Diabetic striatopathy is a rare complication of diabetes, which appears to result from a vascular and metabolic insult to the basal ganglia due to chronic hyperglycemia in the context of poorly controlled type 2 or rarely type 1 diabetes. Clinically, it may be expressed by abnormal movements of 1 body side, typically hemichorea–hemiballism (HH) contralateral to the brain lesions. Brain MRI shows signal abnormalities on contralateral basal ganglia to the symptoms: hyperintensity on T1-weighted and hypointensity or isointensity signals on T2-weighted images. Treatment includes the correction of glycemia and in some patients the addition of specific medications to inhibit abnormal movements, such as neuroleptics, dopamine-release inhibitors, benzodiazepines, or anticonvulsants. The clinical and radiologic course is usually favorable.

Diabetic striatopathy is a well-known complication of diabetes in adults. To our knowledge, only 2 cases have been reported in children. We here report the case of a teenager in whom diabetic striatopathy was revealed by the subacute appearance of hemichorea–hemiballism in the context of weight loss, polyuria, and polydipsia. Glycemia control allowed rapid clinical recovery despite established striatal lesions documented on MRI. We also discuss current hypotheses about pathophysiological processes underlying this entity.

CASE REPORT

This 13-year-old, previously healthy teenager of Uzbek origin noted a subacute progressive appearance of initially intermittent abnormal movements in his left hand 10 days before his first visit to our center. After a 2-week symptom-free interval, the patient noticed the recurrence of these left-sided abnormal movements, this time also involving the leg. The movements were present and continuous when the patient was at rest; they were exacerbated by physical activity and disappeared during sleep. His personal history revealed a significant weight loss of 10 kg in the past 6 months, and his appetite was intact. He also complained of polyuria and polydipsia that appeared in parallel with the onset of abnormal movements. There was no history of autoimmune diseases, neurologic disorders of any kind, or abnormal movements in the family. On admission, the clinical picture was dominated by the presence of continuous irregular movements of low amplitude and abstract
high frequency involving the left arm, mixed with higher-amplitude, brisk jerks involving the left arm and the left leg, consistent with HH. His face was not involved. There was no additional extrapyramidal sign, particularly no rigidity or bradykinesia. Given the context of polydipsia, polyuria, and weight loss, we checked the patient’s glucose levels, which revealed a value of 29 mmol/L (N for random measurement <11.1 mmol/L).

The glycosylated hemoglobin A1c (HbA1c) level was 17.3% (165.6 mmol/mol) (N < 7%), ketonemia (β-hydroxybutyrate) was measured at 0.8 mmol/L (N < 0.4 mmol/L), and the pH was 7.41. These results permitted the diagnosis of diabetes mellitus without ketoacidosis. The results of all other laboratory values on admission are summarized in Table 1, and the later finding of antibodies against glutamic acid decarboxylase finally confirmed the diagnosis of the type 1 diabetes.

Brain MRI (Siemens Avanto 1.5 T; Siemens Healthcare USA, Malvern, PA) was performed 1 day after admission with classic sequences (SE T1, SET2, fluid-attenuated inversion recovery [FLAIR]), susceptibility weighted imaging, and diffusion weighted imaging) (Fig 1). This examination showed an abnormal signal of the right striatum, in the caudate nucleus and putamen, characterized by hypointensity on T2 and FLAIR sequences, hyperintensity on T1 sequences, and restriction on apparent diffusion coefficient sequences, suggestive of subacute ischemia with hemorrhagic alterations. The administration of intravenous insulin at initial dosages of 1.3 IU/kg per day allowed a rapid normalization of blood glucose levels and a clearance of ketones, which permitted to switch to subcutaneous insulin. Less than 24 hours after diagnosis, the patient restarted an oral diet, accompanied by a standard basal–bolus subcutaneous insulin treatment. A week after the correction of glycemia, the movements were still present and disabling. Therefore, tetrabenazine treatment was started, with dosages gradually increased up to 50 mg 3 times a day, and adjusted to 37.5 mg 3 times a day because of side effects (somnolence). After 4 weeks, the disappearance of abnormal movements allowed us to stop tetrabenazine without recurrence of the movements for the 5 months that followed treatment initiation.

A second MRI was performed at 3 months of follow-up with a much better quality related to the absence of movement artifacts. An atrophy of the basal ganglia was noted on the right side, consistent with hemosiderin deposits, particularly well revealed by a T1 hyperintense signal. Susceptibility weighted imaging sequence showed a hypointense signal consistent with calciﬁcations or hemosiderin deposits (Fig 1).1 On the last follow-up visit, at 12 months after onset, the patient had subtle dystonic postures on the left arm while walking, which did not necessitate treatment.

