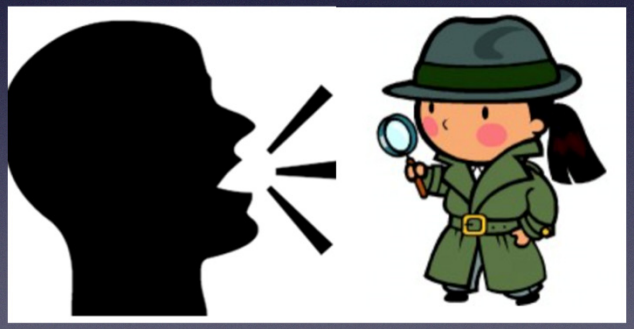
Division of Geriatric Medicine Noon Rounds

Rapidly progressive dementia with language changes: Case presentation and Discussion



May 8, 2023

Objectives

- By the end of this presentation, participants will be able to:
  - Discuss an atypical presentation of a rapidly progressing dementia
  - Describe an approach to the work up for rapidly progressive dementias and the differential diagnosis for potential causes

Case Presentation

- Mr. DJP, 75 year old gentleman referred to Elder Care Outpatient Clinic
- Attended his appointment accompanied by his wife
- Rapid cognitive decline x 6 months

Past Medical History

- Myocardial infarction, February 2011
- Required IABP. CABG with MVR. Difficult to wean off ECMO. LVAD as bridge to heart transplantation July 2011
- Followed by Heart Transplant Clinic
    - Mycophenylate and tacrolimus for immunosuppression
- No reported cognitive concerns

Case Presentation

- March 2022 - difficulties with word finding, particularly nouns
  - Occurred occasionally
  - Remarked to be “out of character”
- Word finding problems, much more noticeable
  - Frequent interruptions in speech due to searching for words
  - Comprehension intact

Case Presentation

- Over 6 months, noticeable progressive language deterioration
- Reduced spontaneous verbal communication
- Able to say short sentences -> yes/no answers
- Word substitutions
- Cognitively slower, problems understanding longer sentences and instructions

Case Presentation

- More socially withdrawn
  - Frustration, but no inappropriate behaviours
- ? Clumsy right hand - poor coordination, dropping items
- Slurring words
- Drooling, slight problems with swallowing

Medications

Allergies: tetracycline - confusion

- Amlodipine 5 mg daily
- ASA EC 81 mg daily
- Calcium carbonate 500 mg daily
- Vitamin D3 1000 units daily
- Finasteride 5 mg QHS
- Mycophelynate 540 mg BID
- Ramipril 2.5 mg QHS
- Tacrolimus 0.5 mg BID
- Tamsulosin 0.4 mg QHS

Functional History

- Independent with basic activities
- Able to assist with shopping, food prep, cleaning and vacuuming
- No longer able use the computer or TV remote
- Stopped driving

Social History

- Born in Montreal, retired travel agent
- Married x 45 years
- 2 children, son (Calgary) and daughter (San Diego)
- Lives in a split level entry home
- Non-smoker, occasional ETOH, no other recreational drugs

