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CASE REPORT

Hemichorea in ketotic hyperglycemia with hyperdense striatum mimicking hemorrhagic transformation in a patient using apixaban

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Abstract

INTRODUCTION: Diabetic striatopathy is a rare condition characterized by unilateral hemichorea and/or hemiballismus in the settings of uncontrolled nonketotic diabetes mellitus. Imaging studies usually reveal striatal abnormality - subtle hyperdensity on CT and T1 hyperintensity on MRI. The resolution of clinical symptoms is prompt when optimal glycaemic control is achieved.

CASE REPORT: We present the case of a 90-year-old male who came to our attention for acute involuntary choreiform movements of his left-sided extremities lasting two-weeks. Apart from that neurological examination was unremarkable. His medical history included hypertension, atrial fibrillation, previous stroke with no residual disability and poorly controlled type 2 diabetes mellitus on metformin treatment. There was no history of movement disorders or exposure to neuroleptics. His glucose level on admission was 512.6 mg/dL, glycated hemoglobin was 14%. CT scan of the head demonstrated an abnormally increased intensity within the right striatum. Treatment consisted of symptomatic treatment of chorea and improvement of blood glucose control. Tiapride was started with a dose of 100mg 4 times a day. The patient was initiated on intensive insulin therapy which included insulin glargine 10 units every evening and 12 units of insulin glulisine 3 times a day with meals. Abnormal movements resolved after normoglycemia was achieved approximately 7 days after admission. Though striatal hyperdensity was still present at follow-up CT scan after 10 days, it was less pronounced.

CONCLUSION: Diabetic striatopathy is a rare but treatable disorder and should be considered in patients with poorly controlled diabetes who present with hemichorea.

INTRODUCTION

Hemichorea is a hyperkinetic movement disorder characterized by excessive unilateral rapid, randomly distributed, and irregularly timed involuntary movements. It can manifest in the settings of uncontrolled diabetes mellitus usually with negative urine ketones. Association with positive urine ketones or diabetic ketoacidosis is uncommon. Because the imaging studies usually reveal striatal abnormality – subtle hyperdensity on CT and T1 hyperintensity on MRI – the condition is also called diabetic striatopathy. The resolution of clinical symptoms is prompt when optimal glycaemic control is achieved. Here, we present a rare association of this syndrome with positive urine ketones in a 90-year old male.

CASE REPORT

90-year-old male came to our attention for acute involuntary choreiform movements of his left-sided extremities lasting two-weeks. Apart from that neurological examination was unremarkable. His medical history included hypertension, atrial fibrillation, hypothyreosis, hyperlipidemia, previous stroke with no residual disability, and poorly controlled type 2 diabetes mellitus on metformin treatment. Further chronic medication included apixaban, combination antihypertensive therapy, levothyroxine, and ezetimibe. There was no history of movement disorders or exposure to neuroleptics. His glucose level on admission was 512.6 mg/dL, glycated hemoglobin was 14%. Biochemistry tests showed no other significant abnormity, arterial blood pH was 7.42, urine ketones were positive. A CT scan of the head (fig.1) demonstrated an abnormally increased intensity within the right striatum. Treatment consisted of symptomatic treatment of chorea and improvement of blood glucose control. Tiapride was started with a dose of 100mg 4 times a day. The patient was initiated on intensive insulin therapy which included insulin glargine 10 units every evening and 12 units of insulin glusine 3 times a day with meals. Abnormal movements resolved after normoglycemia was achieved approximately 7 days after admission. Striatal hyperdensity was still present at follow-up CT scan (fig.2) after 10 days, but it was less pronounced.

DISCUSSION

The most frequent cause of hemichorea is stroke, followed by nonketotic hyperglycemia and cerebral toxoplasmosis as a complication of HIV infection. Many other causes including neoplasms, vascular malformations, vasculitis, or multiple sclerosis have been reported (Hawley & Weiner 2012; Posturna & Lang 2003). Hemichorea and/or hemiballismus in the

