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Case Report

Pediatric Pseudotumor Cerebri Syndrome Secondary to Superior Sagittal Sinus Thrombosis Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Infection and Brief Literature Review

Şiddetli Akut Solunum Yolu Enfeksiyonu Sendromu Koronavirüs 2 ile İlişkili Süperior Sagittal Sinüs Trombozuna Sekonder Pediatrik Psödotumor Cerebri Sendromu ve Literatür İncelenmesi

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ABSTRACT

Pseudotumor cerebri syndrome (PTCS) is characterized by the presence of elevated intracranial pressure in the environment of intact brain parenchyma and cerebrospinal fluid (CSF). PTCS can occur in pediatric populations and cause permanent vision loss if left untreated. It is known that evere acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection predisposes patients to adverse arterial and venous thromboembolic events. Several reports from the literature suggest that cerebral venous sinus thrombosis (CVST) may be a direct complication of SARS-CoV-2 infection. Herein, we have aimed to report a case of PTCS secondary to superior sagittal sinus thrombosis associated with the first episode of pediatric SARS-CoV-2 infection. A previously healthy 13-year-old boy presented to the emergency department in February 2022 with complaints of headache, tinnitus and double vision persisting for four days. His mental status and cranial nerve examination results were normal as revealed during neurological examination performed at admission, but bilateral papilledema was detected in fundoscopic examination. SARS-CoV-2 polymerase chain reaction was negative, while anti-SARS-CoV-2 antibody test was positive. There was no variant study in the case. Contrast-enhanced brain magnetic resonance imaging showed signs of intracranial hypertension and magnetic resonance venography demonstrated the presence of superior sagittal sinus thrombosis. CSF opening pressure was elevated (73 cm H_2O). As measured during lumbar puncture Our patient was accepted as a case of PTCS secondary to CVST associated with SARS-CoV-2 infection. PTCS secondary to CVST associated with SARS-CoV-2 infection was diagnosed and the child was treated with oral topiramate and low-molecular weight heparin. After the treatment, his headache and visual functions improved and then the child was included in our follow-up protocol. Clinicians should consider the risk of acute CVST in SARS-CoV-2 positive patients, especially if neurological symptoms develop. Prompt diagnosis and treatment can prevent vision loss.

Keywords: SARS-CoV-2, pseudotumor cerebri, papilledema, venous thrombosis, headache

ÖZ

Psödotümör serebri sendromu (PTSS), normal beyin parankimi ve beyin omurilik sıvısı (BOS) ortamında artmış kafa içi basıncın varlığı ile tanımlanır. PTSS pediatrik popülasyonda ortaya çıkabilir ve tedavi edilmezse kalıcı görme kaybına neden olabilir. Şiddetli akut solunum yolu enfeksiyonu sendromu-koronavirüs-2 (SARS-CoV-2) enfeksiyonunun hastaları arteriyel ve venöz tromboembolik olaylara yatkınlaştırdığı bilinmektedir. Literatürden çeşitli raporlar, serebral venöz sinüs trombozunun (SVST) SARS-CoV-2'nin 10 doğrudan bir komplikasyonu olabileceğini düşündürmektedir. İlk pediatrik SARS-CoV-2 enfeksiyonu ile ilişkili süperior sagittal sinüs trombozuna sekonder bir PTSS olgusunu sunmayı amaçladık. Daha önce sağlıklı olan 13 yaşında erkek hasta 2022 Şubat ayında son dört gündür baş ağrısı, kulak çınlaması ve çift görme şikayetleri ile acil servise başvurdu. Başvuru sırasında yapılan nörolojik muayenesinde mental durumu ve kraniyal sinir muayenesi normaldi. Fundus muayenesinde bilateral 15 papilödem saptandı. SARS-CoV-2 polimeraz zincir reaksiyonu negatif çıkarken, anti-SARS-CoV-2 antikoru pozitif çıktı. Kontrastlı beyin manyetik rezonans görüntüleme intrakraniyal hipertansiyon belirtileri gösterdi ve manyetik rezonans venografi süperior sagittal sinüs trombozu gösterdi. Lomber ponksiyon BOS 73 cm H_2O ölçüldü. Hastamız SARS-CoV-2 enfeksiyonu ile ilişkili SVST'ye sekonder PTSS olarak kabul edildi. SARS-CoV-2 enfeksiyonu ile ilişkili SVST'ye sekonder PTSS tanısı konulan çocuğa oral topiramat 20 ve düşük molekül ağırlıklı heparin tedavisi başlandı. Tedavi sonrasında baş ağrısı ve görme fonksiyonları düzelen çocuk takibe alındı. Klinisyenler SARS-CoV-2 pozitif hastalarda özellikle nörolojik semptomlar gelişirse akut SVST riskini göz önünde bulundurmalıdır. Hızlı tanı ve tedavi görme kaybını önleyebilir

