

# **Diabetic Striatopathy: A New Challenge in Type-1 Pediatric Diabetic Patients**

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## **Abstract**

Diabetic striatopathy is a neurological condition in diabetic patients characterized by hemichorea- hemiballismus due to vascular and metabolic derangements in basal ganglia. This is a known entity in Type-2 Diabetic adult patients, however, seen very rarely in Type-1 diabetic Pediatric patients. Diabetic striatopathy develops in patients with poor glycemic control in the absence of ketosis. The patient tolerates hyperglycemia for a long time, which results in metabolic injury.

## **INTRODUCTION**

Diabetic striatopathy is an uncommon presentation of diabetes mellitus. It usually presents with hemiballismus-hemichorea. Chorea means “dance-like” in Greek, and refers to rapid, chaotic movements that seem to flow from one body part to another. Many patients have generalized chorea but the majority have asymmetric manifestations and up to 20% have hemichorea [1]. Ballismus is a type of involuntary movement affecting proximal limb musculature, manifesting as jerky, flinging movements of the extremity. The most common etiology of chorea in the pediatric age group is Sydenham’s chorea [2]. In patients of diabetes mellitus, hyperosmolar nonketotic hyperglycemia is responsible for hemichorea – hemiballismus which is commonly seen in type -2 diabetic adult, female patients in the hyperglycaemic hyperosmolar state [3], and very few cases have been reported in the pediatrics age group. Hemichoreic- hemiballismic movements associated with nonketotic hyperosmolar hyperglycemia in diabetic patients are labeled as diabetic striatopathy [4]. It results from vascular and metabolic injury to basal ganglia due to chronic hyperglycemia as a

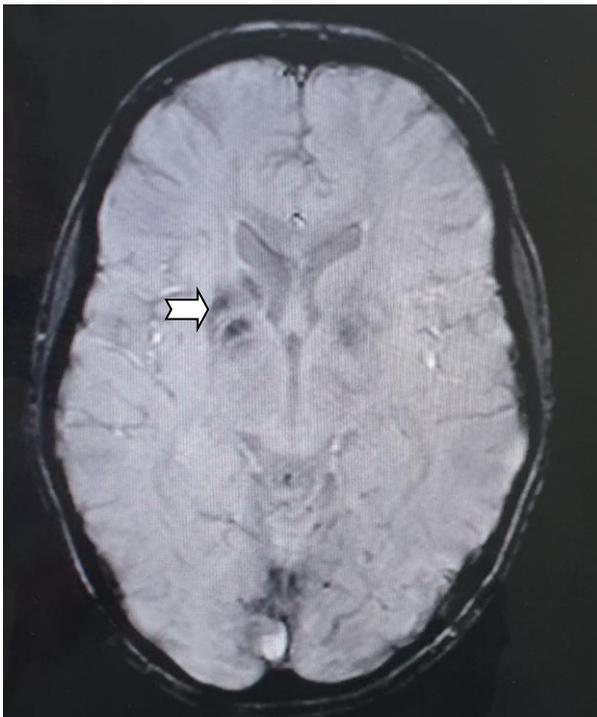
result of poorly controlled type -2 and rarely type-1 diabetes mellitus. We hereby present two cases of diabetic striatopathy who presented to us with abnormal movements of the body.

## **CASE REPORTS**

Case 1: An 11- year- old female presented with abnormal movements of the left hand and left foot for one and a half months. The movements were present continuously throughout the day and disappeared at night during sleep. The patient has known the case of type-1 diabetes mellitus for 3 years and was on the NPH insulin regimen with poor compliance. Family history for diabetes mellitus is negative. Anthropometry revealed short stature 119/125 cm (<-3SD height for age on CDC growth chart), underweight 19/20.3 kg (<-3SD weight for age on CDC growth chart). There were continuous irregular movements of high frequency interrupted by jerks consistent with hemichorea /hemiballismus. Laboratory results revealed HbA1C level- 13.8%, RBS- 300mg/dl, urinary ketones negative, and glycosuria present. Blood osmolality was 300 mosm/kg. Antibodies against glutamic acid decarboxylase (anti-GAD 65) were positive, which confirmed the diagnosis of Type 1 Diabetes mellitus. Anti-insulin antibodies were negative and Anti-tissue transglutaminase also negative. MRI Brain was done on day 4 of admission revealed bilateral basal ganglia hemorrhage and ischemic changes as shown in figure 1 &2. Correction of hyperglycemia was done with titration of insulin dosage. For the abnormal body movements, trihexyphenidyl was started at 0.1 mg/kg and the dosage hiked up for optimal response to 0.2 mg/kg. The patient was discharged under satisfactory conditions after 10 days of hospitalization. This patient did not return for follow-up.