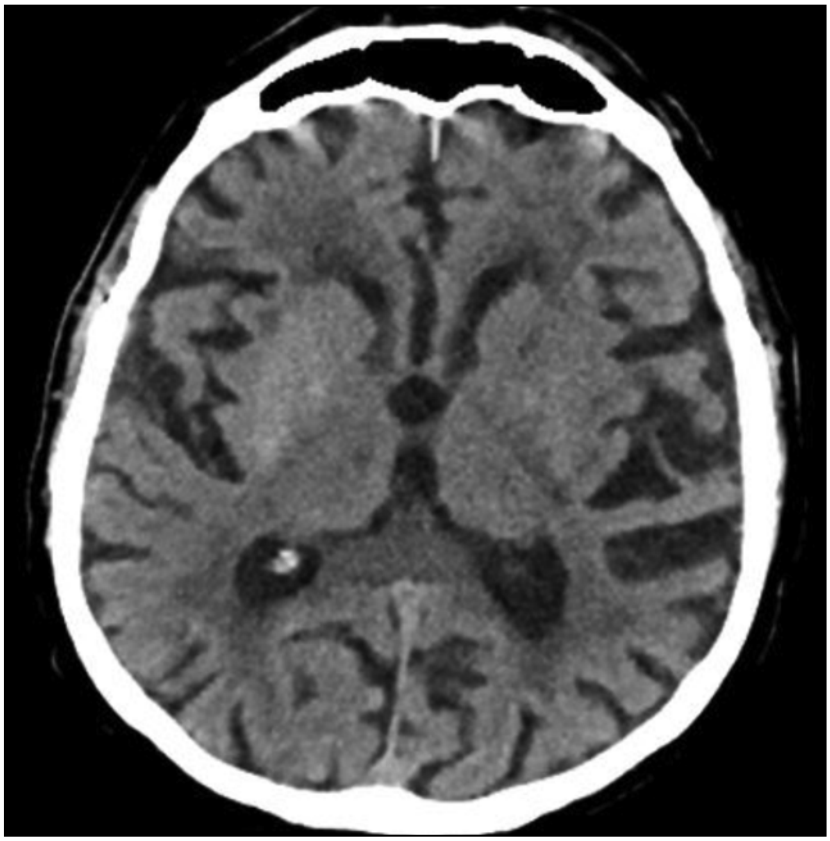

Fig. 1. CT scan at admission

settings of uncontrolled nonketotic diabetes mellitus and prompt resolution of clinical symptoms when optimal glycaemic control is achieved was described in 1960 (Bedwell 1960).

Overall, more than 175 cases have been described. Most of the reported cases occur in elderly female patients of Asian origin, though also Caucasian patients or children can be affected (Chua *et al.* 2020). On the other hand, reports of chorea in the settings of hyperglycemia with positive urine ketones or diabetic ketoacidosis are scarce (Tan *et al.* 2014; Satish 2017; Soysal *et al.* 2012; Das *et al.* 2017) .

Hemichorea has been traditionally attributed to the lesions of the contralateral subthalamic nuclei (STN) (Martin & Alcock 1934), however, MRI studies on post-stroke hemichorea also reported lenticular, cortical, and thalamic regions involvement (Chung *et al.* 2004; Pareés *et al.* 2010). Recently lesion network mapping has revealed that the majority of these regions are functionally connected to the posterolateral putamen (Laganiere *et al.* 2016). Imaging studies on hyperglycemic chorea usually reveal striatal abnormality – subtle hyperdensity on CT, MRI shows T1 hyperintensity, and T2 hypointensity. Surprisingly changes might be bilateral despite the clinical presentation of hemichorea. Imaging abnormalities are only temporary, and median time point for complete resolution of CT abnormalities was 60 days (Chua *et al.* 2020; Oh *et al.* 2002; Lee *et al.* 2016; Mihai *et al.* 2008). Also in our case follow up CT showed partial resolution of striatal hyperdensity after 10 days. Unfortunately, no further imaging was performed after hospital discharge.

The pathophysiology of chorea in the settings of hyperglycemia remains unclear, though several underlying mechanisms have been discussed in the literature. Radiological findings of hyperdense areas in the striatum on CT scans might mimic hemorrhage. Unsurprisingly, petechial hemorrhage has been proposed as an underlying pathology, though some reports arguments against it (Chang *et al.* 1997; Mestre *et al.* 2009; Shan *et al.* 1998). In some cases clinicians can misdiagnose patients and treat them as a symptomatic chorea due to BG hemorrhage (Wilson *et al.* 2011). In our case, hyperdense striatum was initially considered to be the hemorrhagic transformation of ischemic infarct in an anticoagulated patient on apixaban. The decision to stop apixaban and initiate treatment with low-molecular-weight heparin (Fraxiparine) 0.4 ml s.c. twice daily instead was made. After we came up with a diagnosis of diabetic striatopathy four days later, anticoagulation with apixaban was safely resumed. Another theory links chorea to regional blood flow alterations which may contribute to metabolic changes or reactive astrocyte accumulation (Shan *et al.* 1998) Some reports speculated that alterations in dopaminergic activity (upregulation of dopamine receptors, decreased

