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Chimeric antigen receptor T-cell therapy (CAR-T) is a novel immunotherapy used for the treatment of refractory B-cell leukemias and lymphomas. As clinical trials continue to expand, multiple treatment toxicities have been documented. Treatment-associated toxicities are typically systemic, however, focal manifestations have been described. We present a unique case of a 55-year-old female who developed oropharyngeal and laryngeal dystonia following CAR-T therapy. This case points to a possible association between CAR-T therapy and focal head and neck dystonia.

Key Words: Chimeric antigen receptor T-cell therapy, treatment toxicities, adductor laryngeal breathing dystonia, oropharyngeal dystonia.
vocal fold due to recurrence of symptoms. Postoperative stroboscopy showed a decrease in vocal fold dystonia (Video S3). Although the patient continues to experience intermittent dyspnea, she is extremely pleased with her postoperative results and is routinely seen in our clinic for repeated stroboscopy examinations.

**DISCUSSION**

CRS and CRES are the most common toxicities associated with CAR-T treatment. The mechanism of CRS is better characterized as a systemic inflammatory reaction that clinically resembles sepsis. The severity of CRS is graded on a scale of one to four—grade one corresponds to a documented fever above 38 degrees Celsius and grade four corresponds to shock requiring intubation and/or vasopressors. Symptoms typically occur within 24 hours following treatment and peak between 1 to 2 weeks. Interleukin-6 (IL-6) levels are specifically correlated with symptom severity, leading to the utility of tocilizumab (IL-6 receptor blocker) as a standard of care treatment for CRS.

CRES is a central nervous system toxicity that can either occur independently or in concordance with CRS. Similar to CRS, CRES is graded on a scale of one to four—one corresponds to mild neurological impairment and four corresponds to cerebral edema leading to global encephalopathy. Despite being a common adverse reaction documented in up to 40% to 44% of patients, our understanding about the mechanisms of CRES is still incomplete. Reported CRES symptoms can vary drastically and range from focal aphasia, tremors, myoclonus, global delirium, encephalopathy, seizure or seizure-like activity, and comatose states. The onset of CRES symptoms typically occurs within the first week of treatment. In concordance with our study, ancillary studies such as computed tomography, MRI, and an electroencephalogram have not correlated with the type and severity of symptoms. All of these factors point toward a more complex mechanism for CRES and suggests perhaps multiple mechanisms for different manifestations of neurotoxicity.

Our reported case depicts a unique adverse event following CAR-T therapy. Interestingly our patient’s symptoms were localized specifically to the oropharynx and larynx with complete resolution while sleeping. This rare condition is known as adductor laryngeal breathing dystonia (ALBD), described by Grillone and Blitzer in 1994. Their study discussed seven patients with ALBD who were successfully treated with botulinum toxin A injections into the thyroarytenoid muscles. While the etiology of ALBD was not discussed, they did describe many symptomatic similarities to our patient such as persistent stridor, focal dystonia, exacerbated symptoms with exertion, and resolution while sleeping. The disappearance of symptoms during sleep is thought to occur due to decreased brain activity. While a psychogenic etiology could certainly be considered, patients with ALBD typically show little benefit from medical optimization and extensive speech therapy, which was also seen with our patient.

Although we cannot definitively prove causation, the onset of her symptoms following treatment suggests a potential relationship between CAR-T therapy and ALBD. To the best of our knowledge, this is the first reported case of a focal oropharyngeal and laryngeal manifestation following CAR-T therapy.

Given the rapid emergence of clinical trials, immunotherapy has also been an impactful addition to the otolaryngologists’ armamentarium for head and neck malignancies. As indications continue to expand, otolaryngologists should be equipped to understand the mechanism of these drugs and their potential toxicities.

**CONCLUSION**

While CRS and CRES are the most common CAR-T therapy toxicities, ALBD is a potential alternative side effect. We hope that our experience will inform patients and physicians alike about the natural progression and wide array of adverse effects associated with CAR-T therapy.

**BIBLIOGRAPHY**