Case Report

Neurological Disorders due to Recurrent Hypoglycemia

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Abstract

The most important material for the brain tissues is glucose .The brain utilizes around (25%) of the body's glucose, and it's metabolism thought to be primarily by astrocytes through non-insulin dependent (GLUT-1) transporter and insulin dependent (GLUT-4) transporter, but the brain contains very limited stores of glycogen, and therefore it can't regulate it's function for long time without glucose.

So neuronal damage can lead to multiple neurological manifestations as a result of hypoglycemia acutely; stroke like symptoms, movement disorders (tremor, ataxia, difficulty of walking), seizures, coma and death; chronically and repetitive leads to cognitive impairment. Which means clinical picture appears according to the area of neuronal damage.

Keywords: NMDA receptor: N-Methyl-D-Aspartate receptor, WM: White Matter, ischemia, neuronal DNA, Hypoxia, Basal ganglia, cerebral peduncle.

Case Presentation

A 27 years old female patient , known case of T1-DM since age 12 years , has been hospitalized several times due to hypoglycemia and occasionally due to hyperglycemia ,which followed by hypoglycemia . These severe sharp oscillations were seen in blood glucose monitoring, increased up to 500 mg/dL, or severe drop to 25 mg/dL. We couldn't find any cause for explanation of the oscillating glucose levels except non-compliance to treatment .This patient was admitted to central hospital in October- 2015 with :(mild dysarthria, mild dysphagia,head tremor ,left arm tremor ,ataxia and constipation) for three months duration. History of admissions several times to peripheral hospital, with uncontrolled blood sugar and hypoglycemia for the same period.

Physical Examination: The patient was been dysarthric, oriented to place, time and persons. Spastic and ataxic in gait, can walk with help. Pupils equally reactive to light, Gaze evoked horizontal nystagmus, UMN right facial palsy, left 12-th nerve palsy. Hypertonia in both lower limbs with spasticity. Powers in upper and lower limbs, in the right side 5/5, in the left side 4/5**,**

DTR (deep tendon reflexes): brisk reflexes in upper and lower limbs. Sensation intact, no sphincter dysfunction. Lab. Tests (CBC, KFT, LFT, Na+, K+, Ca+, s.iron, s.ferritin, PTH, s.B12, s.Folate, TFT, S. ceruloplasmine, Urinary copper) are normal. CSF analysis (wbc-nil, Rbc-nil, protein -127, glucose-146), blood sugar fluctuated between 25 mg\dl and 500 mg\dl. EEG-diffuse slow wave pattern, Brain MRI at the time of admission to peripheral hospital in July 2015 showed evidence of multiple hyper intense lesions in periventricular, basal ganglia and both cerebral peduncles, more in the right side appears in DWI, T_2 and FLAIR sequences (**Figure 1**) Whole spine MRI is normal.

This patient admitted to central hospital in October 2015 with more deteriorating in clinical presentation, and repeated Brain and whole spine MRI, and we found that the lesions increased in size and in numbers without contrast enhancement (**Figure 2**), without any findings in whole spine MRI.

On follow up after more than 1 year, in December 2016, the patient much better in his clinical features, great improvement in Brain MRI seen in **Figure 3**.

And last follow up for this patient had been in Jun 2017, and his clinical features completely back to normal, Brain MRI in (**Figure 4**).

Discussion

Syndrome hypoglycemia is known since 1924 (1). Most common causes of recurrent hypoglycemia are insulin therapy, which is using in both types diabetes (type 1and type 2) or long acting sulfonylurea drugs for type 2 DM. Chronically can impair the counter regulatory response to hypoglycemia through either impaired awareness of hypoglycemia or hypoglycemia associated autonomic failure. We reviewed more than twenty articles and found that approximately half of the patients with type 1 diabetes were lost response of glucagon and epinephrine to hypoglycemia (2,24).The brain areas that are affected in recurrent hypoglycemia are small and medium sized caudate neurons, neostriatum, hippocampus in the medial temporal lobes, the dentate gyrus and superficial cortical layers, specifically layers 2 and 3, and all areas around cerebrospinal fluids (periventricular white matter, internal capsule, and splenium of corpus callosum) seems to be more affected (3,25) . Low glucose level cause low acetate level, which in turns causes oxaloacetate to form aspartate, and α ketoglutarate to form glutamate (4,5). Aspartate and glutamate build up in the tissue, then interstitial spaces and ultimately CSF space (6). Glutamate and aspartate usually activate glutamate receptors, particularly at the NMDA receptor (7-10). Which is initially leads to sodium and water influx and cause cellular edema (11). This mechanism followed by intra-cellular calcium shifting and causes dysfunction of many intracellular processes (12-15). NMDA receptor activation lead to the production of reactive oxygen species which damage neuronal DNA (16). Ultimately leads to more apoptosis and then stimulate cell death.

