Diabetic striatopathy in pediatric patient: a case report on a reversible and acquired movement disorder

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Abstract

Purpose: To present a rare case of diabetic striatopathy (DS) in a child with type 1 diabetes mellitus (DM) with reversible unilateral hemichorea-hemiballismus.

Case Report: We report a case of an adolescent girl with uncontrolled type 1 DM who presented with hemichorea-hemiballismus of the right extremities. Cranial magnetic resonance imaging (MRI) showed hyperintense signals on bilateral basal ganglia. There was improvement in hemichorea-hemiballismus as blood glucose levels normalized.

Conclusion: A high index of suspicion is required to make a diagnosis of DS in children presenting with abnormal movement disorder and characteristic neuroimaging findings in a background of uncontrolled DM.

Keywords: **Diabetic striatopathy, Diabetes mellitus type 1, hyperglycemia hemichorea-hemiballismus, pediatrics**

Acta Neurol Taiwan 2024;33:23-27

INTRODUCTION

Diabetic striatopathy (DS) is a rare neurologic complication that has an incidence of 1 in 100,000 in the diabetic population; a majority of which are of Asian descent (76.5%)[(1)]. Only 176 patients (male: female = 1:1.7) with a mean age of 67.6 years were identified from 72 articles[(1)]. Among them, 96.6% had type 2 diabetes mellitus (DM) with 17% being newly diagnosed[(1)]. Interestingly, only a limited number of case reports have been documented for DS with type 1 DM in children.

DS predominantly presents with a constellation of movement disorders associated with poor blood glucose control. Chorea, hemichorea, hemiballismus, and seizures may be the presenting symptoms of non-ketotic hyperglycemia in older female adults with type 2 DM, but these findings are unusual in children with type 1 DM. Here, we report a rare case of DS in an adolescent girl with type 1 DM presenting with hemichorea-hemiballismus movements.

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Received July 14, 2022. Revised August 1, 2022
Accepted November 23, 2022

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CASE PRESENTAT ION

A 14-year-old right-handed Filipino girl presented to neurology-outpatient department with 3-week history of uncontrolled, involuntary, irregular movement of her right limbs. She was first admitted in October 2018 and diagnosed with diabetic ketoacidosis with insulin-dependent type 1 DM. Since then, she was maintained on biphasic human isophane insulin with poor compliance to medication and lost follow up. Three weeks prior to admission, our patient experienced sudden, minimal, uncontrolled involuntary writhing movements of her right arm and leg, sparing the tongue, face and neck. This was exacerbated by physical activity, continuous at rest and disappeared during sleep. There was no history of associated weight loss or weight gain, body weakness, sensory changes or alteration in consciousness. There was no history of neurological disorder or abnormal movements in the family. Due to the progression of intensity of the involuntary movement, she was eventually admitted.

On examination, she has a normal weight of 34 kg (Z score 0), a height of 145 cm (Z score <1) and a body mass index (BMI) of 16.2 kg/m^2 (Z score <-1). Significant findings on neurologic examination showed continuous, repetitive, irregular involuntary movement with larger amplitude choreiform to ballistic movement of the right limbs. Motor strength was preserved on both extremities. Cerebellar examination with right finger-to-nose and right heel-to-shin test demonstrates difficulty due to hemichorea-hemiballismus, but the target was reached. On examination of gait, there was a notable superimposed twisting movement of the right leg and foot during the swing phase, making her gait unpredictable and unsteady. There was no evidence of sensory deficit, hypo/hyper reflexia and cranial nerves were normal.

She was initially managed as having Sydenham chorea (SC) of rheumatic fever (RF) with type 1 DM. The 2D echocardiogram, 12-lead electrocardiogram, and anti-streptolysin O were all normal. A cranial computed tomography (CT) was done at the outset revealing an asymmetric hyperdensity of both corpus striatum, more prominently involving the left (see Figure 1A-D). Cranial MRI with contrast (see Figure 1E-H) was also done and showed abnormal signals on bilateral basal ganglia, more on the left with mildly hyperintense T1- and T2-weighted images. The glycosylated hemoglobin was elevated at 15.3% [normal values = <7%]. Blood glucose monitoring ranges from 200-368 mg/dl daily. It took us three weeks to control her blood glucose level. For symptomatic control of hemichorea-hemiballismus, risperidone 0.5 mg/day for 1 week was given and shifted to valproic acid at 15 mg/

