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Case report

CASE REPORT

Anti-$GABA_B$ receptor encephalitis after COVID-19 infection

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Learning points for clinicians

Immune-mediated encephalitis can be triggered by COVID-19 infection. Clinicians should be cognizant of neurological symptoms suggestive for encephalitis in patients with recent COVID-19 infection as early diagnosis and expedient treatment may lead to improved clinical outcomes.

Case report

A 70-year-old man with a history of diabetes mellitus and hypertension was admitted 13 days after developing cough from COVID-19 infection that was diagnosed on home antigen rapid testing. One day prior to presentation, he had an episode whereby he had difficulty expressing himself lasting several minutes, suggestive of ictal aphasia. This symptom recurred the next day, prompting his family to call the ambulance. Examination revealed expressive dysphasia and mild right-sided weakness. Mini-mental state examination score was 24/30.[1]

Routine laboratory tests were unremarkable except for mild hyponatremia (sodium 132 mmol/l, normal 135–145 mmol/l) and iron deficiency anemia (hemoglobin 11.4 g/dl, normal 13.6–16.6 g/dl). Severe acute respiratory syndrome coronavirus 2 real-time reverse transcriptase polymerase chain reaction (PCR) was positive with a cycle threshold value of 38.4. Magnetic resonance imaging of the brain showed left mesial temporal lobe swelling with FLAIR hyperintensity (Figure 1a and b). Cerebrospinal fluid (CSF) analysis showed mildly elevated protein of 0.6 g/l (normal 0.15–0.4 g/l) but no pleocytosis. CSF PCR for herpes simplex virus was negative.

The patient was treated with intravenous (IV) acyclovir, levetiracetam and sodium valproate but continued to develop clinical and electrographic seizures (Figure 1c). Indirect immunofluorescence cell-based assay (Euroimmun AG, Lübeck, Germany) demonstrated the presence of anti-gamma-aminobutyric acid receptor type B (anti-$GABA_B$-R) autoantibodies in serum. Despite the initiation of pulsed IV methylprednisolone, the patient developed super-refractory status epilepticus requiring anesthetic coma with midazolam, propofol and ketamine. Multiple anti-epileptics were required to control his seizures, including levetiracetam, clobazam, lacosamide, gabapentin and perampanel. Whole body computer tomography scan revealed no evidence of malignancy. Further immunotherapy comprising 5 cycles of therapeutic plasma exchange, IV immunoglobulins and IV rituximab were administered without clinical response. IV tocilizumab was considered but withheld in view of severely deranged liver function tests. He eventually regained consciousness after 9 weeks in the intensive care unit, and gradually recovered to become alert and conversant.

Discussion

Anti-$GABA_B$-R encephalitis is an immune-mediated encephalitis that commonly presents with seizures, limbic encephalitis, ataxia and opsoclonus-myoclonus.[2] It can be paraneoplastic in up to 50% of patients, in which there is a strong association with small cell lung cancer.[2,3] A systematic review of 94 anti-$GABA_B$-R encephalitis cases showed that up to 40.7%

