Choreoathetosis in a patient with diabetes mellitus

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A 73-year-old Fijian Indian man presented to the Auckland Hospital Emergency Department (ED) with a two-day history of uncontrollable writhing and jerking movements of his right limbs, severe paroxysmal cramping pain in his right arm and an unsteady gait. He reported no other symptoms including headache, limb weakness or fever. He had had a recent flare of gout in his right wrist and had been commenced on prednisone and colchicine by his general practitioner two days ago.

This patient had multiple co-morbidities, including poorly-controlled type 2 diabetes mellitus (DM), hypertension, gout and chronic renal failure. His chronic renal impairment was related to a background of having one remaining kidney after a live kidney donation in 1984. In 2006 he had been diagnosed with gastric adenocarcinoma and was due for surgical treatment. He had no history of cerebrovascular disease, ischaemic heart disease or peripheral vascular disease. He was an ex-smoker with a 50 pack-year history and did not consume any alcohol. His regular medications were cilazapril 5mg once daily and glipizide 5mg twice daily; however he reported that he "only takes one tablet a day". He had no known drug allergies. Family history was unremarkable.

The patient had been diagnosed with diabetes in 1992. He had a history of poor compliance with his medications and diabetic clinic attendance. At the most recent clinic in 2002 he had been found to have peripheral neuropathy, mild retinopathy and moderate nephropathy at the time. His HbA1c was 9.0%.

On examination the patient appeared to be distressed by his symptoms but fully alert, conscious and oriented. His vital signs were stable including a blood pressure of 140/78mmHg. The most prominent finding was a choreoathetoid movement of both the upper and lower right extremities. His gait was mildly impaired with a tendency to sway to the right. Finger-nose-finger testing was normal. Power and tone were normal in all his limbs. His reflexes were symmetrical with absent ankle reflexes bilaterally. There was a loss of vibratory sensation in his feet. Cranial nerve examination was normal. There was no evidence of inflammation of any joints including his right wrist.

Laboratory studies revealed that complete blood count and electrolytes were normal. His creatinine level was 272umol/L. His random blood glucose level was markedly elevated at 30.7mmol/L as was his HbA1c at 14.0%. The initial impression was that he might have suffered a cerebrovascular accident affecting the basal ganglia. A head computed tomography (CT) scan did not reveal acute haemorrhage or ischaemia, but showed old mild to moderate small vessel ischaemic change in the white matter, predominantly in both frontal lobes. A neurologist suggested that the patient had suffered a probable ischaemic stroke in the deep left white matter.

Prednisone and colchicine were stopped and he was administered eight units of actrapid insulin in the ED. By the second day of admission, his blood glucose level had been reduced to 16mmol/L. He was transferred to the ward and continued on subcutaneous insulin therapy for another day, then restarted on glipizide. Glipizide was increased to 5mg mane and 10mg nocte due to suboptimal control. It was felt that given his history of poor compliance it would be impractical to commence treatment with subcutaneous insulin injections. He was assessed by the physiotherapists regarding his poor balance and discharged home. On discharge, he still had right-sided choreoathetosis but at a slightly reduced level. Aspirin and simvastatin were added as secondary prevention measures for possible ischaemic stroke. The patient and his family were educated about the importance of reducing his cardiovascular risk.

Discussion

The case illustrated posed several diagnostic challenges. Firstly, it was recognised that the patient's main presenting symptom was a unilateral dyskinesia. The movements of his right limbs could best be described as choreoathetosis. The pathophysiological basis of movement disorders such as Huntington's disease (a hyperkinetic disorder) and Parkinson's disease (a hypokinetic disorder) is dysfunction of the extrapyramidal system or basal ganglia. This complex system comprises the caudate striatum, subthalamic nucleus, substantia nigra and parts of the thalamus. The most common cause of unilateral dyskinesia is a focal vascular lesion in the contralateral basal ganglia[2]. In this case, the patient had several major risk factors for cerebrovascular disease, including hypertension and poorly-controlled diabetes mellitus. A CT scan done at more than 48 hours after the onset of symptoms failed to reveal any ischaemic or haemorrhagic changes consistent with a cerebrovascular accident, although there was evidence of old infarcts.

