Case report

A rare case of IGF2 mediated hypoglycemia in a diabetic patient – a praneoplastic manifestation of an adrenal tumor

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Article info

Aim: To learn about rare causes of hypoglycemia.

Case study: Hypoglycemia is most commonly due to antidiabetic drugs. However, it is not always drug induced and it can be observed in other conditions unrelated to diabetes, such as insulinoma, autoimmune disorders, and neoplasia. Herein, we report the case of a rare cause of severe and recurrent hypoglycemia in an 83-year-old diabetic and hypertensive lady who was subsequently diagnosed with adrenal malignancy and hypoglycemia was found to be a paraneoplastic manifestation of the tumor secreting IGF2.

Results and discussion: Although more than 95% of cases of hypoglycemia are due antidiabetic drugs but there are other rare causes of hypoglycemia – malignancy being the most important in the rare causes of hypoglycemia. Persistent hypoglycemia should arouse a suspicion of a rare cause of hypoglycemia. In our case hypoglycemia was due to excessive secretion of IGF2 by the adrenal tumor. Several such case cases have been reported where hypoglycemia was a paraneoplastic manifestation of the tumor. So, we need to be aware of the rare causes of hypoglycemia as it can lead to the diagnosis of the primary tumor, as has been in our case, and it can also significantly affect the course of the treatment.

Conclusions: IGF2 secreting tumor can be a rare cause of hypoglycemia.
1. INTRODUCTION

Hypoglycemia is a common medical emergency in diabetic patients treated with insulin or oral hypoglycemic drugs. However, it can be observed less frequently in other conditions such as insulinomas and rare autoimmune diseases. Paraneoplastic disorders are an exceptional etiological factor of hypoglycemia. In this case, paraneoplastic secretion of insulin-like growth factor 1 (IGF1) or partially processed precursors of IGF2 could be responsible for hypoglycemia.\(^2,3\)

2. AIM

Herein, we report a case of severe and recurrent hypoglycemia in a woman with an adrenal malignancy diagnosed incidentally on routine workup.

3. CASE STUDY

A 83-year-old female, a known diabetic and hypertensive, was admitted with poor oral intake and recurrent episodes of drowsiness and lethargy for 3 days. Her random blood sugar on presentation at hospital was 40 mg/dL. Detailed history and examination failed to reveal any known cause of hypoglycemia. In her past medical history, we noticed the presence of multi-infarct CVA and seizure disorder.

She was admitted for investigation and supportive therapy. Over the next 48 hours she suffered repeated bouts of hypoglycemia. Her symptomatology was particularly characterized by neuroglycopenic signs with fatigue, weakness, headache, dysphasia, and loss of consciousness, without seizures. The Glasgow coma scale was 9/15. In view of this her serum cortisol, growth hormone (GH) and insulin levels were studied which were reported normal. However IGF2 level was found elevated (Table 1). IGF2 and IGF1 ratio was found to be 16.48.

Subsequent workup including CT scans of thorax and abdomen revealed a 6.8 × 6.6 × 6.0 cm right suprarenal mass invading the right lobe of liver with mild ascites (Figures 1–4).

In view of this a diagnosis of non-islet cell tumor hypoglycemia (NICTH) was made.

However, in view of age and extensive comorbidities, patient’s family refused further management. The patient was subsequently discharged on the request of her family members with prescription of prednisolone and advice regarding frequent self-monitoring of blood glucose.

4. RESULTS AND DISCUSSION

NICTH occurs mainly in patients with solid tumors of mesenchymal and epithelial origins and, less frequently, in hematopoietic and neuroendocrine tumors.\(^4\)

Hypoglycemia Table 1. Hormone levels.

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Actual</th>
<th>Normal</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol E</td>
<td>13.39</td>
<td>2–18</td>
<td>mcg/dL</td>
</tr>
<tr>
<td>Cortisol M</td>
<td>20.40</td>
<td>7–28</td>
<td>mcg/dL</td>
</tr>
<tr>
<td>GH</td>
<td>2.718</td>
<td>&lt;10</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Insulin</td>
<td>7.10</td>
<td>&lt;25</td>
<td>mlU/L</td>
</tr>
<tr>
<td>IGF1</td>
<td>&lt;25</td>
<td>55–166</td>
<td>ng/mL</td>
</tr>
<tr>
<td>IGF2</td>
<td>412</td>
<td>71–290</td>
<td>ng/mL</td>
</tr>
</tbody>
</table>

Figure 1. CECT abdomen and pelvis showing 6.8 × 6.6 × 6.0 cm heterogeneous poorly enhancing right suprarenal mass. Arrow indicates adrenal tumor.

Figure 2. CECT abdomen showing tumor invading inferior surface of liver (red arrow) and perihepatic ascites (white arrow).
leads to the diagnosis of the tumor in 50% of cases. In other cases, hypoglycemia occurs after the tumor has been found. Usually, patients report previous hypoglycemic symptoms before the NICTH has been diagnosed. Neuroglycopenic symptoms are more commonly observed than autonomic symptoms due to repeated hypoglycemic events and insidious progression observed with NICTH. In the present case, NICTH was established after excluding all other causes of hypoglycemia with relevant investigations.

The diagnosis of NICTH is based on the findings of hypoinsulinemic hypoglycemia associated with the presence of raised levels of IGF2. The treatment of NICTH should target both a symptomatic management of hypoglycemic episodes and the tumor treatment. Hypoglycemia could be reversible after a successful tumor surgery. Chemotherapy or embolization can reduce the occurrence of hypoglycemia. Glucocorticoids seem to be the most effective symptomatic treatment. They stimulate gluconeogenesis and inhibit the big IGF2 tumor production. This effect is dose dependent and reversible if doses are below a critical level. GH therapy relieves hypoglycemic symptoms although it fails to suppress tumor IGF2 production.

5. CONCLUSIONS

Incidence of diabetes mellitus in India has been steadily increasing and one does get to encounter hypoglycemic patients on a fairly regular basis in day to day practice. However, a high index of suspicion needs to be maintained especially in refractory hypoglycemia in elderly patients and oncological perspective needs to be explored if the index of suspicion is high. Hence this case presented a rare constellation of features which would have otherwise been confusing if correct diagnostic protocols had not been applied.

Conflict of interest
None declared.

References