Family History

- No family history of neurological disorders

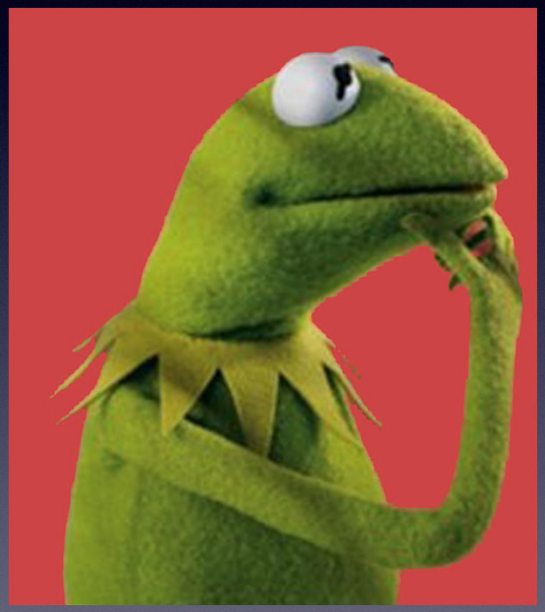
Exam

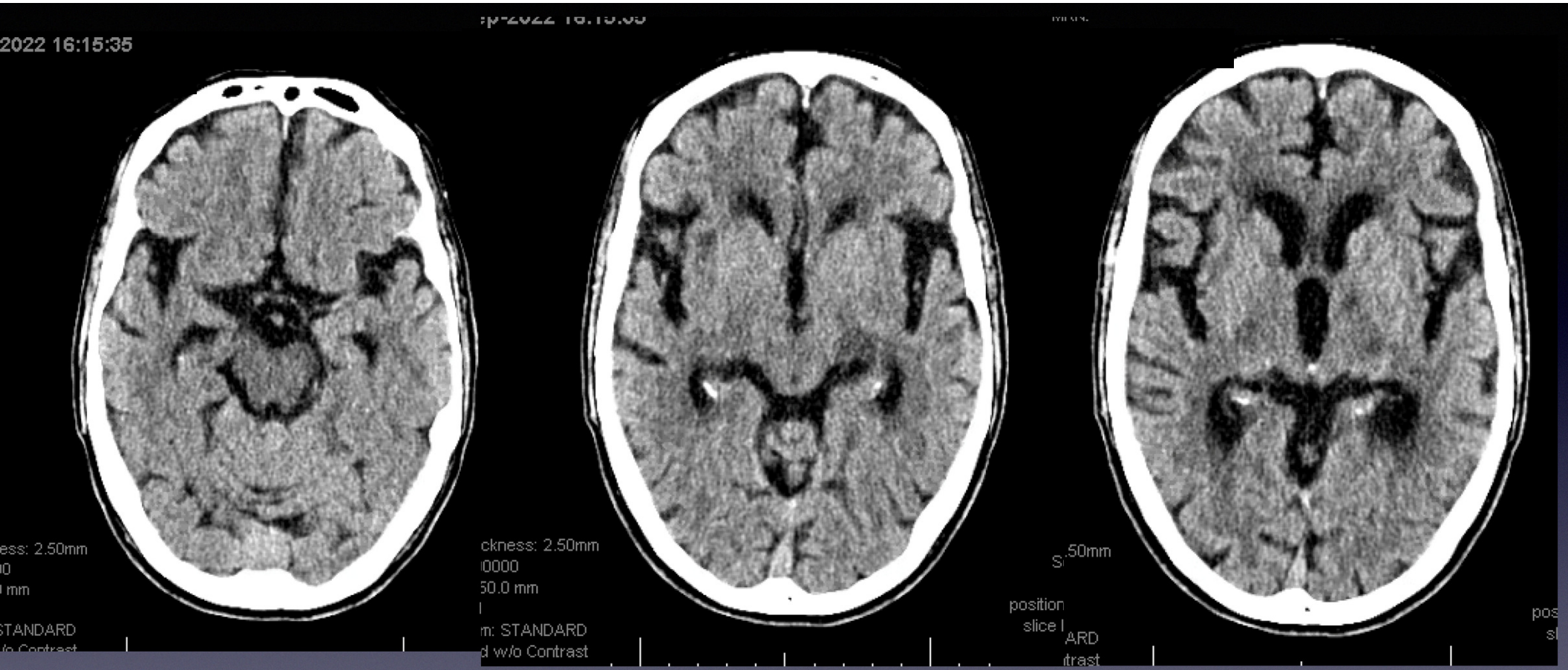
- Afebrile. BP 106/81 mm Hg. HR 99 bpm. RR 14 br/min. 97% on RA
- PERL. Full EOM. Visual fields intact. Mild facial droop right. CN normal.
- Motor - 4/5 right UE extension at elbow and wrist
- Sensory exam, limited due to comprehension, but normal LT/pin prick
- Reflexes brisk bilaterally
- Hoffman sign absent, plantar reflexes equivocal