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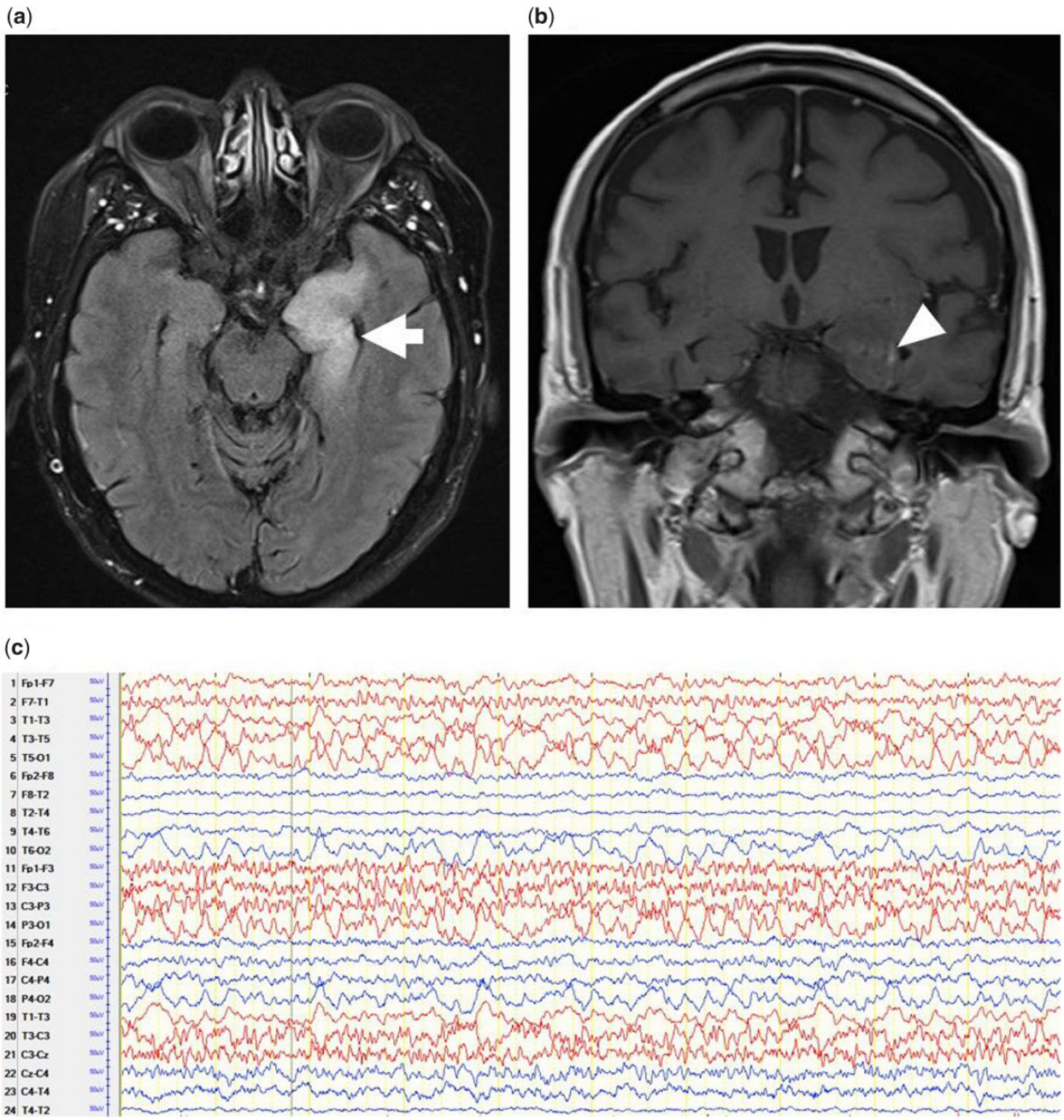

Figure 1. (**a**) Axial magnetic resonance imaging brain showing FLAIR hyperintense signal in the left mesial temporal lobe (arrow). (**b**) Contrast-enhanced coronal T1 sequence demonstrating left mesial temporal lobe swelling with mild contrast enhancement (arrowhead). (**c**) Electroencephalogram showing electrographic seizure manifesting as rhythmic fast activity over the left hemisphere (red tracing).

had an absence of CSF pleocytosis, and 86.3% improved with immunotherapy and/or cancer treatment as indicated.[4]

While cases of encephalitis and indeed autoimmune encephalitis have been reported at the onset and after COVID-19 infection,[5–7] anti-$GABA_B$-R encephalitis post-COVID-19 infection has not been described before. We postulate that molecular mimicry with the production of cross-reactive antibodies to brain antigens and/or the upregulation of pre-existing dysimmune processes by pro-inflammatory mediators in response to COVID-19 infection could have triggered the anti-$GABA_B$-R encephalitis in our patient.[5] Future mechanistic studies are required to delineate these processes and further epidemiological studies will be invaluable to establish the incidence of autoimmune encephalitis during the COVID-19 pandemic.

Conflict of interest: The authors have no conflict of interest to declare.

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