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NEURO-IMAGES

Uncommon relapse after post-herpes simplex encephalitis: an atypical case report

Michele Pistacchi[1] · Sandro Zambito Marsala[2] · Manuela Gioulis[2] · Flavio Sanson[1] · Bruno Giometto[3]

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Introduction

Herpes simplex virus encephalitis (HSVE) is the most common non-epidemic form of viral encephalitis [1], usually presenting with a monophasic course, though 14–27 % of patients, generally children, may develop a recurrent encephalitic episode [2]. The pathogenesis of relapsing HSVE in adults is heterogeneous and may consist in Anti-*N*-methyl-D-aspartate receptor (NMDAR) antibodies mediated encephalitis, whose clinical features include acute psychiatric and cognitive disturbance, seizures, memory deficits, movement disorders ataxia and dysautonomia. Case series with movement disorders [3] have been reported in anti-NMDAR encephalitis post-HSVE most of the relapses recorded are choreatic and occur in children; relapses in adults are rarer and seldom harbour movement disorders. Algorithm for relapses post-HSVE diagnosis has recently been indicated [4].

✉ Michele Pistacchi
michele.pistacchi@ulss4.veneto.it;
michelepistacchi@yahoo.it

[1] Neurology Service, Santorso Hospital, Via Garziere 73, 36014 Santorso, Italy

[2] Neurology Service, San Martino Hospital, Belluno, Viale Europa 22, Belluno, Italy

[3] Clinica Neurologica 2^, Azienda ULSS16 Padova, Padua, Italy

We studied the clinical course of a patient, evaluating any neuroradiological hallmarks that could facilitate early detection.

Case report

A 30-year-old man presenting with fever, headache and dysphasia was admitted to the Neurological Department. Laboratory blood tests showed a C-Reactive Protein (CRP) increase (54 mg/L—n.v. <20 mg/L). Brain computed tomography was normal. Lumbar puncture revealed increased white blood cell count levels (180 cells/μL; lymphocytes, 90 %; monocytes 10 %) and protein content level (133 mg/dL). EEG highlighted disorganised delta–theta activity in the left temporal lobe. Acyclovir (20 mg/kg intravenously every 8 h for 21 days) was empirically administered supposing herpes encephalitis. The patient showed significant improvement in headache and cognition. Afterwards, CSF-polymerase chain reactions (PCR) proved the pathological diagnostic presence of HSV 1, confirming aetiology. Brain MRI demonstrated T2-FLAIR hyper-intensity signal in the left medial temporal lobe, right insula and increased signal in diffusion-weighted images (Fig. 1).

During the following 20-day clinical neurological conditions, instrumental examinations [brain MRI (Fig. 2), EEG] and CSF ameliorated.

A month later, the patient became aggressive with obsessive–compulsive disorders. Immediately, all previous diagnostic examinations were repeated: CSF (cerebrospinal fluid) demonstrated a slight increase in white blood cell count (10 cells/μL; lymphocytes, 90 %; monocytes 10 %) and protein content (145 mg/dL). Once again, brain MRI highlighted hyper-intensity