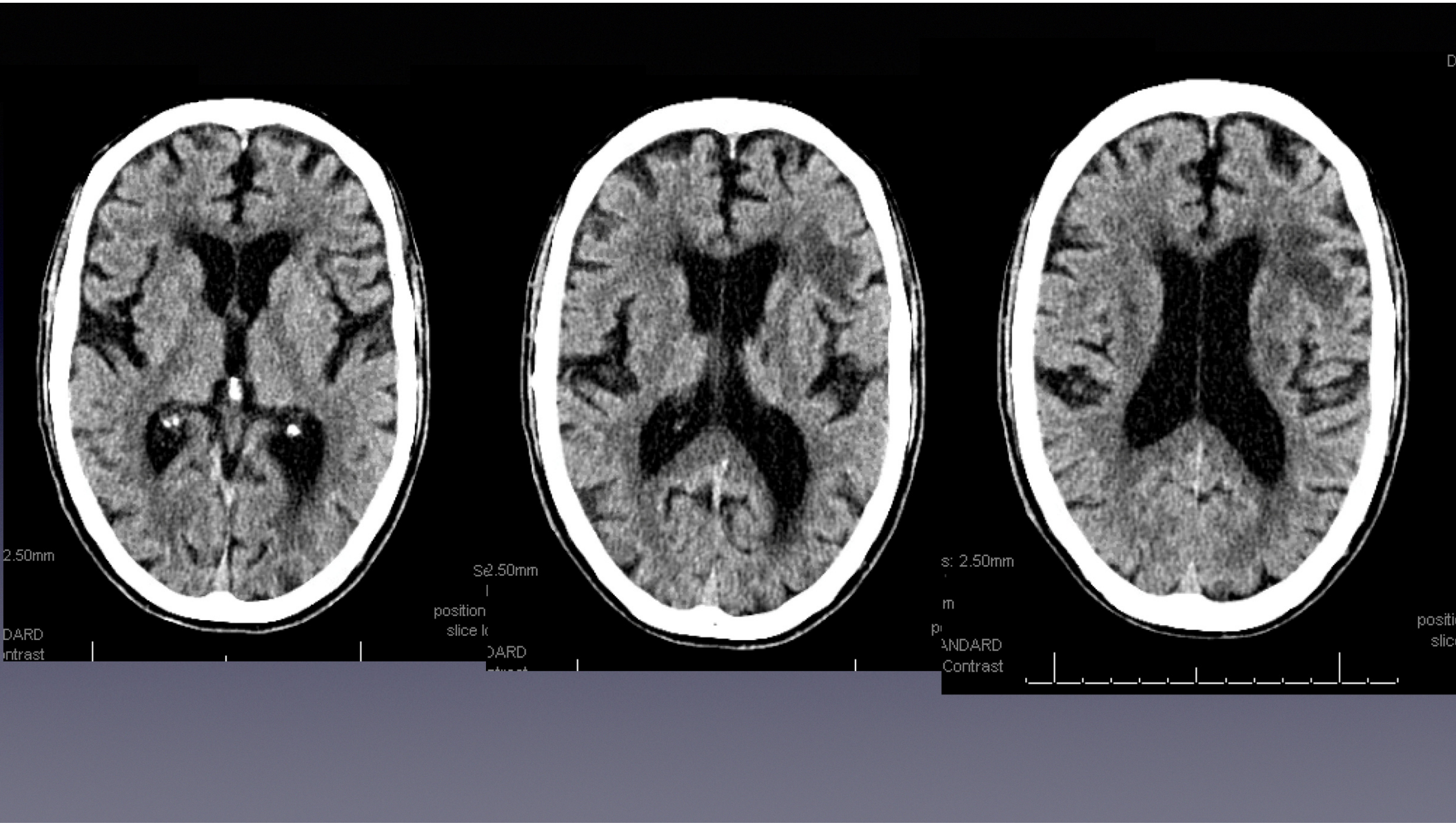
- Reduced spontaneous speech. Effortful, dysarthric speech. Slow speed. Expressive aphasia. Perseverated on certain words and phrases. e.g. repeated his birthday to answer numerous questions.
- Repetition intact at length of a few words and simple phrases
- Difficulty describing “Cookie theft picture” and naming items/pictures
- Auditory comprehension better, following simple instructions and pointing of objects in the room

