A Case of Severe Multiple Sclerosis Reactivation Following Fingolimod Cessation

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Abstract

Case reports of severe rebound disease activity following prolonged interruption or discontinuation of oral Multiple Sclerosis disease modifying drugs (DMD) is being reported more frequently in the literature. The risk of immune reconstitution inflammatory syndrome (IRIS) post Natalizumab (NAT) discontinuation is well known. In fact, it has been shown that disease breakthrough occurs approximately 12 weeks after NAT cessation[1]. Such data is not yet available regarding the risk of disease rebound with other therapies. It is important to elucidate the optimal wash out period when switching from one DMD to another in order to strike a balance between minimizing the risk of opportunistic infections, such as PML, and MS disease breakthrough. Fingolimod (FGD) is considered to be a potent oral therapy for relapsing forms of MS and there have been a few reported cases of disease rebound post FGD discontinuation.

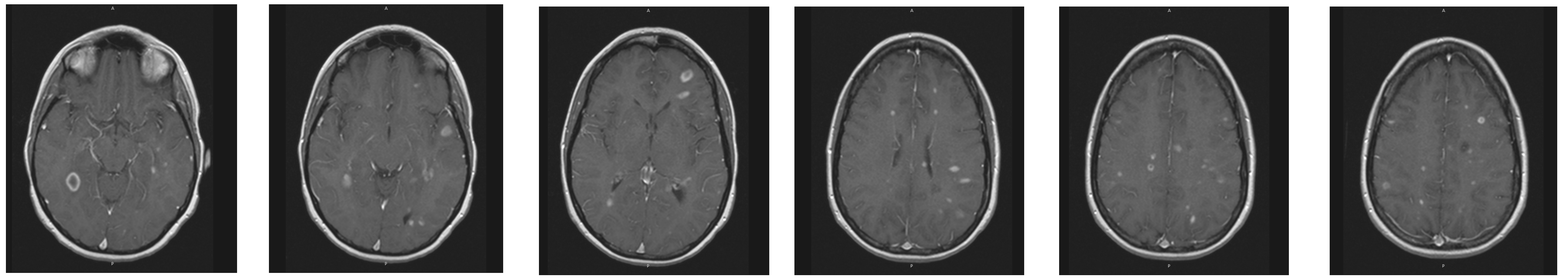
Introduction

Rebound disease activity while changing medication therapies is an emerging consternation among neurology practitioners. Multiple reports of immune reconstitution inflammatory syndrome (IRIS) when transitioning patients between NAT and another DMD have been well documented in the literature. As more novel MS immunomodulation therapies become available, it is important to assess the associated risk and explicate the potential of rebound disease when transitioning between newer therapies. To date, there have been several reports of rebound disease when discontinuing oral MS therapies, with many cases reporting rebound within two months of drug discontinuation[2,3,4,5]. Research on such cases report IRIS-like disease resurgence, which places patients at great risk for progression of disability[3].

Discussion

This case highlights a severe rebound of MS following discontinuation of oral FGD. Of interest ,the severity of disease post drug cessation appears to be much greater than disease burden prior to starting therapy. The resurgence of the immune system post therapy discontinuation needs further investigation. In order to properly balance immune recovery with immune with severe rebound. As previously mentioned, rebound disease after cessation of NAT, FGD and oral Tecfidera (TEC) has documented in the literature [2] . The development and addition of novel immnumodulating drugs and increased incidence of severe rebound disease following cessation of DMD needs to be carefully considered when switching or changing MS therapies.

Case Report



36 year-old Caucasian woman with a history of relapsing remitting multiple sclerosis initially diagnosed in 2005 after presenting to clinic with oscillopsia and nystagmus. She was started on intramuscular interferon beta 1a in 2005, on which she both clinically and radiologically stable. However, between 2010-2011, she developed enhancing lesions in the brain and thoracic spine. Due to progression of disease, she was started on oral Fingolimod (FGD) in 03/2011. FGD was discontinued in 6/2015 after patient expressed desire to conceive. In 08/2015, she developed right sided optic neuritis and ascending paresthesias, initially treated with 3 days of intravenous methylprednisolone (IVMP). After little clinical improvement, she was treated with a second course of IVMP for 3 days. On 10/2015, she remained unable to conceive and was therefore restarted on FGD. Despite re-initiation of FGD, she continued to rapidly decline clinically and soon required the use of a walker for ambulation. She was admitted and treated with 5 cycles of plasma exchange (PLEX) from 10/23/15 to 10/27/15. Howbeit these interventions, her symptoms remained unabated and repeat MRI done on 10/30/15 revealed innumerable enhancing lesions throughout the brain and cervical spine (Figs 1 and 2). On 11/02/15, she received her first dose of IV Rituximab 1000mg, after a second round of PLEX. On 11/18/15 she received her second dose of Rituximab and was later discharged to a rehabilitation facility. On 12/04/15, she was discharged from rehabilitation to home and is now able to walk without assistance. She completed outpatient PT/OT on 2/20/15 and received her third dose of Rituximab 1000mg on 4/26/16. She continues to make clinical improvement and has returned to her baseline activity level.

Fig.1 Innumerable T1 hyperintense lesions scattered throughout brain parechyma which demonstrate postcontrast enhancement.

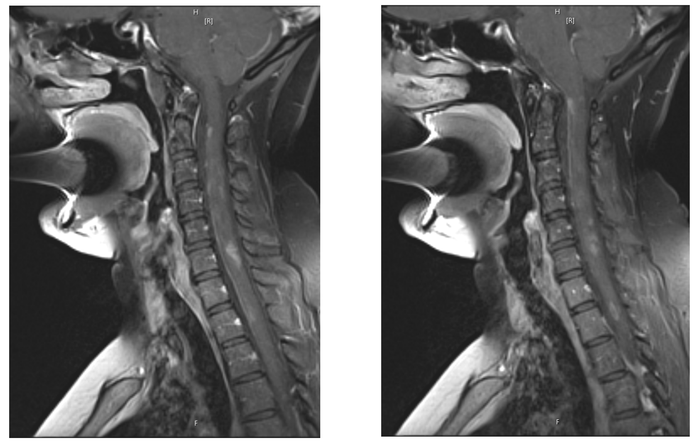


Fig. 2 Numerous lesions scattered throughout the cervical and upper thoracic spinal cord, at all levels, majority of which demonstrate postcontrast enhancement.

Conclusions

The severity of rebound in this case highlights the need to better understand the consequence of lymphocyte redistribution, the rate of immune recovery and factors involved in immune regulation. Preliminary studies suggest possible dysregulation of the S1P1 receptors as a factor in disease rebound post fingolimod cessation[6].

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