Published in final edited form as:

Crit Care Med. 2018 November ; 46(11): e1086–e1087. doi:10.1097/CCM.0000000000003374.

A growing problem of critical illness due to chimeric antigen receptor T cell therapy

Dusan Hanidziar, MD, PhD and
Massachusetts General Hospital Boston MA

Edward Bittner, MD, PhD, MS Ed
Massachusetts General Hospital Boston MA

To the Editor:

We read with great interest the review by Gutierrez and colleagues on critical care considerations for patients receiving chimeric antigen receptor T (CAR T) cell therapy (1). While CAR T cell toxicities have been previously reviewed (2), Gutierrez and colleagues synthesize comprehensive recommendations for their management, tailored specifically for the critical care practitioner. As one would expect, the authors provide an update on the major reasons for ICU admission, i.e. neurotoxicity and cytokine release syndrome (CRS). When severe, these conditions can be life-threatening and require ICU management, including mechanical ventilatory support. We feel that additional caveats pertinent to respiratory management, not discussed by authors, deserve mention. Difficult airway management due to bulky cervical or mediastinal lymphadenopathy, tumor infiltration of tonsils and adenoids and mucosal friability due to coagulopathy can be encountered in patients with leukemias and lymphomas (3). Involvement of the cervical spine by a primary malignancy or metastases and presence of cervical myelopathy should be ascertained before airway manipulation. Full patient cooperation to allow a detailed airway exam may however be hampered by the neurotoxicity of CAR T therapy. Given these risks, it is our opinion that an early and expert airway evaluation including a review of chest and neck imaging should become standard practice to avoid airway emergencies and adverse outcomes.

We would like to recognize the authors for raising the complex issue of fluid management as it may closely relate to respiratory complications. While they point out that respiratory decompensation is frequently preceded by fluid resuscitation, the problem is not discussed in further detail. What are the reasons that volume overload occurs and is it preventable? Maintenance fluid is typically administered to mitigate tumor lysis syndrome or replace insensible losses due to high fevers. Intravenous antibiotics and blood products often provide additional volume. In patients that become hypotensive, empiric fluid boluses are recommended (2). This additional fluid, however, might be tolerated poorly in the setting of pulmonary capillary leak, CRS-related cardiomyopathy or oliguric renal failure. The expertise of intensivists in performing point-of-care cardiac and lung ultrasound to guide

fluid management (4) might prove particularly beneficial for this vulnerable group of patients. In particular, recognition of a new cardiac dysfunction could expedite patient transfer to the ICU and initiation of vasopressor/inotropic support as compared to continued fluid resuscitation on general care floor resulting in fluid overload and respiratory failure.

Finally, we posit the need for individualized physiologic monitoring and ICU management in the future. New CAR T cell products will be introduced for growing list of indications, and administered in combinations with other immunotherapies. As a result, the magnitude and timing of toxicities will likely become increasingly variable and difficult to predict (5). Personalized approaches to inpatient and outpatient monitoring, hospitalization and discharge planning will need to be developed. Patients with extensive comorbidities receiving CAR T cells as a standard of care will likely represent a growing high-risk population. The work by Gutierrez and her colleagues provides an early insight into the complexities and future challenges within this rapidly developing field of critical care.

Acknowledgments:

Dusan Hanidziar is supported by a grant from the National Institute of General Medical Sciences (T32 GM007592).

References

1. Gutierrez C, McEvoy C, Mead E, et al.: Management of the Critically Ill Adult Chimeric Antigen Receptor-T Cell Therapy Patient: A Critical Care Perspective. *Crit Care Med* 2018 6 22. doi: 10.1097/CCM.0000000000003258.
2. Neelapu SS, Tummala S, Kebriaei P, et al.: Chimeric antigen receptor T-cell therapy - assessment and management of toxicities. *Nat Rev Clin Oncol* 2018;15(1):47–62. [PubMed: 28925994]
3. Francisconi CF, Caldas RJ, Oliveira Martins LJ, et al.: Leukemic Oral Manifestations and their Management. *Asian Pac J Cancer Prev* 2016;17(3):911–5. [PubMed: 27039811]
4. Boyd JH, Sirounis D, Maizel J, Slama M: Echocardiography as a guide for fluid management. *Crit Care* 2016; 20:274. [PubMed: 27592289]
5. Teachey DT, Bishop MR, Maloney DG, Grupp SA: Toxicity management after chimeric antigen receptor T cell therapy: one size does not fit ‘ALL’. *Nat Rev Clin Oncol* 2018;15(4):218.