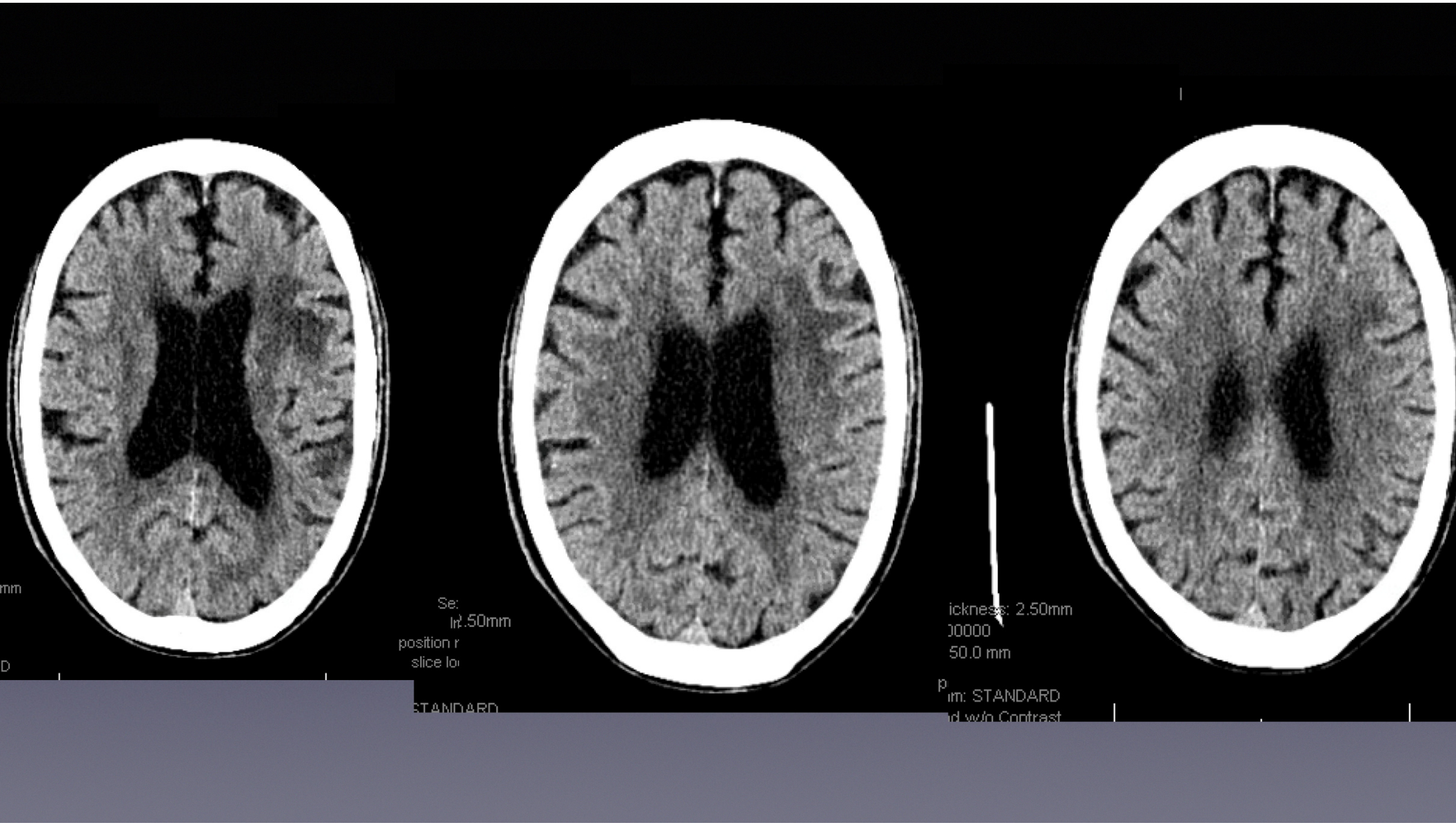
- Attempted MoCA, then MMSE - could not complete tests
- Able to draw simple geometric shapes
- Could write simple words

Thoughts?




