

A Sweet Imbalance: Reversible Middle Cerebellar Peduncle Signal Change in Hypoglycaemic Encephalopathy

Sir,

Hypoglycemic encephalopathy is a reversible metabolic encephalopathy associated with classical radiological involvement of the cortices, hippocampus, and caudate nucleus, which are known to reverse with the correction of hypoglycemia.^[1] Albeit being considered an eminently reversible disease entity, the clinical outcomes may be unfavorable if hypoglycemia is severe and prolonged and may consequently lead to significant morbidity. There are few studies that have examined clinic-radiological correlates of hypoglycemia.^[1-3] The occurrence of bilateral middle cerebellar peduncle diffusion restriction is highly uncommon, and of clinical relevance, as reversibility with the establishment of euglycemia portends favorable outcomes.^[4]

A 69-year-old female presented to our emergency services with the chief complaints of altered sensorium of 3 hours' duration. She was a longstanding diabetic for nearly 20 years, with stringent blood sugar control achieved on three oral hypoglycemic agents (metformin 1000 mg/day, glibenclamide 15 mg/day, and linagliptin 5 mg/day). She had been eating poorly for 3 days prior to the presentation, due to a death in the family. At presentation, her vital signs were stable. She was noted to be in a confusional state, without demonstrable

focal neurological deficits. She had no fever or features of meningeal irritation.

Her random blood sugar in the emergency room was 37 mg/dL. A 100 mL bolus of 25% dextrose was administered, followed by a 10% dextrose infusion. Her renal function test revealed blood urea nitrogen = 27 mg/dL; serum creatinine = 1.8 mg/dL (estimated glomerular filtration rate: 45 mL/min/1.73 m²). HbA1c was 8.2%. Hepatic and thyroid function and serum cortisol levels were in the normal range. Over the next 36 h, her blood sugar levels remained between 70 and 85 mg/dL on dextrose infusion, with a recurrent episode of symptomatic hypoglycemia (blood sugar 54 mg/dL) on the first day, and finally normalized after 36 h of treatment. Electroencephalography (EEG) done on the second day was normal. Magnetic resonance imaging (MRI) of the brain done at presentation showed diffusion restriction in bilateral middle cerebellar peduncles (MCP) [Figure 1]. MR angiography of the head and neck vessels was normal.

With the establishment of euglycemia, her sensorium improved by the second day of admission. Examination done at this stage revealed bilateral symmetrical upper limb incoordination in the form of impaired finger-nose-finger testing, intention tremor, dysidiadochokinesia, and gait ataxia, which gradually improved over the next 2 days. MRI brain

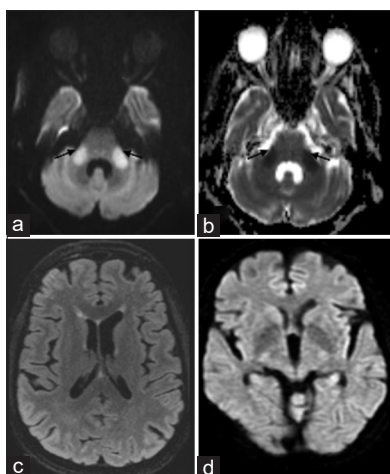


Figure 1: (a) Diffusion-weighted imaging (DWI) and (b) apparent diffusion coefficient (ADC) at presentation show areas of diffusion restriction in bilateral middle cerebellar peduncles (arrows). The supratentorial structures are normal on T2/Fluid-attenuated inversion recovery (FLAIR) (c) and DWI images (d).

repeated on the fifth day demonstrated resolution of the MCP signal change [Supplement 1]. The patient continued to remain asymptomatic at 3 months of follow-up.

Cerebellar dysfunction provoked by hypoglycemia is distinctly uncommon and maybe a rare complication in severe cases. The cerebellum and its connections are, in fact, considered to be privileged sites, which are relatively spared the brunt of hypoglycaemic central nervous system insult due to differential glucose metabolism and/or efficiency of glucose transportation.^[5] Differential glucose metabolism implies that glucose uptake relative to the cerebral cortex is higher in the cerebellum although the rate of glucose metabolism is lower. Hence, the cerebellum is less susceptible to the effects of prolonged and/or severe hypoglycemia. A handful of cases of hypoglycemia-induced cerebellar dysfunction are reported in the literature [Supplement 2],^[5-8] and our case adds to this limited repertoire. The relationship between the duration of hypoglycemia seems to correlate with the development of cerebellar dysfunction, with both prolonged and recurrent episodes of hypoglycemia portending the development of this complication.^[6] Overcontrolled diabetes and insulinoma may be risk factors that may predispose to such a complication. Despite hypoglycemia correction, residual sequelae may persist for several months, with gradual improvement in some cases.^[5]

