Recurrent apnea in a boy suffering from congenital hyperinsulinism in the course of diazoxide treatment.

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Authors declare nothing to disclose

Introduction

Congenital hyperinsulinism (CHI) is a rare disease caused by mutations in genes responsible for regulation of insulin secretion. The most common are mutations of K<sub>ATP</sub> channel. Nowadays we are still not aware of knowledge of exact mutations in 20% of all patients. All of those disregulations lead to inadequate excessive secretion of insulin (Fig. 1). It is the cause of frequent hypoglycemia in individuals suffered from this disease. Prevalence of CHI is estimated at 1:2500 to 1:50000 live births.

First line treatment is a diazoxide therapy. In a case of bad metabolic control or occurring serious side effects of a therapy somatostatine analogs, rapamicine or nifedipine might be used instead of diazoxide.

Case report

Our male patient was referred to the hospital for a first time at the age of 2 months because of episodes of faintness accompanied by hypoglycemia. Laboratory tests confirmed diagnosis of hyperinsulinemic hypoglycemia (Tab. 1).

<table>
<thead>
<tr>
<th>Glucose (mg/dl)</th>
<th>Insulin (µU/ml)</th>
<th>Cortisol (µg/dl)</th>
<th>Growth hormone (ng/ml)</th>
<th>Amonate (µmol/l)</th>
<th>Lactic acid (mmol/l)</th>
<th>F&lt;sub&gt;1&lt;/sub&gt; (mg/dl)</th>
<th>Ketone bodies in urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>15.5</td>
<td>15.9</td>
<td>2.77</td>
<td>&lt;15</td>
<td>2.8</td>
<td>1.33</td>
<td>None</td>
</tr>
</tbody>
</table>

Tab. 1 Laboratory test results

We denied different diagnosis like a inborn metabolic errors. At the beginning he was treated with diazoxide with a good effect. Patient achieved normalization of glycemia and the treatment was well tolerated. Unfortunately in december 2017 he had first episode of apnea which was not connected with hypoglycemia.

Since december 2017 the boy presented next 3 episodes of apneas not related to hypoglycemia, they always appeared once the dose of diazoxide was increased (Fig. 2).

However in the case of our patient during a whole diagnostic process we didn’t find any cardiological (no signs of pulmonary hypertension), neurological (no abnormalities in MRI and EEG) or gastroenterological reasons of apnea.

Because of intolerance to diazoxide we decided to change the way of his treatment and recommended octreotide in multiple daily injections therapy. At the beginning we observed very good reaction and good glycemic control, but after a few days we observed tendencies to hypoglycemia. Because of lack of a good response to the octreotide by itself, we decided to combine two ways of the therapy – and recently the boy is successfully treated with diazoxide in smaller dose (2.9 mg/kg) and octreotide received via personal insulin pump (5,7 mg/kg). Because of secondary adrenal cortex insufficiency caused by octreotide action he also needs to take hydrocortisone orally in supplementary dose. When the dose of diazoxide was decreased no other apnea occured and he’s got good metabolic control (Fig. 3).

Conclusions

There are some reports of kids treated with diazoxide who presented episodes of apneas caused by pulmonary hypertension. In case of our patient we’ve never noticed any features of pulmonary hypertension in echocardiography and physical examination as well as other causes of apnea. It proves that diazoxide might trigger an apnea in different mechanism which is still unknown.

Patients treated with somatostatine analogs might develop supression of counterregulatory systems (e.g. pituitary-adrenal cortex axis) what complicates management of a patient and indicates implementation of supplementary hormonal therapy.

References