Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Author Contributions
Conceptualization: Come, Duarte, Lovero
Data curation: Come, Wainberg, Oquendo, Lovero
Formal analysis: Come, Polanco-Roman, Duarte, Lovero
Funding acquisition: Wainberg, Oquendo, Mello, Lovero
Investigation: Come, Lovero
Methodology: Come, Polanco-Roman, Pathare, Oquendo, Duarte, Lovero
Project administration: dos Santos, Mutemba
Resources: Fumo
Supervision: dos Santos, Fumo, Mutemba, Wainberg, Duarte, Mello
Writing — original draft: Come, Lovero
Writing — review and editing: Come, Polanco-Roman, dos Santos, Fumo, Mutemba, Pathare, Wainberg, Oquendo, Duarte, Mello, Lovero

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Correspondence to Kathryn L. Lovero, PhD, 722 West 168th Street, 9th Floor, New York NY 10032; e-mail: kll2153@cumc.columbia.edu

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Psychosis After Infection With SARS-CoV-2 in an Adolescent: A Case Report

To the Editor:

As many as one-third of patients who have COVID-19 develop long-term neuropsychiatric symptoms, such as anxiety, depression, brain fog, psychosis, seizures, and suicidal behavior.[1] Several case reports have demonstrated the association between psychotic symptoms following infection with COVID-19 in adults.[1,2] In a first episode of psychosis, clinical findings on history, examination, and diagnostic studies may suggest that the psychotic symptoms are due to medical illness, which may be reversible. The presentation can include acute onset, predominance of visual or tactile hallucinations, and association with other neurological symptoms.[3]

We present the case of an adolescent girl who developed an acute episode of psychosis after infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). She presented with psychosis soon after COVID-19 infection. Her laboratory tests were nonrevealing. She responded to olanzapine and was discharged within 5 days. It is important to recognize neuropsychiatric symptoms secondary to COVID-19 in the pediatric population.

CASE REPORT

A 15-year-old girl with no past psychiatric history and no significant family history was brought by her mother to the local emergency department for odd behavior. She had experienced difficulty sleeping for the past 3 days, and earlier that day she had begun acting erratically, telling others that it was time for her to die and complaining of seeing and feeling bugs in her hair. In the parking garage, she fell to the floor and exhibited seizure-like activity for approximately 2 minutes. Her mother reported that she and the rest of the family had been infected with coronavirus disease 2019 (COVID-19) approximately 2.5 weeks prior. The patient was treated with dexamethasone 4 mg for 5 days, which was finished 1 week before presentation without any ill effects. It is uncertain whether the patient's family members had received any type of steroid treatment. Nonetheless, the

TABLE 1 Laboratory Results From the Community Emergency Department and Johns Hopkins All Children's Hospital

Laboratory test	Result
Community emergency department	
β-HCG	Negative
SARS-CoV-2 rapid antigen	Negative
Complete blood count	
White blood cells, 10^9/L	7.8
Red blood cells, 10^{12}/L	4.29
Hemoglobin, g/dL	12.6
Hematocrit, %	39.2
Platelet count, 10^9/L	271
Lymphocytes, %	24 (low)
Neutrophils, %	64
Monocytes, %	12 (high)
Eosinophils, %	0 (low)
Comprehensive metabolic panel	
Sodium, mEq/L	141
Potassium, mEq/L	3.5
Chloride, mmol/L	111 (high)
Carbon dioxide, mmol/L	25
BUN, mg/dL	9
Creatinine, mg/dL	0.74
Glucose, mg/dL	95
Calcium, mg/dL	9.4
Magnesium, mg/dL	2.2
Total bilirubin, mg/dL	0.7
Aspartate aminotransferase, IU/L	19
Alanine aminotransferase, IU/L	27
Alkaline phosphatase, IU/L	69
Total protein, g/dL	7.9
Albumin, g/dL	3.5
Globulin gap, g/dL	4.4 (high)
Lipase, U/L	68
Creatine kinase, U/L	78
Ethyl alcohol, mg/dL	<3.0
Urinalysis	
Protein, mg/dL	100
Ketones, mg/dL	5
Nitrite	Positive
Urobilinogen, mg/dL	4.0
Leukocyte esterase, Leu/μL	Trace
Bacteria	Moderate
Blood, mg/dL	Negative
Glucose, mg/dL	Negative
Urine drug screen	
Opiates	Negative
Methadone	Negative
Phencyclidine	Negative
Amphetamines	Negative
Benzodiazepines	Negative
Cocaine	Negative
Marijuana	Negative
Troponin I, ng/mL	<0.04
Johns Hopkins All Children's Hospital	
C-reactive protein, mg/dL	0.03
Urine drug screen	
Opiates	Negative
Methadone	Negative
Phencyclidine	Negative
Amphetamines	Negative
Benzodiazepines	Negative
Cocaine	Negative
Marijuana	Negative
Ammonia, μmol/L	25
Urinalysis	
Protein, mg/dL	30
Ketones, mg/dL	40
Nitrite	Negative
Urobilinogen, mg/dL	4.0
Leukocyte esterase, Leu/μL	250
Bacteria	Rare
Blood	Negative
Glucose, mg/dL	Negative
Urine culture	No growth
Blood culture	No growth
Acylcarnitine panel	Negative
Very-long-chain fatty acid panel	Negative
Amino acid panel	Negative
Ceruloplasmin, mg/dL	30
Serum copper, ug/dL	103
Thyroid peroxidase antibody, IU/mL	<5
Thyroid-stimulating hormone, μIU/mL	0.19
T_4, ng/dL	1.06
Vitamin B_{12}, pg/mL	428
Folate, ng/dL	8.5
Urine organic acids	Negative
Chlamydia/gonorrhea PCR	Negative
Respiratory virus panel	
SARS-CoV-2	Positive
Adenovirus	Negative
Coronavirus 229E	Negative
Coronavirus HKU1	Negative
Coronavirus NL63	Negative
Coronavirus OC43	Negative
Human metapneumovirus	Negative
Rhinovirus/enterovirus	Negative