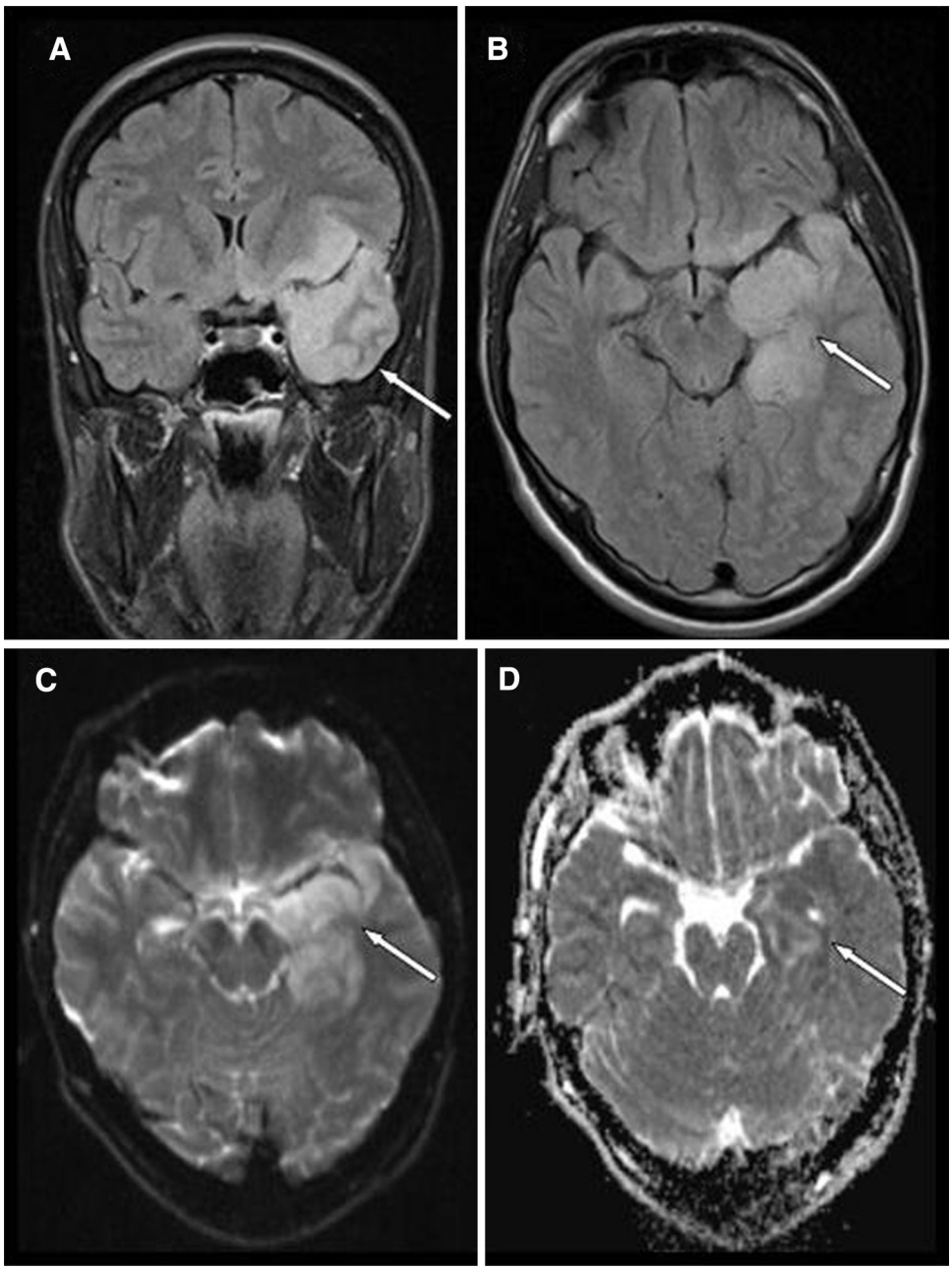

Fig. 1 Initial magnetic resonance imaging: **a** fluid-attenuated inversion-recovery (FLAIR) image, **b** T2-weighted image, **c** diffusion-weighted imaging (DWI) and **d** apparent diffusion coefficient (ADC) map. *Bright spots* are present in both the DWI and corresponding ADC map along with increased T2-Flair signals in the left temporal lobe

in the previously affected regions (Fig. 3) and theta activity in frontotemporal regions was evidenced by EEG.

Suspecting HSVE relapse, empirical acyclovir treatment was repeated. However, HSV-1 PCR analysis did not show the HSV 1 presence in cerebrospinal fluid.

Hence, autoimmune encephalitis was suspected, and serum as well as CSF anti-NMDAR research was positive. Intravenous immunoglobulin treatment (0.4 mg/kg/day for 5 days) was administered.

Nevertheless, few days later, psychiatric symptoms worsened, and the patient needed sedation, restraints, and