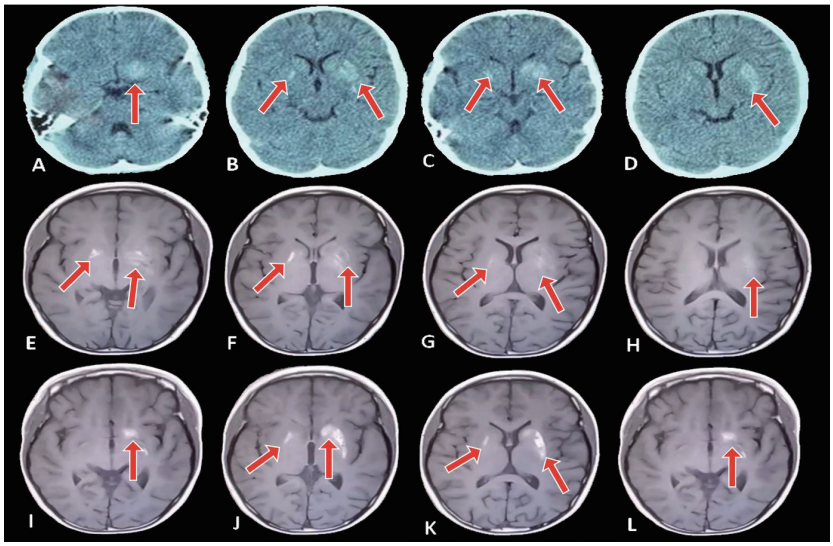

Fig. 1. Cranial computed tomography scan that showed asymmetric hyperdensity of both corpus striatum, more prominently involving the left (red arrow) (A-D). Cranial MRI showing abnormal signals in both basal ganglia, more on the left (red arrows) (E-H). Repeat Cranial MRI two months post-discharge showed increase abnormal signals in both basal ganglia (red arrow) (I-L).

kg/day. The blood sugar levels were better controlled with biphasic insulin maintenance. A month after discharge, the patient's blood sugar ranged from 70-130 mg/dl (normal values: 60-110 mg/dl) that was within acceptable levels already. These resulted in almost near normalization of the blood glucose, there was complete resolution of hemichorea-hemiballismus; however, there remained with subtle infrequent involuntary movement of the right limbs. There was a reduction in the amplitude, frequency and intensity of the hemichorea. The flinging motion, twisting or squirming-like motions of the extremities involved were imperceptible as blood glucose normalized

DISCUSSION

DS is a rare disorder that classically presents with a limited period of choreiform or ballistic movements associated with an episode of non-ketotic hyperglycemia or diabetic ketoacidosis along with characteristic MRI findings[2].

The clinical findings in our case were consistent with striatopathy due to chronic uncontrolled non-ketotic hyperglycemia. The precise etiologic mechanism of DS is not well understood. The pathophysiology is thought to be due to hyperglycemia that dramatically increases neuronal glucose, causing neuronal damage. The high glucose level causes inhibition of astrocytes proliferation resulting in astrocytosis[1]. In a case study, they found out that the basal ganglia are responsible for hemiballism, which contains multiple recent infarcts associated with reactive astrocytosis, suggesting that the ample hypertrophic astrocytes in the lesion may be responsible for characteristic MRI signals[3]. An additional theory suggests an ischemic or metabolic insult. The former inhibits insulin secretion which leads to impaired glucose transport in the brain cells, leading to the release of inhibitory control by gamma-aminobutyric acid (GABA) in the thalamus, which manifest clinically as abnormal body movements, while the latter suggests that regional ischemia is due to diabetic vasculopathy. It is due to the effect of hyperviscosity, which is induced by dehydration due to non-ketotic hyperglycemia, that results in thrombotic obstruction of vessels or occurrence of transient ischemia[2]. The radiologic and pathologic findings in our case demonstrated high signal seen on T1-weighted images can be presumed to induce ischemic changes in the striatum associated with hyperglycemia and hyperviscosity[4].

The main clinical manifestation of DS is the presence of chorea or hemichorea, in which most patients present with unilateral involvement[1]. Our patient had hemichorea-hemiballismus of the right arm, hand, leg and foot. In the Philippines, SC of RF is the most common cause of acute acquired chorea during childhood with a local incidence of 1 per 1000 cases in the school-aged child and a prevalence rate of 1.2-1.3/1000[5,6]. SC is a major sign of acute RF and may be the only sign of RF in some pediatric patients[7]. The characteristic involuntary movement in SC is similar to DS as it is usually asymmetric, present at rest, and disappears during sleep. It is usually aggravated by stress or worsened with anxiety. However, physical findings namely hypotonia and muscular weakness as well as the involvement of bilateral metacarpophalangeal joints producing a "piano-playing" effect is also commonly reported[8,9]. Nonetheless, this was not observed in our patient. Neuropsychiatric symptoms such as irritability, attention deficit and obsessive-compulsive behavior may also exist in SC of RF but not in DS[7]. Lastly, the involuntary movement of DS occurs simultaneously with severe uncontrolled hyperglycemia and is ameliorated with the recovery of blood glycemic level[8]. On the contrary, SC of RF is associated with group A beta-hemolytic streptococcal infection. The neuroimaging findings are typically normal or nonspecific for SC of RF; although some studies of basal ganglia edema have been reported[10]. This is in contrast with MRI findings of striatal hyperintensity signal found in DS.

