A NONSPECIFIC WIDESPREAD INVOLVEMENT OF ENCEPHALITIS IN A COVID-19 PATIENT

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ABSTRACT

Encephalopathic symptoms including headache and altered mental status in hospitalized patients due to Covid-19 infection have been reported frequently in the recent literature.Moreover, neuroimaging correlation of some of these patients have been deonstrated with various forms of encephalitis. We aimed to describe the neuroimaging manifestations of an acute encephalitis with widespread involvement of deep white matter and deep gray matter areas that resolve following steroid treatment in a young male patient. We hope our case will add in the understanding of the range of neurological involvemnets related with Covid-19. More data about neuroimaging and neuropathological examinations are need to determine the neurotropism and particular types of involvements in the central nervous system.

Keywords: *encephalitis, encephalopathy, Covid-19.*

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Introduction

Covid-19 (coronavirus disease 2019) is a viral infectious disease caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), a strain of coronavirus. This virus was first detected in Wuhan, China, in December 2019[(1)] and on 11 March 2020 it was recognized as a pandemic by the World Health Organization (WHO)[(2)]. Most of the cases present with mild to moderate upper respiratory disease, however some progress to severe pneumonia which can rapidly result in massive alveolar injury. In addition, as the pandemic progressed, extrapulmonary manifestations have been started to be increasingly recognized. Encephalopathic symptoms including headache and altered mental status in hospitalized patients due to Covid-19 infection have been reported frequently in the recent literature[(3)].

Moreover, neuroimaging correlation of some of these patients have been demonstrated with various forms of encephalitis. We aimed to describe the neuroimaging manifestations of an acute encephalitis with widespread involvement of deep white matter and deep gray matter areas in a young male patient.

Case presentation

A 32 year old male patient had mild cough and myalgia a week before presentation top ur hospital. Reverse transcriptase-polymerase chain reaction (RRT-PCR) test was positive for Covid-19 on nasopharyngeal swab at that time. He was isolated at home and started to take only supportive treatment including multivitamin and rest. About 2 weeks later, he presented to our hospital with recently developed headache, vertigo, altered mental status,

and involuntary jumping movements in addition to an increase in ongoing symptoms. On physical examination, he was agitated but cooperative with place and time orientation. There were no focal neurological deficit. Meningeal irritation signs were not present. Chest computed tomography (CT) demonstrated patchy peripheral ground-glass opacities with superimposed consolidations located predominantly at lower lobes, suggesting Covid-19 pneumonia (fig. 1). However, the nasopharyngeal swab RRT-PCR test was found to be negative for Covid-19. On the laboratory tests, the white blood cell (WBC) count was in the normal range. C- reactive protein (CRP), Ferritin, and d-dimer were obviously increased. The blood glucose and urea levels were also in the normal range (Table 1).

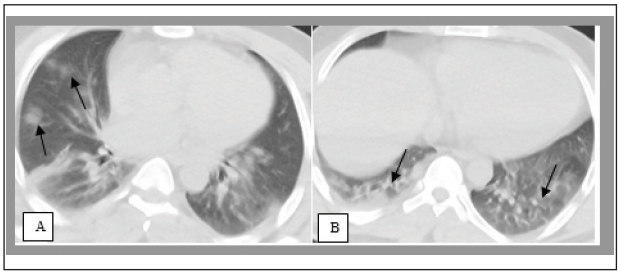

Figure 1: Axial chest CT images (A,B) show nodular and patch GGOs and consolidations (arrows).