2022 16:15:35
ckness: 2.50mm
50.0 mm
m: STANDARD
d w/o Contrast
position
slice l
ARD
trast

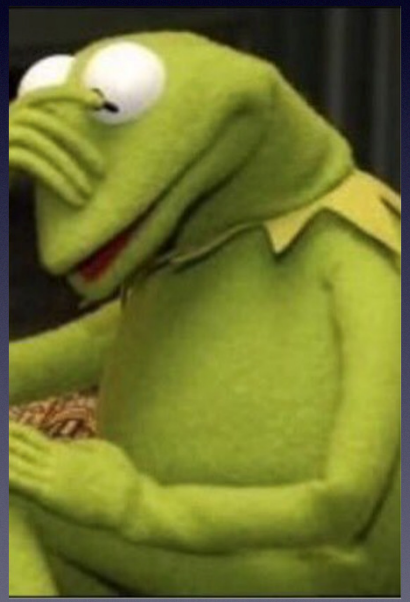

2.50mm
position
slice
Contrast


Se:
.50mm
position r
slice lo
STANDARD
ickness: 2.50mm
00000
50.0 mm
m: STANDARD

CT Scan

- Generalized atrophy
- Background changes consistent with small vessel disease
- Confluent area of attenuation in superior left frontal lobe

Thoughts?



Case Presentation

- Rapid progressive decline in language with more recent atypical features
- Abnormal CT findings
- Less likely to be typical neurodegenerative disease

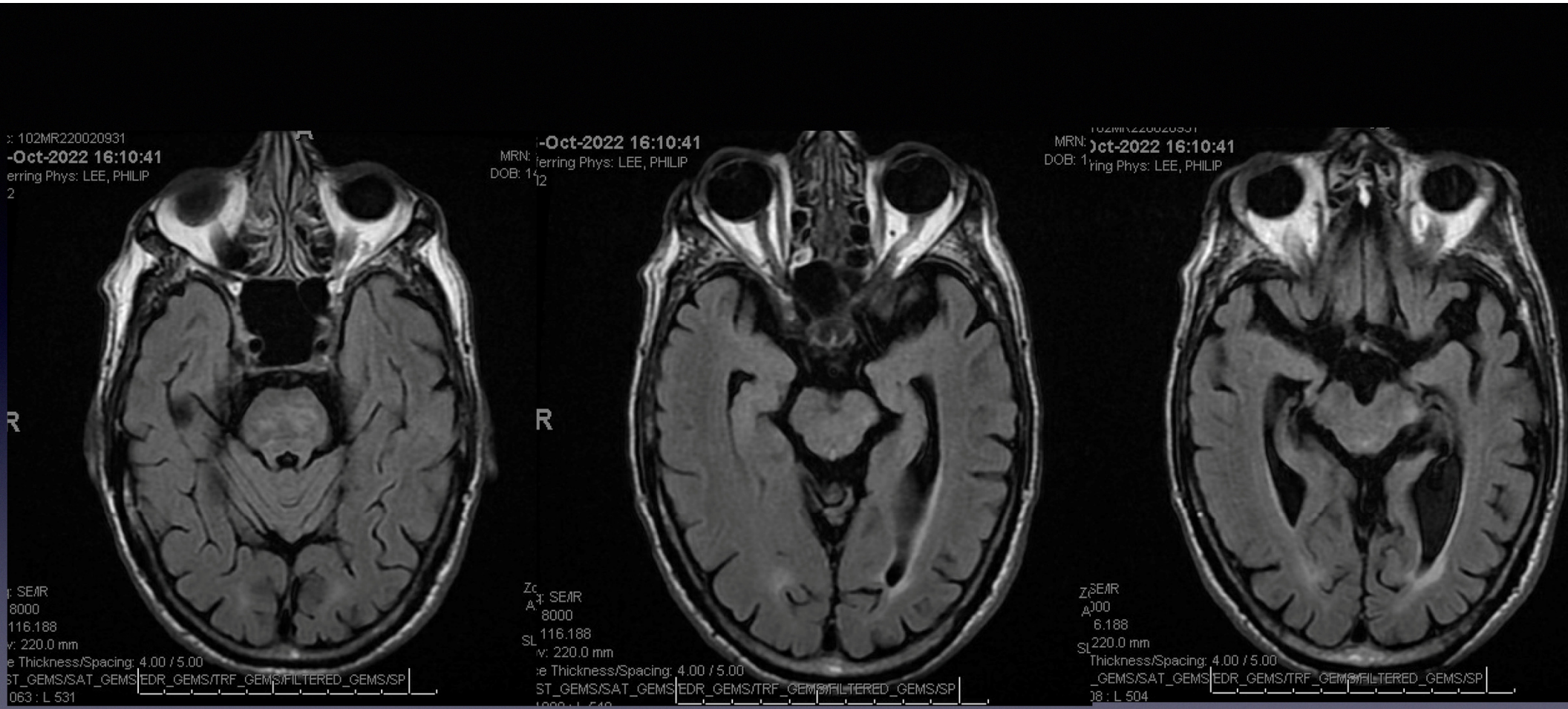
- Immunocompromised state
  - Infectious, VZV, HSV, PML
  - Inflammatory, ADEM
  - Neoplastic, lymphoma
- Paraneopastic

