OBJECTIVE

To describe an unexpected case of acute kidney impairment (AKI) with high-dose chemotherapy and highlight the clinical pharmacist role within this setting.

CLINICAL FEATURES

Stanford BCNU (StaniBCNU) is a high-dose chemotherapy regimen used prior to autologous stem cell transplantation for high-grade lymphoma. It’s a six day protocol, consisting of carmustine, etoposide and cyclophosphamide, Table 1.

Table 1. Stanford BCNU regimen

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose, route</th>
<th>Day</th>
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<tbody>
<tr>
<td>carmustine</td>
<td>450mg/m² IV</td>
<td>-6</td>
</tr>
<tr>
<td>etoposide*</td>
<td>60mg/kg IV</td>
<td>-4</td>
</tr>
<tr>
<td>cyclophosphamide</td>
<td>100mg/kg IV</td>
<td>-2</td>
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<tr>
<td>stem cells</td>
<td>0</td>
<td></td>
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*etoposide phosphate is used at our centre

We describe four recent cases of AKI(1), which occurred with this conditioning regimen at our centre. There was no significant past medical or medication histories on admission for these patients.

Patient 1 was a 28 year old Caucasian male in a complete metabolic remission (CMR) from NK/Tcell lymphoma. His creatine clearance (24 hour urine collection) prior to transplant was 106mL/min.

Patient 2 was a 62 year old Caucasian male in a CMR from relapsed Hodgkins lymphoma. His creatinine clearance (nuclear GFR) prior to transplant was 73mL/min.

Patient 3 was a 39 year old year old Caucasian female in a partial response from relapsed Hodgkins lymphoma. Her creatinine clearance (nuclear GFR) prior to transplant was 106mL/min.

Patient 4 was a 51 year old Caucasian male in a partial response from relapsed follicular lymphoma. His creatinine clearance (nuclear GFR) prior to transplant was 89mL/min.

INTERVENTIONS, PROGRESS AND OUTCOMES

All four cases developed an AKI on D-3 approximately 12 hours after etoposide infusion, from a previously normal baseline, Figure 1. The decision was made to omit cyclophosphamide from the first two cases, and was delivered with a 24 hour delay in the third case. The impact of this omission on long term lymphoma outcomes is uncertain. Complete renal recovery was observed in all four patients, without the need for renal replacement therapy. In the last case, cyclophosphamide was delivered as per protocol, and recovery of renal function was delayed compared to the first three patients.

Significant chemotherapy-related toxicities were observed in all patients, potentially due to increased drug exposure secondary to reduced renal clearance. All four patients suffered severe grade 3-4 mucositis, requiring patient controlled analgesia and total parenteral nutrition for a number of days. A literature search revealed only one prior case of AKI with StaniBCNU conditioning, identifying carmustine as the causative agent(2). Recent paediatric literature also describes unexpected AKI with etoposide phosphate in combination with total body irradiation in paediatric allogeneic stem cell transplant setting(3, 4). These publications suggest the excipients or etoposide alone to be responsible for AKI. Due to the timing of AKI, we are unable to isolate the causative agent and suggest the combination of carmustine with high-dose etoposide could be involved.

The clinical pharmacist made important contributions to multidisciplinary discussions and critical decisions relating to chemotherapy changes, cessation/dose adjustment of concomitant nephrotoxins, and management of transplant complications.

CONCLUSIONS

These cases emphasise the need to be vigilant of renal function monitoring during chemotherapy, in order to minimise possible sequelae of AKI in the autologous transplant setting. We are currently investigating any contributing factors that may necessitate a review of this protocol. Pharmacists contribute expert drug knowledge to improve patient management, particularly in the setting of rare and unexpected events.

REFERENCES