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CASE REPORT

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Autoimmune meningoencephalitis associated with anti-glutamic acid decarboxylase antibody following COVID-19 infection: A case report

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Abstract

Anti-glutamic acid decarboxylase (Anti-GAD) are associated with various neurologic condition; but no meningitis has been reported with it, so far. Evidence demonstrates the associated of autoimmune meningoencephalitis with COVID-19 infection. Here, we report a 44-year-old female with progressive loss of consciousness with anti-GAD65 meningoencephalitis 1 month after COVID-19 infection.

KEYWORDS

anti-GAD, autoimmune meningoencephalitis, COVID-19

1 | INTRODUCTION

Anti-glutamic acid decarboxylase (GAD) are associated with various neurologic conditions, including stiff person syndrome, cerebellar ataxia, and limbic/extralimbic encephalitis, seizure, cognitive impairment, and behavioral disturbance.[1–3] Growing evidence reveals the association of autoimmune meningoencephalitis with COVID-19 infection.[4] Here, we report a patient with anti-GAD65 autoimmune meningoencephalitis, post COVID-19 infection.

2 | CASE PRESENTATION

A 44-year-old female known case chronic bronchitis who was admitted by moderate respiratory distress 1 months ago and received Remdesivir by diagnosis of coronavirus disease 2019 (COVID-19) infection, after 10 days, she discharged with clinical improvement without complication. Twenty days after disease onset, the patient gradually developed memory loss and confusion, therefore, she admitted again. Her past medical history and drug history was negative and had no history of disease in the family. On examination, she was confused without any focal neurological deficits, she did not have fever and meningeal irritation. Her pupils were isochoric and reactive and plantar reflex were down going. Brain computed topography (CT) showed severe hydrocephalus (Figure 1). Brain magnetic resonance imaging (MRI) did not show any other pathologies. Lumbar puncture was done and cerebral spinal fluid (CSF) pressure was normal (12 cm H_2O) and analysis revealed high protein, low glucose and pleocytosis (Table 1) and treatment with ceftriaxone (2 g/BD) and vancomycin (1 g/BD) got started and we continued the treatment. Due to severe hydrocephalus, brain extra ventricular drainage was done for her. The electroencephalography (EEG) showed generalized slow activity. CSF evaluated for fungal, tuberculosis, brucellosis, sarcoidosis, and viral

