Severe Hypoglycemia in a Patient with Acute Renal Failure due to Tumor Lysis Syndrome

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Key words: hypoglycemia, acute renal failure, tumor lysis syndrome

Several mechanisms have been described in the literature to explain the incidence of hypoglycemia in hematologic malignancies. These include increased glucose metabolism in neoplastic tissue, synthesis of insulin-like growth factor-II by tumors, insulin autoimmunity syndrome, and high levels of cytokine production following chemotherapy. However, little data are available on hypoglycemia in patients with tumor lysis syndrome. We present a patient with acute renal failure due to tumor lysis syndrome that appeared after treatment with fludarabine for chronic lymphocytic leukemia. At the same time, severe life-threatening hypoglycemia was diagnosed. With improvement in the clinical and laboratory status, the patient's hypoglycemia was resolved. Our report describes a case of a rarely seen syndrome and submits several hypotheses that might explain this phenomenon, while still leaving it open for further clarification.

Patient Description

A 60 year old woman was admitted to the Department of Nephrology at the Soroka Medical Center because of muscle weakness, paresthesia in the toes and fingers, and vomiting. The patient had suffered from chronic lymphocytic leukemia for several years with recent lymphoma transformation. She had been treated with fludarabine 3 days prior to admission without appropriate hydration. Physical examination revealed signs of hypovolemia such as orthostatic hypotension, plane jugular veins and anemia. Body temperature was normal.

On admission, laboratory findings showed: blood urea nitrogen 170 mg/dl, creatinine 6.1 mg/dl, sodium 132 mEq/L, potassium 9.9 mEq/L, serum pH 7.07, HCO₃⁻ 6 mEq/L, glucose 29 mg/dl, uric acid 45 mg/dl, calcium 6.3 mg/dl, phosphorus 37 mg/dl, lactate dehydrogenase hormone 427–590, white blood cells 1,440, hemoglobin 10.0 g/dl, platelets 137. Electrocardiogram revealed idioventricular rhythm, flattening of P waves, and widening of the QRS complex.

After initial treatment for hyperkalemia in the emergency ward, hemodialysis was performed and hydration initiated. At admission, severe symptomatic hypoglycemia was detected (glucose 29 mg/dl) and intravenous dextrose was started with fast correction of glucose levels, which again fell below 30 mg/dl immediately after cessation of treatment.

Hypoglycemia persisted during the first 5 days of hospitalization, with subsequent complete resolution. Hemodialysis was discontinued after three sessions, with significant improvement in the patient's clinical status and marked improvement in renal function. The patient was not known to suffer from diabetes mellitus. The laboratory data are presented in Table 1.

Comment

It is well known that hypoglycemia may be seen in the clinical course of several tumors. We present a case of acute renal failure due to severe tumor lysis syndrome accompanied by life-threatening hypoglycemia with high levels of C-peptide, inappropriately high for hypoglycemia. Sepsis was ruled out as a possible cause of the hypoglycemia. Furthermore, neither the patient nor any member of her family was known to have been treated by oral hypoglycemic drugs at any time. An assay for sulfonylurea was therefore not considered necessary in this case.

The most common cause of hypoglycemia is increased glucose metabolism in neoplastic tissue with a high histologic grade of malignancy and a high proliferation rate, as in lymphomas and other hematologic malignancies (1, 2). However, our patient had normal glucose levels prior to chemotherapy, and hypoglycemia appeared only after commencement of chemotherapy and the development of the tumor lysis syndrome.

The role of IGF-II has been investigated in a variety of tumors such as hepatocellular carcinoma and non-islet cell tumors (3). Furthermore, IGF-II is known to have insulin-like activity that may reduce glucose plasma levels, but high IGF-II levels are usually accompanied by low insulin values, which was not the case in our patient. Hence, although IGF-II levels were not

Table 1. Patient's laboratory results

<table>
<thead>
<tr>
<th>Tests</th>
<th>Hypoglycemia time resolution values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.91</td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dl)</td>
<td>6.01</td>
</tr>
<tr>
<td>Uric acid (mg/dl)</td>
<td>45.0</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td>37.0</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>29.0</td>
</tr>
<tr>
<td>Insulin (μU/ml)</td>
<td>15.0</td>
</tr>
<tr>
<td>C-peptide (ng/ml)</td>
<td>21.6</td>
</tr>
<tr>
<td>Cortisol (g/ml)</td>
<td>172</td>
</tr>
<tr>
<td>IL-6</td>
<td>Undetectable levels</td>
</tr>
<tr>
<td>TNF</td>
<td>Undetectable levels</td>
</tr>
</tbody>
</table>

* 2 months after the hypoglycemic episode.

