Mild Course of COVID-19 infection in a patient with Rasmussen Encephalitis

Sibel Öz Yıldız (dr_sibeloz@hotmail.com)
Hacettepe University Faculty of Medicine, Department of Pediatric Neurology

Ceren Günbey
Hacettepe University Faculty of Medicine, Department of Pediatric Neurology

Burçak Bilginer
Hacettepe University Faculty of Medicine, Department of Neurosurgery

Kader Karli Oguz
Hacettepe University Faculty of Medicine, Department of Neuroradiology

Bora Gülhan
Hacettepe University Faculty of Medicine, Department of Pediatric Nephrology

Banu Anlar
Hacettepe University Faculty of Medicine, Department of Pediatric Neurology

Dilek Yalızoğlu
Hacettepe University Faculty of Medicine, Department of Pediatric Neurology

Case Report

Keywords: COVID-19, Rasmussen encephalitis, Tacrolimus, Intravenous Immunoglobulin

Posted Date: October 19th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-2119164/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Rasmussen encephalitis (RE) is a rare disease of unknown etiology that affects one hemisphere and causes refractory epilepsy, progressive neurological and cognitive dysfunction. A 17-year-old patient with RE underwent unilateral hemispheric surgery. Her seizures started at nine years old and she underwent left temporal lobectomy at 10 years old. She had been receiving intravenous immunoglobulin and tacrolimus in addition to antiseizure medications. Three weeks after hemispheric surgery, she had COVID-19 infection with mild symptoms. We suggest that light course of COVID-19 infection maybe due to exposure to long-term immunomodulatory treatment.

Introduction

Rasmussen encephalitis (RE) is a rare disease that typically affects one hemisphere, characterized by inflammatory and possibly immune-mediated, drug-resistant epilepsy, and progressive neurological and cognitive impairment. Although the underlying etiology of RE is not exactly known, autoantibodies and cytotoxic T cells may have a role in its pathogenesis [1]. While unilateral hemispheric surgery for epilepsy may decrease seizure frequency, it may result in irreversible loss of motor function. Immune-modulatory treatment including corticosteroids, immunosuppressive drugs, plasmapheresis, intravenous immunoglobulin (IVIG), and tacrolimus have been beneficial treatment options [2]. Here, we present a case of RE treated with IVIG and tacrolimus who had mild symptoms of COVID-19 infection following hemispherectomy.

Case Report

A 17-year-old female patient was diagnosed with RE at nine years old. She initially received steroids, IVIG in addition to polytherapy with antiseizure medications (ASM). During the course of the disease, she developed prominent the left temporal atrophy (Figure-1A,1B), video-EEG monitoring study showed hemispheric asymmetry with slowing on the left side, interictal discharges and seizures consolidated over the left temporal area. Palliative resective surgery with left temporal lobectomy and amygdalohippocampectomy was performed at 10 years of age (Figure-1C). The frequency of seizures initially decreased after surgery, however seizures originating from extratemporal areas, predominantly from left frontal region persisted. She was started on tacrolimus at 12 years in addition to ongoing treatment with IVIG and steroids. Parents remained reluctant to further epilepsy surgery for a long time until both parents and the patient decided to pursue with surgery due to persistence of seizures and poor ambulation. She had epilepsia partialis continua, daily focal aware motor seizures, and weekly focal onset aware motor seiuzures evolving to bilateral tonic clonic seizures. She was maintained on polytherapy with lacosamide, zonisamide, levetirasetam, clobazam, tacrolimus and IVIG. Presurgical evaluation revealed that speech and language functions were transferred to the unaffected right hemisphere as shown by functional magnetic resonance studies. She finally had left anatomical hemispherectomy at 17 years old (Figure-1D). She was seen at follow up visit three weeks after surgery, she was noted to have decreased appetite, poor fluid intake and she was admitted for intravenous
hydration. History at the time of admission revealed that she had headache for two days and a serous nasal discharge for a day. She had no complaints of fever, cough, shortness of breath, loss of taste and smell, diarrhea, chest pain, and muscle pain. The patient’s vital signs were stable, lungs were clear to auscultation and the chest radiograph was normal, COVID-19 PCR was positive. Other laboratory investigations revealed hemoglobin: 8.8 gr/dl (11.7-15.5), absolute lymphocyte count: 790 µL (1.200-3.600), absolute neutrophil count: 1540µL (1.800-6.400), C-reactive protein was slightly elevated at 1.44 mg/dl (0-0.8), serum creatinine 1.15 mg/dl (0.26-0.77). Complete blood count and serum biochemistry were otherwise normal. The patient was observed in the hospital for three days without further complaints, her kidney function tests returned to normal levels following hydration.

Long term tacrolimus exposure was thought to be one of the risk factors for impaired kidney function tests. Tacrolimus was discontinued following surgery as well as IVIG treatment. Also antiseizure medications, levetiracetam, lacosamide, and zonisamide were decreased to prevent further kidney injury. She was discharged with home isolation recommendations. She has been seizure free after surgery.

**Discussion**

The signs and symptoms of SARS-CoV-2 infection are stated to have a milder course in children compared to adults [3,4]. In a meta-analysis; severe COVID-19 infection was found to be more common in patients with an underlying disease, detected in 5.1% of children with comorbidities and 0.2% without comorbidities. Comorbid conditions such as obesity, chronic respiratory disease, cardiovascular disease, neurologic disorders, immun, metabolic, hematologic, malign, renal, gastrointestinal disorders, pose significant risk factors for severe COVID-19 infection [5]. The frequency of seizures increased in 27% of epileptic patients exposed to COVID-19 [6]. Seizure exacerbation and frequent seizures were related to history of exposure to COVID-19, suggesting the adverse impact of COVID-19 on seizure-related problems, inappropriate changes of ASM and non-response to ASM [6].

