Navigating troubled waters: Hyperglycaemic Hyperosmolar State precipitated by Nephrogenic Diabetes Insipidus

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INTRODUCTION

- Hyperglycaemic hyperosmolar state (HHS) is a common medical presentation, typically occurring in older patients with Type 2 diabetes mellitus.
- Mortality rates of up to 60% have been reported.
- We describe a rare case of HHS, likely to be precipitated post-lithium-induced nephrogenic diabetes insipidus (DI).

CASE HISTORY

- A 62-year-old female with bipolar disorder presented to ED with lethargy, confusion and reduced mobility.
- Past medical history: bipolar disorder, hypothyroidism and recurrent UTIs.
- Medication history: lithium (>10 years duration), diazepam, olanzapine, sodium valproate and levothyroxine.
- She remained persistently hypernatraemic with Na > 170 mmol/L despite commencement of intravenous fluids.
- 10 days after admission, her blood glucose was noted to be 35 mmol/L with serum osmolality of 398 mOsm/kg.
- She was deemed to be in HHS and treatment commenced with fixed rate insulin infusion and 0.9% saline.
- Over the next few days, the patient’s clinical state deteriorated and she was transferred to ITU.
- Despite a fall in blood glucose, her plasma Na remained persistently elevated despite intravenous 0.45% saline.
- She remained polyuric with an increasing plasma osmolality and a low urine osmolality. This prompted the consideration of nephrogenic DI as a concomitant pathology.
- Overnight water deprivation test confirmed the diagnosis of DI.

RESULTS

<table>
<thead>
<tr>
<th></th>
<th>Pre-HHS treatment</th>
<th>Post-HHS treatment</th>
<th>Post-DI treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mmol/L)</td>
<td>35</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>Serum Osmolality (mOsm/kg)</td>
<td>398</td>
<td>350</td>
<td>289</td>
</tr>
<tr>
<td>Urine Osmolality (mOsm/kg)</td>
<td>-</td>
<td>219</td>
<td>267</td>
</tr>
<tr>
<td>Serum Na (mmol/L)</td>
<td>176</td>
<td>150</td>
<td>144</td>
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</tbody>
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MANAGEMENT

- Amiloride with hydrochlorothiazide was started as treatment for nephrogenic DI.
- Subsequent improvement was observed with falling serum osmolalities and plasma sodium.
- Her plasma glucose remained stable on oral anti-hyperglycaemic agents.

Discussion & Learning Points

- Nephrotoxic renal effects of lithium may occur even within what is considered a therapeutic range.
- Lithium acts through entering the collecting ducts through epithelial sodium channels (ENaC) and inhibits signalling pathways (adenylate cyclase and glycogen synthase3-beta) causing disruption of the aquaporin-2 structure. These changes are initially reversible but thereafter can become permanent.
- Following recovery of hyperglycaemia, persistent polyuria and hyperosmolar state, should prompt consideration of differentials to include diabetes insipidus.
- Amiloride and hydrochlorothiazide are effective in the treatment of nephrogenic diabetes insipidus.
- It is important to recognise the two conditions may coexist in the same patient, so that appropriate therapies may be initiated.

References: