Usefulness of brain ^{18}Fluorodeoxyglucose positron emission tomography in the diagnosis and follow-up of neuropsychiatric systemic lupus erythematosus: a case report

Sirs,

A 77-year-old female followed for systemic lupus erythematosus (SLE) with cutaneous and articular involvement as well as triple positive antiphospholipid syndrome under vitamin K antagonists was admitted for cognitive disorders arisen a few weeks before. As SLE was quiescent for several months, she was not receiving any specific treatment. Hydroxychloroquine had been stopped for two years because of retinal toxicity. International normalised ratio was in the therapeutic range.

Physical examination showed malar rash and frontal lobe syndrome characterised by disturbances in attention, memory, language and perseveration as well as the presence of primitive reflexes.

Frontal Assessment Battery (12/18) and Mini-Mental State Examination (28/30) showed cognitive decline involving lexical fluency and executive function. Laboratory tests revealed decreased levels of C3 and C4 and a significant elevation of anti-dsDNA antibodies. Anti-ribosomal P antibodies were found positive. Albuminuria/creatininuria ratio was at 193 mg/mmol leading to renal biopsy showing class III glomerulonephritis. Brain Magnetic Resonance Imaging (MRI) found no inflammatory nor ischaemic lesions. Cerebrospinal fluid (CSF) analysis was normal. Brain ^{18}Fluorodeoxyglucose positron emission tomography with computed tomography (^{18}F-FDG PET/CT) showed a diffuse cortical hypometabolism, involving mainly the frontal regions, with relative striatal hypermetabolism, suggesting an advanced fronto-temporal dementia or an encephalitis.

Neuropsychiatric systemic lupus erythematosus (NPSLE) associated with lupus nephritis was evoked. The patient was treated with methylprednisolone pulses followed by tapering prednisone, as well as 6 cyclophosphamide infusions. ^{18}F-FDG PET/CT imaging and neuropsychological assessment were performed 2, 4 and 8 months after initiation of treatment, as shown in Figure 1. Follow-up was associated with a clear improvement of both neuropsychological symptomatology and ^{18}F-FDG metabolism. This positive evolution was consistent with NPSLE mimicking fronto-temporal dementia.

The definition of neuropsychiatric domain is limited in the last ACR-EULAR classification criteria for SLE since this domain only includes three criteria (acute confusional state/delirium, psychosis, seizure). In a cohort of patients with suspected NP-SLE, using the clinical diagnosis as gold standard, the sensitivity of the proposed criteria was 87% and the specificity was

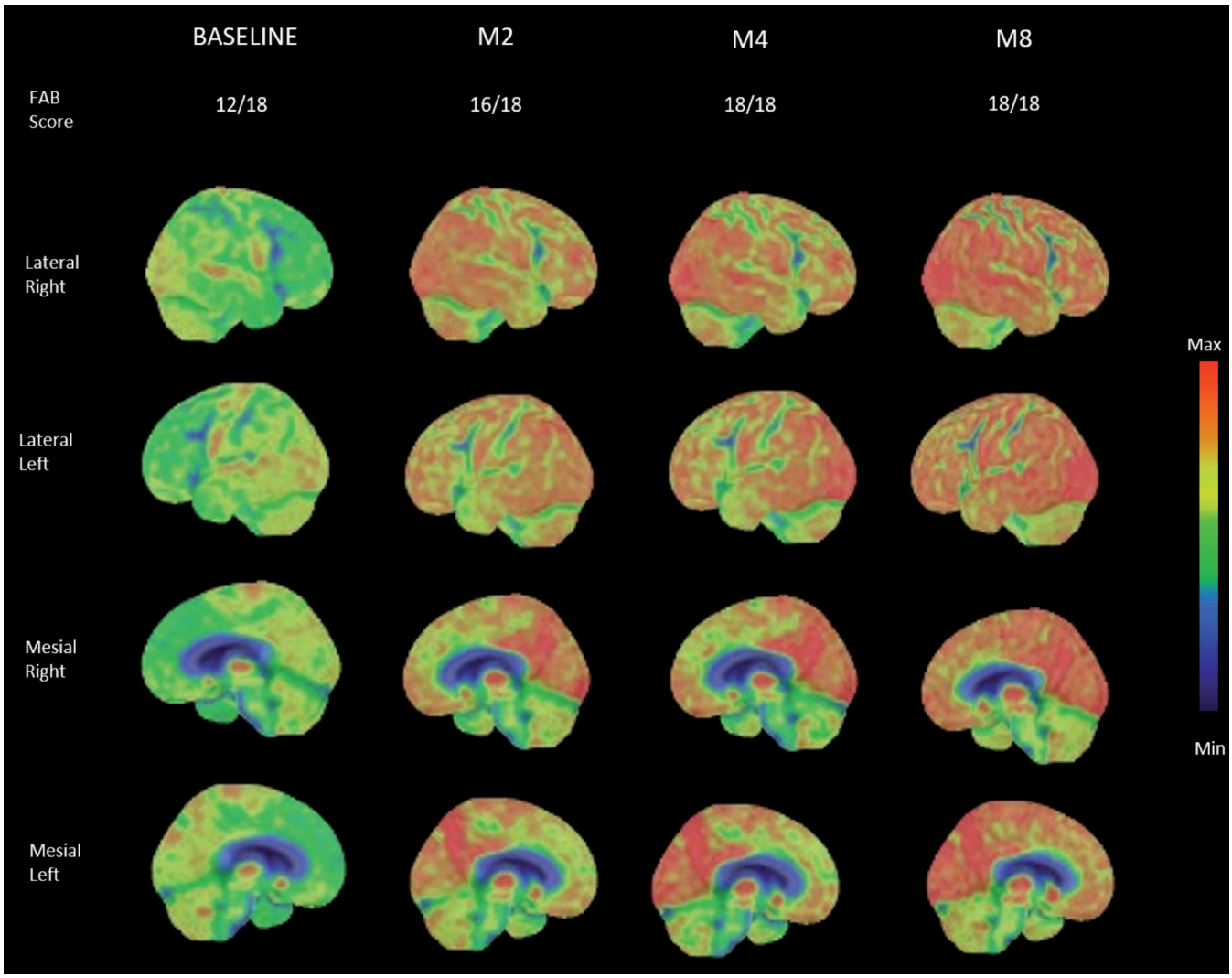

Fig. 1. On-treatment normalisation of cognitive decline according to FAB (top line) and normalisation of diffuse cortical hypometabolism in brain 18F-FDG PET/CT (bottom illustrations). FAB: Frontal Assessment Battery; 18F-FDG PET/CT: 18Fluorodeoxyglucose positron emission tomography with computed tomography; M: month.

74%. The authors recalculated by adding six other neuropsychiatric syndromes to the neuropsychiatric domain, increasing sensitivity to 90% without impacting on specificity (1).

Recent strategies to determine whether a neuropsychiatric manifestation is attributable to SLE *versus* a competing comorbidity include patient activity assessment, neuropsychological tests, autoantibodies testing, CSF examination and neuroimaging for brain structure and function (2, 3). When MRI is normal and SLE is controlled, neuropsychiatric manifestations may be mistakenly attributed to steroid intolerance. Further investigation is then needed to diagnose NPSLE (3, 4).

Conventional MRI is the current neuroimaging gold standard for the assessment of patients with NPSLE but 40–50% of MRI are found normal. Structural MRI cannot detect damage such as neuronal dysfunction, axonal damage, microstructural changes or perfusion abnormalities, particularly found in diffuse inflammatory NPSLE. Advanced functional imaging techniques such as functional MRI as well as ^{18}F-FDG PET/CT could be helpful to better define NPSLE syndromes and their mechanisms (5, 6).

Indeed, while ^{18}F-FDG PET imaging was originally confined to the field of oncology, new applications in inflammatory and infectious disorders are emerging. In inflammatory encephalopathies, ^{18}F-FDG PET is especially relevant to detect abnormal brain metabolism in patients with normal MRI (7). Concerning NPSLE, data from small early studies showed that ^{18}F-FDG PET is extremely sensitive in detecting brain metabolic abnormalities in both clinical and latent CNS involvement (8, 9). The most common finding is a diffuse cortical hypometabolism, with relative striatal and/or limbic hypermetabolism (7-9). Several studies have reported that NPSLE affects the parieto-occipital lobes. However, there was no significant correlation between clinical symptoms and brain metabolic abnormalities on ^{18}F-FDG PET (8, 10). Weiner *et al*. showed that, in the presence of both severe or mild NPSLE symptomatology, ^{18}F-FDG PET was abnormal in 100% of the cases, while MRI was able to detect only 67% of the severe NPSLE and 30% of the mild NPSLE (8). So, ^{18}F-FDG-PET allows the early detection of reversible brain lesions, before structural damage, for which adequate treatment could improve the prognosis. Complete normalisation of ^{18}F-FDG uptake after treatment has been shown in few patients with NPSLE (10). However, longitudinal follow-up data remain scarce.

Our case illustrates the potential diagnostic contribution of ^{18}F-FDG PET/CT in lupus patients with central diffuse manifestations particularly when brain MRI and CSF analysis are not informative. ^{18}F-FDG PET/CT is sensitive for the early detection of NPSLE lesions, it seems useful to investigate the underlying pathological mechanism and it could be an effective follow-up neuroimaging tool. Such as functional MRI, limits of these neuroimaging techniques remain their high cost and their availability in routine care. The future challenge is to design large studies that assess these techniques in the management of NPSLE.

G. Vial[1], *MD*
N. Gensous[1], *MD, PhD*
M. Meyer[2], *MD, PhD*
P. Duffau[1], *MD, PhD*

[1]Department of Internal Medicine and Clinical Immunology, Saint Andre Hospital, University Hospital Center of Bordeaux; [2]Department of Nuclear Medicine, Haut-Lévêque Hospital, University Hospital Center of Bordeaux, Pessac, France.

Please address correspondence to:
Pierre Duffau
1 rue Jean Burguet,
33000 Bordeaux, France.
E-mail: pierre.duffau@chu-bordeaux.fr

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