**DISCUSSION**

The clinical presentation of our patient is consistent with HH revealing diabetic striatopathy. This is a well-known complication of diabetes in adults. Adult patients at particular risk are those with type 2 diabetes and a history of poorly controlled glycemia. In rare cases, HH due to underlying striatopathy is the initial manifestation revealing their diabetes. For unclear reasons, these patients usually lack the presence of ketone bodies in their urine or blood (nonketotic hyperglycemia). Their brain MRI shows lesions in the striatum, either contralaterally to the clinical manifestations2 or more rarely bilaterally. The prognosis of abnormal movements in that situation is usually good, and generally, most symptoms disappear completely after a few days, weeks.

**TABLE 1 Laboratory Results**

<table>
<thead>
<tr>
<th>Tests</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood gases</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.41; P02 = 4.9 kPa; Hb = 146 g/L; potassium = 3.9 mmol/L; sodium = 128 mmol/L; glycemia = 21.4 mmol/L; lactates = 1.0 mmol/L; bicarbonate = 22.8 mmol/L; base excess = −12 mmol/L</td>
</tr>
<tr>
<td>Urine</td>
<td></td>
</tr>
<tr>
<td>Glucosuria</td>
<td>268.2 mmol/L (N = 0.1–0.9 mmol/L)</td>
</tr>
<tr>
<td>Endocrinological</td>
<td></td>
</tr>
<tr>
<td>Insulin not measurable</td>
<td>&lt; 0.2 mIU/L</td>
</tr>
<tr>
<td>Peptide C (fasting)</td>
<td>165 pmol/L (N = 500–1200 pmol/L)</td>
</tr>
<tr>
<td>Immunologic</td>
<td></td>
</tr>
<tr>
<td>Anti-GAD65: positive</td>
<td>14.3 IE/mL (N &lt; 10 IE/mL)</td>
</tr>
<tr>
<td>Anti-insulin: negative</td>
<td></td>
</tr>
<tr>
<td>Anti-IA2: negative</td>
<td></td>
</tr>
<tr>
<td>Anti-islets: negative</td>
<td></td>
</tr>
<tr>
<td>Antitransglutaminase: negative</td>
<td></td>
</tr>
<tr>
<td>TSH: 0.939 mIU/L (N = 0.400–4.000)</td>
<td></td>
</tr>
<tr>
<td>FT4: 14.0 pmol/L (N = 10.3–23.8)</td>
<td></td>
</tr>
<tr>
<td>T3: 0.90 mmol/L (N = 0.80–2.70)</td>
<td></td>
</tr>
<tr>
<td>T4: 70.0 mmol/L (N = 60.0–150.0)</td>
<td></td>
</tr>
<tr>
<td>Urea: 3.1 mmol/L (N = 2.8–7.1)</td>
<td></td>
</tr>
<tr>
<td>Creatinine: 45 pmol/L (N = 21–88)</td>
<td></td>
</tr>
<tr>
<td>Sodium: 128 mmol/L (N = 135–143)</td>
<td></td>
</tr>
<tr>
<td>Potassium: 3.8 mmol/L (N = 5.5–5.1)</td>
<td></td>
</tr>
<tr>
<td>Osmolality: 284 mmol/kg</td>
<td></td>
</tr>
<tr>
<td>Calcium: 2.28 mmol/L (N = 2.20–2.52)</td>
<td></td>
</tr>
<tr>
<td>Phosphate: 1.51 mmol/L (N = 1.05–2.00)</td>
<td></td>
</tr>
<tr>
<td>Protein: 85 g/L (N = 64–80 g/L)</td>
<td></td>
</tr>
<tr>
<td>AST: 45 U/L (N = 14–50 U/L)</td>
<td></td>
</tr>
<tr>
<td>ALT: 41 U/L (N = 8–39 U/L)</td>
<td></td>
</tr>
</tbody>
</table>

ALT, alanine aminotransferase; anti-GAD65, anti–glutamic acid decarboxylase; anti-IA2, antibodies anti–tyrosine phosphatase; AST, aspartate aminotransferase; FT4, free thyroxine; Hb, hemoglobin; P02, carbon dioxide; T3, triiodothyronine; T4, thyroxine; TSH, thyroid-stimulating hormone.
or more rarely months after the normalization of blood glucose levels. Sometimes, it is nevertheless necessary to introduce a specific drug treatment, such as that used in our patient. Other options include neuroleptics, dopamine release inhibitors, benzodiazepines, or anticonvulsants. The radiologic course may be delayed, with normalization of the images only after a prolonged period of time, ranging from a few weeks to 6 years. This clinical presentation seems extremely rare in children.

