Official Journal of the Irish Medical Organisation

Ir Med J; November/December 2022; Vol 115; No. 10; P703

December 15th, 2022

CAR-T Cell Therapy in Refractory DLBCL in a Patient with Congenital Haemophilia A

K. Chmielowiec, C. Neill, F. Sayers, H. Manson, R. McKeown, G. Benson

Department of Clinical Haematology, Belfast City Hospital, Belfast BT9 7AB, Northern Ireland.

We present a 49-year-old man with severe haemophilia A diagnosed with Diffuse Large B-Cell lymphoma (DLBCL) having presented with 7-year history of asymptomatic right-sided neck swelling. His past medical history included congenital severe haemophilia A with no inhibitor and successfully treated tuberculosis and hepatitis C. He was Hepatitis B immune via inoculation and HIV negative. Following diagnosis of lymphoma he commenced R-CHOP chemo-immunotherapy. He had 670 disease free days. Two years later during a routine follow up and detection of lymphadenopathy he underwent a CT scan, which showed recurrence, this was confirmed with lymph node biopsy. Patient was commenced on R-ESHAP chemo-immunotherapy and proceeded to autologous stem cell transplant. All three cycles were administered as inpatient during which he received daily prophylactic recombinant factor VIII. Following treatment he was noted to be in complete metabolic remission. Following cycle three he proceeded to high dose BEAM conditioning therapy followed by stem cell rescue. He received daily prophylactic recombinant factor VIII, followed by infusion at 160units/hr after initial loading dose of 3,000 units when platelet count fell below 50. Target factor VIII levels were maintained between 60-100%. There was no haemophilia related bleeding during that time. He had 126 disease free days following haematopoietic stem cell transplant. Following second disease relapse he was referred and approved for CAR-T cell therapy with axicablegene ciloleucel. Following re-infusion of cells his recovery was complicated by neutropenic fever, cytokine storm syndrome treated with tocilizumab and central venous line sepsis. As of publication date he continues to be in remission.

Immune function modulation due to factor administration even in the absence of chronic viral infection contributes to increased risk of malignancy in patients with haemophilia. Haematomas can also be easily mistaken for tumours and vice versa in patients with haemophilia. The difference in management of patients with haemophilia is the added risk of bleeding due to congenital factor deficiency; however, with appropriate prophylaxis there was no observed increase in bleeding episodes in literature. Our patient did not have any unexpected bleeding that was related to haemophilia during his treatment, including his CAR-T therapy. Treatment of lymphoma especially DLBCL is given with curative intent, therefore dosing regiments should not be reduced based solely on background of haemophilia.

There is not much literature about patients with haemophilia being excluded from clinical trials, however the issues with participation appears to be related to patients' willingness to participate in clinical trial, rather than their diagnosis of haemophilia being an exclusion criteria. Deranged coagulation profile is not an exclusion criteria to participate in the CAR-T cell therapy trial, which our patient was consented for. Patients have also reported in questionnaires that if they had no knowledge about clinical trial they were less motivated to participate and that physicians should provide patients with clear and unbiased information on the clinical research and communicate better. This would improve patient understanding of different clinical research steps, why participation is required, including expected benefits to either patient himself or benefiting society as a whole.

Corresponding Author:
Karolina Chmielowiec
Department of Clinical Haematology,
Belfast City Hospital,
Belfast BT9 7AB,
Northern Ireland.
E-Mail: Karolina.Chmielowiec@belfasttrust.hscni.net

References:

1. Cruz MS, Santillan J, Lesser J, Ortiz L, Forzani L, Plaza P. *Surgery in a patient with Haemophilia A and Lymphoma.* Case Reports in Haematology Volume 2020, Article ID 4852428. 1-4.
2. Neelapu SS, Locke FL, Bartlett NL, Lekakis LJ et al. *Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma.* N Engl J Med 2017; 377:2531-2544.
3. Rutherford SC, Martin P, Chapin J. *Management strategies in patients with diffuse large B-cell lymphoma and severe haemophilia.* Haemophilia (2015), 21, e411-e455.
4. Rutherford SC, Martin P, Tam W, DeSancho MT, Chapin J. *Clinical course and haemostasis strategies in patients with severe haemophilia A and diffuse large B-cell lymphoma (DLBCL): a single centre experience and review of literature.* Abstracts/Thrombosis Research 133 S2 (2014) S170-S225.