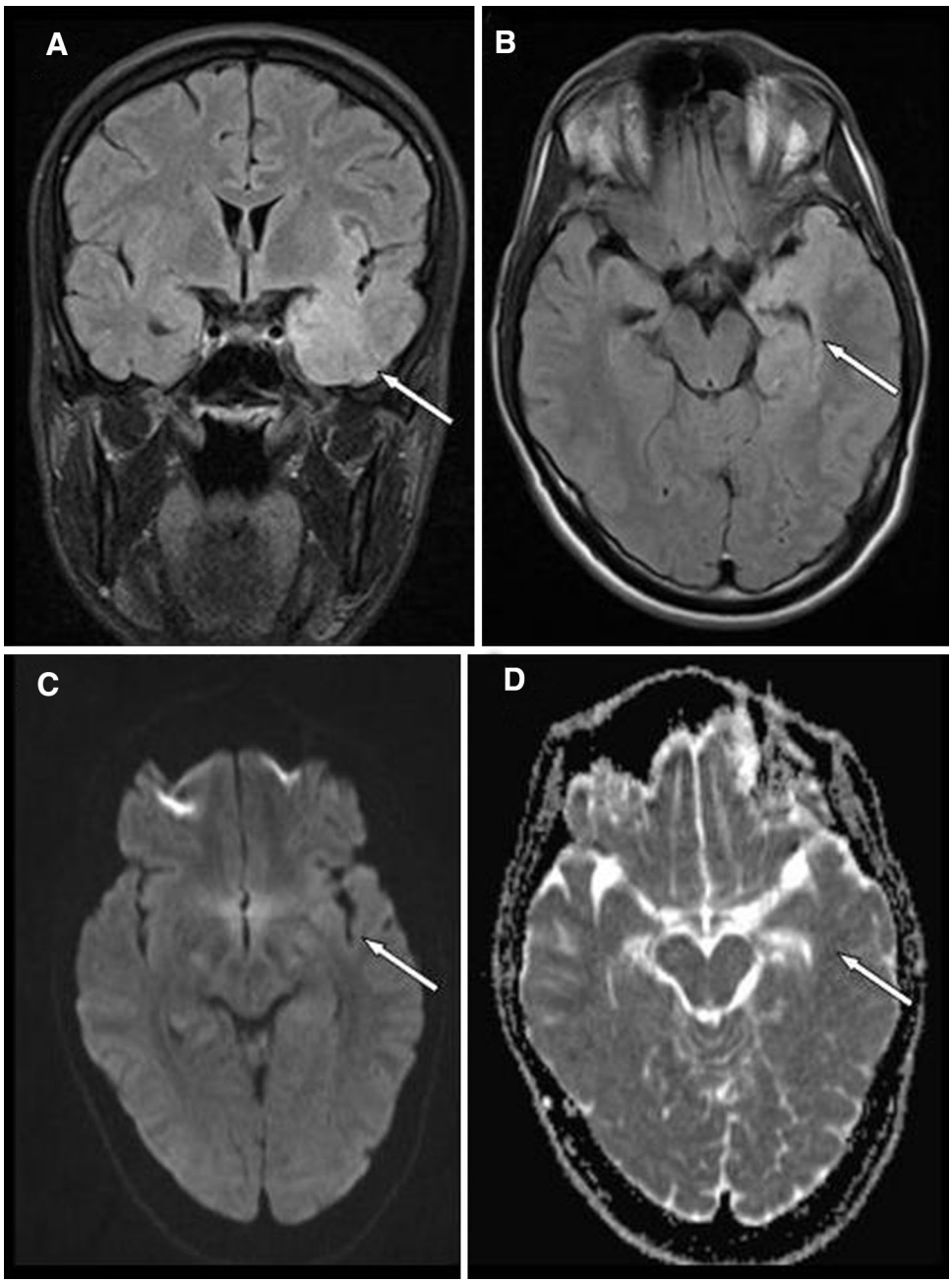

Fig. 2 Images obtained at follow-up magnetic resonance imaging study 21 days after acyclovir treatment: **a** fluid-attenuated inversion-recovery (FLAIR) image, **b** T2-weighted image, **c** diffusion-weighted imaging (DWI) and **d** apparent diffusion coefficient (ADC) map. A slight improvement is observed in the area of high signal intensity in the left temporal lobe

antipsychotic treatment; therefore, plasmapheresis treatment was considered.

After three plasmapheresis sessions, the patient's conditions improved; cognitive assessment evaluated with mini mental state examination (MMSE) scored 14/30. After five sessions, a significant improvement in neurological and psychiatric symptoms was noticed and MMSE scored 27/30.

Two months later, neurological symptoms and neuroradiological clinical pictures had greatly improved (Fig. 4).

