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LETTER TO THE EDITOR

Clinical and MRI improvement in a case of progressive multifocal leukoencephalopathy

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Dear editor,

Progressive multifocal leukoencephalopathy (PML) is a severe demyelinating CNS disease due to lytic infection of oligodendrocytes by the John Cunningham polyomavirus (JCV), an opportunistic agent requiring immunosuppression to become active, commonly complicating HIV infections, lymphoproliferative disorders or immunosuppressive therapies [1]. PML has been reported in immune-mediated rheumatologic disorders, such as systemic lupus erythematosus (SLE). Currently, no therapies have been approved [2], but many broad-spectrum nucleoside-analogue chemotherapeutics have been tested to inhibit JCV replication. Among these, cidofovir, an acyclic nucleotide-phosphonate analogue of deoxycytosine-monophosphate, has been employed with various outcomes, alone or in combination with mirtazapine, an agonist of serotonin-receptor-2A (5HT2AR) blocking the JCV entry into glial cells. Although the restoration of host adaptive-immune response is the first purpose of PML therapy, a paradoxical excess of immune reconstitution may cause the PML-immune reconstitution inflammatory syndrome (PML-IRIS). In this condition, the administration of intravenous corticosteroids is associated with a more favourable outcome [3]. Here we report the first PML-IRIS in an SLE patient, responsive to treatment with intravenous prednisolone, cidofovir, and oral mirtazapine.

A 39-year-old HIV-negative woman with a 10-year history of SLE, taking oral prednisone (5–10 mg/daily) and azathioprine (100 mg/daily), was referred to another institution for progressive dizziness and gait instability (Table 1 for details). Neurological examination showed ataxia, left arm dysmetria and gaze-evoked nystagmus (Fig. 1f). Rheumatologic screening demonstrated a non-active SLE status. CSF polymerase chain reaction assays were positive for JCV (35.132 JCV-DNA copies/mL). Brain MRI showed a lesion in the left cerebellar hemisphere involving the ipsilateral middle cerebellar peduncle, with incomplete irregular marginal gadolinium enhancement. A diagnosis of PML was presumed. Azathioprine therapy was stopped, corticosteroid treatment reduced and oral mirtazapine (30 mg/day) was started [2]. Nevertheless, over the following 2 months, her neurological conditions deteriorated and she was referred to our institution. MR imaging and spectroscopy (Fig. 1a, b) showed increase of lesion size and gadolinium enhancement, and highly altered metabolism, suggesting PML-IRIS. Administration of intravenous prednisolone (1000 mg/daily for 5 days) led to significant clinical improvement. A cyclic therapy with cidofovir (5 mg/kg once every 2 weeks for 5 months) was associated. Over the following months the patient regained her ability to perform daily-living activities independently; CSF JCV-DNA

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