Case Report / Olgu Sunumu

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A Case of Acute Necrotizing Encephalopathy Associated with SARS-CoV-2 on the Background of Takayasu's Arteritis and Intensive Care Management

Takayasu Arteriti Zemininde SARS-CoV-2 İlişkili Akut Nekrotizan Ensefalopati Gelişen Bir Hasta ve Yoğun Bakım Takibi

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Abstract

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) typically leads to mild infectious disease in children, although both acute infection and multisystem inflammatory syndrome in children can cause severe complications. Additionally, SARS-CoV-2 is a neurotropic virus that can present with a wide spectrum of neurological symptoms. Acute necrotizing encephalopathy of childhood (ANE) is a rare acute encephalitis characterized by symmetrical lesions in the thalamus with variable involvement of the white matter, brainstem, and cerebellum. It usually develops after viral infection in genetically predisposed patients. Although the prognosis is poor, some patients respond to steroid and intravenous immunoglobulin (IVIG) treatment. In this case report, we present the case of an 11-year-old patient with no previously known disease who developed SARS-CoV-2-related ANE that did not respond to steroid and IVIG treatment. Our patient was incidentally diagnosed with Takayasu arteritis, and brain death occurred in the 32nd hour of admission.

Keywords: SARS-CoV-2, acute necrotizing encephalopathy, Takayasu arteritis

Öz

Şiddetli akut solunum sendromu-koronavirüs-2 (SARS-CoV-2) literatürde genellikle çocuklarda hafif bir bulaşıcı hastalık seyrine yol açar, ancak hem akut enfeksiyon hem de çocuklarda multisistem enflamatuvar sendrom ciddi komplikasyonlara neden olabilir ayrıca nörotropik bir virüs olup geniş bir spektrumda nörolojik semptomla prezente olabilir. Çocukluk çağının akut nekrotizan ensefalopatisi (ANE), talamusta tipik, simetrik lezyonlarla, beyaz cevher, beyin sapı ve serebellumun değişken tutulumuyla karakterize, nadir bir akut ensefalittir. Genetik olarak yatkın hastalarda genellikle viral enfeksiyon sonrası gelişebilir. Hastalığın prognozu kötü olmakla beraber bazı hastalarda steroid ve intravenöz immünoglobulin (IVIG) tedavisine yanıt alınmaktadır. Olgu olarak daha önce bilinen bir hastalığı olmayan 11 yaşında SARS-CoV-2 ile ilişkili ANE gelişen, steroid ve IVIG tedavisine yanıt vermeyen, başvurusunun 32. saatinde beyin ölümü gerçekleşen ve insidental olarak Takayasu arteriti tanısı alan hasta sunulmuştur.

Anahtar Kelimeler: SARS-CoV-2, akut nekrotizan ensefalopati, Takayasu arteritis

Introduction

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) usually leads to a mild course of infectious disease in children than in adults, but acute infection and multisystem inflammatory syndrome can cause serious complications. Neurological symptoms are predominantly reported in adults, ranging from mild headaches to seizures, peripheral neuropathy, stroke, demyelinating disorders, and encephalopathy. Acute

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necrotizing encephalopathy (ANE) of childhood is a rare disease usually characterized as acute encephalitis by typical, symmetrical lesions in the thalamus, white matter, brainstem, and cerebellum. It can usually develop after viral infection in genetically predisposed patients. Although the prognosis of the disease is poor, some patients benefit from steroid and IVIG treatment. Here, we present a patient who developed SARS-CoV-2-associated ANE and did not benefit from any treatment. The patient died at 32 hours of hospitalization and was diagnosed incidentally with Takayasu's arteritis.

Case Report

An 11-year-old male patient with no known disease before complained of high fever, weakness, and headache for two days. He was admitted to the hospital with generalized tonic-clonic seizures on the second day of his symptoms. Due to the patient being of foreign nationality, there is no record within Turkey's vaccination program, and there is no available information regarding their vaccination status abroad. In the emergency department, midazolam was used to the patient due to his seizure; the patient was unconscious, had shallow breathing, and was intubated in the emergency department. In addition, inotropic support was started for fluid-resistant hypotension.

Hypodense areas and signs of cerebral edema were detected on non-contrast cranial computer tomography (CT), and the patient was pre-diagnosed with encephalitis, so anti-edema treatment, ceftriaxone, vancomycin, and oseltamivir started. In the first physical examination after admission to our intensive care unit, his pupils were fixed and dilated, Glasgow Coma scale was 3, and he had no brainstem reflexes.

Cranial magnetic resonance imaging (MRI) showed diffuse, symmetrical edema and signal changes consistent with pathological contrast enhancement in the thalamus, both sides of the cerebral crus of the mesencephalon, and in the pons at the 6th hour of admission to the intensive care unit (Figure 1A, B, E, F-H) and diffusion-weighted MRI showed diffusion restriction only in a focal area in the pons (Figure 1C, D). IVIG and pulse methylprednisolone treatment was started for the patient prediagnosed with ANE.

