Huge intracortical lesion determining acute relapse in multiple sclerosis


The Multiple Sclerosis Centre – Veneto region (CeSMuV), Department of Neurosciences, and *Neuroradiology Unit, University Hospital of Padova, Italy

**Introduction.** Histological and magnetic resonance imaging studies have disclosed that grey matter inflammation and degeneration constitute a relevant aspect of multiple sclerosis (MS) pathology. Indeed, cortical lesions and atrophy can be observed at disease onset, increase over the course of the disease and play a significant role in determining the progressive physical and cognitive deterioration observed in MS patients. Up to date, however, no association between acute clinical relapses and cortical lesions has been described.

**Patients**
We report clinical and MRI findings in a series of five MS patients who had clinical relapses characterized by the acute appearance of cortical symptoms due to the development of large, snake-like, cortical inflammatory lesions. Symptoms were: 1) acute Wernicke’s aphasia mimicking stroke, 2) agraphia with acalculia not associated to motor deficit or linguistic disturbance, 3) hypophonia of the left arm followed by muscle twitching of the hand, spreading to arm and face, 4) acute onset of left lower limb paroxysmal hypertonia, 5) temporal lobe status epilepticus with psychotic symptoms mimicking encephalitis. The lesions were observed by double inversion recovery (DIR) and phase-sensitive inversion recovery (PSIR) MRI. In all the patients a detailed differential diagnostic work-up was performed. The symptoms completely recovered after high-dose steroid therapy.

---

**Case 1.** A right handed 36-year-old men with a recent diagnosis of clinical isolated syndrome based on the McDonald/Polman criteria, having dissemination in space of lesions and presence of IgG oligoclonal bands in the cerebrospinal fluid, presented at the emergency room with a clinical relapse characterized by acute Wernicke’s aphasia, mimicking an inchaemic stroke. However, the patient had not risk factors for cerebrovascular pathology and an accurate differential diagnosis workup excluded both atherosclerotic and embolic pathologies. CT scan was normal. DIR and PSIR sequences disclosed a huge snake-like cortical lesion selectively involving the superior and middle temporal gyrus of the left hemisphere. Then, the patient was treated with high-dose steroid therapy with complete recovery of the symptom within 4 weeks. Thus, the criterion of the dissemination in time of the lesions and the definite diagnosis of relapsing remitting MS could be achieved.

**Case 2.** A 32-year-old left-handed female, with a recent diagnosis of relapsing remitting MS, not yet treated with disease modifying drugs, developed an acute agraphia with acalculia not associated to motor deficit or linguistic disturbance. DIR sequence disclosed a quite large cortical lesion in the right frontal lobe involving the premotor cortex. High dose steroid therapy was followed by the complete recovery of the symptom.

**Case 3.** A 45-year-old man with a five-year history of relapsing remitting MS and treated with interferon beta, acutely developed a moderate hypotonia of the left arm. The deficit progressively worsened over the following 48 hours. There, he developed muscle twitching of the hand, spreading to arm and face. DIR sequence disclosed a large intracortical lesion involving the precentral gyrus. The symptoms completely disappeared after five days of high-dose steroid therapy.

**Case 4.** A 36-year-old female with a six-year-history of relapsing remitting MS, who interrupted glatiramer acetate therapy for planning a pregnancy, presented at the ER complaining the acute onset of left lower limb paroxysmal painful hypertonia. The symptom became continuous and highly disabling within 24 hours. DIR disclosed the presence of an extended leukocortical (mixed) lesion in the right hemisphere involving the motor cortical area. The patient was treated with baclofen and high-dose steroids with an almost complete recovery. In the subsequent year, however, the patient developed a left leg hypertonia that required continuous treatment with baclofen. No white matter lesions were observed along the cortical-spinal tract and in the spinal cord that could explain the symptom.

**Case 5.** A 21-year-old boy with a recent diagnosis of relapsing remitting MS treated with interferon beta, having no previous history of psychological problems or epilepsy, suddenly developed a mental confusion with behavioural changes. MRI examination and cerebrospinal fluid analysis excluded infectious disease. The possible abuse of drugs was investigated and excluded. DIR and PSIR images disclosed the presence of several cortical lesions in the frontal lobes, and a huge cortical lesion in the uncus of the right temporal lobe. The EEG disclosed a temporal epileptic focus. The symptoms dramatically improved with high dose steroids and carbamazepine therapy. The diagnosis of temporal lobe epilepsy due to MS cortical lesions was definitely achieved.

**Discussion**
MS relapses are classically considered to be associated to the development of inflammatory white matter lesions involving functional systems. Grey matter pathology, on the contrary, has been associated to the progressive phase of MS, characterized by the accumulation of physical and cognitive disability. Our observations indicate that a ‘cortical relapse’ has to be taken into consideration in MS, especially in the presence of unusual symptoms of unclear interpretation. The symptoms observed in our patients had the clinical features of MS relapses: they had an acute presentation, lasted more than 24 hours, were explained by the magnetic resonance imaging findings and recovered after high-dose steroids. In all our cases the vascular nature of the lesions was excluded. The routine magnetic resonance imaging investigation in MS should include sequences aimed at visualizing cortical lesions, such DIR or PSIR, especially in the presence of symptoms that suggest a cortical dysfunction.

**Conclusion**
‘Cortical relapses’ constitute a new clinical entity and the inclusion of cortical lesions in the MRI diagnostic criteria for MS needs to be carefully evaluated.

Acknowledgement: This work was supported by grants from the University of Padova, Inter-area Project N. CPDA099394, and from the Italian Minister of Public Health, RF GR-2010-2313255