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CASE REPORT

Repeated hypoglycemia and cognitive decline A Case Report

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Abstract

OBJECTIVE: Diabetes mellitus has a high incidence in general population and goes by high morbidity by specific micro vascular pathology in the retina, renal glomerul and peripheral nerves. In type 1 DM, intensive therapy can prevent or delay the development of long-term complications associated with DM but hypoglycaemia especially severe hypoglycaemia defined, as a low blood glucose resulting in stupor, seizure, or unconsciousness that precludes self-treatment is a serious threat. Hypoglycaemia that may preferentially harm neurons in the medial temporal region, specifically the hippocampus, is a potential danger for the brain cognitive function which several studies failed to detect any significant effects, whereas others indicated an influence on it. A young diabetic case presented here with severe cognitive defect. Great number of severe hypoglycaemic or hyperglycaemic attacks and convulsion episodes were described in his medical history.

RESULTS AND CONCLUSION: Neuroradiologic findings on CT and MRI, pointed that global cerebral atrophy that is incompatible with his age. Brain perfusion studies (SPECT, ^{99m}Tc-labeled HMPAO) also showed that there were severe perfusion defects at superior temporal region and less perfusion defects at gyrus cingulim in frontal region. These regions are related with memory processing. Severe cognitive defect in this patient seems to be closely related these changes and no another reason was found to explain except the repeated severe hypoglycaemic episodes.

Introduction

A patient with severe cognitive defect, which is caused by hypoglycemia, and also with other diabetic complications is documented and discussed by the literature findings.

Case

A man who is 42 years old now has been diagnosed as type 1 DM for 25 years and has been hospitalized several times (approximately twice a months) because of severe hypoglycemic coma or hyperglycemic keto-ascidosis. After having generalized tonic-clonic convulsions twice a week in 1990, he had been ordered to use a Phenobarbital tablet twice a day. In spite of taking medicine, convulsion history was similar to it was before. He had been well in daily routine activities till February 2001, when he experienced convulsions and was hospitalized in intensive care unit at the local state hospital. After two months follow up, he was discharged but during that time he had a difficulty doing his daily routine. Two months later general condition of the patient worsened, and readmitted to the same hospital for four months again. After this second hospitalization, he was referred to medical faculty hospital without a clear-cut diagnosis and a panacea. On admission; blood pressure, fever, respiration and pulse were in normal limits, physical examination were other wisely normal except severe cachexia of the patient. He was conscious but orientation to place, time and person was deteriorated. Cranial nerve examination was normal but in motor examination muscle atrophy and mild contracture were found in four extremities. Muscle power was 2–3/5 in proximal and 2/5 in distal both upper and lower extremities. All deep tendon reflexes were lost except the triceps (+/–) reflex. Abdominal superficial reflexes, cremaster and anal reflexes were lost, and also he had incontinence and encompresis. Sensorial examination showed long glowe and socks type hypoalgesia-hypoesthesia. Position sense was lost in lower extremities and decreased in upper extremities. Blood analyses showed no pathologic finding except the blood glucose level (Renal, hepatic functions, B12, Folic acid, infectious disease – Sy, Hepatitis, HIV –, inflammatory disease – RF, ANA, Sedimentation vs –). Mixed type sensorimotor polyneuropathy was found in EMG examination. Diffuse slow wave pattern was seen in EEG. Cerebral imaging showed severe atrophy in bilateral temporal region whereas bilateral superior temporal and frontal hypo perfusion was found in SPECT. Mini Mental State Test (MMST) score was 12 and 14 in repeated examinations. So a severe cognitive defect was detected. Severe sharp oscillations were seen in blood glucose monitoring like excess elevations up to 400 mg/dl or severe drops down to 30 mg/dl and this was not related with given insulin dosage. We couldn't find any cause for explanation of the oscillating glucose levels. Insulin antibody was negative in blood, and there was no pathologic finding at abdominal imaging. Muteness, perioral dyskinesia and anxiety were seen in severe blood glucose level drops about 15 mg/dl without any of warning signs abruptly and in a waxing and waning manner.

Discussion

Both type 1 and type 2 DM have similar complication rate (1). In type 1 DM, intensive therapy can prevent or delay the development of long term complication associated with DM (2) but hypoglycemia especially severe hypoglycemia, defined as a low blood glucose resulting in stupor, seizure, or unconsciousness that precludes self treatment (3), is a serious threat. Based on neuropathologic evidence, it has been proposed that severe hypoglycemia may preferentially harm neurons in the medial temporal region, specifically the hippocampus (4). Case studies have repeated deficits in delayed declarative memory after a severe hypoglycemia with