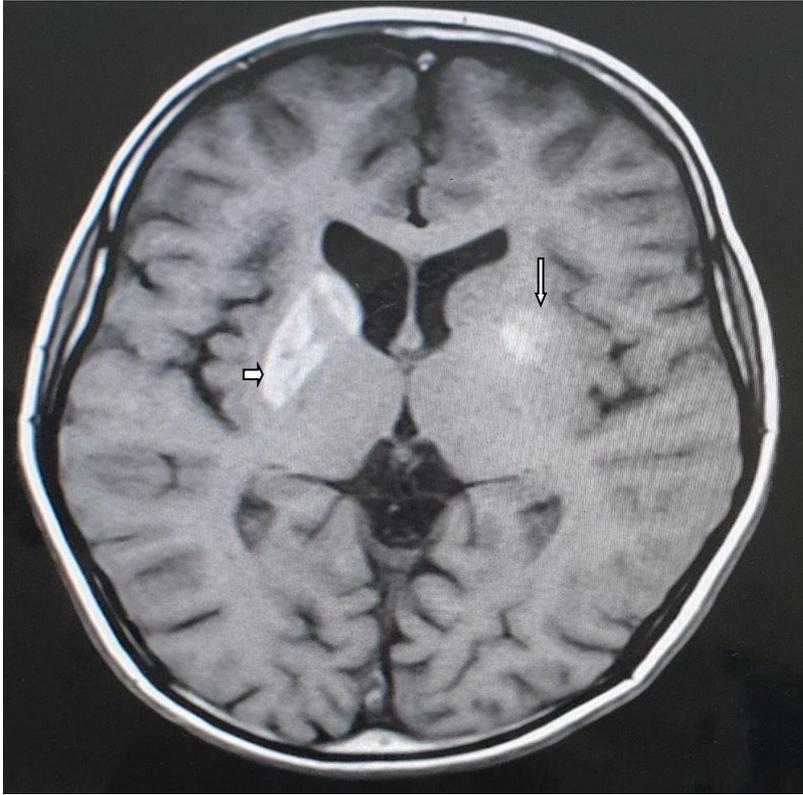


**Figure 1:** T1 showing hyperintensity in bilateral basal ganglia more on the right side.



**Figure 2:** GRE sequence showing blooming in basal ganglia right more than left due to hemorrhage

Case 2: A 10 Years old Female presented with abnormal movements of the left upper and lower limbs for 7 days. The patient was known as a case of Type 1 DM for 2 years was on NPH insulin regimen with poor compliance. There was no family history of diabetes mellitus in a family member. The anthropometry revealed short stature 110/123cm (<-3SD height for age on CDC Growth chart), Underweight 18/20.7kg (<-3SD weight for age on CDC Growth chart). She had periodic choreiform and ballistic movements of the left upper and lower extremities that ceased during sleep. Initial laboratory values revealed RBS-568mg/dl, HB1Ac 10%, Urinary ketones-negative. Blood osmolality was 298 mosm/kg. MRI-Brain showed asymmetrical T1 hyperintensity is noted in bilateral basal ganglia (more on the right side) with no diffusion restriction, post-contrast enhancement as shown in figure 3. Antibodies against glutamic acid decarboxylase (anti-GAD 65) were positive, which confirmed the diagnosis of Type 1 Diabetes mellitus. Anti-insulin antibodies were negative and Anti-tissue transglutaminase also negative. Correction of hyperglycemia was done with titration of insulin dosage. For the abnormal body movements tablet Trihexyphenidyl 0.1mg/kg, tablet Clonazepam 0.015mg/kg/day started and then dosage hiked up for optimal response (Table Trihexyphenidyl 0.3mg/kg/day, Tablet Clonazepam 0.03mg/kg/day, Tablet Haloperidol 0.015mg/kg/day. This patient was discharged on a basal-bolus regimen, on follow-up after 1 month of discharge the patient showed improvement in terms of choreiform movements and improvement in glycemic control. This patient remained on regular follow – up 3 monthly showed improvements in dyskinetic movement so haloperidol and trihexyphenidyl tapered and stopped.



**Figure 3:** is showing bilateral hyperintensity in basal ganglia more on the right side.

EEG was not done in both cases as after MRI images, the diagnosis of diabetic striatopathy was made and patients improved with treatment.

Weight and height were mentioned for the patient as a part of the general physical examination and to see nutritional adequacy on follow-up.

## **DISCUSSION**

Diabetic striatopathy presents with hemiballism-hemichorea in patients with poorly controlled hyperglycemia. Chronic hyperglycemia causes vascular and metabolic injury to basal ganglia causing contralateral hyperkinetic movements. The neuroimaging shows lesions, such as hyper attenuation of basal ganglia on CT scan, the hyperintensity of basal ganglia on MRI (T1w imaging).

The clinical findings in our cases are consistent with striatopathy as a result of non-ketotic hyperglycemia. The exact etiopathogenesis of diabetic striatopathy and non-ketosis is not fully understood. Two major hypotheses have been purposed to explain the likely etiology: ischemic versus metabolic insult [5].

The difference in the incidence of striatopathy in type-2 diabetic patients as compared to type-1 is due to pathophysiology of dyskinesia. In HHS, the Krebs's cycle activity is suppressed in the brain due to hyperglycemia and shifts to anaerobic cycle. This shift in HHS causes the brain to metabolize GABA to succinic acid via semialdehyde pathway hence depleting GABA levels in the brain. This leads to release of inhibitory control by GABA in thalamus resulting in hyperkinetic movement, whereas in diabetic ketoacidosis (DKA) acetoacetate produces in the liver and GABA levels will not be deranged hence rarity in DKA patients [6-7]. The non –ketotic hyperglycemia suppresses insulin secretion which leads to impaired glucose transport in brain cells. Impaired glucose transport leads to diminished functioning of GABAnergic inhibitory transmission in the striatum which manifests clinically as abnormal body movements. This metabolic hypothesis does not explain why after good glycemetic control movements cease to disappear in a few patients [8-9].

The ischemic hypothesis suggests that regional ischemia is due to diabetic vasculopathy. Under the effect of hyperviscosity which is induced by dehydration due to non-ketotic hyperglycemia, a thrombotic obstruction of vessels or transient ischemia is liable to occur. Although obstruction of the microvascular lumens in the affected striatum has seldom been observed histologically [8-9].

In most cases of diabetic striatopathy, hyperglycemia is usually present without ketoacidosis, as seen in our patients too, which explains the fact that these patients tolerate persistent hyperglycemia leading to changes in basal ganglia. The exact reason behind the basal ganglia lesion is still unclear. In typical Hemiballismus-Hemichorea patients, MRI findings of

hyperintensity in basal ganglia are due to the accumulation of manganese in gemistocytes (astrocytes with large protein content found in acute brain injury). Histopathological findings in adult diabetic patients with Hemiballismus-Hemichorea revealed areas of gliosis, accumulation of gemistocyte, and loss of neurons. The majority of data in diabetic Hemiballismus-Hemichorea is on adult patients, as few as 3 pediatric patients have been reported as per our knowledge/literature. Hence, more studies are required in pediatric patients who present with nonketotic hyperglycemia [10-11].

Most patients with hemichorea-hemiballismus improve with improved glycemic control and neuroleptic drugs. The exact duration of anti chorea treatment is not known. The most common drugs used for choreiform movements are neuroleptics drugs (haloperidol/risperidone), selective serotonin reuptake inhibitor (escitalopram), dopamine depleting agent (risperidone tetrabenazine), GABAergic drugs (clonazepam/Gabapentin). The complete clinical with or without radiological improvement may take from 2-28 days [3]. The rationale for using trihexyphenidyl in our cases is due to its antidyskinetic effect [12]. The mean time of improvement in our case 1 was 30 days and case 2 was 3 months.

To conclude, close monitoring is required in patients who have hyperglycemia without ketosis as these patients have more tendencies to develop HH and early institution of therapy along with glucovigilance in these patients can prevent long term morbidity.

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