		Reference range
WBC	7.39 K/uL	3.98-10.2
CRP	28.1 mg/L	0-5.0
Ferritin	508,93 ng/L	22-274
d-dimer	2240 ng/mL	0-500
Blood glucose	124 mg/dL	70-105

Table 1: The laboratory findings

Cranial CT showed no intracranial hemorrhage but patchy areas of periventricular hypodensities were demonstrated (fig. 2). Contrast-enhanced 3T (Tesla) magnetic resonance imaging (MRI) of the brain revealed prominent bilateral T2w and Flair hyperintensities in the periventricular white matter and the centrum semiovale, with involvement of bilateral medial temporal lobes, basal ganglia, thalami, brain stem and cerebellar white matter. Cortical gray matter and corpus callosum were spared. On postcontrast images there was no pathological enhancement. A few foci of hemorrhages were noted within the left basal ganglia and thalamic lesions. At that time, there was no restricted diffusion (fig. 3).

However, about 1 week later restricted diffusion has been demonstrated in the basal ganglia (fig. 4). There were no toxic exposure in his personal history and no metabolic abnormality in the laboratory tests

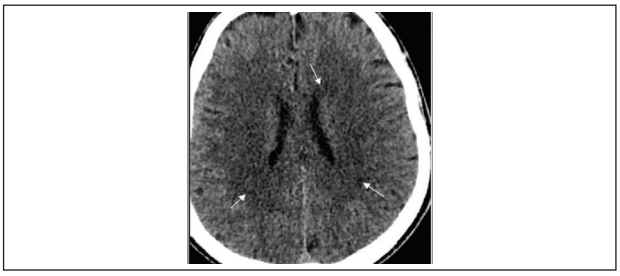

Figure 2: Nonenhanced axial CT image shows faint patchy hypodensities within the periventricular white matter (arrows).

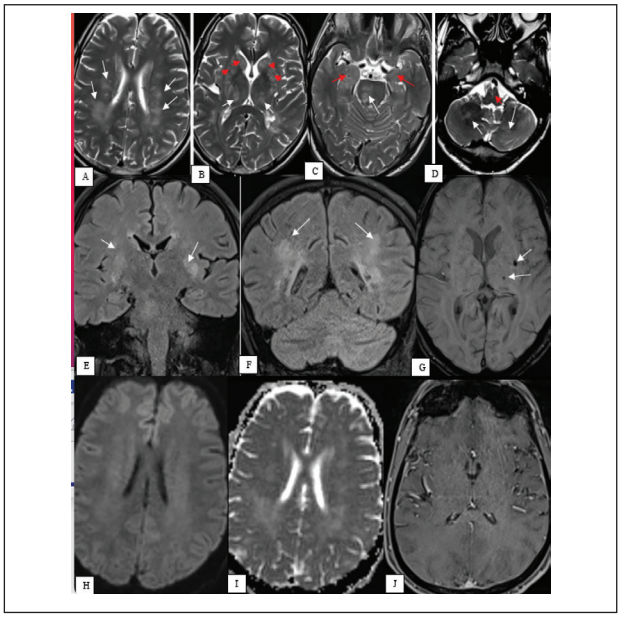

Figure 3: Contrast-enhanced cranial 3T MRI scans. Axial T2w images (A, B, C, D) demonstrate prominent hyperintensities in the periventricular white matter (A, white arrows), bilateral basal ganglia (B, red arrowheads) and thalami (B, white short arros), pons (C, White arrow) and bilateralş medial temporal lobes (C, red arrows), medulla oblongata (D, red arrow) and cerebellum (D, white arrows). Note the sparing of the corpus callosum. These hyperintensities are also shown on coronal fluid-attenuated inversion recovery (Flair) images (E, F; white arrows). Axial susceptibility-weighted image (SWI) at the level of basal ganglia and thalami shows blooming artifact in the left putamen and thalamus (G, White arrows). Axial diffusion-weighted image (H; b = 2000 sec/mm^2) and the corresponding apparent diffusion coefficient (ADC) map (I) show no restricted diffusion . There is no contrast enhancement on the postcontrast T1w image (J).

Serum vasculitis markers were also negative. Lumbar puncture (LP) was performed and revealed no elevation of leukocytes in cerebrospinal fluid (CSF), but it was remarkable for increased protein level (0,85 g/L). In addition, RRT-PCR tests for herpes simplex virüs (HSV) and SARS-CoV-2 was negative on CSF analysis. CSF bacterial culture showed no growth.

