involving the putamen[11]. Moreover, improvement of the imaging findings usually lags the resolution of symptoms.

Many mechanisms have been proposed to explain NHHH. The most widely accepted theory is that during

states of non-ketotic hyperglycemia, the Kreb's cycle is inactivated, and the brain shifts to the anaerobic pathway and uses GABA as an energy source which ultimately gets depleted. The depletion of GABA, acetylcholine and resulting metabolic acidosis produces basal ganglia dysfunction leading to chorea. Inversely, ketones in DKA are used as an energy source producing GABA as a metabolite, hence the rarity of NHHH in children where T1D is much more common than T2D. However, this hypothesis does not explain why the manifestations are usually unilateral and don't resolve promptly after glycemic control. Other theories include basal ganglia ischemia, hemorrhage, ion deposition and increased dopamine secretion[14]. Interestingly, our patient did not have urine ketones throughout his initial admission for abnormal movements. He did however have urine ketones on follow-up when his symptoms had completely resolved.

NHHH tends to have a good prognosis. The abnormal movements are reversible and the mainstay of treatment is achieving adequate glycemic control. However, symptoms may persist for weeks despite normoglycemia necessitating the addition of a therapeutic agent. Most commonly used drugs are dopamine antagonists such as haloperidol and risperidone, anticonvulsants such as valproic acid and topiramate, or benzodiazepines such as diazepam and clonazepam[15]. Our patient's symptoms persisted for few weeks despite improved glycemic control for which he required valproic acid that was titrated to control his symptoms. His symptoms eventually resolved after 6 weeks and valproic acid was stopped.

Conclusion :

NHHH is a rare complication of diabetes mellitus especially in children. It is important for clinicals to have a high index of suspicion for NHHH in a patient with choreiform movements and hyperglycemia because the mainstay of treatment is achieving glycemic control. More importantly, as more youth are diagnosed with T2D and other rare forms of diabetes, the diagnosis of NHHH is important to recognize.

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