IGF = insulin-like growth factor
measured in our patient, this mechanism can be ruled out as a possible cause of the hypoglycemia. There are reports in the literature of insulin autoimmune syndrome with hypoglycemia, hyperinsulinemia, and insulin and pro-insulin antibodies in patients who had not been exposed to exogenous insulin in the past [4]. Usually plasmapheresis is used to reduce the antibody body pool. In our patient the hypoglycemia resolved spontaneously without the need for additional therapy.

It is known that several cytokines (interleukins 1 and 6, tumor necrosis factor) may induce hypoglycemia, loss of body weight, and anorexia. Investigations have shown that IL-1 may be responsible not only for elevated insulin levels but also for elevated glucagon levels. This remains a controversial issue. Although it was anticipated that high levels of cytokine-interleukins would be found in a patient with tumor lysis syndrome treated by chemotherapy, in our patient IL-1 and TNF-α levels in the serum were normal.

Extrapancreatic production of insulin by tumor cells was unlikely since the insulin and glucose levels normalized soon after resolution of the renal failure. Furthermore, the patient was not treated by drugs known to stimulate endogenous insulin production in the pancreas.

Despite the fact that renal failure may be a possible explanation for the C-peptide and insulin elevation due to reduced clearance of insulin in the kidney [5], hypoglycemia is an unusual occurrence in this setting. Thus, the mechanism underlying the hypoglycemia needs further investigation.

References

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Acute Lindane Poisoning in a Child
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Key words: lindane poisoning, insecticide, ingestion, seizures, metabolic acidosis

Lindane, an organochlorine insecticide belonging to the hexachlorocyclohexane family, is widely used as a therapeutic insecticide for humans and animals. It can be absorbed by ingestion, inhalation, or dermal exposure. The primary target of action is the central nervous system. Lindane toxicity has been reported to occur mostly by way of dermal exposure. This report presents a case where intoxication occurred through ingestion.

Patient Description
A 3½ year old male Bedouin child from a rural area was admitted to the Children's Emergency Room because of a short attack of seizures that occurred at home. A short while before, he had ingested an unknown quantity of an unidentified liquid insecticide used for treating animals and passed spontaneously. A day after admission the child's parents showed us the material responsible for the poisoning. It was identified as a 55% lindane solution used as an animal insecticide. They had bought the insecticide somewhere on the West Bank; there was no manufacturer's name on the label, only a sticker stating the lindane concentration.

On admission the child was lethargic and irritable. He exhibited nausea, vomiting and tremor. His temperature was 37.2°C; pulse 150 beats/minute, blood pressure 110/70 mmHg, and respirations 23/minute. Initial arterial blood gases showed pH 7.28, pCO₂ 41 mmHg, pO₂ 95 mmHg, and HCO₃⁻ 20.0 mmol/L. The hemoglobin level was 11.3 g/dl and white blood cell count 14,400/mm³.

Other laboratory results were: serum sodium 140 mEq/L, potassium level 3.8 mEq/L, chloride 105 mEq/L, blood urea nitrogen 35 mg/dl, creatinine 0.9 mg/dl, creatine phosphokinase 50 U/L, alanine aminotransferase 41 U/L, and aspartate aminotransferase 35 U/L. X-ray films of the chest and electrocardiogram were normal. In the emergency room there was a repeat occurrence of general clonic-tonic seizures that were arrested by intravenous injection of diazepam solution (0.2 mg/kg). The child was hospitalized in the General Pediatric Department for further observation. He continued to be lethargic, irritable and nauseous, was still vomiting and had tremors. The child developed a third episode of general clonic-tonic seizures that lasted for about 2 minutes and passed

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