Chorea-Ballismus Associated with Hyperglycemia

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ABSTRACT
Chorea-ballismus which is a rare complication of nonketotic hyperglycemia may be the first symptom of type 2 diabetes mellitus. In this paper, we present two patients, who had involuntary movements and were diagnosed as having ballismus-chorea associated with nonketotic hyperglycemia. While one of the patients was not diagnosed with diabetes mellitus, the other one did not administer insulin therapy for a long time which was prescribed. The patients were investigated by cranial imaging and biochemical tests. The symptoms improved in one of them within hours, however, it took days to improve for the other one. This clinical situation, which is thought to be caused by hyperglycemia, cerebral ischemia and failure of gamma-aminobutyric acid (GABA) and which probably improves with regulation of blood glucose levels, should be kept in mind by emergency physicians, because it can be the first presentation of type 2 diabetes mellitus.

Key words: Ballismus, Chorea, Nonketotic hyperglycemia

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Case 1
A right-handed 73-year old male patient presented because of involuntary movements in the left arm and leg and occasionally in his mouth and tongue. It was learned that the patient who had hypertension had coronary by-pass operation for two times and anticoagulant treatment was initiated when atrial fibrillation was found in investigations performed because development of right hemiparesis in 2009. Endarterectomy was also performed in the patient in whom 90% narrowing was found in the left internal carotid artery during investigations performed for stroke.
The patient who was receiving antiaggregant and anticoagulant treatment had no known diabetes. On neurological examination, right sequel homonymous hemianopsia and right hemiparesis were found. In addition, high-amplitude, irregular movements in the proximal part of the left arm, lower-amplitude involuntary movements which he could not control in the distal part of the left foot and accompanying irregular, involuntary movements in the tongue and chin such as opening the mouth and waggling the tongue-chin were observed.

At the time of presentation, the blood glucose level was found to be 515 mg/dl. Ketone was negative on complete urinalysis. The pH value in venous blood gases test was found to be 7.3. The patient was evaluated to have non-ketotic hyperglycemia. Biochemical parameters and hemogram were found to be normal. The INR value was found to be 2.3. Serum osmolarity was calculated to be normal (260 mosm/l).

On cranial computerized tomography (CT), hyperdense lesions were noted in bilateral putamen and globus pallidus with predominance on the right side (Figure 1). In addition, hypodense lesions which might be compatible with ischemia were present in the areas of supply of the left posterior cerebral artery and right posterior inferior cerebellar artery. On DWI (Diffusion-Weighted-Imaging) -ADC (Apparent Diffusion Coefficient) weighted magnetic resonance imaging (MR), no lesion compatible with acute ischemia was observed. On T2-weighted MR sections, bilateral hypointens areas were observed with predominance in the right putaminal area in addition to the old ischemic sequel lesion (Figure 2). The patient was evaluated to have “non-ketotic hyperglycemia-related chorea-ballismus” as result of the investigations performed. Ballistic-choreic movements regressed approximately 12 hours after the blood glucose was reduced and all complaints disappeared in days. The patient needed no therapy other than regulation of blood glucose and intravenous hydration.

Case 2

A 62-year old right-handed male patient presented with involuntary movements in his left arm and leg which had been lasting for one day. It was learned that the patient who had hypertension, hyperlipidemia and type II diabetes for one year did not administer insulin for the last one month. The patient reported that weakness developed in his right side three years ago, but improved in a short time and he did not refer to any physician. On neurological examination, irregular, high-amplitude ballistic movements were observed in his left arm and leg. The patient could not sit and walk because of these movements.

At the time of presentation the blood glucose was found to be 930 mg/dl and (+++) glucose was found on complete urinalysis, but ketone was negative. pH value in the venous blood gases test was found to be 7.3. Biochemical tests were found to be normal except for increased urea and creatinine levels and a sodium value of 119 mmol/l. Serum osmolarity was also found to be normal (240 mosm/l). A diagnosis of “non-ketotic hyperglycemia-related chorea-ballismus” was made. Cranial CT and DWI-ADC weighted MR examinations were found to be normal. It was learned that the patient’s complaints regressed 4 days after the blood glucose was reduced and the patient was followed up with haloperidol (2x5 drops) treatment.