To our knowledge, only 2 similar cases have been reported so far in that age category. The first pediatric case was described by Mihai et al in 2008. They reported the case of a previously healthy 15-year-old girl with a history of sudden-onset repeated involuntary movements involving her right side, including her foot, arm, and face. She had initially presented with paraesthesia of the right leg, face, and all the right side of her body, with symptoms increasing during exercise and disappearing during sleep. This paraesthesia was followed by the development of abnormal movements involving the right body side, including her face. A diagnosis of Sydenham chorea was first considered, but the search for antistreptolysin antibodies (antistreptolysin-O) was negative. An electroencephalogram, a brain computed tomography scan, a brain MRI, and blood tests in search of autoimmune diseases (eg, encephalitis, systemic lupus erythematosus, Wilson’s disease) came back normal. Her blood tests showed hyperglycemia at 20.3 mmol/L and HbA1c levels of 13.9% (128.4 mmol/mol), and urine tests showed glycosuria and ketonuria; all of these results confirmed the diagnosis of type 1 diabetes. Insulin treatment was started, and after 24 hours of treatment the blood glucose levels were corrected and the abnormal movements had disappeared.

In 2012, Alves et al published the second case of a boy known for type 1 diabetes mellitus since the age of 2 months. His follow-up was irregular, and the metabolic control of his disease was poor. He had been taking human insulin on a regular basis for several years and was admitted at 8 years because of subacute onset of uncontrolled upper limb movements. HH was noted on examination, with movements involving mainly the patient’s right side, worsening with the initiation of physical activity, and disappearing when the patient was asleep. There was no other neurologic manifestation or general symptoms. At the time of admission, blood samples showed slightly elevated blood glucose levels of 8.7 mmol/L, as well as glycosuria 3 months before hospitalization; the patient’s HbA1c levels were 13.5% (124 mmol/mol), indicating poor metabolic control over the previous 3 months. Renal and liver functions, electrolytes, and thyroid function were normal. Investigations for additional immunologic diseases were negative. The brain MRI showed abnormal signals in the striatum, bilaterally and symmetrically. The patient was initially treated with valproic acid (16 mg/kg per day). Two days later the abnormal movements had disappeared.

The most frequently accepted pathophysiological hypothesis for diabetic striatopathy involves cerebral local hypoperfusion due to hyperviscosity that follows chronic hyperglycemia. This hypoperfusion
leads to anaerobic metabolism, which in turns reduces the levels of γ-aminobutyric acid. Its decreased concentration leads to an increase in thalamocortical activity, causing abnormal movements like HH. In most cases, hyperglycemia associated with diabetic striatopathy is nonketotic and is therefore not complicated by acidosis at diagnosis. This fact may explain the patient’s tolerance to chronic hyperglycemia, likely to be necessary to cause the aforementioned pathologic changes in the basal ganglia. The details of the mechanisms that underlie the basal ganglia lesions remain to be clarified. In typical cases, cerebral MRI shows hyperintense signal of the putamen, in T1-weighted images, probably reflecting the accumulation of manganese in gemistocytes (ie, astrocytes with large protein content found during acute brain injury). The rare histopathological studies of autopsied adults revealed the presence of gliosis, the accumulation of gemistocytes and a localized loss of neurons, without evidence of hemorrhage or infarct. Similar studies in the pediatric population are wanting, and specific pathologic mechanisms in that age group remain to be understood.

In conclusion, diabetic striatopathy is a rare entity in childhood with easy-to-treat neurologic manifestations, which must be recognized and treated appropriately to avoid additional deterioration of the patient’s health and appearance of diabetic-related complications.

ABBREVIATIONS

DS: diabetic striatopathy
HbA1c: hemoglobin A1c
HH: hemichorea–hemiballism

REFERENCES

Diabetic Striatopathy in Childhood: A Case Report
Tamara Faundez, Philippe Klee, Sylviane Hanquinet, Valérie Schwitzgebel, Pierre R Burkhard and Christian M Korff
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An error occurred in the article by Faundez et al, titled “Diabetic Striatopathy in Childhood: A Case Report” published in the April 2016 issue of Pediatrics (2016;137[4]; doi:10.1542/peds.2014-3761). On page 1, in the list of authors, the copy reads: “Tamara Faundez, MD,a Philippe Klee, MD, PhD,b Sylvianne Hanquinet, MD,c Valérie Schwitzgebel, MD,b Pierre R Burkhard, MD,d and Christian M Korff, MDa.” Author affiliation copy reads: “aDepartment of Pediatric Neurology, Child and Adolescent, bEndocrinology and Diabetes Unit, Department of Child and Adolescent, “Pediatric Radiology Unit, Department of Radiology, and “Neurology Unit, Department of Clinical Neurosciences, University Hospitals of Geneva, Switzerland”.

This should have read: “Tamara Faundez, MD,a Philippe Klee, MD, PhD,b Sylvianne Hanquinet, MD,c Valérie Schwitzgebel, MD,b Pierre R Burkhard, MD,d and Christian M Korff, MDa.” Author affiliation copy: “aDepartment of Pediatric Neurology, Child and Adolescent, bEndocrinology and Diabetes Unit, Department of Child and Adolescent, cPediatric Radiology Unit, Department of Radiology, and dNeurology Division, Department of Clinical Neurosciences, University Hospitals of Geneva, Switzerland.”

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