Radiology

Letters to the Editor

Clinical Course of a Patient with Radiographically Described Acute Necrotizing Encephalopathy (ANE)

From

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Editor:

We write in reference to a previously reported case of acute necrotizing encephalopathy (ANE) associated with acute SARS-COV-2 infection (1). A 58-year-old woman with hypertension presented with cough, fever, and altered mental status. She was somnolent but arousable, with bilateral ptosis and conjugate tonic downgaze. She initially was right hemiparetic, and over days became quadriplegic. SARS-CoV-2 RT-PCR testing was positive via nasopharyngeal swab. Initial cerebrospinal fluid (CSF) testing was unavailable. Later, SARS-CoV-2 RT-PCR was performed on the CSF and was negative.

Initial treatment was with 2 grams/kg of intravenous immunoglobulin in divided doses, without clinical improvement. High-dose steroids (IV methylprednisolone 1000 mg daily for a total of 5 days) were then given, followed by 40 mg prednisone for five days via percutaneous endoscopic gastrostomy tube. After supportive care, the patient demonstrated physical and cognitive improvement, with decreasing ophthalmoplegia, speaking in short answers, and participating with physical therapy. She was discharged to subacute rehabilitation.

The patient recovered considerably; four months after hospitalization, her sensory and motor examination were normal. There was residual psychomotor slowing. She was able to perform activities of daily living, although she was not yet driving. Modified Rankin Scale was 3. Repeat MRI brain without contrast showed residual T2 hyperintensities and hemosiderin deposition in the medial thalami; the former were significantly improved from previous. MRI T2 hyperintensities in the bilateral medial temporal lobes had resolved (Figure).

Several cases of COVID-19 associated ANE have now been reported (Table). Most show MRI abnormalities in the thalamus, putamen, hippocampus, medial temporal lobes, and amygdala, associated with illnesses (1-5). The brainstem, cerebellum, cerebral peduncles, and

pons may also be involved. (2-5). The neuroinvasive mechanism of ANE is not known; there are two possible hypotheses, the immune-mediated neurotoxicity and neuronal retrograde dissemination (6). SARS-CoV and SARS-CoV-2 are similar in structure, and both can penetrate through the neuroepithelium of the olfactory nerve and olfactory bulb by an interaction between the viral spike" protein and host cell surface protein angiotensin-converting enzyme 2 (ACE2). In the brain, ACE2 is expressed in the brainstem, hypothalamus, motor cortex, and raphe nucleus (7). Immunotherapy has some role in the treatment of COVID-19 associated ANE, as described in the literature (1, 4,5).

References

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Table: Case Report Summaries of COVID-19 associated ANE

Study	Geographic location	Age	Gender	Co-morbidities	Symptom onset/ onset of neurologic syndrome (Days)	CNS/ PNS Symptomatology	Nasopharyngeal SARS-CoV 2 RT- PCR	CSF SARS-CoV 2 RT-PCR	MRI	Treatment	Outcome
Poyiadji et al [1] Case report ANE	Detroit, MI, USA	58	F	HTN	4 days after cough, fever and myalgia	AMS	Positive	Negative	BL thalamic and medial temporal lobe hemorrhages	IVIG+ IVMP+ HCQ+ AZI	Recovered
Dixon et al [2] Case report ANE	London, UK	59	F	Transfusion dependent aplastic anemia	10 days after fever, cough, sorethroat, myalgia, dyspnea and headache	AMS, Seizures	Positive	Negative	Symmetrical hemorrhagic lesions in the amygdalae, putamen, brainstem, and thalamic nuclei	levetiracetam, ceftriaxone, aciclovir, amoxicillin, clarithromycin, steroids	Died
Elkady et al [3] Case report ANE	Egypt	33	F	None	4 days after fatigue, fever, headache, nasal congestion	Status epilepticus, coma,	Positive	Not tested	BL hemorrhagic thalamic and cerebellar lesions	IVMP +IV midazolam+ valproic acid	Died
Virhammar et al [4] Case report ANE	Sweden	55	F	None	7 days after Fever, myalgia, pneumonia	Lethargy, unresponsiveness, stupor, multifocal myoclonus	Positive	Negative x 3 (N gene was positive)	BL thalamic, hypocampal, medial temporal lobes, cerebral peducnle and pontine lesions	IVIG+ acyclovir+PLEX+ Convalescent plasma	Recovered
Delamarre et al [5] Case report ANE	France	51	M	None	21 days after fever, cough, pneumonia	Unresponsivess, comatos	Positive	Negative	BL Thalami, cerebellum, brainstem, supratentorial grey and	IVMP 1 gm x 3 days, IVIG 2 gm/kg over 5 days	Recovered

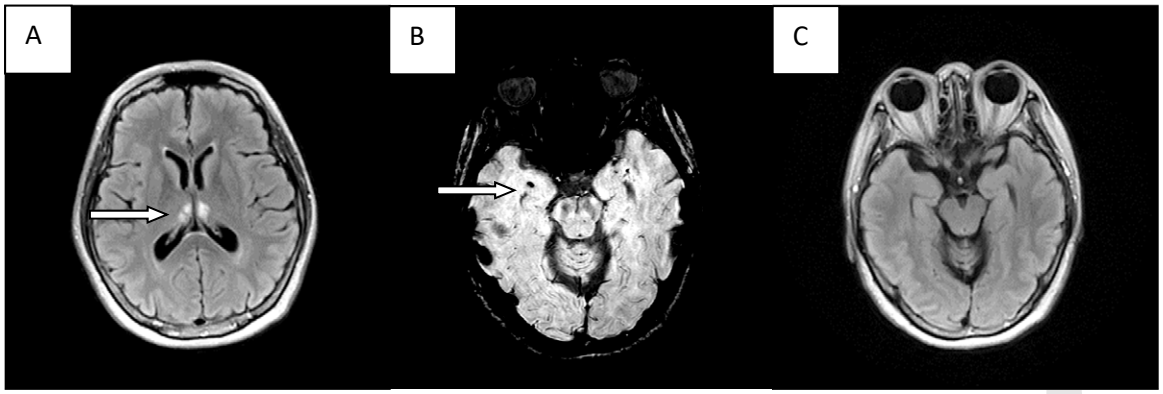

Figure: Images in a 58-year-old woman with acute necrotizing encephalopathy (ANE) associated with acute SARS-COV-2 infection. Brain MRI without contrast 15 weeks after ANE onset. MRI demonstrates residual T2 FLAIR hyperintensity within the thalami (*A,* white arrow*)* with residual hemosiderin deposition indicated by hypointense signal intensity on susceptibility-weighted images (*B,* white arrow). *C,* Earlier T2 hyperintensities in the bilateral medial temporal lobes had resolved.