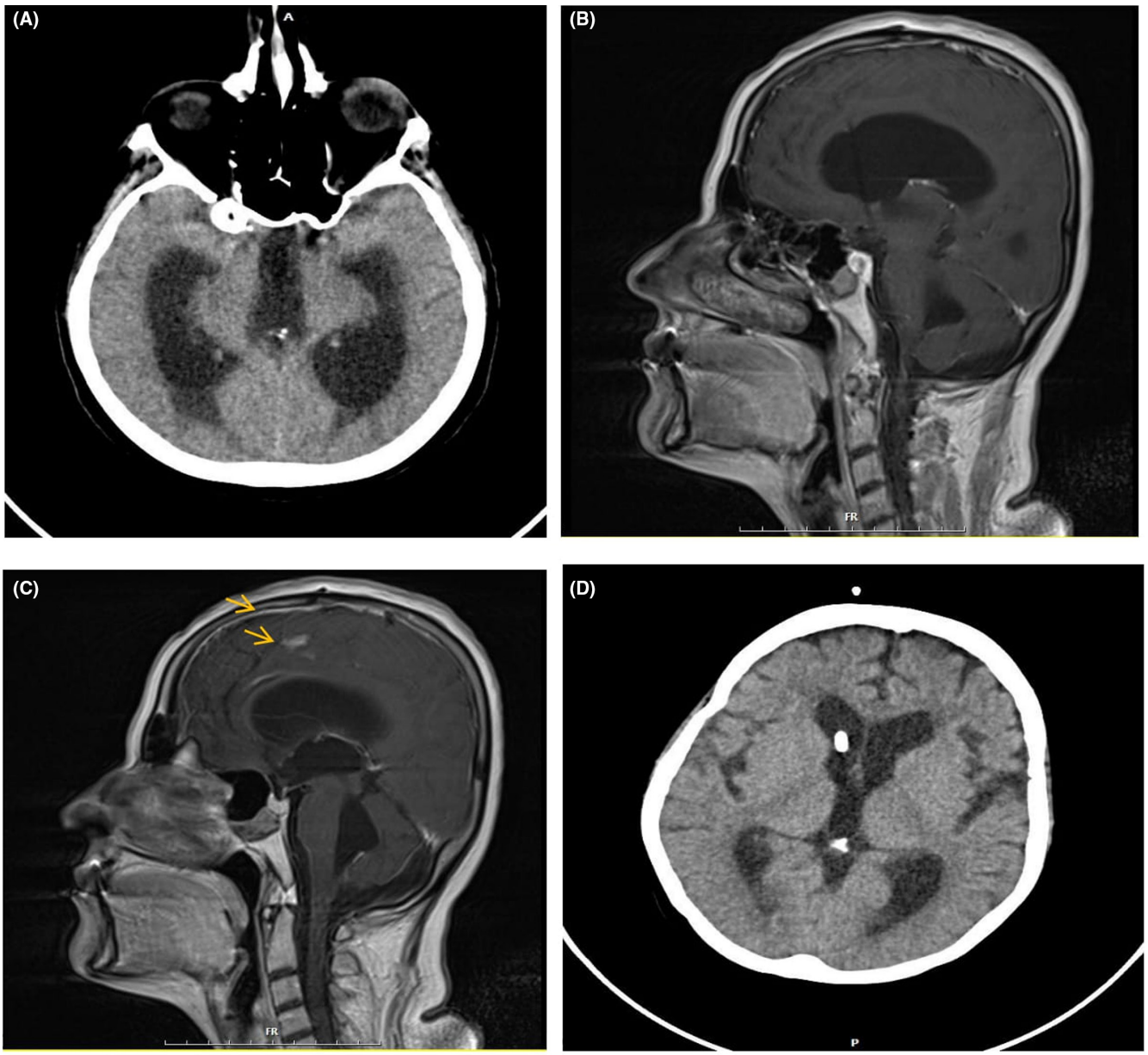

FIGURE 1 (A) Axial view Brain CT without contrast demonstrates severe hydrocephalus before extra ventricular drainage. (B, C) Sagittal view Brain MRI (T1) with gadolinium shows meningeal enhancement (Yellow arrow). (D) Axial Brain CT without contrast after extra ventricular drainage, that shows hydrocephalus was reduced.

infections including HSV-1,2 and CMV, and autoimmune antibodies, and they came back positive for anti-GAD65 (Table 1). Malignancy and vasculitis work-up were negative. Due to the negative CSF culture, antibiotics discontinue and was started 7-day course of 1 g/day IV methylprednisolone and she responded very well to medication and became conscious again and oriented without hallucination and illusion. Unfortunately, patient had pulmonary thromboembolism (PTE) in hospitalization, and she died.

3 | DISCUSSION

Neurological manifestations are reported in 6%–36% of patients with COVID-19. They could be divided in to direct (viral), secondary and post (para) infections (autoimmune) and varying from self-limiting mild symptoms such as insomnia to the most sever manifestations, such as stroke, meningoencephalitis, Guillain–Barre syndrome (GBS), acute disseminate encephalomyelitis (ADEM), and others.[5,6] Meningeal or parenchymal

TABLE 1 Laboratory data.

Test	Result
Serum	
BS	90
WBC	7.9
Hbg	11
Plt	130
ESR	97
CRP	94
HBs-Ag	Negative
HCV-Ab	Negative
HIV-Ab	Negative
HBc-Ab	Negative
Blood culture	Negative
Collagen vascular tests	Normal
Paraneoplastic panel	Negative
Autoimmune panel	
Anti-GAD65	Positive (15)
CSF analysis	
WBC	High
PMN	90
Lymphocyte	10
RBC	10
Protein	High
Glucose	Low
Lactate	15.1
Gram stain	Negative
CSF Culture	
Bacterial	Negative
Viral	Negative
Fungi	Negative
CSF PCR	
HSV	Negative
EBV	Negative
HIV	Negative
Mycobacterium tuberculosis	Negative
Brucella	Negative
Borrelia burgdorferi	Negative
COVID-19	Negative
Paraneoplastic panel	Negative
Autoimmune panel	
Anti-GAD65	Positive (15)
Amphiphysin	Negative
CV2	Negative
Ri	Negative
Yo	Negative
Hu	Negative
SOX1	Negative
Recoverin	Negative
PNMA2 (Ma2/Ta)	Negative