Anahtar kelimeler: SARS-CoV-2, psödotümor serebri, papilödem, venöz trombozu, baş ağrısı

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INTRODUCTION

Pseudotumor cerebri syndrome (PTCS) is characterized by a constellation of symptoms due to elevated intracranial pressure with an unclear etiology absolutely in the presence of normal brain parenchyma and cerebrospinal fluid (CSF) constituents[1]. PTCS can be classified as primary and secondary depending on whether the etiologic agent is identified or not[1]. Intracranial venous thrombosis has been implicated as a cause for intracranial hypertension secondary to CSF outflow obstruction[2].

Since the beginning of the coronavirus disease-2019 pandemic, a diverse spectrum of neurological manifestations associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, including headache, seizures, altered mental status, aseptic meningitis, and also intracranial hypertension has been identified[3]. Furthermore, SARS-CoV-2 infection deteriorates coagulation pathways, predisposing infected individuals to venous thromboembolism[4]. Underlying pathomechanisms include endothelial dysfunction with increased levels of von Willebrand factor, systemic inflammation induced by the activation of Toll-like receptors (TLRs), and a procoagulatory state established via activation of tissue factor pathway[4]. We report a pediatric patient with secondary PTCS associated with sagittal sinus vein thrombosis emerged after SARS-CoV-2 infection, which to our knowledge a similar case has not been cited in the literature so far.

CASE REPORT

A previously healthy 13-year-old boy presented to the emergency department in February 2022 with complaints of headache, tinnitus and diplopia persisting for four days. His mental status and cranial nerve examination results were normal as revealed during neurological examination performed at admission, but bilateral papilledema was detected in fundoscopic examination detailed ophthalmologic examination revealed stage 3 papilledema, minimal dilation of the blind spot, bilateral enlargement of optic nerve sheaths up to a diameter of 6 mm, and increased peripapillary retinal nerve fiber layer thickness. During visual acuity test he could count fingers from a distance of 4 meters. SARS-CoV-2 polymerase chain reaction test from a nasopharyngeal swab was negative but SARS-CoV-2 immunoglobulin (Ig) G IgM rapid test was positive for SARS-CoV-2 infection in the patient who had been exposed to SARS-CoV-2 infection 10 days previously. There was no variant study in the case. Routine blood test results were their normal limits. Brain magnetic resonance imaging revealed partially empty sella turcica, enlargement of the bilateral perioptic nerve in the subarachnoid space, and optic nerve tortuosity. Magnetic resonance venography revealed subacute dural venous sinus thrombosis in the short segment at the level of the superior sagittal sinus vertex (Figure 1). Echocardiograms, results of Doppler ultrasonography examinations, genetic thrombophilia panel, hemostasis and rheumatological tests were within normal limits. The opening pressure at the lumbar puncture was as high as 73 cm H_2O. Biochemical parameters of CSF were not remarkable. Results of detailed viral and bacterial serologic tests were not pathologic. Acetazolamide and low-molecular weight heparin were started in the patient who was diagnosed with PTCS secondary to sagittal sinus vein thrombosis associated with SARS-CoV-2 infection. Due to metabolic acidosis and taste disturbance, acetazolamide was replaced with topiramate. On the third day of treatment, his headache and ocular complaints improved significantly. Control ophthalmological examination revealed normal visual acuity and peripapillary retinal nerve fiber layer thickness. Papilledema was regressed completely and bilateral optic nerve sheath diameters were reduced to 4 mm. The patient is still being followed up with

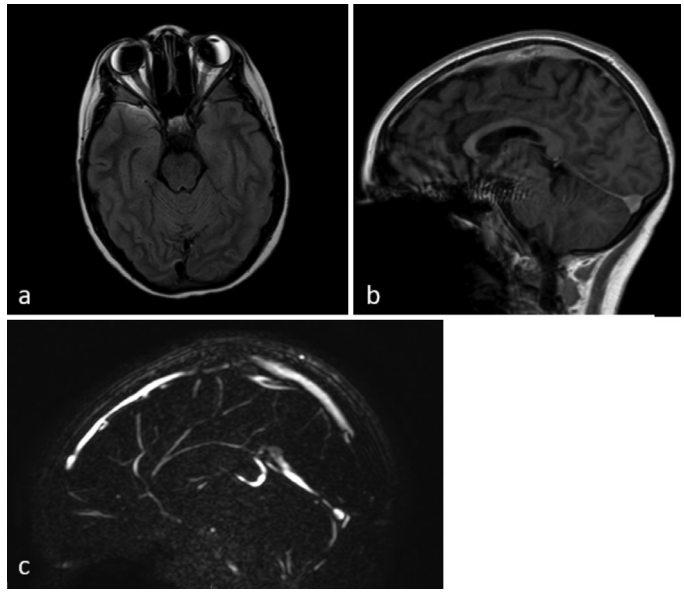

Figure 1. a) Axial FLAIR image showing protrusion of the optic nerve head and optic nerve tortuosity. **b)** Sagittal contrast-enhanced T1 image demonstrating focal hypointensity in superior sagittal sinus due to partial thrombosis. **c)** Sagittal TOF magnetic resonance venography displaying lack of flow in the short segment of the superior sagittal sinus

topiramate and low molecular weight heparin. Informed consent was received from the family.

