

COVID + Neurology

NORAN NEUROLOGICAL CLINIC

SEPTEMBER 8TH, 2020

CONOR RYAN

PEDIATRIC NEUROLOGY

Neurological Involvement

Children

- Rare

Adults

- Headache is most common symptom
- Dizziness frequently reported
- Complications in minority, but occur throughout the nervous system

Overview

- Neurotropism
- Pediatric involvement
- Adult involvement and stroke risk
- Chronic neurological disorders
- Telemedicine and neurology

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- **Neurotropism**
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Neurotropism

- Not strongly neurotropic per se
- Involves ACE2 receptors, infection often heralded with loss of smell from olfactory impairment
- Yet, limbic encephalitis is very rarely seen (contrasted to HSV encephalitis, with similar mode of entry)
- Autopsy studies showed (1) olfactory impairment limited to olfactory bulbs, (2) subcortical hemorrhages, (3) cortical and subcortical edema, and (4) nonspecific white matter abnormalities
 - Coolen T, et al. Early postmortem brain MRI findings in COVID-19 non-survivors. *Neurology*. 2020 Jun 16;10.1212/WNL.0000000000010116. doi: 10.1212/WNL.0000000000010116.

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Case Series of 4 pediatric patients

Study:

Neurologic and Radiographic Findings Associated With COVID-19 Infection in Children

Omar Abdel-Manna, MD; Michael Eyre MD; Ulrike Lobel, MD; et al.

JAMA Neurol. Published online July 1, 2020. doi:10.1001/jamaneurol.2020.2687

27 children with **multisystem inflammatory syndrome in children (MIS-C)**

4 (**15%**) with neurological symptoms (encephalopathy, headache, focal deficits)

