LETTER

COVID-19–associated acute necrotising encephalopathy successfully treated with steroids and polyvalent immunoglobulin with unusual IgG targeting the cerebral fibre network

A recent case report described the radiological features of a suspected COVID-19 necrotising haemorrhagic encephalopathy.¹ We present here a description of clinical, biological, radiological and immunological features of a COVID-19 patient case, evocative of virus-associated acute necrotising encephalopathy (ANE) possibly mediated by antibodies. Patient’s representative consent has been obtained in agreement with the journal’s policy.

A 51-year-old man without personal or family history of neurological disease was hospitalised after 10 days of fever and cough. COVID-19 was diagnosed by reverse-transcriptase PCR on nasal swab and bilateral ground-glass opacities on thoracic CT scan. At day 12, he was admitted in intensive care unit (ICU) for non-invasive ventilation. The result of the neurological examination was normal. At day 21, while the patient had been weaned off oxygen, he became unresponsive and rapidly comatose (Glasgow Coma Scale 6: E1, V1, M4) with a disconjugated gaze. The patient was groaning and showing rhythmic movements of the right upper limb. An urgent brain MRI, including diffusion-weighted imaging (DWI) and MR angiogram, ruled out vertebrobasilar ischaemic stroke; gradient echo T2*-weighted images excluded haemorrhage and thrombus in the venous system. It revealed only subtle hyperintensities in bilateral thalami on FLAIR sequence (figure 1). Consciousness impairment required tracheal intubation. He was hyperthermic (39°C) without shock. Blood and cerebrospinal fluid (CSF) samples revealed thrombopenia and lymphopenia, mild inflammatory response (C reactive protein, ferritin and fibrinogen), CSF albumin-cytological dissociation with increased CSF IgG antibodies (91.9 mg/L, normal 10–30 mg/L) and altered blood–brain barrier integrity (CSF/serum albumin index=17.3, normal <6.5) (online supplementary material). An electroencephalogram revealed symmetrical background activity.
of low-voltage delta waves without spatial organisation, triphasic waves or paroxysmal activity. He showed unresponsive coma (Glasgow Coma Scale=3), pyramidal syndrome, right-sided sixth nerve palsy and no corneal reflex. A second brain contrast-enhanced MRI at day 22 revealed progressing lesions with diffuse hyperintense lesions in the thalami, cerebellum, brainstem, supratentorial grey and white matters on FLAIR images without gadolinium-enhanced lesions (figure 1).

At this time, the patient no longer had respiratory viral excretion (two negative RT-PCR at 48-hour interval on tracheal aspirations). A second CSF sampling revealed no meningitic cytological pattern and PCR results were negative for SARS-CoV-2 and other common viruses (online supplementary material). Anti-ganglioside autoantibodies were not found in patient’s serum (immunodot anti-ganglioside 5003; GA Generic Assays, Dahlewitz, Germany) and autoantibodies against myelin oligodendrocyte glycoprotein were not found in serum and CSF (cell-based assay, FA 115-1003-50; Eurolmmun, Lübeck, Germany). Anti-neuronal autoantibodies against intracellular (immunodot PNS9DIV-24; Ravo, Freiburg, Germany) and surface (cell-based assays: NMDAR, AMPAR, GABABR, AMPA1/2, Caspr2, Lgi1, DPPX, FA 112D-1003-6; Eurolmmun) neuronal antigens were negative in serum and CSF. Indirect immunofluorescence (performed by the immunological laboratory) revealed a specific and atypical IgG staining on monkey cerebellum slices (Ref 504225; Inova Diagnostic, San Diego, USA) and on rat hippocampal slices (Eurolmmun) (figure 1). No specific staining was observed on other tissues (rat stomach, kidney and liver and on HeLa cells). On monkey cerebellum (data not shown), a staining around Purkinje cells, evoking basket cells, was associated with neuronal antigens. On monkey cerebellum (data not shown), a staining around Purkinje cells, evoking basket cells, was associated with neuronal antigens.

IgG staining on monkey cerebellum slices (EuroImmun) (figure 1). No specific staining was observed on other tissues (rat stomach, kidney and liver and on HeLa cells). On monkey cerebellum (data not shown), a staining around Purkinje cells, evoking basket cells, was associated with neuronal antigens. On monkey cerebellum (data not shown), a staining around Purkinje cells, evoking basket cells, was associated with neuronal antigens.

The fulgurant evolution of lesions on MRI should alert clinicians on the interest of repeating brain imaging in case of impaired consciousness after COVID-19 infection. The remarkable efficacy of an early treatment by high-dose steroids and polyvalent immunoglobulin to stop the process should invite clinicians to consider it as soon as a central nervous system infection has been ruled out. COVID-19-mediated ANE with IgG antibodies emerging from peripheral tissues and targeting the cerebral fibre network around basal ganglia is a possible new entity that should be further studied.

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