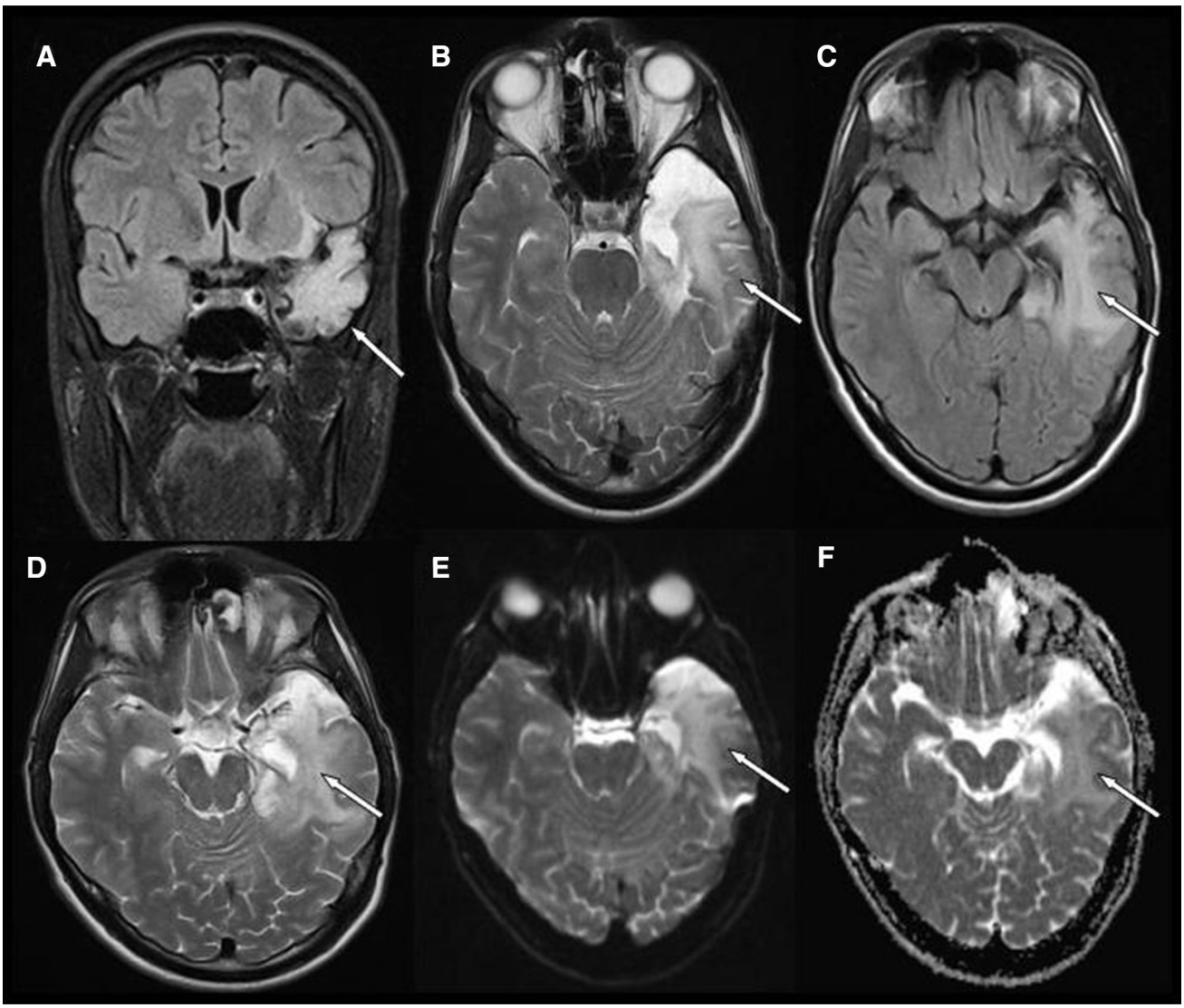

Fig. 3 Magnetic resonance imaging of NMDAR antibodies post-HSVE obtained in the hospital emergency department: **a** fluid-attenuated inversion-recovery (FLAIR) image, **b–d** T2-weighted image, **e** diffusion-weighted imaging (DWI) and **f** apparent diffusion coefficient (ADC) map. This sequence of the brain shows increased signal intensity of the left temporal area, consistent with NMDAR antibodies post-HSVE

Discussion

Anti-NMDAR encephalitis is a rare disease in adults, more often developing as an idiopathic autoimmune syndrome following HSV encephalitis. Diagnosis should be suspected when patients affected by HSV encephalitis show worsening clinical conditions after previous recovery or improvement. Clinical presentation has a heterogeneous spectrum complicated by psychiatric manifestations; neuroimaging might help in early detection. Antiviral therapy failure increases the suspicion of possible autoimmune encephalitis. The absence of HSV in cerebrospinal fluid