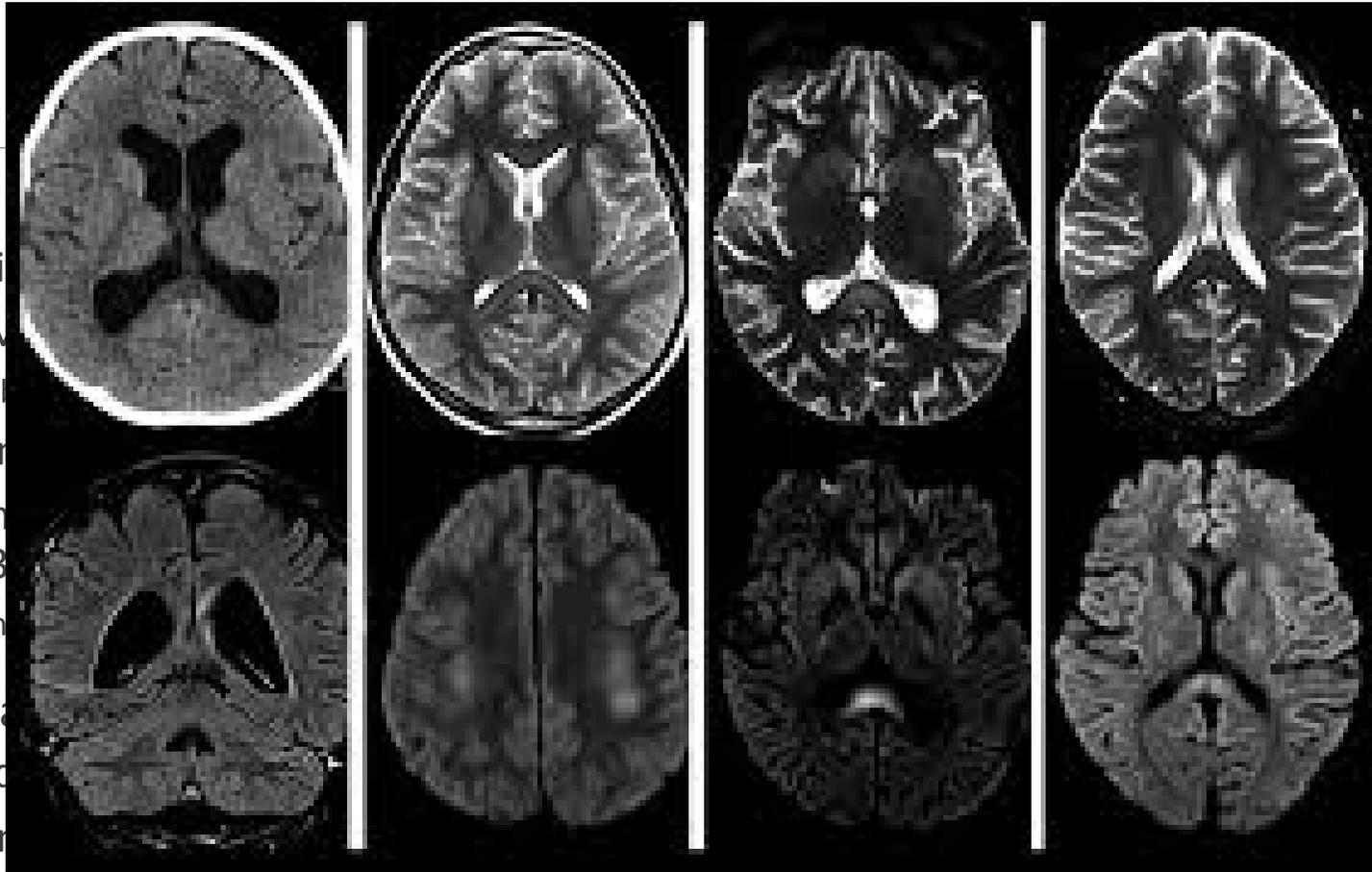
Case

Results

- 4 / 27 children
- All with MRI
- Afro-Caribbean
- Confusion
- Improvement days 17-30
- Treatment

Neurological

- Nothing
- CSF unremarkable



limited in 2 (50%,

n 1).

es negative.

Other pediatric case reports/series

Bilateral thalamic lesions in child with MIS-C

- Rash, fever, respiratory failure, cardiac dysfunction, encephalopathy; no concerning CSF findings.
- MRI with bilateral lateral thalamic changes; EEG with slowing; these improved by discharge on day 15
- Treatment: empiric antibiotics (48 hours), IV steroids, IV immunoglobulin, anakinra, prophylactic anticoagulation, and supportive therapy for MIS-C diagnosis
 - Abel D, et al. Encephalopathy and bilateral thalamic lesions in a child with MIS-C associated with COVID-19. Neurology. 2020; doi: 10.1212/WNL.0000000000010652.

Adult MRI – no distinctive findings

- Responsive to immunotherapy
 - Perrin P, et al. **Cytokine release syndrome-associated encephalopathy** in patients with COVID-19. Eur J Neurol. 2020; doi: 10.1111/ene.14491.
- Ischemic stroke (27%), leptomeningeal enhancement (17%), encephalitis (13%, younger); in 64 covid patients undergoing MRI
 - Kremer S, et al. Neurologic and neuroimaging findings in COVID-19 patients: A retrospective multicenter study. Neurology. 2020; DOI:10.1212/WNL.0000000000010112.

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Adult neurological involvement

Over >50% of hospitalized covid patients have neurological symptoms

- Nonspecific (common)
 - Headache
 - Dizziness
 - Altered mental status
 - Myalgia
- Focal neurological findings
 - Anosmia and dysgeusia (common)
 - Stroke
 - Demyelinating features (central or peripheral)
- Albacovid study in Spain: 841 patients (66 +/- 15 years) (Neurology 2020;95:e1060-e1070)
- Garcia-Monco JC, et al. Neurological manifestations in a prospective unselected series of hospitalized COVID-19 patients. *Neurol Clin Pract.* 2020; 1-25, doi:10.1212/CPJ.0000000000000913.
- Paterson RW, et al. The emerging spectrum of COVID-19 neurology: clinical, radiological and laboratory findings. *Brain.* 2020 Jul 8:awaa240. doi: 10.1093/brain/awaa240.

Adult studies

Central Nervous System

- Non-inflammatory Encephalopathy (normal imaging and CSF) – delirium
- Encephalitis/Encephalomyelitis/ADEM (some with hemorrhage) with para-infectious inflammation on imaging and in CSF – **immuno-responsive**
- Brainstem encephalitis/cerebellitis with confusion, ataxia, dysarthria, and dysphagia

Immune-therapy treatment of choice when indicated, with outcomes often favorable.

Cerebrovascular

- Cerebral infarctions, secondary to **hypercoagulable** state – most severe complications
- Vasculitis w/wo encephalitis, w/wo infarctions
- Posterior reversible encephalopathy syndrome (w/wo hemorrhage)

Peripheral Nervous System

- Guillain-Barre syndrome and inflammatory brachial plexopathy
- Generalized muscle weakness, proximal > distal
- No evidence for NMJ impairment

Risk of Acute Ischemic Stroke in adults

COVID -- 31 / 1916 (1.6%)

INFLUENZA -- 3 / 1486 (0.2%)

Odds ratio of **8.1**

- Merkler AE, et al. Risk of ischemic stroke in patients with Coronavirus Disease 2019 (COVID-19) vs patients with influenza. JAMA Neurol. 2020, doi:10.1001/jamaneurol.2020.2730.

Role for prophylactic anticoagulation. Consideration for children (severe MIS-C, risk factors).