Multisystem inflammatory syndrome (MIS-C) in children is well defined in children with history of COVID-19 infection [7]. Age younger than one year, increased viral load, and having a chronic disease are risk factors that increase the severity of MIS-C [8]. Our patient had a mild course of COVID-19 infection despite the infection occurred following a major surgical procedure, and the course was complicated with impaired kidney function which could be due to poor intake perioperatively and medication toxicity.

In a multicenter study by Belli et al.; advanced age and comorbid conditions had a negative effect in patients with liver transplant and COVID-19 infection. However, COVID-19 infection had a mild course in patients receiving tacrolimus, and lower the mortality rate, suggesting a protective effect of tacrolimus in COVID-19 infection. Tacrolimus inhibits calcineurin and suppresses the early stage of T-cell activation, reducing the production of many cytokines such as tumor necrosis factor-alpha and interferon-gamma, especially proinflammatory cytokines, subsequently attenuating the cytokine storm in COVID-19 infection [9]. In a prospective study by Solanich et al., 56 adults with severe COVID-19 infection were compared with respect to treatment, the mortality rate was found to be lower in patients who received pulse
methylprednisolone and tacrolimus in addition to the standard treatment when compared with those who received standard treatment only [10].

Contradictory findings have also been reported, albeit with small number of cases. In a retrospective case series of 835 patients with COVID-19, of whom 46 (5.5%) received immunosuppressive therapy before diagnosis of the infection, 20 received oral steroids (43%), 12 mycophenolate (26%), and 11 tacrolimus (24%). Patients who had previously received immunosuppressive therapy had worse outcomes and increased mortality, regardless of comorbid conditions. The authors hypothesized that while immunosuppression might be beneficial in the later stages of the disease, patients on immunosuppressive therapy prior to contracting SARS-CoV-2 develop more severe COVID-19 infection due to the impaired antiviral immune response [11].

Intravenous immunoglobulin is a blood product obtained from healthy donors and contains polyclonal immunoglobulin gamma used in primary and secondary immun deficiencies, neuroimmunological diseases such as Chronic Inflammatory Demyelinating Polyneuropathy, Guillain-Barré syndrome, autoimmune/inflammatory conditions, and infectious diseases [12]. COVID-19 induces an inflammatory response with macrophage hyperactivation, especially in the lungs, leading to a cytokine storm responsible for serious lung and systemic complications [13], therefore IVIG has been used in the early stage treatment of COVID-19 infection to inhibit the production of inflammatory cytokines in macrophages [14]. Intravenous Ig treatment was found to reduce hospital stay and mortality in patients with moderate to severe COVID-19 infection [15].

Our patient contracted the infection soon after she underwent hemispheric surgery for refractory epilepsy. She had abnormal kidney function tests at the time of the diagnosis of COVID-19 infection which could be attributed to long term medication exposure and low fluid intake perioperatively. At the time she had the infection, serious subtype, of COVID-19 infection was more prevalent globally. Her mild COVID-19 infection course following a major surgical intervention, in the setting of medical complications was in contrast to the course expected in patients with immunodeficiency and several neurological comorbidities.

The COVID-19 pandemic remains a significant health problem globally, despite the severity of the disease seem to decrease over time, new treatment approaches are needed particularly for patients with serious medical conditions.

**Conclusion**

We conclude that our patient might have had a mild course of COVID-19 due to prior IVIG and tacrolimus treatments, despite she had a serious neurological disease with refractory epilepsy, progressive motor and cognitive decline. Tacrolimus may be one of the immune-modulatory treatment options in selected patients with COVID-19 infection, further studies are required to determine its possible use.
Abbreviations

RE; Rasmussen encephalitis, IVIG; Intravenous immunoglobulin, ASM; Antiseizure medications, EEG; Electroencephalography, MIS-C; Multisystem inflammatory syndrome

Declarations

Ethics approval and consent to participate: Ethical approval was waived by the local Ethics Committee of University in view of the retrospective nature and case of the study and all the procedures being performed were part of the routine care. Written informed consent was obtained from the parent. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Consent for publication: Written informed consent was obtained.

Availability of data and material: Not applicable

Competing interests: The authors declare no conflicts of interests.

Funding: No

Authors' contributions: Sibel Öz Yıldız and Dilek Yalınıçoğlu contributed to design the study, collect the data, draft the initial manuscript, and revise the manuscript; Sibel Öz Yıldız, Ceren Günbey, Burçak Bilginer, Kader Karli Oguz, Bora Gülhan, Banu Anlar, and Dilek Yalınıçoğlu treated the patients and reviewed the manuscript; Sibel Öz Yıldız, Dilek Yalınıçoğlu, Ceren Günbey, Kader Karli Oguz collected data and reviewed the manuscript; Dilek Yalınıçoğlu contributed to design the work and critically review the manuscript and supervise the whole process; All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Acknowledgements: None

References


Figures
Figure 1

Representative axial Fluid-attenuated inversion-recovery (FLAIR) images obtained chronologically. At initial presentation of the patient (A), a subtle T2 hyperintensity in the left mesial temporal structures is seen (arrow) which is manifest along with volume loss at an image obtained a year later (double thin arrows B). Corresponding image at a year later, shows resection site with adjacent encephalomalasia of left temporal lobectomy including amygdalohippocampectomy (C). Fluid-filled space with basal ganglia atrophy and signal abnormalities due to performed left hemispherectomy is seen (D).