Cyclophosphamide is an alkylating agent used in immunosuppressive and antineoplastic therapies. 1,4 NCCN Category 1 recommended treatment for breast cancer. In moderate (20 to 50 mg/kg) and high dose (30 to 50 mg/kg) IV doses it induces acute hyponatremia. 5 It is a commonly used chemotherapy agent. Clinical presentation includes myelosuppression, bone marrow depression, nausea, vomiting, diarrhea, and encephalopathy. 1

CASE DESCRIPTION

A 53-year-old female with past medical history of ductal carcinomas in situ of the left breast status post lumpectomy and radiation therapy presented with newly diagnosed Stage IIIA pT1c pN2a IDC of the right breast.

She underwent bilateral mastectomies and received low-dose cyclophosphamide treatment for breast cancer—however less than ten cases have been reported. 1,4-6

CASE DESCRIPTION CONT.

• She was started on dose-dense AC therapy: 1 Docetaxol at 60 mg/m² total dose 106 mg. 2 Cyclophosphamide at 600 mg/m² total dose 1000 mg IV (rounmed down from 1056 mg) equivalent to 14.4 mg/kg.

• No side effects were noted during the treatment.

• She was admitted to the intensive care unit (ICU) for endotracheal intubation and mechanical ventilation.

• Evaluation for another etiology for her altered level of consciousness was negative.

Emergent laboratory results

<table>
<thead>
<tr>
<th>Sodium</th>
<th>Potassium</th>
<th>Creatinine</th>
</tr>
</thead>
<tbody>
<tr>
<td>113 mmol/L</td>
<td>7.7 mmol/L</td>
<td>1.40 mg/dL</td>
</tr>
</tbody>
</table>

Electrolytes were quickly corrected within twenty-four hours with 3-4 mmol/L of sodium and 0.9% normal saline treatment to 140 mmol/L and 1.40 mg/dL

She was extubated and transferred to the floor for further monitoring within two days.

On discharge from the hospital, her physical exam was normal with neurological status intact.

Discharge laboratory results

<table>
<thead>
<tr>
<th>Sodium</th>
<th>Potassium</th>
<th>Creatinine</th>
</tr>
</thead>
<tbody>
<tr>
<td>137 mmol/L</td>
<td>3.3 mmol/L</td>
<td>0.45 mg/dL</td>
</tr>
</tbody>
</table>

HOSPITAL COURSE

Mild hyponatraemia is a known side effect of chemotherapeutic agents. 1,4,6

Cyclophosphamide in high (>30 to 50 mg/kg) and moderate (20 to 30 mg/kg) IV doses has been shown to induce severe hyponatremia. 3,4,11

This case represents an extremely rare event of symptomatic hyponatremia associated with low-dose cyclophosphamide therapy (<15 mg/kg), in the treatment of malignancy.

In our patient:

• no structural brain lesions to explain altered mental status
• no other definitive etiology to explain sudden hyponatremia
• no risk factors such as concurrent recreational drug use
• while patients are recommended to increase fluid intake post treatment to prevent hemodynamic instability, the patient was treated with hemodynamic optimization and hydration.

Hypothetically we evaluated the patient’s daily fluid intake and output which was within normal parameters.

There is one documented case of successful continued treatment with cyclophosphamide and concurrent 0.9% saline hydration. 6 We did not reintroduce cyclophosphamide therapy.

HYPOTHESIS

Hypotheses for mechanism of cyclophosphamide-induced acute hyponatremia 4,12:

1. Direct toxic effect of cyclophosphamide or its metabolites on renal collecting tubule epithelium and release of vasopressin.

2. Antidiuretic hormone-like activity of cyclophosphamide or its metabolites and resulting inability to excrete dilute urine.

FOLLOW UP

• She presented for continued chemotherapy.

• She had no recollection of events from her arrival for cycle 1 chemotherapy to release from the ICU.

• Physical exam examination at one positive, 8

• Memory loss but no other neurological deficits. She was very hesitant to continue therapy given her recent complication.

• She has since completed chemotherapy and is undergoing radiation therapy. No further electrolyte disturbances were noted for the duration of treatment.

DISCUSSION

Severe hyponatremia can lead to psychosis, seizure, permanent brain damage, coma, and death. 4,12

Low-dose cyclophosphamide is a commonly used therapy in treatment of many cancers. 1

If a patient presents following treatment with fatigue, lethargy, or altered level of consciousness, clinicians must include hyponatremia in the differential diagnosis. 1,13

Clinicians should be aware of this potentially serious adverse effect regardless of treatment dose and duration. 1,7

Only prompt diagnosis and immediate management can help prevent significant and permanent neurological deficits. 4,12

There is one documented case of successful continued treatment with cyclophosphamide and concurrent 0.9% saline hydration. 6 We did not reintroduce cyclophosphamide therapy.

CONCLUSION

Patients should be monitored before and after receiving low-dose cyclophosphamide therapy for breast cancer with early follow-up.

The emotional trauma patients may endure from this complication including ICU admission, memory loss, fear or refusal of further therapy, and residual neurological deficits should not be overlooked.

REFERENCES