In our case there is a young diabetic patient presented with symptoms of dysarthria, dysphagia, head tremor, left arm tremor, ataxia and constipation, for three months duration. Here brain MRI images which is available and most sensitive for diagnosis, showed large multiple hyper intense lesions

in periventricular, basal ganglia and both cerebral peduncles. Patients with extensive cortical and WM involvement often present a diagnostic challenge. Similar changes can also occur with hypoxia, hyperammonemia, encephalitis, after seizures, or may be drug-induced (17, 18). Splenial lesions have been reported in seizures, anti-epileptic drug withdrawal or toxicity, alcohol abuse, encephalitis, and electrolyte derange-ments (19, 20). The medical literatures described similar cases with sparing of the thalamus, brain stem and cerebellum, and this may help to differentiate hypoglycemia from hypoxic brain injury, which often involves the thalamus (17,21,22,23), but the our patient had good size lesions in both cerebral peduncles, which was not mentioned in medical literatures. Clinical context, and past medical history from the patient and family should narrow diagnostic considerations and showed evidence of non-compliance of the patient for controlling here blood sugar, with predominance recurrent hypoglycemia and drops blood sugar to 25mg\dl for long period .During the admission in our department, we consulted endocrine team for strict therapy regimen to control here blood sugar.

One year later on follow up and after repeating brain MRI images, we found that all brain MRI lesions disappeared.

Conclusion

Recurrent hypoglycemia can cause multiple neurological dysfunctions, according to the area of neuronal damage. Reversible brain MRI changes were established in our case with cerebral peduncles involvement similar to others CNS disorders that are usually affecting brain stem. Physicians should discuss the best way of treatment and prevention to achieving blood sugar control.

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Figures

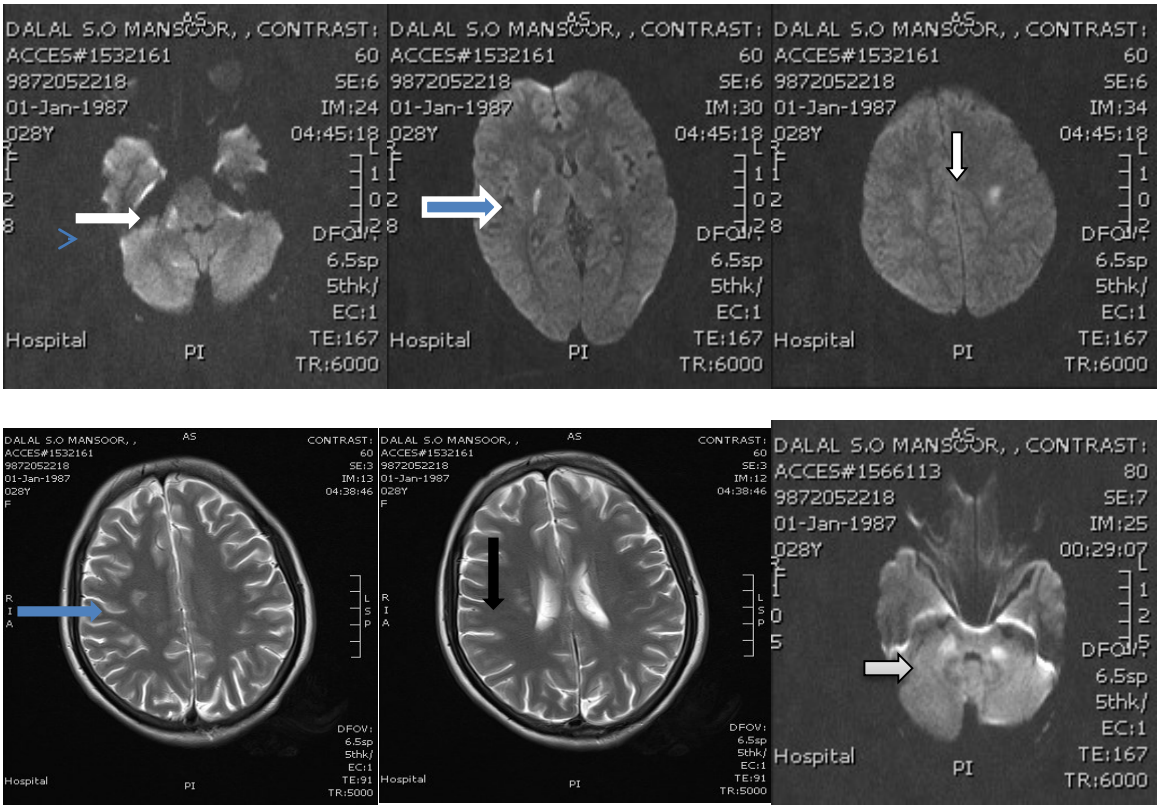

Figure 1. (First admission in July 2015 to peripheral hospital) Brian MRI T_2, DWI and FLAIR.

