Severe tumefactive rebound of multiple sclerosis following fingolimod cessation

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Accepted 12 May 2016

DESCRIPTION
Fingolimod is an oral sphingosine-1-phosphate receptor modulator approved for the treatment of active relapsing-remitting multiple sclerosis (RRMS). Recent reports have highlighted the possible risk of rebound disease activity after withdrawal of fingolimod. We describe a case of a patient who developed severe tumefactive lesions on discontinuing fingolimod treatment.

A 32-year-old woman with RRMS escalated treatment from interferon β to fingolimod due to ongoing relapses. She developed side effects on fingolimod including persistent lymphopenia (<0.3). The fingolimod dose was reduced to alternate days. The patient noticed cognitive decline with progressive memory loss. JC-virus serology was previously positive, with a titre of 2.41. Cerebrospinal (CSF) studies and MRI were performed to exclude progressive multifocal leukoencephalopathy (PML). CSF JC-virus PCR was negative. MRI with contrast showed ongoing MS disease activity, but no evidence of PML.

We aimed to switch treatment from fingolimod to alemtuzumab. The patient discontinued fingolimod in May 2015. However, only by July 2015 did the side effects related to fingolimod resolve. The patient started a modified diet and low-dose naltrexone therapy. She now declined treatment with alemtuzumab, anticipating further side effects. However, she consented to repeat MRI in 2 months and further discussion to reconsider alemtuzumab was carried out.

In August 2015, she was admitted with a severe MS relapse. Examination revealed acute left hemisensory disturbance and tetraparesis. She also reported of dysphagia, weight loss, balance disturbance and worsening of memory. MRI demonstrated severe rebound disease and numerous contrast-enhancing tumefactive MS lesions (figures 1 and 2). She was
treated with intravenous steroids and alemtuzumab leading to partial neurological recovery after 6 months.

Cessation of natalizumab has been associated with life-threatening rebound of MS. However, such severe rebounds have rarely been reported after stopping fingolimod.\(^1^\)\(^,\)\(^2\) Of such cases, tumefactive lesions are more infrequently described.\(^3\) Immunosuppression with steroids has been previously used to treat such relapses after fingolimod cessation. De Masi et al\(^3\) reported the use of selective immune adsorption (SIA) as an alternative to treat a patient with a relapse following cessation of fingolimod therapy. They considered SIA as the rebound was refractory to intravenous steroid therapy. Our patient stabilised on steroids and alemtuzumab.

Learning points

- Although relapses following the cessation of fingolimod are uncommon, it is important to be aware of the potential risk and advise patients to not stop treatment abruptly.
- It is important to carefully plan switching from oral therapy in multiple sclerosis, avoiding prolonged periods without treatment.

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