inflammation often indicates a treatable disorder and clinicians should consider infectious, neoplastic, and autoimmune diseases in patients with undifferentiated meningoencephalitis.[7] and varying from self-limiting mild symptoms such as insomnia to the most severe manifestations, such as stoke, meningoencephalitis, Guillain–Barre syndrome (GBS), and others.[5,6] Studies carried out since the COVID-19 outbreak have revealed conflicting statistics on the incidence of meningoencephalitis in various countries.[8] It may be speculated that cases of meningoencephalitis related to COVID-19 may not actually reflect direct viral invasion to CNS, post-/para-infection immune pathologies might come in to play in some of the clinical presentations. Also, might COVID-19 include an autoimmune response after a latent period. Various neurological symptoms were reported in meningoencephalitis associated with COVID-19 infection. Confusion or altered mental status was the most frequently reported symptom accounting in 22.22% of cases.[9,10] The presence of specific neural autoantibody, such as GAD65 and VGKC complex antibodies, is a key early differentiating feature between causes of autoimmune meningeal and encephalitis because identifying these antibodies often lead to treatment initiation without a need for invasive testing such as brain biopsy.[7] Twenty-eight articles reporting 48 patients with infectious or immune-mediated COVID-19 CNS-disease, 5 patients presented with meningoencephalitis and 11 cases with autoimmune encephalitis.[11] Zamani et. al., 2021, conducted a systematic review of 26 case reports on COVID-19-related meningoencephalitis that all patients presented with altered mental status and mild/moderate pleocytosis or proteinorrhachia in CSF.[4] Anti-GAD antibody is found in some neurological syndromes, including stiff-person syndrome (60%–80%), limbic encephalitis (17%), cerebellar ataxia (2%), epilepsy (2.1%–5.4%), and Miller Fisher syndrome, eye movement disorders, palatal myoclonus and Parkinson's disease rarely occur.[12–14] But no cases have reported with anti-GAD65 meningitis, so far (Table 2). Clinicians should carefully consider the possibility of a false-positive result when an autoantibody is present in the serum but not the CSF, if the autoantibody does not fit the patient's clinical syndrome, or if the autoantibody is only present at low titers (<1:80).[7] The interesting finding of our case is presentation of GAD-65 with meningoencephalitis

TABLE 2 The studies that introduced anti-GAD65 encephalitis.

Reference	Gender	Age (year)	COVID-19 PCR	Clinical manifestation	MRI	EEG	CSF	Serum Antibody
(8)	6 Male 3 Female	Mean: 60	positive	Loss of consciousness, Fever, seizure and Agitation	Generalize atrophy	Indeterminate	COVID-19 PCR: Negative Two cases: abnormal sugar One case: 60 leukocytes	Indeterminate
(15)	5 Male 1 Female	Mean 49	Positive	Loss of consciousness, agitation and delirium	3 cases: cortical or white matter hyper intensities, contrast enhancement	Indeterminate	Elevate protein without pleocytosis Viral PCR: negative	Indeterminate
(11)	2 Male 3 Female	Mean 55	Positive	Seizure, confusion, hallucination and headache	One case: intracranial hemorrhage	Indeterminate	One case: Positive COVID PCR 4 cases: lymphocytic pleocytosis	Indeterminate
(16)	Female	27	Negative (post-vaccination)	Confusion, anxiety, headache	Normal	Mild generalized slowing without epileptiform abnormalities	WBC:19 Protein:43	Indeterminate
(17)	7 Male 4 Female	Ranged from 24–75	One patient: negative Another: negative	Confusion and coma Psychotic symptom and seizure	Cerebellar, hippocampus and temporal lobe signal change and leptomeningeal enhancement	Indeterminate	Mild elevated protein and WBC 3 cases: positive COVID-19 PCR	Indeterminate
(18)	Female	50	Post vaccination/ Not done PCR COVID-19	Worsening behavioral changes and dizziness	Multiple new plaque in periventricular, juxta cortical and cortical	Indeterminate	Not done	NMDA And anti-COVID-19 IgG
(19)	Female	62	Post vaccination/ Not done PCR COVID-19	Fever and headache	Normal	Indeterminate	Lymphocytic pleocytosis Elevated protein	Indeterminate
(20)	Male	66	Not done	Memory deficit, ataxia, confusion	Brain stem and temporal encephalitis	Diffuse slowing	Normal	GAD
(21)	Female	45	Not done	Gait difficulty, gaze palsy and spasms	Encephalitis	Indeterminate	Indeterminate	GAD

TABLE 2 (Continued)

Reference	Gender	Age (year)	COVID-19 PCR	Clinical manifestation	MRI	EEG	CSF	Serum Antibody
(22)	Female	35	Not done	Memory deficit, psychiatric disturbance and seizure	normal	Indeterminate	Mild lymphocytic and elevated protein	NMDA
(23)	Female	23	Not done	Fever and headache	Diffuse leptomeningeal enhancement and white matter signal change	Indeterminate	Elevated protein and cellularity Anti-GFAB and anti-MOG	Anti-MOG
(24)	Male	54	Not done	Confusion	Normal	Indeterminate	Lymphocytic pleocytosis	GAD
(25)	male	8	Negative	Fever and headache	Indeterminate	Indeterminate	10 lymphocyte and elevated protein	Indeterminate

after COVID-19 infection that high titer of GAD-65 antibody was present in the serum and the CSF sample.

4 | CONCLUSION

Suspicion for autoimmune meningoencephalitis is heightened in patients with subacute disease onset because inflammatory and autoimmune causes of meningoencephalitis may be treatable if identified early in a course of illness. Also, GAD-65 antibody could cause meningitis in addition to encephalitis, but this need future investigation.

AUTHOR CONTRIBUTIONS

All the authors have contributed equally to conception, design, manuscript preparation, critical revision, and finalization. All the authors agree to be accountable for all aspects of the work.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the finding of this study are available within the article.

CONSENT

Written informed consent was obtained from sister of the patient to publish this report in accordance with the journal's patient consent policy.

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