- **1683 admissions, 23 (1.4%) developed ischemic or hemorrhagic stroke, with high morbidity and mortality**
 - Hernández-Fernández F, et al. Cerebrovascular disease in patients with COVID-19: neuroimaging, histological and clinical description. Brain. 2020 Jul 9:awaa239. doi: 10.1093/brain/awaa239.
- **844 admissions, 20 (2.4%) developed ischemic stroke in Philadelphia study, with high rates of cerebrovascular risk factors (95% hypertension, 60% diabetes, age >50, et al)**
 - Rothstein A, et al. Acute cerebrovascular events in hospitalized COVID-19 patients. Stroke. 2020 Jul 20:STROKEAHA120030995. doi: 10.1161/STROKEAHA.120.030995.
- **6 patients with underlying atherosclerosis and large vessel strokes during covid infection**
 - Lapergue B, et al. Large vessel stroke in six patients following SARS-CoV-2 infection: a retrospective case study series of acute thrombotic complications on stable underlying atherosclerotic disease. Euro J Neurol. 2020; 1-14, doi: 10.1111/ene.14466.

Rare complications in adults

Guillain Barre Syndrome

- Helbok R, et al. Guillain-Barré syndrome in a patient with antibodies against SARS-COV-2. Eur J Neurol. 2020 Jun 12. doi:10.1111/ene.14388.
- Kilinc D, et al. Guillian-Barré syndrome after SARS-CoV-2 infection. Eur J Neurol. 2020; doi:10.1111/ene.14398.

Miller Fisher and polyneuritis cranialis

- Gutiérrez-Ortiz C, et al. Miller Fisher syndrome and polyneuritis cranialis in COVID-19. Neurology. 2020 Apr 17; doi: 10.1212/WNL.0000000000009619.

Generalized myoclonus

- Rábano-Suárez P, et al. Generalized myoclonus in COVID-19. Neurology. 2020; doi:10.1212/WNL.0000000000009829.

Iatrogenic (?) brachial plexopathy injury (prone positioning for 11 days)

- Diprose WK, et al. Bilateral upper limb neuropathies following prone ventilation for COVID-19 pneumonia. Neurol Clin Pract. 2020, doi:10.1212/CPJ.0000000000000944.

EEG findings in adults

- EEGs revealed slowing in some patients.
- Periodic discharges seen uncommonly, generalized > lateralized with frontal involvement.
 - Periodic discharges could represent underlying brain injury from infectious/parainfectious process.
- No other potentially epileptogenic abnormalities.
 - Vespignani H, et al. Report of EEG Finding on Critically Ill Patients with COVID-19. *Ann Neurol*. 2020; doi:10.1002/ana.25814.

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Epilepsy

No significant associations between COVID and patients with epilepsy

No special precautions for management

Parkinson Disease

No increased rates of disease incidence, disease complications, or Parkinson's symptoms

Based on one cohort of nonadvanced PD patients ->

COVID-19 risk and mortality did not differ from the general population

(Fasano A, et al. COVID-19 in Parkinson's disease patients living in Lombardy, Italy. *Mov Disord.* 2020 Jul;35(7):1089-1093. doi: 10.1002/mds.28176.)

Guidelines

Multiple Sclerosis

- Conflicting data on if disease-modifying therapy / immunosuppression leads to higher risk of COVID
- Guidelines available for isolating after pulse therapy, spacing dosing intervals of infusions, etc
 - Spreading natalizumab to every 6 weeks (vs every 4 weeks)

Neuromuscular disorders and EMG performance

- via American Academy of Neuromuscular and Electrodiagnostic Medicine

Infantile spasms

- via Child Neurology Society

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Tele-medicine

Personal experience – improved care

- Able to arrange earlier and more frequent visits to manage control of seizures/headaches/etc and medication side effects, especially helpful for those living distant from clinic.

One study on the topic (~90% satisfaction by providers and caregivers, ~5% needed in-clinic f/u)

- The authors concluded that telehealth was rapidly and satisfactorily implemented in a child neurology outpatient setting, and that preliminary findings indicate sustainability post-pandemic.
- Rametta SC et al. Analyzing 2,589 child neurology telehealth encounters necessitated by the COVID-19 pandemic [published online ahead of print 2020 Jun 09]. *Neurology*. 2020.
doi: 10.1212/WNL.0000000000010010.

Summary

Neurotropism

- Despite olfactory bulb involvement, little evidence of spread to brain.

Pediatric involvement

- Most neurological complications of COVID in children (central and peripheral nervous systems) are rare, and usually exist as complications of multisystem inflammatory syndrome (15% of MIS), and can be amenable to immunotherapy.
- Neurological testing in children notable for MRI abnormalities in splenium of corpus callosum.

Adult involvement and stroke risk

- Distinctive EEG or CSF findings are not present; variable MRI findings in adults
- Inflammatory encephalopathy treatable with immunotherapy
- Cerebral infarction from hypercoagulable state occurs in 1.6% of adults, suggesting anticoagulation may be beneficial in stroke prevention. Need in children can be considered.

Chronic neurological disorders

- No effect on epilepsy, Parkinson disease, and most chronic neurological disorders.
- Guidelines available for management of neurological disorders and immunosuppression.

Telemedicine

- Telemedicine has been working well and is promising form of care regardless of epidemic.