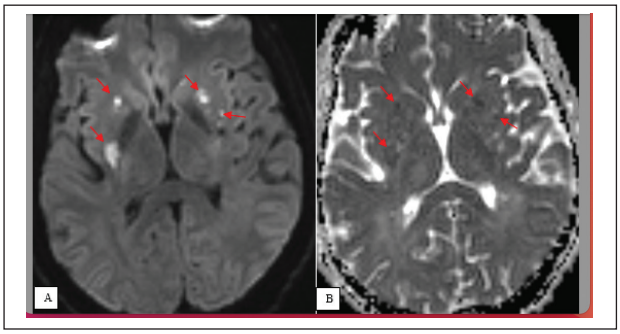

Figure 4: Axial diffusion-weighted image (A; b = 2000 sec/mm^2) and the corresponding apparent diffusion coefficient (ADC) map (B) show restricted diffusion at bilateral basal ganglia (red arrows).

Therefore, Covid-19 related autoimmune encephalitis was considered after detailed exclusions of other causes. Two days later, he was intubated due to respiratory distress, but before that there was no hypoxic or anoxic episode. Due to the increased level of CSF protein, pulse steroid during 3 days and then maintainence steroid treatment was started. After a week, he was extubated and the chest CT showed regression of the pneumonic infiltrations (fig. 5).

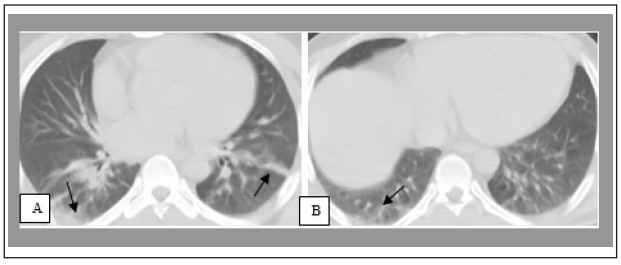

Figure 5: Axial chest CT images at discharge (A, B) show prominent regression in the pneumonic infiltrations. Some persistent subpleural densities at lung bases were noted (A, B; black arrows).

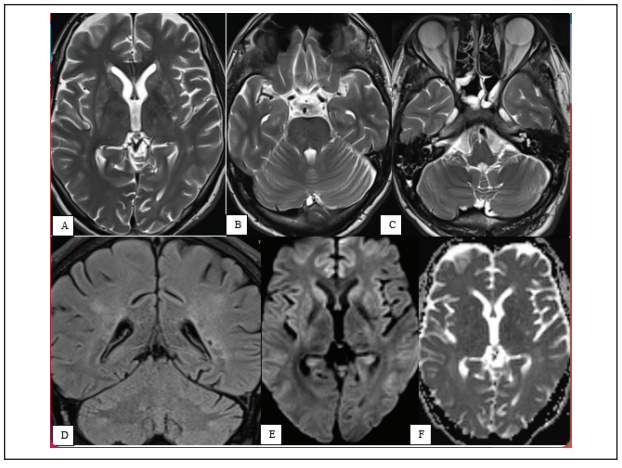

Figure 6: 3T MRI scans performed at discharge. Axial T2w images (A, B, C) and coronal Flair image (D) demonstrate prominent regression of the hyperintensities. Axial diffusion-weighted image (E; b = 2000 sec/mm^2) and the corresponding apparent diffusion coefficient (ADC) map (F) show no restricted diffusion anymore.

On control brain MRI the pathological increased T2w signal intensities and the restricted diffusion have been shown to be resolved prominently (fig. 6). He was discharged from the hospital with a planned neurological outpatient control.