(continued)

TABLE 1 Continued

Laboratory test	Result
Influenza A	Negative
Influenza B	Negative
Parainfluenzae 1	Negative
Parainfluenzae 2	Negative
Parainfluenzae 3	Negative
Parainfluenzae 4	Negative
Respiratory syncytial virus	Negative
Bordetella pertussis	Negative
Bordetella parapertussis	Negative
Chlamydia pneumoniae	Negative
Mycoplasma pneumoniae	Negative
Encephalitis panel (serum)	
AMPA-R antibody	Negative
Amphiphysin antibody	Negative
AGNA-1	Negative
ANNA-1	Negative
ANNA-2	Negative
ANNA-3	Negative
CASPR2-immunoglobulin G	Negative
CRMP-5-immunoglobulin G	Negative
DPPX Ab IFA	Negative
GABA-B-R antibody	Negative
GAD65 antibody	Negative
GFAP	Negative
IgLON5	Negative
LGI1-immunoglobulin G	Negative
mGluR1 antibody	Negative
NIF	Negative
NMDA-R antibody	Negative
PCA-1	Negative
PCA-2	Negative
PCA type Tr	Negative
Cerebrospinal fluid results	
Volume	2 mL
Color	Colorless
Glucose, mg/dL	66
Protein, mg/dL	20
Red blood cells, per mm^3	218
White blood cells, per mm^3	2
Meningitis panel	
Escherichia coli	Negative
Haemophilus influenzae	Negative
Listeria monocytogenes	Negative
Neisseria meningitidis	Negative
Streptococcus agalactiae	Negative
Streptococcus pneumoniae	Negative
Cytomegalovirus	Negative
Enterovirus	Negative
Herpes simplex virus type 1	Negative
Herpes simplex virus type 2	Negative
Human herpesvirus 6	Negative
Human parechovirus	Negative
Varicella zoster	Negative
Cryptococcus gattii	Negative
Herpes simplex virus PCR	Negative
Anti-NMDA antibodies	Negative

(continued)

TABLE 1 Continued

Note: AGNA-1 = anti-glial nuclear antibody -1; AMPA-R = α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor; ANNA = anti-neuronal nuclear antibody; BUN = blood urea nitrogen; CASPR2 = contactin-associated protein 2; CRMP = collapsing response-mediator protein; DPPX Ab IFA = dipeptidyl aminopeptidase-like protein 6 antibody immunofluorescence assay; GABA-B-R = gamma aminobutyric acid type B receptor; GAD65 = glutamic acid decarboxylase 65-kilodalton isoform; GFAP = glial fibrillary acidic protein; HCG = human chorionic gonadotropin; IgLON 5 = immunoglobulin-like cell adhesion molecule 5; LGI1 = leucine-rich glioma inactivated 1; mGluR1 = metabotropic glutamate receptor 1; NIF = neuronal intermediate filament; NMDA-R= N-methyl-D-aspartate receptor; PCA-1 = Purkinje cell cytoplasmic autoantibody; PCR = polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; T_4, thyroxine.

patient was the only one of her family who presented with hallucinations. Initial laboratory tests including urine drug screen were negative (Table 1). While in the emergency department, the patient was alert and oriented but continued to experience paranoia, delusions, and hallucinations. She did not display any fluctuation in cognition, attention, or arousal. Psychiatric consultation was obtained, and the consulting physician recommended that further neurological workup, including lumbar puncture, be performed. The patient had an episode of agitation in which she reported hallucinations as well as anxiety and attempted to elope despite attempts at redirection. After receiving haloperidol for agitation, she was transferred to Johns Hopkins All Children's Hospital for further care.