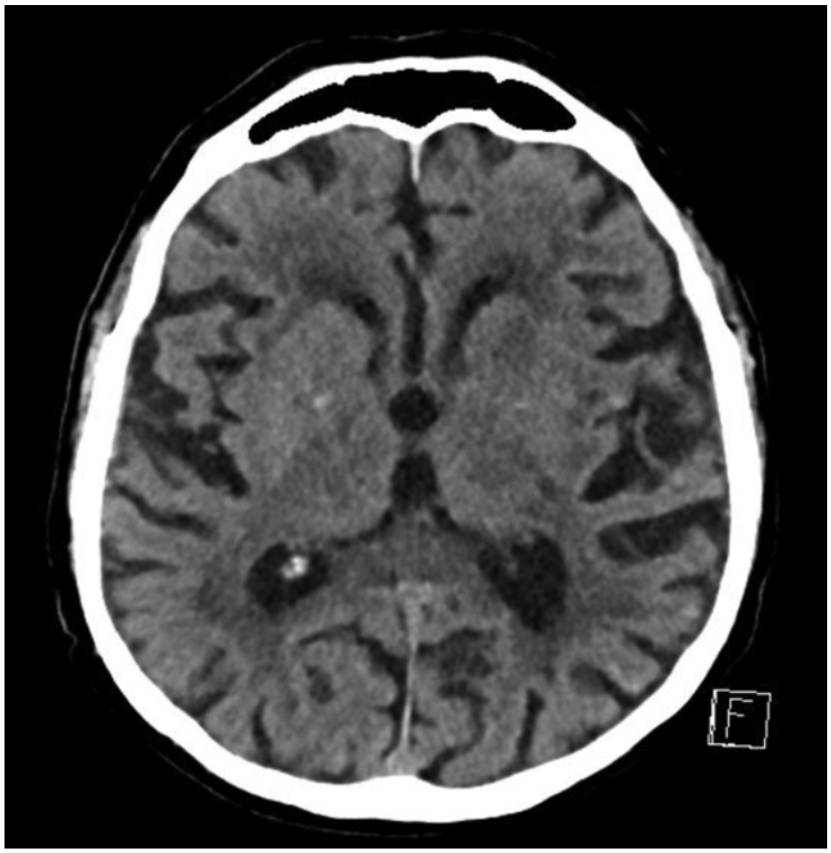

Fig. 2. Follow up CT scan

dopaminergic activity (DA) catabolism) could be the cause (Battisti *et al.* 2009). Others presumed metabolic changes leading to decreased synthesis of neurotransmitters acetylcholine or gamma-aminobutyric acid (GABA). In ketotic patients, acetoacetate can be used to synthesize GABA, which could explain why nonketotic patients are more prone to suffering from chorea (Oh *et al.* 2002). Also, autoimmune etiology involving possibly anti-GAD65 antibodies have been proposed (Ahlskog *et al.* 2001). Others suggested reversible mineral deposition (e.g. calcium) (Shan *et al.* 1998) and osmotic demyelination syndrome (Duker & Espay 2010).

The prognosis of most patients, especially of younger age, is favorable. Though in about 20% of cases symptoms may reappear despite tight glycemic control. Rarely also persistent chorea was reported. Interestingly, a literature review of published cases showed shorter recovery time (two days) in patients who received insulin treatment only when compared to insulin treatment and additional anti-chorea medication (14 days to recovery). This might be due to the fact that anti-chorea medication was initiated in patients who were more severely affected (Chua *et al.* 2020; Oh *et al.* 2002; Lee *et al.* 2014; Ahlskog *et al.* 2001). In our case, we included booth insulin treatment and anti-chorea medication. The time to resolution of symptoms was only 7 days.

CONCLUSION

Hemichorea in the settings of ketotic hyperglycemia in patients with uncontrolled diabetes mellitus is a rare but treatable disorder and should be considered in patients with poorly controlled diabetes who present with hemichorea. CT findings of hyperdense striatum might mimic hemorrhage, but the presented case demonstrates that patients can be safely anticoagulated.

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