REBOUND OF DISEASE ACTIVITY AFTER DISCONTINUATION OF NATALIZUMAB OR FINGOLIMOD CAN BE SUCCESSFULLY TREATED WITH AUTOLOGOUS HAEMATOPOIETIC STEM CELL TRANSPLANTATION

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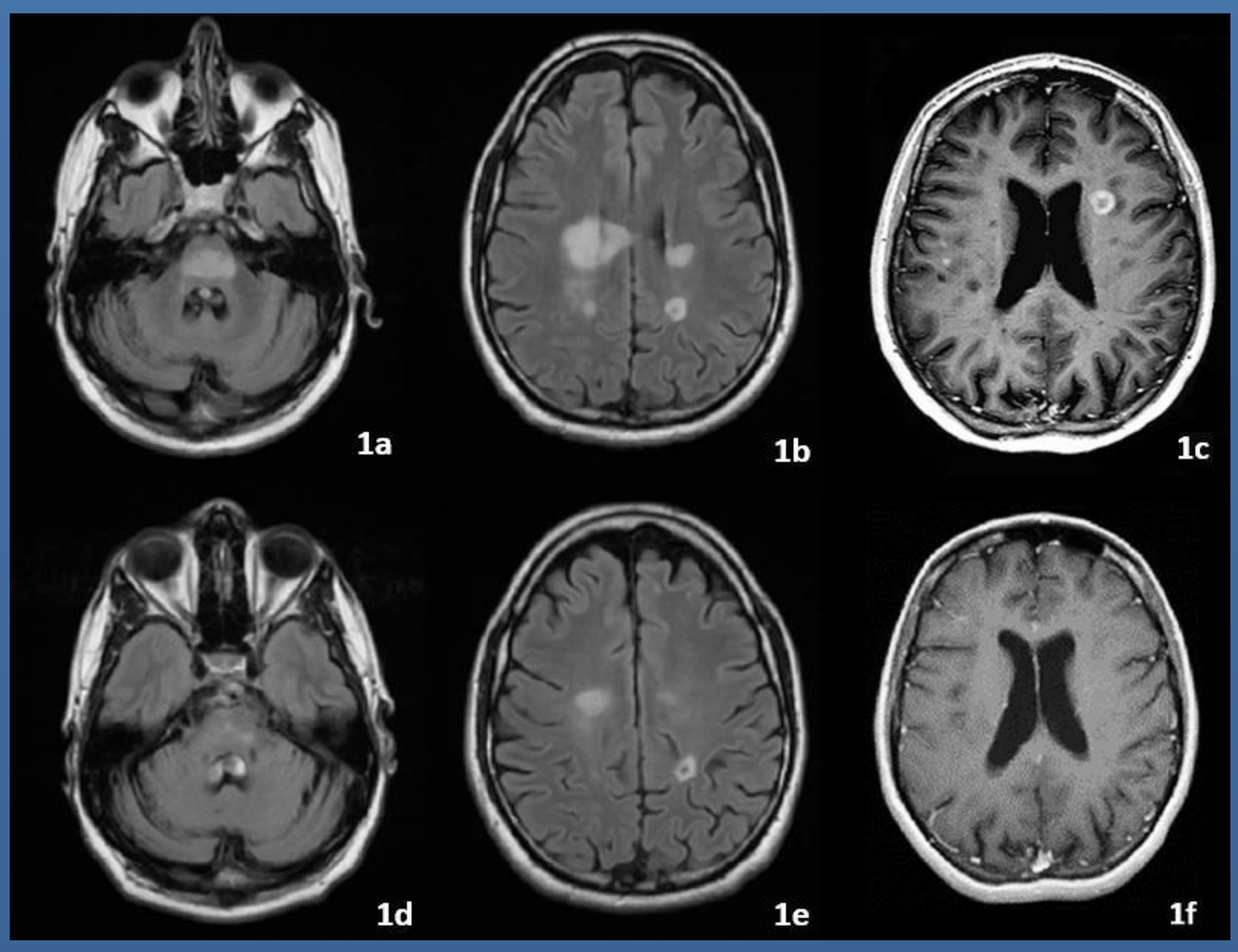
Discontinuation of natalizumab (NTZ) and, more rarely, fingolimod (FTY) therapy can be followed by a recurrence of disease activity increasing to a level beyond the pre-treatment level, often resulting in significant irreversible disability. Several strategies to control the rebound of inflammatory activity have been tested with unsatisfactory results and yet the best therapeutic approach needs to be found. Here we report two cases of dramatic recurrence of disease activity after interruption of NTZ and FTY, successfully treated with autologous haematopoietic stem cell transplantation (AHSCT).



Patient #1 was treated for 7 years with NTZ and he was almost free from disease activity, but in January 2014 the therapy was suspended considering the high risk of developing a progressive multifocal leukoencephalophaty (PML). In April 2014 he experienced a severe relapse reaching a high disability level (EDSS 8), he was treated with plasmapheresis and i.v. cyclophosphamide (CY) with only partial recovery, followed by a new clinical relapse and persistent disease activity at MRI. It was decided to treat the patient with intense immunosuppression with BEAM (carmustine, cytarabine, etoposide and melphalan) followed by AHSCT. Transplantation was followed by a marked clinical improvement (EDSS 3) and disappearance of clinical and MRI activity.

Patient #2 was treated with FTY for 3 years, suspended for a planned pregnancy. Four months after the discontinuation of FTY a severe relapse occurred (EDSS 6.5). She was treated with steroids and i.v. CY, with only partial improvement and MRI signs of activity were still persistent. The patient was therefore treated with intense immunosuppression followed by AHSCT. After 9 months no relapses occurred (EDSS 3) and MRI does not show any evidence of disease activity.

Several studies have demonstrated that AHSCT has a profound effect on relapses and has the capacity to completely suppress MRI activity with an effect that is maintained with time. The present cases indicate that AHSCT can be a possible strategy in MS cases with a severe rebound of disease activity after discontinuation of NTZ or FTY treatment, unresponsive to the usual conventional therapies.

Figure 1. a-b *MRI pre AHSCT pt.1.* ***c*** *MRI pre AHSCT pt.2.* ***d-e*** *MRI post AHSCT pt.1. f MRI post AHSCT pt.2.*