Discussion

Movement disorders related with hyperglycemia may be in the form of chorea and/or ballismus. The second most common cause of hemiballismus following stroke is known to be hyperglycemia (2). The picture of hyperglycemia-related ballismus-chorea (HRBC) is observed between the ages of 50 and 80 years in poorly controlled diabetes patients (3,4). The diagnosis of diabetes is frequently made after involuntary movements occur. Improvement of the clinical picture in hours, a blood glucose value of 400-1000 mg/dl and regression of involuntary movements with regulation of hyperglycemia in most patients are considerably typical. While cranial CT imaging is normal in some patients, hyperdense lesions in the basal ganglion region which is the known radiological finding of hyperglycemia-related ballismus-chorea is observed in some other patients. On cranial MR examination, hyperintense lesions are observed in the putamen and caudate nucleus especially in the T1 sequence. In previously published series of HRBC cases, it was reported that lesions with different intensities could also be observed in the T2 sequence or cranial MR examination might be normal (1,5,6).

As observed in the patients reported here, regulation of blood glucose is the most efficient factor in improvement of involuntary movements and abnormal movements disappear in hours. However,
Hemiballismus may continue for more than three months in 20% of the patients (2). Atypical HRBC cases who started, did not improve and showed late recurrence after regulation of hyperglycemia have also been reported (6). Although the findings in these patients are generally reversible, the picture may get worse in conditions accompanied by hyperosmolarity/hyperviscosity and even mortality may be observed (5). In our patients, the picture of HRBC occurred acutely. In the first patient, the involuntary movements regressed 12 hours after the blood glucose was reduced and improved completely in days and no additional treatment was required. In the second patient, the complaints regressed 4 days after the blood glucose was reduced and the patient was followed up with haloperidol treatment. Hyponatrema in our second patient was thought to be dilutional hyponatrema which developed secondarily to hyperglycemia. In acutely developed hyperglycemia, dilutional hyponatrema may develop because of transfer of fluid from the cells to the plasma due to the hypertonicity of the extracellular fluid and osmotic difference of water. With each 100 mg/dl increase in serum glucose, serum osmolarity increased by 1.9-2.1 mosm and serum sodium decreases by 1.6-1.8 mEq/L. In long-lasting hyperglycemia, sodium loss and actual hyponatrema may occur as a result of osmotic diuresis (7).

The pathophysiology of HRBC is not clear. Increased vascular resistance due to tissue edema arising from hyperglycemia, increased viscosity, decreased metabolic rate in brain cells, inactivation of Krebs cycle because of hyperglycemia and consumption of GABA by the brain in order to obtain energy may be in question. It is known that among basal ganglion cells GABA has inhibitor function, glutamate has activating function and acetylcholine has modulator function. It is thought that decreased regional blood supply because of hyperglycemia and consumption of GABA which is an inhibitory transmitter play a role in the pathophysiology. In this case, focal seizures occur if the cerebral cortex is affected primarily (focal motor seizures including most frequently epilepsy partialis continua) and dyskinesias occur, if the subcortical structures are affected primarily (4,8,9).

Improvement of symptoms with normalization of serum glucose concentration suggests a metabolic pathology and acute occurrence of the event suggests a vascular pathology. Continuance of chorea despite normalization of blood glucose in some patients and the fact that abnormal movements are generally observed on the one side of the body are contradictory to a metabolic pathology, while the fact that chorea may be observed bilaterally and observation of only neuron loss, gliosis and reactive astrocytosis, but not infarction or hemorrhagia are contradictory to vascular pathology (9,10). Chang et al. defended that this clinical picture might have developed as a result of transient ischemia potentiated by hyperglycemia based on the imagings (cerebral MR and MR spectroscopy) performed in the acute period and remission phases in 18 HRBC patients (5).