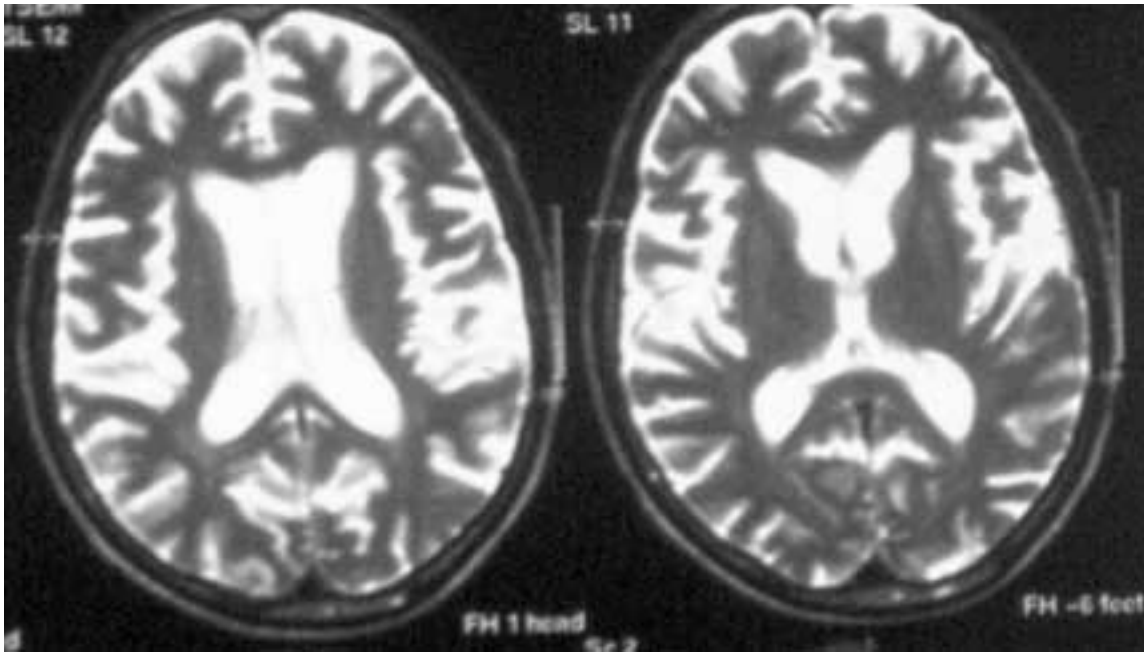

Fig. 1. Axial T2 MRI images showed bilateral severe temporal and frontal lobe atrophy.

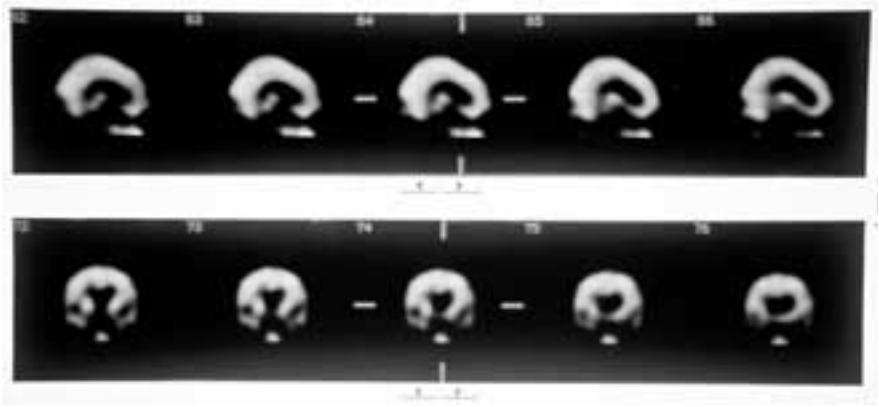

Fig 2. Brain perfusion SPECT was performed by using a single headed gamma camera (Siemens e. cam Single USA) equipped with a low-energy high-resolution collimator. Tc-99m HMPAO was prepared according to the manufacturer's instructions and a 740 MBq dose was administered intravenously while the patient was lying supine in a quiet room with eyes closed and ears plugged. The imaging protocol acquired 64 frames at 30 seconds per frame with 360° rotation of the detector 20 min after the injection. Images were reconstructed in a transaxial plane parallel to the orbitomeatal line. Transaxial, sagittal and coronal tomographic slices were obtained and evaluated visually. Bilateral temporal lobe hypo perfusion was observed. Additionally, perfusion of the frontal lobes was decreased slightly.

subsequent damage to the medial temporal region (5). Besides the effect of single severe hypoglycemic episode, the effect of repeated hypoglycemia on cognitive function has also been discussed controversially thus far. Several studies failed to detect any significant effects (6), whereas others indicated an influence of hypoglycemia on cognitive function (5, 7, 8).

A young diabetic case presented here with severe cognitive defect. Great number of severe hypoglycemic or hyperglycemic attacks and convulsion episodes were described in his medical history. Neuroradiologic findings on CT and MRI, showed that global cerebral atrophy which is incompatible with his age (Figure 1). Brain perfusion studies (SPECT, Tc–99m HMPAO) also showed that there were severe perfusion defects at superior temporal region and less perfusion defects at gyrus cinguli in frontal region (Figure 2). These regions are related with memory processing. Severe cognitive defect in this patient seems to be closely related these changes and no another reason was found to explain except the repeated severe hypoglycemic episodes.

In health, severe hypoglycemia does not occur because of the efficient systems the body has to detect and deal with a falling blood glucose concentration. In DM, the mechanisms of counter regulation are impaired. Previous mild hypoglycemia can induce "hypoglycemia unawareness" and thereby lead to diminished warning symptoms (9) and also diminished the glycaemic thresholds for cognitive dysfunction to lower plasma glucose level (10). Onset of counter regulation is likely to be brain function and, these impairments are seen in some patients with long disease duration. Loss of the efficiency of these mechanisms increases the risk not only of hypoglycemia *per se* but also of severe episodes with clinically significant cognitive dysfunction (11).

We also observed the condition, "hypoglycemia unawareness" in our case. Severe blood glucose level drops till to 30–40 mg/dl had no clinical signs of hypoglycemia and blood glucose level gave an enormous response, which it is not compatible with given external insulin supplementations. So that, many unpredictable hypoglycemic episodes were observed. The patient was experienced two generalize tonic-clonic convulsions. Both frequency of hypo or hyperglycemic episodes (twice a month for 25 year) and convulsions (twice a week for ten year), and concordance of the two situations are extreme values. This may be explaining these neuroradiologic, neurophysiologic and clinical findings.

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