Discussion

Neurological manifestations ranging from headache, myalgia, hyposmia/anosmia, hypogeusia/ageusia to more severe situations including altered mental status, ischemic and hemorrhagic stroke and encephalitis have been reported in varied frequencies in the literature. In a case series of 214 patients, neurological complications have been observed in 36.4% of the overall cases including impaired consciousness (14.8%) and acute cerebrovascular diseases (5.7%) and the more severe complications were reported in patients with more severe infection[4]. In another study reported from France, neurological manifestations were reported to be present in 84% of patients with Covid-19 admitted to the ICU[5]. Acute cerebrovascular diseases particularly acute ischemic stroke were reported up to 6% of hospitalized patients with severe inflammatory state[6]. We also reported various neuroimaging complications seen in our patients including stroke, splenial corpus callosum lesion and spondylodiscitis complicated with psoas abscess in our previous studies[7,8]. In the pathophysiology of the neurological complications seen in Covid-19, the hyperinflammatory-hypercoagulable state called as cytokine storm and neurotropism of the virus itself that may be associated with direct or autoimmune encephalitis have all been suggested[9-11]. Furthermore, the relation between sinusitis and retrograde trans-synaptic transfer through the olfactory nerve has also been included in the pathophysiological bases of Covid-19 related neurological involvements[12].

In addition, the disease related systemic comorbidities associated with the critical illness, including hypoxia, seizure and hypoglycemia may be the primary cause of the neurological complications or may interfere with the pattern the virüs related encephalopathic involvements[5,13-17]. Two neuroimaging findings, leukoencephalopathy and microhemorrhages involving white matter diffusely in a characteristic pattern, that were believed to be related with hypoxia in critically ill patients with COVID-19 were reported by Radmanesh et al. The authors suggested demyelination or disruption of blood-brain barrier for underlying

pathogeneses[18]. Meningitis and encephalitis was first described with the involvement of the wall of the right lateral ventricle, the right mesial temporal lobe and hippocampus in a 24 year old male patient with Covid-19. The specific SARS-CoV-2 RNA was reported to be detected in a CSF but not in the nasopharyngeal swab in this patient[19]. A multicenter study from Turkey demonstrating brain MRI findings in patients in the ICU with Covid-19 infection reported nonspecific patterns of involvement of encephalopathy. The most common imaging finding was cortical signal intensity abnormalities on Flair images (37%), accompanied by cortical diffusion restriction, leptomeningeal enhancement, or cortical blooming artifact in some of these patients[20]. In our patient neither hypoglycemia nor significant hypoxia was present at presentation. There were two attacks of seizure before presentation to our hospital, but there was no status epilepticus and the deep white matter involvement and relave symmetricity of the findings did not suggest postictal changes.

Although some specific involvements can be encountered in some specific types of encephalopathies like HSV encephalitis, most of the reported patients with Covid-19 related encephalitis nonspecific involvements have been demonstrated. The medial temporal lobes were involved bilaterally as in HSV encephalitis, but the insular cortices and inferolateral frontal lobes were spared. In addition, the deep gray matter including the thalamus and basal ganglia are typically spared in HSE. The concurrent involvement of the medial temporal lobe, periventricular and cerebellar white matter and deep gray matter areas is not specific for any types of encephalopathy on neuroimaging. A review evaluating the findings of CSF analysis in 113 patients identified in 67 studies reported that CSF protein was elevated in 100% of the fatal cases with an average of 61.28 mg/dl and in 65.0% in non-fatal cases with an average 56.73 mg/dl[21]. In our patient the CSF protein level was also increased. The cell count, glucose levels, and albumin level were within normal ranges as in the reported CSF findings from the multicenter study of Turkey reporting CSF findings obtained 10 of their patients with cortical signal intensity abnormalities[20].

