

## 935 A CASE REPORT OF PEDIATRIC ADENOVIRAL REACTIVATION AFTER CAR T-CELL THERAPY

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**Background** The patient is an 11-year-old male with pre-B acute lymphoblastic leukemia (ALL) in second relapse 15 months after a hematopoietic stem cell transplant (HSCT) who presented for anti-CD19 CAR T-cell therapy with tisagenlecleucel. Tumor burden prior to therapy revealed ~60% bone marrow involvement by leukemia without CNS disease. He received Fludarabine/Cyclophosphamide for lymphodepletion followed by CAR T-cell infusion on D0 (Image 1). He developed grade 1 CRS, grade 1 neurotoxicity for which he received Tocilizumab and 10 days of dexamethasone, and carHLH (grade 3 transaminitis, hyperferritinemia, coagulopathy) for which he received 5 days of Anakinra (figure 1). He developed abdominal pain and tenesmus that progressed to hematochezia on D+12. CT abdomen revealed bowel wall thickening and mucosal hyperenhancement suggestive of pancolitis. Stool viral panel and Clostridium difficile were negative. He was empirically treated for typhlitis with Zosyn and switched to Cefepime/Flagyl without improvement. Fecal Adenovirus resulted positive while CMV and enterovirus were negative. Blood Adenovirus was detected at <190 copies/mL. Endoscopy showed crypt epithelial apoptosis with scattered atrophy and loss. Colonic biopsy was positive for Adenovirus. The patient slowly improved and discharged on D+36.

**Methods** Adenovirus infection leads to significant morbidity and mortality among pediatric HSCT patients.<sup>1-3</sup> After infection, adenovirus persists in mucosal lymphocytes but competent host immunity prevents viral expansion in gut epithelial cells [4]. When host immunity is compromised, viral reactivation can lead to adenoviremia resulting in enteritis, hepatitis, and death.<sup>2,5</sup> Historically, supportive care has been used with cidofovir reserved for fulminant disease. Recently, viral specific T-cells (VSTs) have shown promise.<sup>6</sup>

A recent study noted that adenovirus was the most common identifiable pathogen in a cohort of pediatric patients receiving CAR T-cells.<sup>7</sup> However, previous studies have not identified it as a common cause of post-CAR infections.<sup>8</sup> Pre-infusion disease burden, lymphodepleting regimens, carHLH, neutropenia duration, hypogammaglobulinemia, high grade CRS, and previous HSCT have been identified as risk factors for infections.<sup>7-9</sup>

We propose three contributors to adenoviral reactivation in the gut during CAR T-cell treatment (Image 2):

1. Pre-infusion lymphodepletion destroys gut mucosal lymphocytes, spreading viral particles to host epithelial cells and reactivating infection.
2. CAR T-cell expansion leads to generalized immune dysregulation/contraction during CRS and HLH/MAS
3. Immune blockade blunts immune regulation.

**Conclusions** Adenovirus should be considered in patients who develop gastrointestinal symptoms (abdominal pain, diarrhea, tenesmus, hematochezia) after CAR infusion. Further research is needed to identify those at risk for severe disease who may warrant additional treatment.

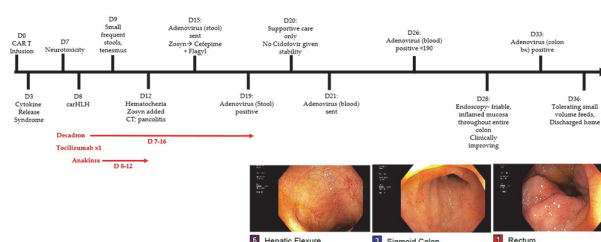
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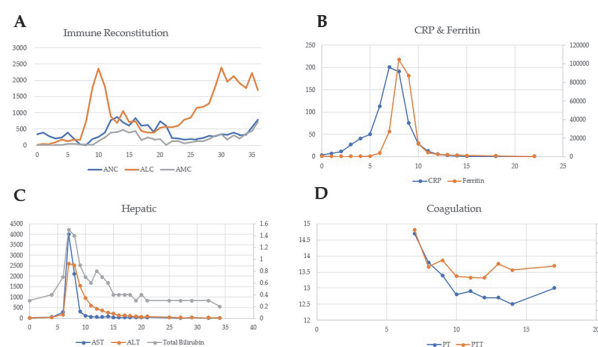
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**Consent** Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

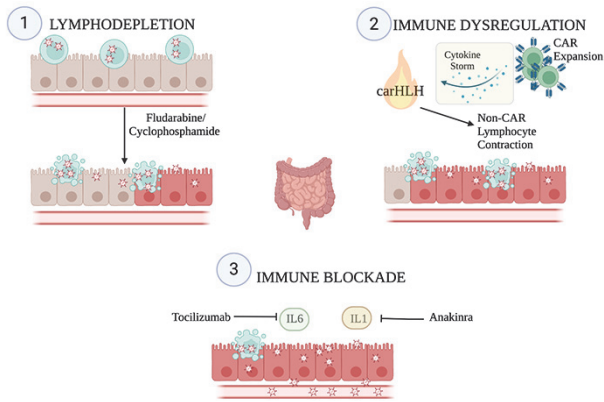
### Patient Timeline



**Abstract 935 Image 1** Patient timeline with endoscopic findings Hospital course (black), immune modulation (red), and associated endoscopy showing inflammatory changes at the hepatic flexure, sigmoid colon, and rectum



**Abstract 935 Figure 1** Laboratory trends Laboratory values over time for immune reconstitution (A), inflammatory markers (B), hepatic toxicity (C), and coagulopathy (D). Absolute Neutrophil Count (ANC), Absolute Lymphocyte Count (ALC), Absolute Monocyte Count (AMC), C-reactive protein (CRP), Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Prothrombin Time (PT), Partial Thromboplastin Time. Days (x axis). Cell counts in cells/microliter, CRP in mg/L, Ferritin in ng/mL, AST and ALT in IU/L, Total bilirubin in mg/dL, PT and PTT in seconds.



**Abstract 935 Figure 2** Contributors of adenoviral reactivation Lymphodepletion (1), carHLH (2), and immune modulation (3) as potential contributors to adenoviral reactivation

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