In cranial CT angiography, diffuse cerebral edema, tonsillar herniation, fourth ventricular hemorrhage, and absence of intracranial blood flow supported brain death. In the arterial phase of CT angiography, concentric stenosis areas and enlargements in the lumen of the left vertebral artery, subclavian artery, left common carotid artery, and cervical segment of the internal carotid arteries on both sides and concentric wall thickening in the stenosis areas were observed (Figure 1I). In addition, there was extravasation and pseudoaneurysm appearance from the left vertebral artery (Figure 1I).

Takayasu arteritis (TA) was considered in the radiological findings. Thoracic abdominal computed tomography also showed a slight increase in vessel wall thickness supporting vasculitis in the thoracic aorta, which is more prominent in the supra-aortic branches. In the viral serology tested for the etiology of acute necrotizing encephalopathy, Coronavirus disease-2019 (COVID-19) IgG, and also the SARS-CoV-2 polymerase chain reaction of the patient was positive (Table 1).

The patient, who developed multiple organ failure secondary to hyper inflammation, died at the 12th hour of his admission to the intensive care unit. In light of this information, the patient was diagnosed with ANE and multi-organ failure due to SARS-CoV-2, which developed underlying Takayasu arthritis.

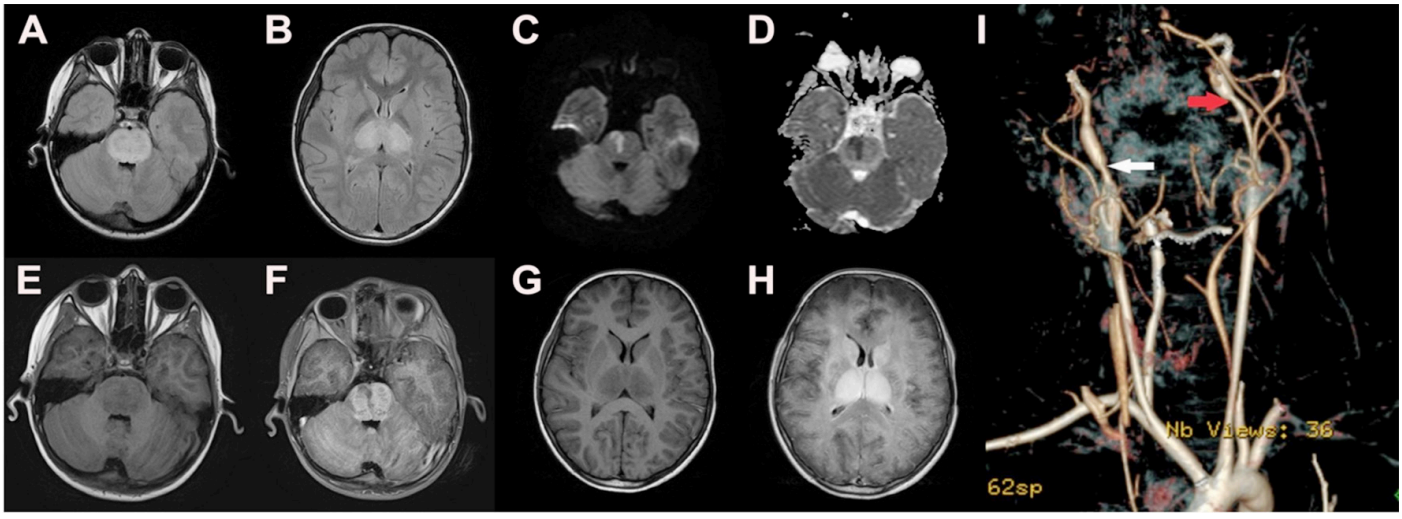

Figure 1. A, B) Diffuse edema in the pons, thalamus, C, D) Diffusion restriction in the pons, E-G) Hypointensity due to edema in the pons, thalamus, caudate nucleus, F-H) Diffusion-limiting area in the thalamus, caudat nucleus, I) Stenosis in both internal carotid arteries