Conclusion

In this report, we tried to demonstrate a widespread acute encephalitis in a patient with recent diagnosis of Covid-19. The nonspecific involvement and resolution of the neuroimaging findings along with the clinical signs and symptoms with steroid treatment has been shown. We hope our case will add to the understanding of the range of neurological involvement related with Covid-19. More data about neuroimaging and neuropathological examinations are needed to determine the neurotropism and particular types of involvements in the central nervous

References

1) Huang C, Wang Y, Li X, et al. . Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395: 497-06 10.1016/S0140-6736(20)30183-5.
2) Mahase E. Covid-19: WHO declares pandemic because of "alarming levels" of spread, severity, and inaction. BMJ 2020; 368: m1036. 10.1136/BMJ.m1036.
3) Weiss P, Murdoch DR. Clinical course and mortality risk of severe COVID-19. Lancet 2020; 395: 1014-15 10.1016/S0140-6736(20)30633-4
4) Mao L, Jin H, Wang M, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. JAMA Neurol 2020 Apr 10 [Epub ahead of print].
5.) Helms J, Kremer S, Merdji H, et al. Neurologic Features in Severe SARS-CoV-2 Infection. N Engl J Med 2020 Apr 15 [Epub ahead of print] 10.1056/NEJMc2008597.
6) Li Y, Wang M, Zhou Y, Chang J, Xian Y, Mao L. Acute cerebrovascular disease following COVID-19: a single-center, retrospective, observational study. SSRN Electron J. 2020.
7) Berrin Erok, Ali Önder ATcai Hakan Önder. Neurological Complications Encountered in Imaging Studies in Association with Covid-19: a single-center analysis. Eur J Clin Exp Med 2022.
8) Erok B., Kıbıcı K. COVID-19 Infection Manifesting with Lumbar Spondylodiscitis Complicating With Psoas Abscess without Pneumonia. Indian J of Neurosurgery. 2021. DOI: 10.1055/s-0041-1741405
9) Moriguchi T, Harii N, Goto J, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. Int J Infect Dis 2020; 94: 55-58.
10) Poyiadji N, Shahin G, Noujaim D, Stone M, Patel S, Griffith B. COVID-19-associated Acute Hemorrhagic Necrotizing Encephalopathy: CT and MRI Features. Radiology 2020 Mar 31: 201187.
11) Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020; 395(10229): 1033-1034.
12) Giacomelli A, Pezzati L, Conti F, et al. Self-reported olfactory and taste disorders in SARS-CoV-2 patients: a cross-sectional study. Clin Infect Dis. 2020; ciaa330.
13) Kelley BP, Patel SC, Marin HL, Corrigan JJ, Mitsias PD, Griffith B. Autoimmune Encephalitis: Pathophysiology and Imaging Review of an Overlooked Diagnosis. AJNR Am J Neuroradiol 2017; 38(6): 1070-1078.

14) Cianfoni A, Carlo M, Cerase A, et al. Seizure-induced brain lesions: a wide spectrum of variably reversible MRI abnormalities. Eur J Radiol 2013; 82(11): 1964-1972.
15) Muttikkal TJ, Wintermark M. MRI patterns of global hypoxic-ischemic injury in adults. J Neuroradiol 2013; 40(3): 164-171.
16) Bathla G, Police B, Agarwal A. Neuroimaging in patients with abnormal blood glucose levels. AJNR Am J Neuroradiol 2014; 35(5): 833-840.
17) Fanou EM, Coutinho JM, Shannon P, et al. Critical Illness-Associated Cerebral Microbleeds. Stroke 2017; 48(4): 1085-1087.
18) Radmanesh A, Derman A, Lui YW, et al. COVID-19 -associated diffuse leukoencephalopathy and microhemorrhages. Radiology 2020 May 21.
19) Moriguchi T, Harii N, Goto J, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. Int J Infect Dis 2020; 94: 55-58.
20) Kandemirli SG, Dogan L, Sarikaya ZT, et al. Brain MRI Findings in Patients in the Intensive Care Unit with COVID-19 Infection. Radiology. 2020; 297(1): E232-E235. doi:10.1148/radiol.2020201697.
21) Medha Tandon, Saurabh Kataria, Jenil Patel, et al. Comprehensive Systematic Review of CSF analysis that defines Neurological Manifestations of COVID-19. International Journal of Infectious Diseases 104 (2021) 390-397.

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