THE RARE NEUROLOGIC MANIFESTATIONS OF ACUTE HYPOGLYCEMIA; DYSKINESIA AND HEMIPLEGIA

S. Aktan, M.D.* / C. Aykut, M.D.** / G. Tughan, M.D.

* *Associate Professor, Department of Neurology, Faculty of Medicine, Marmara University, İstanbul, Turkey.*
** *Research Assistant, Department of Neurology, Faculty of Medicine, Marmara University, İstanbul Turkey.*

SUMMARY

Hypoglycemia causes alterations in consciousness such as confusion and stupor, as well as seizure and sudden hemiparesis.

In this article, neurologic manifestations of acute hypoglycemia and probable causes have been reviewed in connection with two cases encountered.

The first patient developed orofasciobuccal and upper limb dyskinetic movements while the second patient displayed transient hypoglycemic hemiplegia.

The dyskinetic movements are attributed to the increase of glutamate which is the excitatory neurotransmitter in the striatum, particularly in the caudate nucleus. It is also presumed that the transient hypoglycemic hemiplegia is due to hemodynamic alterations in cortical watershed areas.

Key Words: Hypoglycemia, dyskinesia, hemiplegia.

INTRODUCTION

Hypoglycemia may cause alterations in consciousness such as confusion and stupor as well as seizure and sudden hemiparesis. Diabetes mellitus, alcoholism, and sepsis alone or in combination accounted for 90% of cases of hypoglycemia. Among other causes responsible for hypoglycemia are fasting, terminal malignant diseases, insulinomas, insulin abuse, gastroenteritis, and myxedema (1-3).

In this article, neurologic manifestations of acute hypoglycemia and its probable causes are discussed in connection with two cases encountered.

The first patient developed orofasciobuccal and upper limb dyskinetic movements due to prolonged hypoglycemia. The other patient developed sudden hemiparesis which improved completely with intravenous hypertonic glucose administration. Both cases are reported due to these unigue manifestations.

CASE REPORTS

CASE 1-A 52-year-old woman with chronic liver disease was admitted to our hospital with hematemesis accompanied by hepatosplenomegaly. HBS Ag was positive while anti-HBs antibody was negative. Further laboratory investigations were unremarkable with slight elevation in serum GOT and GPT values. Hematemesis was stopped with conservative measures and her general condition was stable. She was kept in hospital for further evaluation and treatment.

Days following her admission she became agitated and the next day she was confused and then she became stuporous. On neurological examination, she was stuporous. With noxious stimuli, she could not move her right leg. She experienced upper limb and orofasciobuccal dyskinetic movements. The plantar response was extensor on the right side. Her serum glucose level was 20mg% in multiple examinations. Hypertonic glucose was useless in recuscitating the patient and her coma deepened (E1V1M1 according to the Glascow Coma Scale). The dyskinetic movements disappeared and she died after 10 days. Cranial CT on the first day of coma revealed no remarkable lesions or generalized brain swelling.

CASE 2-A 48-year-old woman with chronic renal insufficiency developed hyperpotassemia during hospitalization. She was immediately given insulin and hypertonic glucose for the treatment of hyperpotassemia. In 20 minutes she became lethargic and developed right hemiparesis. Her serum glucose level was 25mg/100ml in repeated examinations. She was given intra venous hypertonic glucose with subsequent complete resolution of her neurological deficit.

DISCUSSION

In chronic liver dissease, mental confusion due to hypoglycemia is a common clinical disorder. During the course of chronic liver disease hypoglycemia is believed to be due to an abnormality in glycogen metabolism (4).

The cortex, hypocampus, cerebellum, and striatum are the most vulnerable parts of the brain that are affected from hemodynamic altrations such as hypoxia, hypotension, and hypoglycemia (5). Ischemia and hypoxia affect border zones between major arteries and end artery zones at the cortex. Striatum, particularly the caudate nucleus on the other hand is more susceptible to hypoglycemia than the cortex (6,7).

In recent experimental studies in the rat, the nucleus caudatus and putamen (caudoputamen) have been shown to be very vulnerable to hypoglycemia. Small and medium sized neurons are predominantly damaged, whereas the larger neurons are markedly more resistant (8-10).

The membrane depolarization in the striatum during hypoglysemia was believed to induce elevation of intracellular calcium concentration and initiate cell death in vulnerable neurons (11). However recent studies show that massive calcium loading does not occur in hypoglysemia (12,13). So it is concluded that, calcium accumulation is not responsible for neuronal necrosis in hypoglysemia as it is in ischemia. The elevated intracellular calcium concentrations during hypoglycemia leads to release of neurotransmitters, especially glutamate and aspartate in the striatum (14).

Recent studies have implicated that excitatory transmitter substances such as glutamate, have neurotoxic properties when applied intracerebrally (10). Glutamate is the most effective excitatory neurotransmitter in the caudate nucleus (15). The possible cause of hypoglysemic nerve cell injury in this nucleus is probably due to the excitotoxic effect of glutamate. Furthermore, intrastriatal injection of a glutamate receptor antagonist protects the caudate nucleus against hypoglycemic neuronal damage in rats (10,13,14,16).

