**INTRODUCTION**

Graft-versus-host disease (GVHD) is common after allogeneic hematopoietic stem cell transplant (SCT) but has rarely been reported after autologous stem cell transplant (ASCT). Acute GVHD after ASCT can involve the gastrointestinal tract and rarely the skin and liver and presents with diarrhea, skin rash, and jaundice, respectively, similar to that in allogeneic SCT. Early recognition and prompt treatment can reduce disease progression, morbidity, and mortality. We report here four patients of multiple myeloma who developed acute gut GVHD following ASCT. All patients showed complete recovery after treatment except one patient who later develops chronic GVHD, requiring prolonged immunosuppression.

**CASE REPORT**

A total of 207 patients underwent ASCT at Bone Marrow Transplant center of BLK Super Speciality Hospital from January 2010 to December 2017, of which 135 had multiple myeloma, and others had lymphoma (Hodgkin and non-Hodgkin) and acute promyelocytic leukemia. Autologous acute GVHD developed in 4 patients all of whom had multiple myeloma. We retrospectively analyzed the data of these patients developing autologous GVHD. The study was approved by Hospital Ethical committee. The patient characteristics and outcome have been described in Table 1. Of these four patients, two had received RVD (lenalidomide, bortezomib, and dexamethasone) and two had received CVD (cyclophosphamide, bortezomib, and dexamethasone) before ASCT. All patients received melphalan 200 mg/m² as conditioning regimen. The median stem cell dose was 5.31 × 10⁶ cells/kg (range, 2.77–7.33 × 10⁶ cells/kg). The median days of neutrophil and platelet engraftment were 10.5 (range, 10–12) and 17 (range, 15–23) days, respectively. All patients developed green-colored, large volume, watery loose stools after engraftment (median 13.5 days of ASCT) clinically suggestive of acute gut GVHD. Patients were evaluated for infective causes of diarrhea including stool examination for Clostridium difficile and blood cytomegalovirus-polymerase chain reaction, and all were negative. Sigmoidoscopy was done in all patients and histopathology of the specimens showed evidence of gut GVHD with apoptosis in crypts, cryptitis, and crypt loss in focal areas [Figure 1a-c].

**ABSTRACT**

Graft-versus-host disease (GVHD) has rarely been reported after autologous stem cell transplant (ASCT). GVHD risk is more after ASCT for multiple myeloma compared to lymphoma. Clinical manifestations and treatment of acute GVHD post ASCT are similar to those after allogenic SCT. We report here our experience of acute GVHD following ASCT for multiple myeloma.

**Key words:** Autologous graft-versus-host disease, autologous stem cell transplant, multiple myeloma

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The patients were treated with intravenous methylprednisolone 2 mg/kg as the first-line treatment. One patient also received second-line treatment with etanercept. The patients were followed for a median of 3 months, ranging from 2 to 6 months. At the time of last follow-up, all patients were in remission for GVHD, except one patient who later developed chronic GVHD (limited and oral), requiring prolonged treatment with steroids.

### DISCUSSION

Autologous GVHD is a rare condition which has been reported in patients undergoing autologous SCT for multiple myeloma. Of 38 patients treated with autologous SCT for multiple myeloma at our center over 8 years, 13 patients (34%) developed acute gut GVHD not responding to steroids, eight patients underwent autologous SCT for multiple myeloma, six of whom did not respond to steroids, and five patients presented early after SCT, with a median delay of 2 days after SCT. The patients were treated with intravenous methylprednisolone 2 mg/kg as the first-line treatment. One patient also received second-line treatment with etanercept. The patients were followed for a median of 3 months, ranging from 2 to 6 months. At the time of last follow-up, all patients were in remission for GVHD, except one patient who later developed chronic GVHD (limited and oral), requiring prolonged treatment with steroids.

### Table 1: Characteristic of patients with multiple myeloma developing acute GVHD post-ASCT

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age/Sex</th>
<th>Myeloma type and stage</th>
<th>Treatment before ASCT</th>
<th>Myeloma status before ASCT</th>
<th>CD 34+ cell dose (x10⁶ cells/kg)</th>
<th>Day of neutrophil engraftment</th>
<th>Day of GVHD onset</th>
<th>Grade of GVHD (according to biopsy)</th>
<th>Treatment given</th>
<th>Response to GVHD treatment</th>
<th>Days to respond</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57 year/Male</td>
<td>IgG kappa, ISS-3</td>
<td>RVD×4 cycles</td>
<td>CR</td>
<td>7.23</td>
<td>10</td>
<td>13</td>
<td>III</td>
<td>IV MP 2 mg/kg/day</td>
<td>Responded but 2 days later developed limited chronic GVHD</td>
<td>2 days</td>
</tr>
<tr>
<td>2</td>
<td>25 year/Male</td>
<td>Kappa light chain, ISS-2</td>
<td>30 Gy RT to spine f/b RVD×4 cycles</td>
<td>PR</td>
<td>3.83</td>
<td>12</td>
<td>16</td>
<td>IV</td>
<td>IV MP 2 mg/kg/day</td>
<td>CR</td>
<td>3 days</td>
</tr>
<tr>
<td>3</td>
<td>54 year/Male</td>
<td>IgA lambda, ISS-3</td>
<td>CVD×6 cycles f/b lenalidomide maintenance</td>
<td>VGPR</td>
<td>2.77</td>
<td>10</td>
<td>14</td>
<td>III</td>
<td>IV MP 2 mg/kg/day</td>
<td>CR</td>
<td>3 days</td>
</tr>
<tr>
<td>4</td>
<td>56 year/Male</td>
<td>IgG kappa, ISS-2</td>
<td>30 Gy RT to spine f/b CVD×9 cycles f/b RD for 4 months</td>
<td>PR</td>
<td>6.80</td>
<td>11</td>
<td>12</td>
<td>III</td>
<td>IV MP 2 mg/kg/day etanercept 25 mcg s/c</td>
<td>CR</td>
<td>6 days</td>
</tr>
</tbody>
</table>

and drugs. Rarely, mucositis can be severe and life-threatening.\textsuperscript{[3]} Autologous GVHD, though rare, should be considered in the differential diagnosis of severe unexplained diarrhea after ASCT.

In allogeneic SCT, the GVHD is due to an immunologic attack on the recipient’s skin, gastrointestinal tract, and liver by donor lymphocytes due to the mismatch of histocompatibility antigens.\textsuperscript{[4]} However, patients undergoing ASCT do not have this mismatch, and therefore, pathophysiology of GVHD after ASCT is mainly due to diminished self-tolerance secondary to an altered immune system.\textsuperscript{[1,2]} Newer drugs used for multiple myeloma treatment such as immunomodulators and proteasome inhibitors, both of which our patients had received, have been postulated to alter regulatory T-cell function that could potentially lead to GVHD in these patients.\textsuperscript{[5]} The prevalence has been found to be consistently higher among patients with multiple myeloma compared to lymphoma.\textsuperscript{[1,2]} The diagnosis and management of autologous GVHD are similar to that of acute GVHD after allogeneic SCT. These cases highlight the need for high index of suspicion of autologous GVHD, particularly in multiple myeloma patients, and need urgent treatment.

**ACKNOWLEDGMENT**

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**REFERENCES**


