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# Exploring the Adverse Effects of CAR-T Therapy: A Cases Report of Potential MINOCA in CAR-T

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# Exploring the Adverse Effects of CAR-T Therapy: A Case Report of Potential MINOCA in CAR-T

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## INTRODUCTION

The discovery and application of Chimeric Antigen Receptor T-Cell Therapy (CAR-T) has marked a new era in cancer treatment. CAR-T is a novel therapy with a relatively small treatment population, and we have yet to identify the full spectrum of its adverse effects.[1] There are well-established approaches to the most common adverse effects, principally cytokine release syndrome (CRS), but there is limited literature discussing the nature of cardiotoxicity in CAR-T, much less its mechanism or management.[2,3] This case study discusses the development of myocardial infarction with no obstructive coronary atherosclerosis (MINOCA) in a patient treated with CAR-T.

## CASE PRESENTATION

A 48-year-old man with a history of Stage IV Diffuse Large B-Cell Lymphoma refractory to R-CHOP alternating with high-dose methotrexate and cytarabine, craniospinal irradiation, and haploidentical stem cell transplant, underwent CD 19-directed CAR-T. His post-treatment course was complicated by marrow aplasia and infection, but he ultimately responded to therapy and achieved complete remission.

Five months after undergoing CAR-T, the patient presented with persistent malaise and vague abdominal pain. Initial assessment found him to be cachectic and frail, and he was admitted for further investigation of failure to thrive (FTT). An extensive workup of endocrine, metabolic, and infectious causes of FTT was unrevealing. Labs showed stable neutropenia (ANC 0.4) and anemia (Hgb 9.7) with no evidence of adrenal insufficiency, thyroid dysfunction, vitamin deficiencies, nor bacterial, viral, or fungal infections. EGD did not reveal any significant gastrointestinal pathology, only patches of chronic, mild inflammation.

On the sixth day of hospitalization, the patient reported left shoulder pain. Telemetry showed an acute increase in heart rate, from a baseline sinus tachycardia of 100-110 bpm to 130-140 bpm. EKG revealed new inferior ST segment elevations. Echocardiography identified newly depressed ejection fraction (45%) and basal to mid-anterior and anteroseptal wall motion abnormalities, where previous studies had shown normal EF and no segmental wall motion abnormalities. High-sensitivity troponins were elevated and continued to rise from – 344 ng/L followed by 366 ng/L in the setting of normal renal function. Subsequent cardiac catheterization revealed no obstructive coronary artery disease. Altogether, the evidence for myocardial injury in the absence of obstructive coronary artery disease culminated in a diagnosis of MINOCA.

A multi-disciplinary team including Cardiology and Hematology-Oncology reviewed possible etiologies of cardiac injury. Although the patient had previously received doxorubicin chemotherapy (total of 229 mg, 20 months prior to this admission), the acute onset of ST elevations and dynamic troponins were atypical for anthracycline-induced cardiomyopathy.[4] Similarly, the presentation was not typical for stress-induced cardiomyopathy, especially in the absence of an acute trigge.[5]

The constellation of cardiac findings was attributed to myocarditis, but the underlying cause remained unclear. The patient was not taking any medications commonly associated with myocarditis. Infectious workup was negative including blood cultures, urine cultures, influenza A and B, respiratory pathogen panel, EBV, CMV, tuberculosis and aspergillus testing. Of note, testing for coxsackie A and B, HIV, and HSV was not performed. Previous reports have posited a CRS-mediated mechanism of cardiac injury in CAR-T, but CRS typically peaks days after treatment, and would be uncommon months after CAR-T infusion.[6] Another proposed mechanism considers off-target cross-reactivity, leading to an autoimmune myocarditis.[6] The next best steps to workup myocarditis would have been further infectious testing, cardiac MRI, endomyocardial biopsy, but these were deferred as the patient was high-risk for invasive procedures and the findings were unlikely to change clinical management.

Besides myocarditis, other etiologies of MINOCA include coronary vasospasm, coronary microvascular dysfunction, and thrombophilia[7]. These were not further investigated during the patient's hospitalization.

## DISCUSSION

CAR-T is a novel therapy with a relatively small treatment population, and we have yet to uncover the full spectrum of its effects. This case illustrates the potential for MINOCA as a result of CAR-T-induced myocarditis. Other possible etiologies of MINOCA include coronary vasospasm and coronary microvascular dysfunction, but there is no available literature on these pathologies in CAR-T. Identifying similar cases will allow for further characterization of susceptible patient populations, underlying mechanisms, and preventative strategies.

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