The patient had a significant background of poorly-controlled diabetes and the administration of prednisone is likely to have precipitated the acute hyperglycaemic episode on admission. An interesting question that arises is whether the temporal relationship between the commencement of prednisone and onset of dyskinesia is of significance. A survey of the literature revealed that chorea or ballism is a rare but recognised complication of hyperglycaemia without ketosis. According to a meta-analysis, in the period 1985 to 2001 only fifty-three cases of this condition had been reported[3]. The patients described with chorea or ballism with associated hyperglycaemia were mostly elderly with diabetes, with an average age of 71[3]. The average age of patients with dyskinesia secondary to a focal vascular lesion was generally lower, around 66[3]. Interestingly, most of the reported cases thus far were of Asian origin[2-4]. The chorea/ballism has been unilateral in most cases, although generalised chorea has also been reported.

More recent reports of patients with unilateral symptoms have documented characteristic brain imaging findings within the corresponding contralateral striatum. These include high density changes without mass effect on CT. However, there have been several cases with no CT changes, as in the case illustrated[5]. High signal intensity on T1-weighted magnetic resonance imaging (MRI) scans have almost consistently been found in cases when an MRI was performed at presentation. In most cases, the imaging features had completely reversed on follow-up scans and correlated well with clinical improvement[2]. Positron emission tomography (PET) scans in patients with hemichorea/ballism secondary to hyperglycaemia have shown reduced cerebral glucose metabolism[4] and concomitant hypoperfusion in the contralateral basal ganglia seen on single photon emission computed tomography (SPECT)[2-6].

Previous studies have shown that chorea associated with hyperglycaemia may resolve with the correction of blood glucose level[2]; or may be slow, taking months to resolve[6]; or may be persistent[5]. However in the majority of cases the prognosis of hemichorea/ballism secondary to non-ketotic hyperglycaemia has been favourable. A meta-analysis found that the abnormal movements had resolved in 97% of patients within 6 months[3].

Researchers have endeavoured to provide an explanation for the association between hyperglycaemia and chorea/ballism. An early hypothesis was that in hyperglycaemia, cerebral metabolism shifts to the anaerobic pathway with inhibition of the Krebs cycle. Gamma-aminobutyric acid (GABA) may then be utilised as an alternative energy source leading to a reduction of GABA in the basal ganglia and subsequent chorea[3]. However the phenomenon of delayed recovery despite normalisation of blood glucose has led some researchers to question this hypothesis. Some entertain the possibility that delayed improvement may simply be part of the natural history of diabetic chorea[6].

With the consistent finding of hyperintensity on T1-weighted MRI of patients with chorea/ballism associated with hyperglycaemia, researchers are recognizing this as a unique clinicoradiological syndrome[3]. Unilateral findings on MRI also argue against a solely metabolic mechanism of disease.

The current consensus appears to be that of a multifactorial aetiology where both vascular and metabolic factors play a role. Pre-existing microangiopathic disease and damage such as lacunar infarction leading to local failure in vascular autoregulation during an episode of hyperglycaemia is one possibility[1,4]. Another explanation is that transient focal cerebral ischaemia during a period of hyperglycaemia may lead to partial striatal damage, as opposed to complete infarction. This may then cause transient regional metabolic failure[4].

The unique clinicoradiological syndrome of chorea, non-ketotic hyperglycaemia and high signal intensity on T1-weighted brain MRI may have significant implications in the case illustrated. Several important questions arise. Would an MRI brain study have been a useful investigation in this case? Would diagnosis of this particular syndrome affect management? As described earlier, the detection and correction of hyperglycaemia could potentially lead to full recovery in some patients diagnosed with this syndrome. Thus, the clinical prognosis of this syndrome would be more favourable than if the patient had sustained a cerebral infarct. However, given his background of poor compliance with medications, long-term prognosis may be poor. In this case, it seems that achieving good glycaemic control would be an important part of management, regardless of the aetiology of the dyskinesia. Educating the patient and his family about the importance of reducing other cardiovascular disease risk factors would be essential.

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