



Hemoadsorption-Based Strategy for Refractory Chimeric Antigen Receptor T Cell Therapy-Associated Toxicity: A Single Centre Experience



Pasquale Esposito (1,2), Massimiliano Gambella (3), Elisa Russo (1,2), Anna Maria Raiola (3), Novella Conti (2), Elisa Porcile (4), Stefania Bianzina (5), Monica Centanaro (4), Emanuele Angelucci (3), Francesca Viazzi (1,2)

Affiliations:

1. Department of Internal Medicine (DIMI), University of Genova, Genova, Italy
2. Unit of Nephrology, Dialysis and Transplantation, IRCCS Ospedale Policlinico San Martino, Genova, Italy
3. Unit of Hematology and Cellular Therapy, IRCCS Ospedale Policlinico San Martino, Genova, Italy
4. Anesthesiology and Intensive Care Unit, IRCCS Ospedale Policlinico San Martino, Genova, Italy
5. Neonatal and Pediatric Intensive Care Unit, Emergency Department, IRCCS Istituto Giannina Gaslini, Genova, Italy

Introduction

Chimeric antigen receptor T cell (CAR-T) therapy represents a breakthrough in the management of relapsed/refractory hematologic malignancies. Despite its efficacy, it is frequently complicated by cytokine release syndrome (CRS), which can progress to life-threatening organ dysfunction and may not respond to pharmacologic interventions.

Methods

We retrospectively analyzed patients who received CAR-T therapy for hematologic malignancies between 2020 and 2023, focusing on those treated with hemoadsorption. Data collected included demographics, comorbidities, CAR-T details, complications, treatments, and outcomes. Inflammatory markers (IL-6, ferritin, CRP) were measured to assess changes during hemoadsorption. Outcomes included CRS resolution, disease progression, and death. Disease staging, diagnosis and grading of CRS, Immune effector Cell-Associated Neurotoxicity Syndrome (ICANS), acute kidney injury (AKI), and performance status followed established clinical criteria and guidelines.

Results

Among 48 patients, four developed grade 4 CRS unresponsive to standard therapy, including tocilizumab, corticosteroids, and anakinra. These patients—all with high tumor burden and poor performance status—underwent extracorporeal hemoadsorption as additional rescue therapy. Treatment was delivered using continuous veno-venous hemodiafiltration (CVVHDF) with a CytoSorb® cartridge and AN69ST hemofilter.

Hemoadsorption began a mean of 5.2 ± 1.7 days post-CAR-T infusion. One patient, who had refractory IL-6 elevation and pre-existing cardiomyopathy, died shortly after the procedure. The remaining three experienced marked IL-6 reduction (till to -95%), hemodynamic stabilization, improved respiratory function, and renal recovery (Table 1). Two of these patients later succumbed to either disease progression or infection; one survived at least two months after discharge.

Conclusions

This case series highlights the potential role of hemoadsorption as an adjunctive approach for severe CAR-T-related CRS unresponsive to conventional treatment. The therapy was well tolerated and associated with clinical improvement and reduction in inflammatory markers. Nonetheless, further prospective studies with larger cohorts are necessary to validate these findings, refine patient selection, and define optimal integration with existing therapies.

PATIENT	#1	#2	#3	#4
Clinical Features				
Age, years	69	47	77	75
Sex	F	F	M	F
Hematological diagnosis	NOS-DLBCL	NOS-DLBCL	MCL	NOS-DLBCL
Previous therapy lines	2	2	3	2
Disease Stage	4B	4A	3SB	4B
CAR-T Therapy				
Lymphodepletion regimen	Fluda 25 mg Cy 250 mg	Fluda 25 mg Cy 250 mg	Fluda 30 mg Cy 500 mg	Fluda 25 mg Cy 250 mg
CAR-T product	Tisagenlecleucel	Tisagenlecleucel	Brexucabtagene	Tisagenlecleucel
Post-infusion complications				
CRS	Yes	Yes	Yes	Yes
-Onset from infusion	0	1	2	1
-Max stage	4	4	4	4
ICANS	Yes	Yes	Not valuable	Yes
-Max stage	4	3	-	4
Other toxicities			Coagulopathy	Cardiomyopathy
Peak IL-6 (ng/L)	>5000 *	4842	4575	2974
Day from infusion	3	3	5	4
Peak CRP (mg/L)	148	221	82	46.6
Peak Ferritin (µg/L)	6564	50565	29330	56401
Peak sCr (mg/dl)	1.9	2.4	1.7	1.5
AKI stage	3	3 (with oliguria)	2	3
Pharmacological treatment				
Tocilizumab	Yes	Yes	Yes	Yes
-Cumulative dose (mg)	1920	1920	1500	1600
Corticosteroids (dexamethasone)	Yes	Yes	Yes	Yes
-Cumulative dose (mg)	170	540	790	270
Anakinra	Yes	Yes	Yes	Yes
-Cumulative dose (mg)	700	1300	700	1400
Blood purification treatment				
Days from CAR-T infusion	7	3	6	5
Modality	CVVHDF	CVVHDF	CVVHDF	CVVHDF
Dialysis Membranes	modified AN69S + CytoSorb®	AN69S + CytoSorb®	modified AN69S + CytoSorb®	AN69S + CytoSorb®
HA cycles	2	3	4	1
CVVHDF Duration (days)	6	11	5	1
Delta IL-6 (%)	-95	-88	-67	-18
CRS resolution	Yes	Yes	Yes	No §