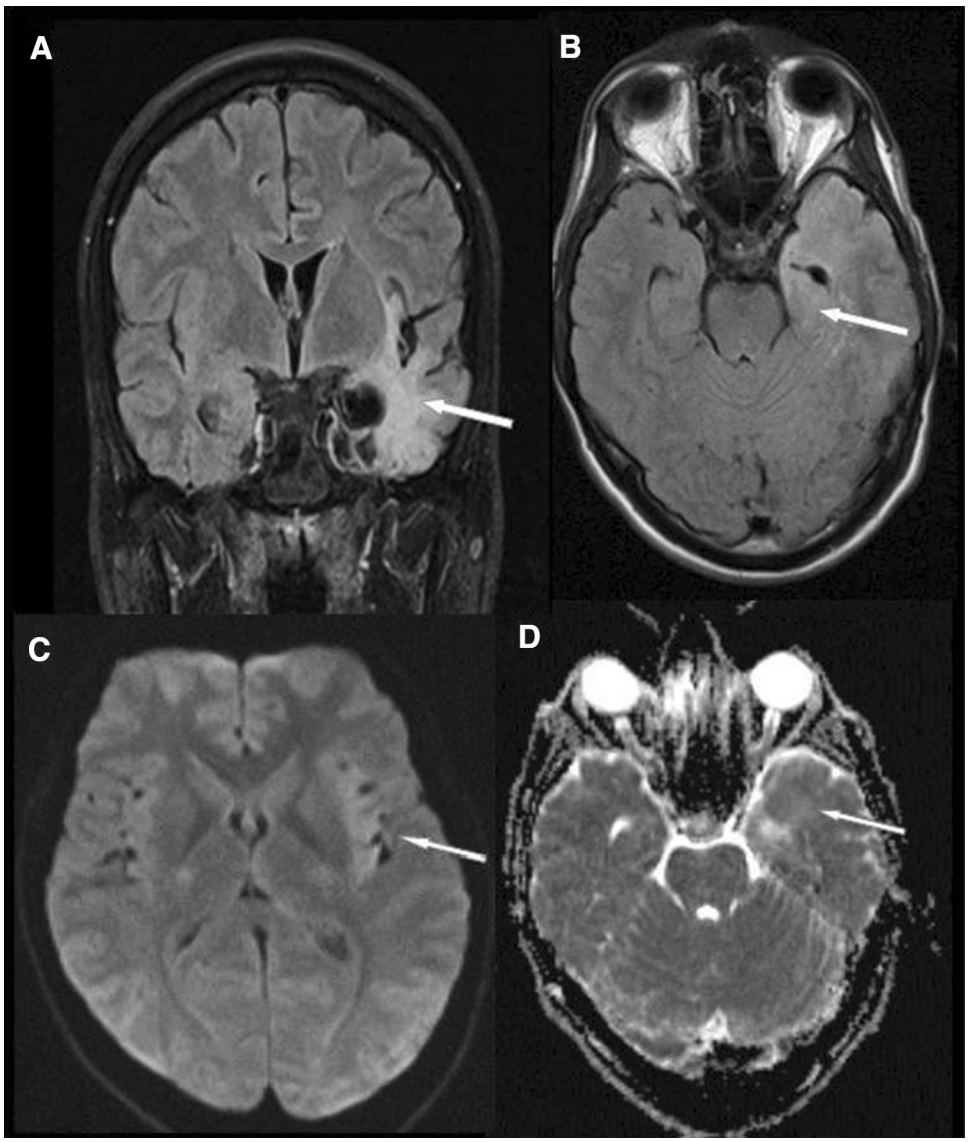

Fig. 4 Images obtained at follow-up magnetic resonance imaging study 2 months after NMDAR antibodies post-HSVE event: **a** T2-weighted image, **b** fluid-attenuated inversion-recovery FLAIR image, **c** diffusion-weighted imaging (DWI) and **d** apparent diffusion coefficient (ADC) map. This follow-up brain scan shows the attenuation in left temporal lobe signal abnormalities

proved through PCR support autoimmune aetiology. Quick supposition may provide the correct diagnostic pathway toward an ad hoc treatment.

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Conflict of interest The authors declare that they have no conflict of interest.

Ethical Standard The authors declare that they acted in accordance with ethical standards laid down in the 1964 Declaration of Helsinki.

Informed consent Informed consent for publication was obtained from the patient.

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