Post-infectious brainstem encephalitis associated with SARS-CoV-2

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INTRODUCTION

Immune-mediated neurological sequelae following infection with SARS-CoV-2 are becoming increasingly evident, and can affect both peripheral and central nervous systems.[1, 2] We report a post-infectious brainstem syndrome in a patient with Covid-19 who presented with generalized myoclonus, ocular flutter with convergence spasm and acquired hyperekplexia. Clinical improvement was seen following corticosteroids, highlighting this as a possible treatment in patients where a post-Covid-19 autoimmune encephalitis is suspected.

CASE PRESENTATION

A 65-year old woman presented with a one-week history of widespread involuntary movements, diplopia and cognitive decline having experienced fever, cough and myalgias the week before.

She had a past medical history of presumed Alzheimer's disease, osteoarthritis and gastroesophageal reflex disease. The diagnosis of Alzheimer's disease had been made 3 years earlier on the basis of a 12-month history of amnestic symptoms including repetitive questioning and navigational difficulties. At her functional baseline she could mobilise unaided, leave the house independently and wash without assistance. She was fluent in English, but her native language was Arabic. Mini-mental state examination score eight months prior to presentation was 20/24. Regular medications included a rivastigmine patch 4.6mg/24 hours, omeprazole and solifenacin.

Collateral information from her son reported that two weeks prior to presentation she had developed non-productive cough, fever and myalgias. She had also experienced two days of diarrhea which spontaneously resolved. Her son suffered from similar symptoms and both members of the household self-isolated for suspected Covid-19.

Although these symptoms gradually improved, seven days later she developed involuntary movements, initially in the right hand and upper arm. Over the next 48 hours these movements became unremitting and generalized, involving the face and all four limbs. She began to only speak in her native Arabic, before developing progressive speaking difficulties and increasing confusion. Over this time she also described worsening vision with difficulty reading, struggling to focus and intermittent double vision. In the twenty-four hours prior to admission, she experienced well-formed visual hallucinations of people in the house and seeing objects flying around the room, prompting attendance to hospital.

The most prominent feature on neurological examination was widespread, stimulus-sensitive myoclonus involving the tongue and all four limbs, associated with hyperekplexia without habituation to tactile, visual and auditory stimuli (see video). There was a full range of extraocular eye movements with associated ocular-facial synkinesis. Saccadic eye movements were interrupted by ocular flutter and prominent convergence spasm with miosis on visual fixation (see video). She was alert and orientated to place but not time (day/year) and was only able to follow single stage commands. She had a non-fluent aphasia and difficulty repeating sentences. Perseveration, echopraxia and marked mirror movements were evident on motor testing, but constructional apraxia was absent. Allowing for persistent myoclonus, the remainder of the neurological examination was normal.

Combined throat and high nasal swab reverse-transcriptase polymerase-chain-reaction testing was positive for SARS-CoV-2. Chest X-ray demonstrated bilateral peripheral pulmonary infiltrates in the mid and lower zones consistent with Covid-19. Complete blood examination including lymphocyte count was normal. C-reactive protein was raised at 21 mg/L. D-dimer was 1800 ug/L (normal<500).

Magnetic resonance imaging of the brain with contrast, including 3D volumetric FLAIR and diffusion weighted imaging, was normal. Cerebrospinal fluid (CSF) examination showed a white blood cell count of 1 cell/μL (normal<5 cells/uL), normal protein and glucose with matched oligoclonal bands in serum and CSF. Standard CSF neuro-viral PCR panel and PCR for SARS-CoV-2 were negative.

Extensive antibody screening including for anti-NMDA-R, anti-GAD, anti-CASPR2/LGI1 antibodies, ganglioside antibodies and a panel of anti-neuronal antibodies in serum and CSF were negative. Anti-glycine receptor and anti-DPPX antibodies were negative.

Computed tomography of the chest, abdomen and pelvis confirmed lung changes of Covid-19 but no evidence of malignancy. Electroencephalogram was within normal limits with no cortical correlate to the myoclonus. FDG-PET scan was consistent with pneumonitis with no other pathological uptake seen.

Levetiracetam 750mg twice daily and clonazepam 0.25mg twice daily were commenced and over the following week there was partial improvement in myoclonus and hyperekplexia, but no significant improvement in cognition, mobility, or eye movement abnormalities. Repeat testing for SARS-CoV-2 on day 5 and day 7 were negative and no symptoms of active Covid-19 infection were seen during her admission.

The patient was discussed in our multidisciplinary teleconferencing meeting and as the most likely cause of her neurological syndrome was felt to be a post-infectious immune-mediated encephalitis a decision was made to treat with corticosteroids.

Fourteen days following onset of neurological symptoms (21 days following onset of Covid-19 symptoms) she was commenced on intravenous methylprednisolone 1g per day for three consecutive days. This was followed by oral prednisolone 60mg (1mg/kg), with a plan to wean this to cessation over a period of 4-6 months.

Following initiation of corticosteroids there was slow progressive improvement in her neurological symptoms. Upon discharge from hospital (10 days after steroids) she was able to mobilize with one stick and cognition had returned to her previous baseline. There was ongoing fine myoclonus however this was continuing to improve.

CONCLUSION

This case expands on emerging literature describing post-infectious immune-mediated neurological sequelae affecting the central nervous system in patients with Covid-19. While causation is difficult to prove, the temporal profile of symptoms developing one week following Covid-19 clearly implicates viral infection as a contributing factor.

While we could not identify evidence of inflammation on neuroimaging, this is not uncommon in other forms of autoimmune encephalitis[3], and her clinical presentation was strongly suggestive of a post-infectious cortical but predominantly brainstem syndrome.

Although it is unclear whether treatment with steroids was a contributing factor to her improvement or whether this was part of the natural history of her illness, this case highlights a possible role for steroids in patients where a post-Covid-19 autoimmune encephalitis is suspected, after exclusion of appropriate mimics. Resolution of fever and respiratory symptoms prior to commencing treatment together with repeated negative coronavirus PCR and normal lymphocyte count reassured us she was no longer actively infected and made us more comfortable in starting corticosteroids rather than considering other immunomodulatory options like intravenous immunoglobulin or plasma exchange.

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