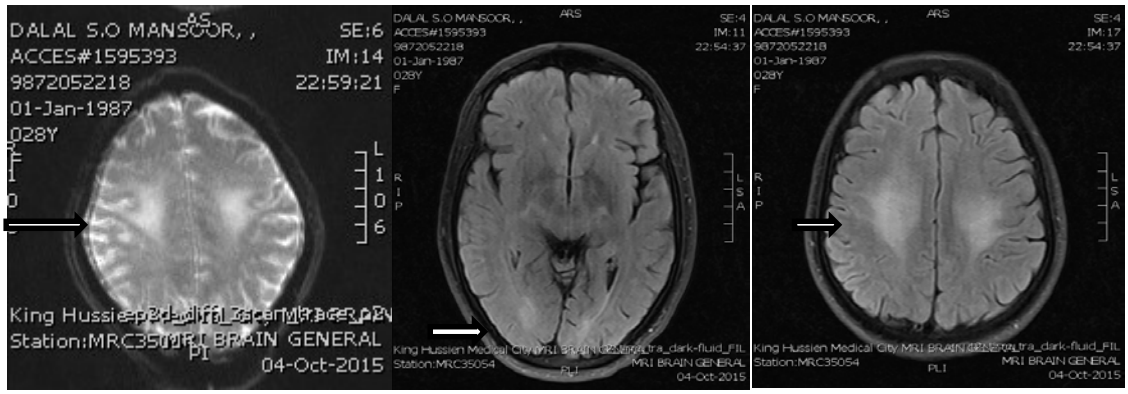

Figure 2. Brain MRI T_2 and FLAIR.

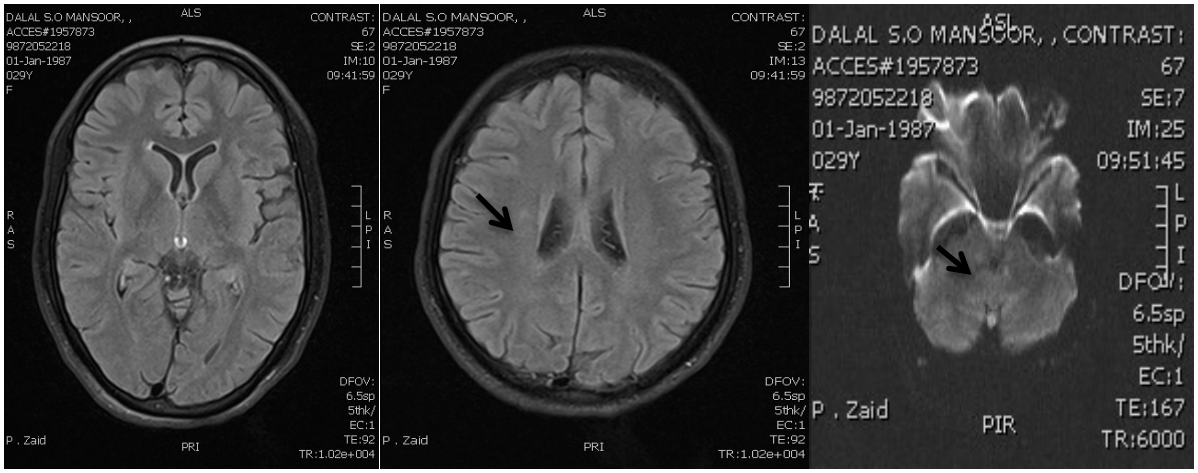

Figure 3. Brain MRI DWI and FLAIR.

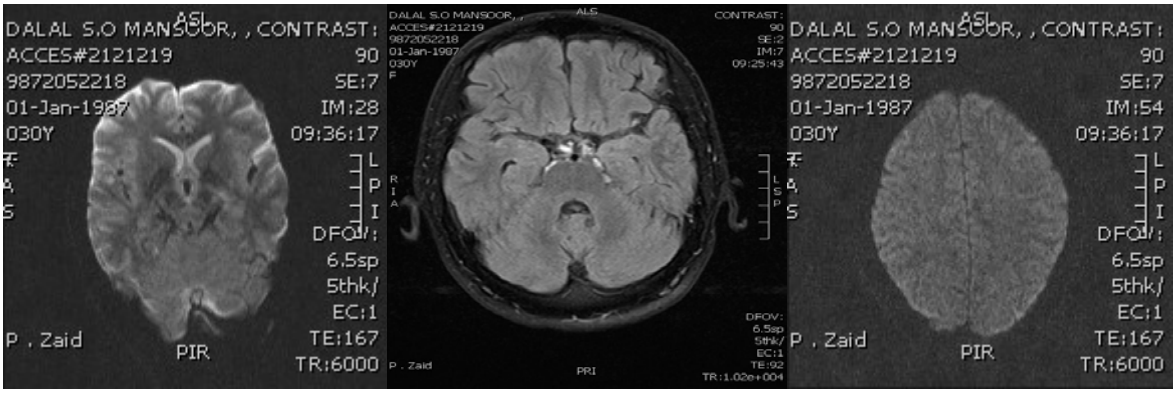

Figure 4. Brain MRI DWI and FLAIR.