In a study in which Oh et al made a meta-analysis of 53 patients, some different results were obtained in addition to the above-mentioned characteristics. 91% of the patients were Asian and this was related with poor diabetes control or genetic properties in underdeveloped countries. Female/male ratio was found to be relatively close to each other compared to previous data. While bilateral chorea was observed in 6 of the patients, hemichorea was observed in the other patients and focal neurological deficit was reported in 15 patients. Hyperintens areas in the putamen in T1-weighted sections were observed in all patients. Findings obtained in T2 weighted examinations were variable. While contralateral flashing was observed in 46 patients with hemichorea, ipsilateral flashing was observed in 1 patient. Bilateral flashing was observed in 6 patients with bilateral chorea. Abnormal movements improved in 1 day-10 months (mean: 6 months) with blood glucose regulation. In the majority of patients, regulation of blood glucose was sufficient to control chorea-ballismus. In some patients, treatment with haloperidol or other drugs was required. Recurrence was observed in 13.6% of the patients and among these patient, hyperglycemia was found in 4 patients in whom blood glucose was measured. It has been reported that recurrence may be observed in 2 years and occurs mostly on the same body side. It was reported that hyperintensity in T1-weighted sections disappeared with improvement in chorea in 19 of 22 patients in whom cranial MR follow-up was done and chorea did not improve, although flashing returned to normal in 2 patients. SPECT (Single Photon Emission Computed Tomography) was performed in 8 of the patients. Hypoperfusion was found in the contralateral basal ganglion, while hypoperfusion was observed in the early phase and subsequently hypoperfusion was observed in 4 patients. Hyperperfusion in the early phase was associated with increased blood flow as a response to decreased blood glucose due to insulin treatment. It was reported that hypoperfusion might be related with disrupted neuronal metabolism or ischemia due to vascular insufficiency or a combination of these two factors (1).

Shan et al. proposed a hypothesis by combining the factors which were thought to be involved in the pathophysiology in their study which aimed to explain MR signal changes in HRBC (9). According to this hypothesis, dysfunction of GABAergic neurons in the caudate nucleus and putamen caused by hyperglycemia and cerebral ischemia leads to HRBC. It is thought that the neurons in the indirect pathway become functionally insufficient and the neurons in the direct pathway are preserved during ischemia. It is known that the neurons in the direct pathway which are preserved functionally start to be fired because of reduced epileptic threshold in hyperosmolarity and this excessive activity in the direct pathway leads to metabolic irregularity. At the end of all this process, astrocytes are stimulated and observation of gemistocytes which are swollen reactive astrocytes and neuronal loss and gliosis in the striatal region in acute and chronic injuries in autopsy studies is explained in this way (9,11). Since petechial hemorrhages are observed in the indirect pathway by where ischemic damage is present with the highest rate, they may be observed as hyperdens areas on CT. While no lesion compatible with acute ischemia was observed on cranial CT, DWI/ADC and T2 section MR in the early phase in our patients, bilateral hyperdense basal ganglia lesion was noted on CT in our first patient with predominance on the right side and on T2 sequence MR, this lesion was observed to be hypointense. MR examination of our second patient was normal. Although T1 sequence MR imaging is not performed under emergency conditions, it was thought that the other radiological findings might be compatible with the findings observed in HRBC.

Both patients presented here were evaluated to be HRBC with their clinical and radiological properties and responses to
treatment. It should be kept in mind that this clinical picture in the pathogenesis of which hyperglycemia, cerebral ischemia and consumption of GABA are thought to be involved and which generally improves with regulation of blood glucose may be the first cause of presentation to the emergency department especially in patients whose diabetes is not known and rapid intervention should be performed.

References


