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Imatinib has become the standard primary approach for the treatment of a newly diagnosed chronic phase myeloid leukemia (CML) patient, recently. Complete cytogenetic response is achieved on the majority of patients under treatment, but the disease remains in molecular level and after discontinuation of the drug, relapses occur inevitably. In imatinib era centers are referring only the patients, who has imatinib resistance or patients with high relapse risk. Secondly, the period from diagnosis to transplantation is an importantominator. In imatinib era CML patients will first undergo a trial of imatinib and according to the response they will be referred to the allogeneic transplant program. There is lack of data about the impact of delayed referral and emerging imatinib resistance on allogeneic transplant outcome. We have performed a case-matched control analysis in our CML (n: 173). CML patients who received imatinib before transplantation (n=20), were matched according EBMT (Gratwohl) score with imatinib naive ones (n=40). The median age at transplant in the imatinib group was 39 (19-57), gender F/M: 10/10, disease status 1st CP:13, 2nd ones (n matched according EBMT (Gratwohl) score with imatinib naive

Engraftment for neutrophil

coming to multi-organ failure. We conclude that HSV-6 encephalitis complicates approximately 10% of T cell depleted allo-HSCT. Poor yield of routine CSF, MRI and EEG examination calls for high index of suspicion and CSF examination for HSV-6 PCR. Prompt antiviral treatment with foscarin appears effective.

| Table-1: HSV-6 Encephalitis following allo-HSCT |

<table>
<thead>
<tr>
<th>Age (Year)</th>
<th>Sex</th>
<th>Onset/Day</th>
<th>Manifestation</th>
<th>HSV-6 CSF (copy/ml)</th>
<th>HSV-6 Blood (copy/ml)</th>
<th>Outcome</th>
<th>Other viral infections</th>
<th>Follow-up Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>46F</td>
<td>+41</td>
<td>Amnesia, confusion, seizure</td>
<td>4700</td>
<td>Negative</td>
<td>Complete resolution</td>
<td>Herpes zoster</td>
<td>Alive 12 months</td>
<td></td>
</tr>
<tr>
<td>66F</td>
<td>+103</td>
<td>Confusion, somnolence, disorganized speech</td>
<td>225,000</td>
<td>22,500</td>
<td>Transient improvement</td>
<td>CMV</td>
<td>Died day = 147</td>
<td></td>
</tr>
<tr>
<td>41M</td>
<td>+60</td>
<td>Amnesia, confusion, tremor</td>
<td>Positive*</td>
<td>200</td>
<td>Complete resolution</td>
<td>None</td>
<td>Alive 36 months</td>
<td></td>
</tr>
<tr>
<td>39M</td>
<td>+35</td>
<td>Amnesia, confusion, seizure</td>
<td>4800</td>
<td>100</td>
<td>Complete</td>
<td>BK virus resolution</td>
<td>Alive 6 months</td>
<td></td>
</tr>
<tr>
<td>58F</td>
<td>+83</td>
<td>Seizure, confusion</td>
<td>600</td>
<td>2700</td>
<td>Complete resolution</td>
<td>None</td>
<td>Died day = 120</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: M- male, F- female, allo-HSCT- allogeneic hematopoietic stem cell transplant, MRI- Magnetic resonance imaging, HHV- Human herpes virus, Prot- Protein, Leu- Leukocytes, CSF- Cerebrospinal fluid, WM- white mater, * Quantitative PCR not available

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**HUMAN HERPESVIRUS-6 ENCEPHALITIS FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION**

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Approximately 50% recipients of allo-HSCT develop human herpes virus-6 (HHV-6) viremia detectable by polymerase chain reaction amplification (HHV-6 PCR), but the clinical significance of this asymptomatic viremia is unclear. Five of 53 (9.4%) patients who received Alemtuzumab (total dose, 40 mg) supported conditioning (CY-TBI = 3, BU-TBI = 1, Flu-Mel = 1, MUD = 1, MMRD = 1) and Tacrolimus as GVHD prophylaxis subsequently developed HHV-6 encephalitis whilst receiving antiviral prophylaxis (Valaciclovir = 4 and Valganciclovir = 1). Acute GVHD (grade II = 1, grade III = 2, grade IV = 2) preceded encephalitis and had necessitated, prednisone = 5, Infliximab = 1, Alemtuzumab = 1, and Daclizumab = 1. HSV-6 encephalitis became apparent at 41-103 days (median 60 days) presenting with confusion (n=5), amnesia (n= 3) and seizures (n=2). MRI revealed non-specific white matter changes in 4 and a non enhancing medial temporal lobe lesion in one of the patients. CSF was elevated in 4 patients (table-1); CSF-plaqenclotysis was mild with a median of 3- lymphocytes/hpf. HSV-6 PCR on blood (plasma) revealed 100-22,500 (median 1200) DNA copies/ml. CSF PCR was positive in all 5 patients at 600-225,000 (median 4700) copies/ml. CSF HHV6 was several fold higher than plasma levels (table-1). EEG was nonspecific in all 5 patients. Intravenous administration of foscarin resulted in neurological improvement at 8-13 days (median 11) and negative plasma PCR at 30-66 (median 50) days; recovery of short-term memory loss was more prolonged. In the patient with negative plasma PCR, CSF PCR became negative on 30th day of therapy. Four patients had complete neurological recovery, one patient (#2) had transient improvement before succumbing to multi-organ failure. We conclude that, HSV-6 encephalitis complicates approximately 10% of T cell depleted allo-HSCT. Poor yield of routine CSF, MRI and EEG examination calls for high index of suspicion and CSF examination for HHV-6 PCR. Prompt antiviral treatment with foscarin appears effective.