Another unusual feature in our patient was the distinctive radiological findings in the form of bilateral MCP involvement. Radiological findings in hypoglycemia usually demonstrate signal change in the cerebral cortex, hippocampus, caudate nucleus, basal ganglia, corona radiata, centrum semiovale, and rarely, splenium of the corpus callosum and internal capsule.^[1,9] Uncommonly, central pontine myelinolysis may be triggered by rapid shifts in blood glucose, including sudden and precipitous hypoglycemia.^[10] MCP involvement is considered extremely rare

and may portend poor outcomes in terms of cerebellar sequelae, unlike our case.^[4] The MCPs are predominantly composed of white matter fibers originating from the contralateral pontine nuclei traversing to the cerebellum. Hypoglycemia probably leads to intramyelinic edema of these fibers, responsible for the MRI findings. A plausible concern in our patient may have been a stroke, keeping in mind the diffusion restricting nature of the lesions. However, rapid resolution and absolute symmetry keenly disfavored this supposition. It is also possible that this patient's individual neurometabolism favored decreased glucose uptake: utilization ratio in the middle cerebellar peduncles compared to the cortex, making them susceptible to hypoglycemic injury. This mechanism has been previously reported by Kim *et al.*,^[7] supported by **fluorodeoxyglucose (FDG)**-positron emission tomography (PET).

Usually, bilateral symmetrical MCP involvement may be demonstrated by a host of conditions, with hypoglycemia being a largely uncommon etiology. In a series of 27 patients with bilateral MCP involvement, only one patient had hypoglycemia as the underlying cause.^[4] Other diseases that involve bilateral MCP include neurodegenerative conditions, including multiple system atrophy, spinocerebellar ataxia, Wilson's disease, stroke, hypertensive encephalopathy, demyelinating diseases, Behcet disease, human immunodeficiency virus (HIV) encephalopathy, and lymphoma.^[4]

Cerebellar dysfunction is a rare manifestation of hypoglycemia and may present with unusual neuroradiological correlates. It is imperative to recognize and correct it promptly to prevent long-term neurological sequelae.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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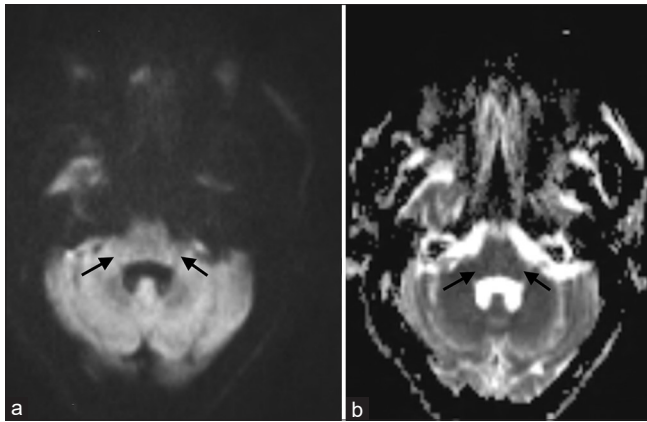
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Supplement 1: (a) Diffusion-weighted imaging (DWI) and (b) apparent diffusion coefficient (ADC) at 72 h show the resolution of the areas of diffusion restriction in the middle cerebellar peduncles (arrows)

Supplement 2: Summary of published reports of cerebellar dysfunction associated with hypoglycemia

Author/year of publication	Age/sex of the patient	Duration of symptoms	Clinical features	Radiological features	Outcome
Berz <i>et al.</i> /2008 ^[5]	51 yrs/male	12 h; symptoms developed after self-overdosing of insulin	Limb dysmetria, gait ataxia, dysarthria	MRI showed small vessel ischemic changes	Resolution over 3 months
Shwaninger <i>et al.</i> /2002 ^[6]	41 yrs/male	Two years history of recurrent hypoglycemia due to insulinoma	Severe gait ataxia, mild intention tremor	MRI brain showed bilateral posterior limb (internal capsule) and middle cerebellar hyperintensities on T2 images (PET) brain: normal	Persistence of MRI signal change, but some clinical improvement in cerebellar features at 4 months after resection of insulinoma
Kim <i>et al.</i> /2000 ^[7]	52 yrs/female	12 h	Ataxia, dysarthria, tremor, giddiness	MRI brain normal; FDG-PET showed decreased glucose uptake: utilization ratio and increased glucose leak in the cerebellum	Complete resolution of cerebellar features over 12 h, following hypoglycemia correction
Agrawal <i>et al.</i> /2014 ^[8]	55 yrs/female	8 h	Sudden onset of postural imbalance and incoordination with focal cerebellar signs on the left side	MRI brain normal	Complete resolution of cerebellar features within 20 min of the administration of glucose