PB2260 CIDOFUOR FOR THE TREATMENT OF ADENOVIRUS INFECTION IN PEDIATRIC PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT): A SINGLE CENTER EXPERIENCE

**Topic:** 30. Infections in hematology (incl. supportive care/therapy)

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**Background:** Adenovirus (ADV) infection is usually self-limited and asymptomatic in immunocompetent individuals but is a cause of morbidity and mortality in immunocompromised pediatric patients undergoing HSCT. In particular, impaired T-cell immunity following HSCT increases the risk of viral reactivation and/or infection. Patients developing ADV-associated disease present with a broad variety of clinical manifestations ranging from mild gastroenteric or respiratory symptoms to severe hemorrhagic enteritis, cystitis, hepatitis, pneumonia, encephalitis, myocarditis or multiple organ involvement. Currently, no specific drugs are approved for the treatment of ADV infection. Cidofovir, a nucleotide analogue inhibiting viral DNA replication, has potential for therapeutic activity against ADV.

**Aims:** We retrospectively evaluated efficacy and safety of cidofovir in pediatric patients undergoing HSCT with ADV infection.

**Methods:** We identified cases of ADV infection following HSCT in pediatric patients treated in our Institution since December 2015. Patient characteristics are summarized in the Table. ADV-DNA was monitored in peripheral blood twice weekly in the first 100 days post-HSCT, then once monthly in the first year after HSCT. Cidofovir was started when blood ADV-DNA was > 1000 copies/mL in symptomatic patients.

**Results:** Eight patients out of 76 who underwent HSCT (11 from haploidentical donors) between December 2015 and February 2022 developed ADV infection: 7 were male; median age was 8.5 years (range 2-15 years). Pre-transplant diagnosis was severe aplastic anemia for 3 patients, the remaining 5 patients were diagnosed with acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), Cooley disease, Fanconi anemia and hyper IgM X-linked immunodeficiency. One patient received HLA identical SCT from a family donor, one patient underwent matched and another mismatched unrelated donor SCT, 5 patients received haploidentical SCT: one unmanipulated with post-transplant cyclophosphamide and 4 with B- Tα/β depleted graft. Median time to ADV infection was 90 days (range 23-170 days). ADV-DNA was isolated by RT–PCR in blood in 7/8 patients; ADV-DNA was isolated by RT-PCR in bronchoalveolar lavage fluid and pericardial fluid in 4 and one patient who developed severe interstitial pneumonia and pericardial effusion, respectively. None of the patients received probenecid for kidney protection. In our cohort, cidofovir was given at the dose of 1 mg/kg/three times a week, in order to prevent kidney injury. Patients received a median of 9 (range 8-14) cidofovir doses. 7/8 patients cleared ADV viremia and resolved pericardial and pulmonary manifestations.

**Image:**

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Summary/Conclusion: ADV infection is a potentially life-threatening complication after HSCT, with an increased incidence in pediatrics and in patients undergoing haploidentical HSCT, consistent with our experience, with no approved standard treatment. Cidofovir represents a valid therapeutic option. Our treatment schedule at the dose of 1 mg/kg/3 times a week showed 87.5% resolution with no major hematological or renal toxicities requiring dose adjustment for concomitant nephrotoxic agents or treatment discontinuation. Our schedule was well-tolerated and feasible for outpatient administration, resulting in a median disease resolution of 3 weeks. Although very encouraging, these results should be confirmed by larger cohorts of patients.