Table 1. Laboratory test findings

Laboratory parameters	Value	Normal range
White blood cell	20.76x10^9/L	4.8-12x10^9/L
Absolute neutrophil count	19.29x10^9/L	1.7-8.1x10^9/L
C-reactive protein	304 mg/L	0-5 mg/L
Interleukin-6	5297.8 pg/mL	0-3.4 pg/mL
Creatinine	2.01 mg/dL	0.4-0.8 mg/dL
Aspartate aminotransferase	23672 U/L	0-37 U/L
Alanine transaminase	9387 U/L	0-32 U/L
Lactate dehydrogenase	17913 U/L	0-298 U/L
Sodium	155 mEq/L	132-146 mEq/L
Brain natriuretic peptide	19083 ng/L	<125 ng/L
Troponin I	>25000 ng/L	<45 ng/L
D-dimer	>10000 ng/mL	<500 ng/mL
Ammonia	228 µmol/L	11.2-35.4 µmol/L
Post-mortem lumbar puncture cerebrospinal fluid parameters	White blood cell: 40 cells/mm^3 Red blood cell: 10,720 cells/mm^3 Protein: >2.500 mg/L Glucose: 70 mg/dL	
Cerebrospinal fluid, polymerase chain reaction test, and culture	Negative	
RANBP2, the mitochondrial disease-specific mutation in exome analysis	Negative	
Metabolic test for inherited metabolic disease	Negative	

Discussion

We present a patient with SARS-CoV-2 related ANE and incidentally diagnosed with TA, who did not benefit from steroid or IVIG treatment, and at the 32nd hour of the hospital administration, brain death occurred. It was aimed to draw attention to the relationship of ANE with SARS-CoV-2 and to elucidate the underlying mechanisms in an undiagnosed and untreated patient with vasculitis that may cause high mortality. The vascular endothelium plays a role in regulating vascular tone in addition to maintaining vascular hemostasis. Therefore, endothelial dysfunction is the primary determinant of microvascular dysfunction. In the literature, it has been shown that SARS-CoV-2 causes direct viral infection and diffuse endothelial inflammation in the endothelial cells.[1]

SARS-CoV-2 infection can cause primer pulmonary disease and complications, venous thromboembolism, acute kidney, and liver injury, cytokine release, septic shock, disseminated intravascular coagulation, and neurological complications.[2] However, most neurological complications result from the systemic effects of SARS-CoV-2, such as cytokine release, immune-mediated inflammatory syndromes, and hypercoagulability.[3]

Maury et al.[4] reported neurologic symptoms in 73% of hospitalized COVID-19 patients, 13-40% had non-specific encephalopathy, less commonly acute demyelinating encephalomyelitis (n=13), and 4 of the patients diagnosed with ANE.ANE is a parainfectious disease primarily reported in pediatric patients. The autopsy of a patient with ANE showed no cellular inflammatory response in areas of necrosis.[5] However, it is accepted that immune-mediated, uncontrolled inflammation after viral infections may cause ANE. There is no standard treatment for ANE, and in the case series of Vanjare et al.[6] ANE, related mortality was reported as 40%; limited studies show that using anti-virals, IVIG, and steroids may increase the effectiveness of the treatment.There are limited cases of COVID-19-associated ANE, and only one resulted in death.[7] Therefore, we think that the rapid progression of the disease in our patient cannot only be explained by the combination of SARS-CoV-2 and ANE. Furthermore, it is considered that accompanying vasculitis may have changed the prognosis of the disease.

TA is a rare idiopathic granulomatous vasculitis in children. The systemic inflammatory response often may not correlate with the vessel wall's inflammatory process. Skipping lesions in affected segments and intact segments seen together along the artery in our patient is characteristic of TA. Although the earliest detectable lesion by imaging methods is localized narrowing or irregularity in the arterial lumen, our patient's stenosis and aneurysm formation may indicate the chronicity of the disease. Since it is not a common vasculitis, clinicians often do not consider TA in the differential diagnosis, and the diagnosis can take even years after the first onset of symptoms.[8]

In this paper, we offer a compelling clinical scenario that describes the development of ANE as a result of SARS-CoV-2

infection in a patient suffering from Takayasu's arteritis, a rare autoimmune vasculitis. This case serves as an illustration of the complex interactions between Takayasu's arteritis, viral infection, and the emergence of severe necrotizing encephalopathy.

Conclusion

The given case demonstrates the necessity for increased awareness and varied management techniques due to the complex relationship between Takayasu's arteritis, SARS-CoV-2 infection, and the resulting severe necrotizing encephalopathy.

This report meets with ethical standards by including informed consent, author contribution clarification, a statement of no conflict of interest, and an assurance that no financial disclosures were made. This commitment emphasizes the equality of all contributions and the lack of external funding.

Ethics

Informed Consent: Informed consent was obtained.

Authorship Contributions

Surgical and Medical Practices: E.U., B.Ç.A., R.B., A.Ö.P., S.Ö., O.P., E.K., S.E., Concept: E.U., G.G., Design: E.U., G.G., Analysis or Interpretation: E.U., B.Ç.A., R.B., A.Ö.P., S.Ö., O.P., E.K., S.E., Literature Search: E.U., G.G., B.Ç.A., R.B., A.Ö.P., S.Ö., O.P., E.K., S.E., Writing: E.U., G.G.

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