In our first patient,the appearence of orofasciobuccal and upper limb dyskinetic movements in the acute phase of hypoglycemic state is attributed to elevated concentrations of glutamate in the striatum, particularly in he caudate nucleus. When coma deepened, the dyskinetic movements disappeared indicating glutamate mediated hypoglycemic neuronal damage. In this patient we also observed right lower limb paresis and Babinski sign. Just like ischemic and hypoxic states, the 'border zone' and 'end artery zone' areas are vulnerable to hypoglycemia. Cerebral perfusion pressure and blood flow of this patient have already been reduced in these regions that are called 'watershed areas'. The infarct occurring in those areas without any arterial obstruction is called "watershed infarct" (1, 17). The lower limb paresis can be explained as a watershed infarct.

The second patient developed transient hypoglycemic hemiparesis that is related to hemodynamic changes occurring in the cortical "watershed areas".

In the late stages of hypoglycemia, cranial CT may show low density areas in the cerebral cortex with contrast medium enhancement (17). These CT findings represent the course neural cell damage by severse hypoglycemia.

In our first case the cranial CT that was performed on the first day of hypoglycemic coma showed no remarkable lesion in the 'border zone' areas which is in agreement with the description of Iwai et al. (17).

Hypoglycemia, besides other neurological signs, may cause dyskinesia and hemiplegia. Early diagnosis and treatmet with hypertonic glucose may completely reverse the neurological deficit. In the near future the use of glutamate receptor antagonists may be useful in the treatment of late diagnosed hypoglycemic neurological signs.

REFERENCES

1. *Malouf R, Brust JCM. Hypoglycemia: causes, neurological manifestations, and outcome. Ann Neurol. 1985; 17:421-430.*
2. *Foster CW, Hart RG. Hypoglycemic hemiplegia: two cases and a clinical review. Stroke 1987: 18:944-946*
3. *Wallis WE, Donaldson I Scott RS. Hypoglycemia masquerading as cerebrovascular disease. Ann Neurol. 1985; 18:510-512*
4. *Iber FL, Latham PS. Normal and pathologic physiology of the liver. In: Sodeman WA, Sodeman TM (eds). Sodeman's Pathologic Physiology Mechanisms of Disease. Philedelphia: WB Saunders 1985: 875-909.*
5. *Brierley JB, Brown AW, Meldrum BS. The nature and time course of the neuronal alterations resulting from oligemia and hypoglycemia in the brain of macaca mulatta. Brain Res. 1971; 25:483-499.*
6. *Kalimo H, Ollson Y. Effects of severe hypoglycemia on the human brain: neuropathological case reports. Acta Neurol Scand 1980; 62:345-356.*
7. *Smith ML, Auer RN, Siesjo BK. The density and distribution of ischemic brain injury in the rat following 2-10mm of forebrain ischemia. Acta Neuropathol (Berl). 1984; 64:319-332.*
8. *Wieloch T. Hypoglycemia induced neuronal damage preventad by an N-methyl D-aspartate antagonist. Science 1985; 230:681-683.*
9. *Kalimo H, Auer RN, Siesjo BK. The temporal evolution of hypoglycemic brain damage. III. Light and electron microscopic finding in the rat caudoputamen. Acta neuropathol (Berl). 1985; 67:37-50.*
10. *Linden T, Kalimo H, Wieloch T. Protective effect of lesion to the gluta matergic cortico striatal projections on the hypoglycemic nerve cell injury inthe rat striatum. Acta Neuropathol (Berl). 1987; 74: 335-344.*
11. *Harris RJ, Wieloch T, Sywen L. Cerebral extracellular calcium activity in severe hypoglycemia in relation to extracellular potassium and energy state. J Cereb Blood Flow Metab. 1984; 4:187-193.*
12. *Siesjo BK, Deshpande JK. Electrolyte shifts between brain and plasma in hypoglycemic coma. J Cereb Blood Flow Metab. 1987; 7:789-793.*
13. *Simon RP, Schmidly JW, Meldrum BS. Exitotoxic mechanisms in hypoglycemic hippocampal injury. Neuropathol App Neurobiol. 1986; 12:567-576.*
14. *Westerberg, E, Wieloch T. Lesions to corticostriatal pathways ameliorate hypoglysemia induced arachidonic acid release. J Neurochem. 1986; 47:1507-1511.*
15. *Fonnum I. Glutamate: a neurotransmitter in mammalian brain. J Neurochem. 1984; 42:1-11.*
16. *Simon RP, Schmidley JW, Meldrum BS. Excitatory amino acid and calcium content of subarachnoid spinal fluid during hypoglycemia in the rat. Neuroscience Letters. 1986; 71:370-374.*
17. *Iwai A, Sokomoto T, Kinoshita Y. Computed tomographic imaging of the brain after hypoglycemia coma. Neuroradiology 1987; 29:398-400.*