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**CD154:CD40 CO-STIMULATORY BLOCKADE AT PRIMARY BMT PROMOTES ALLOGENEIC ENGRAFTMENT IN SECONDARY BMT BY BLOCKING SENSITIZATION**

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Introduction: The morbidity associated with ablative conditioning has prevented the widespread application of bone marrow (BM) transplantation (BMT) to treat autoimmune diseases and hemoglobinopathies. To reduce the risk-benefit ratio of establishing chimerism, less-toxic approaches for conditioning recipients have been pursued. As one approaches the threshold for conditioning, failure of durable chimerism occurs with an increasing frequency. In the present studies, we evaluated the effect of non-ablative conditioning regimens on sensitization after graft failure and BM re-transplantation. Materials and Methods: Recipients were infused with MHC-disparate BMC in the context of costimulatory material and/or anti-CD154 (day 0) and/or anti-CD154 (day 5) DTH response. The values are reported as mean fluorescence intensity (MFI). The Ab titers were 4.9 ± 2.6 MFI in mice treated with anti-CD154 and 4.0 ± 0.4 in mice treated with both anti-CD154 and anti-CD154 resembled the Ab level in naive mice (3.4 ± 0.5). Ab titers were significantly higher in mice treated with anti-CD154 mAb alone (47.7 ± 71.3; P < 0.05) and the non-mAb treated group (123 ± 54.7). Conclusion: These results suggest that CD154+CD40 co-stimulatory blockade used at the time of primary BMT promotes allogeneic engraftment in secondary BMT after engraftment failure. The mechanism is that anti-CD154 inhibits B cell activation and generation of alloantibody after primary BMT. Circulating anti-donor Abs are therefore the critical hurdle for the success of secondary BMT. These findings could have a significant impact on management of clinical recipients who have failed at primary BMT and require retransplantation.

The impact of early onset of hemophagocytosis after transplantation on the outcome of allogeneic stem cell transplantation

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[Introduction] Recently, the concept of early onset of hemophagocytosis after transplantation has been proposed, but the incidence, pathological findings and prognosis have not clarified. We analyzed how the early onset of hemophagocytosis after transplantation affects the outcome of allogeneic stem cell transplantation.

[Patients and methods] Fifty-two patients received their transplants at the Nagoya First Red Cross Hospital from May 2005 to April 2006. Forty-five patients of the 52 patients received marrow aspiration in early stage of transplantation (until day 30), and were included in the current study. Patients’ ages were from 17 to 65 (median 42) years old. Forty patients were malignant diseases, and 5 patients were non-malignant diseases. Nineteen patients received reduced intensity stem cell transplantation (RIST) regimen, and 36 patients received conventional regimen. Thirty-two patients received BMT, 8 patients received PBSCT, and 5 patients did CBT. Cells of bone marrow were retrospectively analyzed by a pathologist, and they were divided into three groups according to the intensity of pathological findings of hemophagocytosis as group A (no hemophagocytosis), group B (mild hemophagocytosis) and group C (severe hemophagocytosis). We compare three groups with the clinical parameters.

[Results] Twenty-two patients were included in group A (49%), 13 patients in group B (29%), and 10 patients in group C (22%). The average of maximum T-bilirubin in early stage of transplantation (until day 30) was 1.60 mg/dl (group A), 2.68 mg/dl (group B), and 6.49 mg/dl (group C). There was significant difference between A and C group (P < 0.01). Similarly, the average of maximum creatinine was 0.78 mg/dl (group A), 0.75 mg/dl (group B), and 1.26 mg/dl (group C). There was significant difference between A group and B group (P < 0.01). Disease free survival until day 100 was 45% (group A), 77% (group B) and 40% (group C) (P = 0.02).

[Conclusion] It is supposed that the occurrence of hemophagocytosis until day 30 were well associated with elevation of T-bilirubin and creatinine, and early mortality. To confirm a clinical significance of hemophagocytosis, further studies are needed.