CT and MRI are the two most common imaging modalities to identify striatal anomalies of DS. One study showed a sensitivity of 95.3% and 78.8% for MRI and CT, respectively[1]. In our patient, the CT scan showed asymmetric hyperdensity of both corpus striatum, more prominently involving the left whereas the cranial MRI revealed abnormal signals in both basal ganglia, more intensely noticeable on the left. This unique imaging finding though not specific, when combined with hyperglycemia and the presence of chorea is pathognomonic of the condition[1]. Asymmetric chorea is characteristically related to contralateral basal ganglia lesion. However, the correlation between the

neuroimaging findings and the patient's symptoms remains ambiguous. Though, reports in 2020 showed an inconsistency rate of 9% between laterality of symptoms and neuroimaging studies[1]. Some patients with unilateral neuroimaging lesions manifest chorea in bilateral limbs, whereas some with bilateral striatal abnormalities show the unilateral manifestation of chorea while others show symptoms in the side of the body ipsilateral to the side of the neuroradiological lesion[11-14]. In the 2020 study, they pointed out that the majority of patients with DS present with hemichorea as opposed to only 9.7% with bilateral limb involvement[1]. In our patient, T1-hyperintense signals were found in the bilateral basal ganglia but more so on the left correlating it with the contralateral affected right limb, indicating that the higher the intensity signals in the basal ganglia the more severe the manifestation of involuntary movement. In the recent case report, the author concluded that the range of T1-weighted high signal in the striatum was closely related to the severity of the disease[11]. This study likewise affirmed that there was no significant correlation found between the side of the body affected and the location of striatal abnormalities[8]. Nevertheless, these clinical and neuroradiologic mismatch gave us a significant challenge to establish the underlying pathogenesis and neurological localization of DS[14].

The mainstay treatment for DS is glycemic control[1,2]. Among patients given glucose-control-only therapy, the median recovery time was two days, whereas the median recovery time of patients receiving anti-chorea medications with successful treatment was 14 days[1]. Although, some patients with chorea could be successfully treated with glucose control only. However, the majority of children need additional anti-chorea medications for symptom control[1,2]. The effective symptomatic treatment of chorea has not been well established, although some reports used valproic acid in escalating doses[15]. It has a slow onset of action therefore it needs at least 2 weeks before considering as ineffective. A neuroleptic drug, like risperidone at 1-2mg per day has also been found to be effective in controlling the chorea[15]. However, they increase the risk of tardive dyskinesia[15]. In general, secondary chorea improves with treating the underlying medical abnormality. Our patient had disabling hemichorea-hemiballismus that interferes with her daily activity hence symptomatic treatment was given.

Most reported cases of DS that include follow-up imaging suggest that the associated T1 hyperintensity is resolved along with the movement symptoms as hyperglycemia is corrected[16]. In one study, 16 of 52 patients who were treated by only controlling hyperglycemia had complete resolution of their chorea, and the remainder generally improved with standard treatments targeting hyperkinetic movement[16]. Our patient's hemichorea-hemiballismus completely disappeared after 2 months with insulin and anti-chorea medication.

Upon repeating the cranial MRI two months after discharge, there was an increase in the extent of the intermediate to high T2 and T1 weighted signals in both basal ganglia (see Figure 1I-L). In a 2020 descriptive study, the shortest follow-up resolution time on CT was 10 days compared to 60 days on MRI, implying that MRI may be a more accurate tool for tracking the resolution of striatal anomalies in follow-up studies[1]. The same study points out that an increase in striatal hyperintensity might reach its maximum level in an average of 90 days following hospital discharge as opposed to the repeat cranial MRI of our patient during the 2nd month of treatment where it showed no improvement, instead documented with the progression of striatal abnormalities on bilateral basal ganglia. This finding in our patient needs immediate follow-up since there is a relatively high overall recurrence rate of 20% even after the resolution of striatal anomaly[1]. This highlights the need for regular examination regardless of the neuroimaging findings.

One limitation in our case report has been the relatively short duration of follow up. Our patient has been unable to see us in the clinic as the patient and her family has gone back home to their province. Thus, we were also unable to do a follow up MRI. Despite these limitations, we were able to document the presence of DS in a patient with type 1 DM and involuntary movements.

CONCLUSION

Due to its rarity, DS is an underdiagnosed neurologic manifestation of type 1 DM in children. A high index of suspicion is needed among patients with hemichorea/hemiballismus and uncontrolled DM, as this is a potentially reversible disorder that can be managed with

adequate glucose control.

Conflicts of Interest

The authors have no financial conflicts of interest.

Author's role

Conceptualization: Maela P. Palisoc, Roland Dominic G. Jamora. Data curation: all authors. Formal analysis: all authors. Investigation: all authors. Methodology: all authors. Project administration: Maela P. Palisoc, Roland Dominic G. Jamora. Supervision: Maela P. Palisoc, Roland Dominic G. Jamora. Validation: Maela P. Palisoc, Roland Dominic G Jamora. Visualization: all authors. Writing—original draft: Maela P. Palisoc, Annfel Jave S. Navarro. Writing—review & editing: all authors.

Study Funding

The study has no funding support

Ethical Standards

The authors state that they have obtained verbal and written informed consent from the patients for the inclusion of their medical and treatment history within this report.

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