

Daratumumab Induced Acute Reversible Psychological Symptom in a Multiple Myeloma Patient: An Unreported Tale of Daratumumab

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1. Abstract

Multiple Myeloma (MM) is second most common currently incurable haematological cancer. Significant improvement has been made in management of MM and integration of daratumumab-an anti-CD38 humanised monoclonal antibody with other anti-MM treatments has improved the MM survival considerably. However this novel drug can lead to unpleasant side-effect such as acute psychosis which has not been previously reported.

3. Introduction

Multiple myeloma (MM) is an incurable haematological malignancy with an incidence of 4.5 to 6.0 per 100,000 people per year in Europe, with a mortality of 4.1 per 100,000 people per year [1]. MM is the second most common haematological malignancy in the United States of America causing 2% of deaths from cancer [2]. Over the last 15 years significant improvement has been made in the management of MM and survival has improved significantly [3].

Daratumumab is an IgG1 κ human monoclonal antibody (mAb) that binds to the CD38 protein expressed at a high level on MM tumour cells surface. One study suggests that daratumumab can induce myeloma cell death through complement-dependent cytotoxicity, antibody-dependent cell-mediated cytotoxicity, and antibody-dependent cellular phagocytosis as MM tumor cells express CD38 [4]. A more recent study showed significant improvement in overall response (OR) and progression free survival (PFS) when daratumumab containing regimen was used to treat MM [5].

4. Method and Material

A 73 years old male patient with relapsed MM was started on daratumumab monotherapy infusion as 4th line treatment. Pre-medication was given with montelukast, methyl prednisolone and

chlorpheniramine as per institutional protocol. Within 3 hours of starting the daratumumab infusion patient became confused. Examination did not show any signs of infection and his vital parameters were all within normal limit and did not show any change from baseline. He complained of headache. His daughter reports he couldn't remember a conversation they had shortly before. Patient remains confused and paranoid for 48 hours and he tried to escape from in-patient ward and he was wandering around naked. He had no cognitive impairment prior to this.

The patient was started with broad-spectrum intravenous antibiotics despite clinically he was not showing any signs and symptoms of infection and his inflammatory markers remain normal. Multiple blood cultures, urine cultures remain negative. As his confusion and paranoia deteriorated, he was commenced on treatment dose intravenous aciclovir to cover for possible meningo-encephalitis. A Lumbar Puncture (LP) was performed and cerebrospinal fluid (CSF) samples were sent for bacterial/viral/ Cryptococcus/ TB infection but there was no positive yield. He also underwent computerised tomographic (CT) scan & magnetic resonance imaging (MRI) scan of brain and both these scans showed only involuntional age-related changes and did not show no acute changes attributable for his symptoms of confusion and paranoia. Immunophenotyping of CSF did not show plasma cell or any malignant cell. All his electrolytes remain normal as well

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normal thyroid functions.

His psychological condition started to improve after 48 hours and normalised to baseline before he was discharged after 5 days from the start of daratumumab infusion. Psychological symptoms such as this with daratumumab have not been reported in English literature. The exact mechanism how daratumumab has caused confusion and paranoia is not clear. However, it may be due to the fact that CD38 antigen also expressed in adult human brain [6] and interaction of daratumumab with CD38 antigen of brain cells has caused confusion and paranoia in this patient. However, further research should be conducted for further evaluation.

5. Conclusion

In an effort to treat currently incurable MM, we shall continue to use this relatively new drug more often either as single agent or in combination with other drugs and we shall see some unseen and unpleasant adverse events and hence the treating physicians need to be mindful about the consequences.

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