At Johns Hopkins All Children's Hospital, her bizarre behavior persisted. She was suspicious of staff and appeared internally preoccupied. She began to ask permission excessively of her mother for meals and toileting. She described persistent hallucinations and delusions of reference. An extensive diagnostic evaluation was performed (Table 1). Magnetic resonance imaging of the brain, ultrasound of the ovaries and pelvis, and electroencephalogram were unremarkable. A lumbar puncture was performed with unremarkable cell counts, glucose levels, and protein levels. A meningitis panel and encephalitis panel were obtained and were negative. As the patient had a positive response to an olanzapine 5-mg disintegrating tablet that was given before imaging, olanzapine 5 mg was started at bedtime for persistent psychosis. An additional 2.5 mg was added in the morning within 2 days for an episode of paranoia after she attempted to stab the hospital sitter with a spoon. Her

symptoms improved, and she was discharged home within 5 days. At a follow-up appointment 1 week after discharge, her symptoms had all but resolved. As she continued to stabilize, the plan had been to gradually wean off olanzapine over the course of 6 months as tolerated. However, she was lost to follow-up.

DISCUSSION

There is limited information about the neuropsychiatric impact of COVID-19 infection in the pediatric population. In adults, neuropsychiatric symptoms associated with COVID-19 such as psychosis typically occur within days to weeks after the infection.[2] Children and adolescents have similarly shown that most neuropsychiatric symptoms develop after the acute respiratory infection resolves.[4] Our case adds to the emerging body of data on neuropsychiatric symptoms in youth with COVID-19 infection.

This patient had no past psychiatric history, and her presentation was not consistent with delirium, as she did not have disturbance in attention, awareness, or cognition. Although she received a short course of low-dose dexamethasone before the presentation of psychotic symptoms, there were no psychotic symptoms during the dexamethasone treatment. Additionally, she had completed the dexamethasone treatment more than 1 week before the onset of her psychotic symptoms, making the steroid exposure an unlikely cause of her symptoms.[5] Given that COVID-19 infection preceded the psychotic symptoms by 2 weeks, the remaining explanation was psychosis secondary to COVID-19 infection.

A notable strength of this case report is the thorough medical evaluation the patient received. Given her abrupt presentation of psychosis, she appropriately had a comprehensive medical workup for secondary causes of psychosis, and these were all negative or normal. While the neuropsychiatric symptoms of COVID-19 are typically thought to be due to inflammation, others have reported cases of adults in which inflammatory markers are normal, and the same has been seen in some cases of anti-*N*-methyl-D-aspartate receptor encephalitis.[6] One case series also described a teenager with psychosis after infection with COVID-19 who had normal serum inflammatory markers.[7] One possibility is that symptoms were mediated by a specific antibody or antibodies that are not routinely tested, such as those proposed by Bartley *et al.*[7] This may be one possible explanation for her elevated globulin gap.

This report has limitations. As a single case report, there is no comparison or control group. Causation cannot be definitively linked to infection with COVID-19. While many antibodies were tested in this patient, some specific antibody tests performed in other research studies were not available to perform.

This case highlights the potential for neuropsychiatric sequelae from COVID-19 infection in the adolescent age group. It is important for clinicians to recognize that such complications can arise in youth affected by COVID-19 so that treatment can be guided appropriately.

PATIENT PERSPECTIVE

With the medication, I felt like my body was able to work for me again. I was no longer seeing anything in the dark. I was no longer hallucinating.

Reena Thomas, MD
Michael J. Hernandez, MD
Roy Thomas, DO, MPH

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Dr. Thomas is with Johns Hopkins All Children's Hospital, St. Petersburg, Florida. Dr. Hernandez is with University of South Florida, Tampa. Dr. Thomas is with Northwestern McGaw Family Medicine Residency at Delnor Hospital, Geneva, Illinois.

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Author Contributions
Writing — original draft: Thomas, Hernandez, Thomas
Writing — review and editing: Thomas, Hernandez

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Correspondence to Reena Thomas, MD, Johns Hopkins All Children's Hospital, 880 6th Street South, Suite 420, St. Petersburg, FL 33701. e-mail: thomas.reena1@gmail.com

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