DISCUSSION

Although children and adults had comparabie PTCS symptoms, demographic characteristics differ, and children are reported to have a higher incidence of secondary PTCS[5]. In the pediatric population, the most common causes of secondary PTCS are treatment with tetracycline antibiotics, and synthetic growth hormone, withdrawal from chronic corticosteroid therapy, and cerebral venous sinus thrombosis (CSVT)[6]. Since the beginning of the SARS-CoV-2 pandemic, many entities have been defined in the clinical course of the infection, one of which is an increase in the risk of thrombosis by disrupting the coagulation system leading to CSVT[7]. To date, in the literature, CSVT secondary to SARS-CoV-2 infection has been reported in 41 cases with a female predominance (53.7%) and a mean age of 50.1±16.5 years. In these patients, CVST was localized in the transverse and superior sagittal sinus in 63.4% and 46.3% of the cases, respectively[8].

Our case will contribute to the literature due to being the first pediatric case with PTCS associated with superior sagittal sinus vein thrombosis secondary to SARS-COV-2 infection. Despite the female predominance in the literature, our case was male. Again, in terms of thrombosis localization, contrary to the literature, superior sagittal sinus venous thrombosis was demonstrated in our case.

In patients with CVST secondary to SARS-COV-2 infections, headache, low-grade fever, and gastrointestinal symptoms are the most common initial symptoms. However, clinicians should be alerted for a wide range of symptoms such as seizures, signs of intracranial hypertension, decreased consciousness, altered sensorium, and typical stroke symptoms, all of which can occur within hours, days, or weeks without any specific time frame, complicating the already challenging diagnostic decision-making process for CVST even further[8,9]. Our patient had headache, a symptom that can be seen separately in both CVST and PTCS. However, tinnitus and diplopia, which are not typical for CVST, but classical symptoms for PTCS, were present in our patient.

Swelling of optic disc in the setting of SARS-CoV-2 infection was proposed to have many possible etiologies including ischemic optic neuropathy, papillophlebitis, optic neuritis, and retinal vein occlusion. The presence of normal visual acuity and color vision along with normal pupillary responses and the absence of associated retinal hemorrhages or venous tortuosity in our patient made us exclude these above-mentioned etiologies.

The etiology of neurologic symptoms in SARS-CoV-2 infection and multisystem inflammatory syndrome in children (MIS-C) have not been well described. Neurological symptoms in MIS-C are rarely seen compared to other organ system involvements. MIS-C was not considered in the differential diagnosis because clinical and laboratory parameters of our patient did not comply with the definition of MIS-C determined by Centers for Disease Control and Prevention/the World Health Organization[10].

The main goals of treatment for PTCS are to prevent vision loss and to relieve symptoms of elevated intracranial pressure. As an acceptable first-line therapy, carbonic anhydrase inhibitors provide effective management of PTCS by decreasing the production of CSF[11]. The treatment process of our patient was initiated with acetazolamide and maintained with topiramate due to the side effects of acetazolamide. In addition, as classical treatment for CSVT, low-molecular weight heparin was used. This combination was found to be well tolerated and beneficial without relevant side effects.

Although conduction of further studies is needed to establish a definitive cause-effect relationship, inflammation triggered by SARS-CoV-2 infection in association with the state of hyperviscosity and hypercoagulability may induce intracranial hypertension in some infected individuals.

Therefore, we suggest that in patients with confirmed SARS-COV-2 infection presenting with unexplained neurological symptoms including severe, persistent headache or papilledema, a high degree of suspicion for CSVT should be always kept in mind.

Ethics

Informed Consent: Informed consent was received from the family.

Peer-review: Externally peer reviewed.

Author Contributions

Concept: M.C.Y., Ç.G., Design: M.C.Y., Ç.G., G.S.U., Ö.Ö., S.H.K., E.Y., U.Y., Data Collection or Processing: M.C.Y., Ç.G., G.S.U., Ö.Ö., S.H.K., E.Y., U.Y., Analysis or Interpretation: M.C.Y., U.Y., Literature Search: M.C.Y., Ç.G., U.Y., Writing: M.C.Y.

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