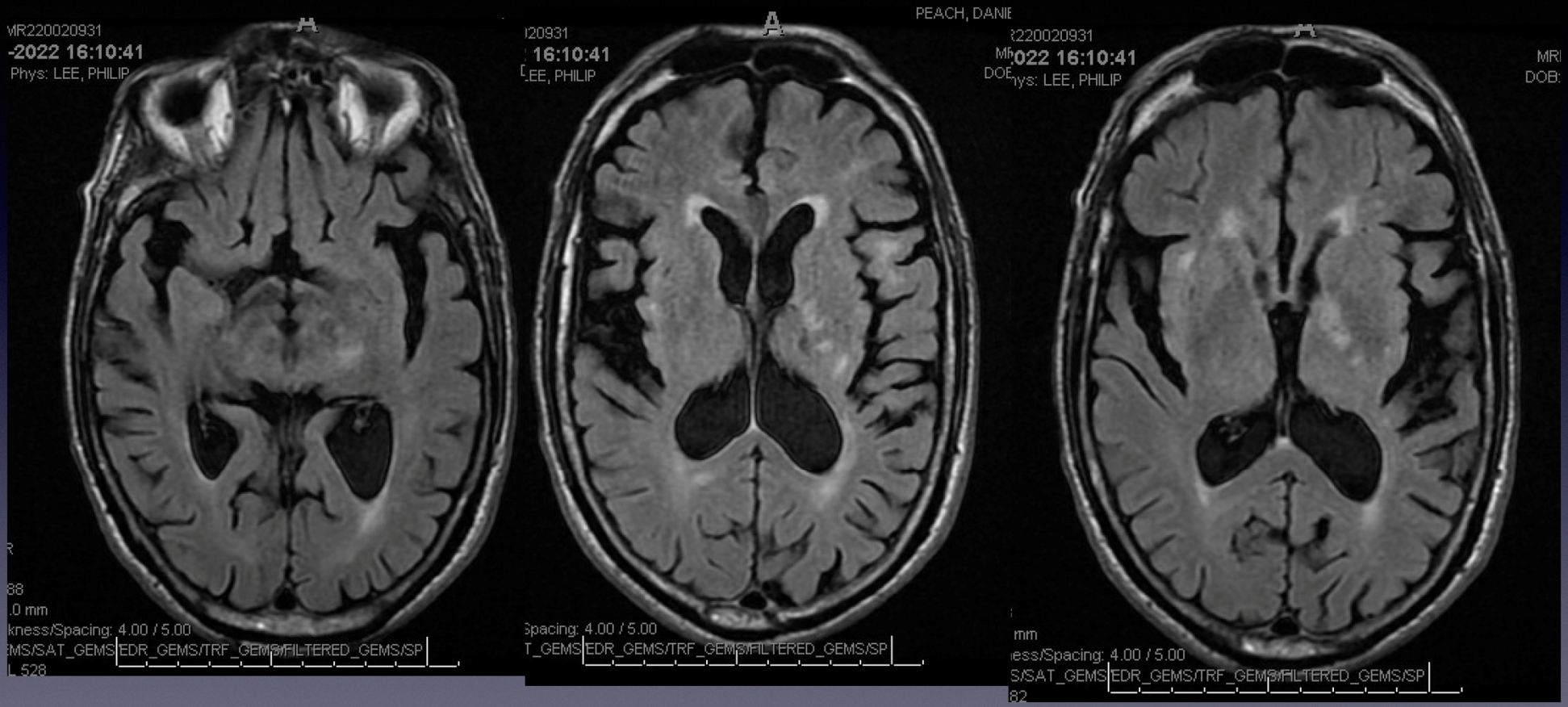
Case Presentation

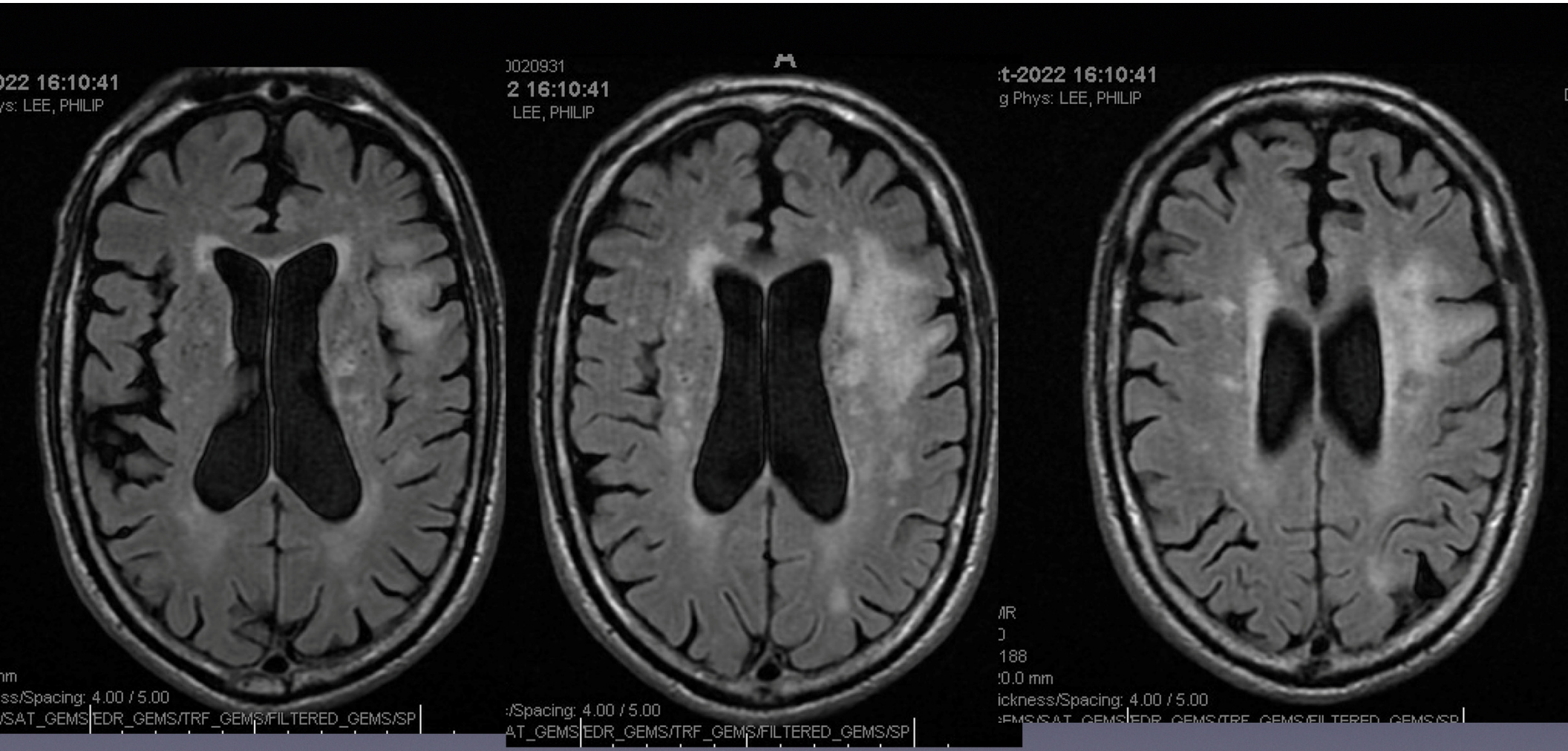
- Needs further investigations to determine etiology
- Needs MRI, LP, bloodwork
- Given rapidity of decline and complexity of investigations, admitted to Geriatric Medicine (*Huge thanks to my colleagues)
- Consultation requested from Neurology and Heart Transplant team

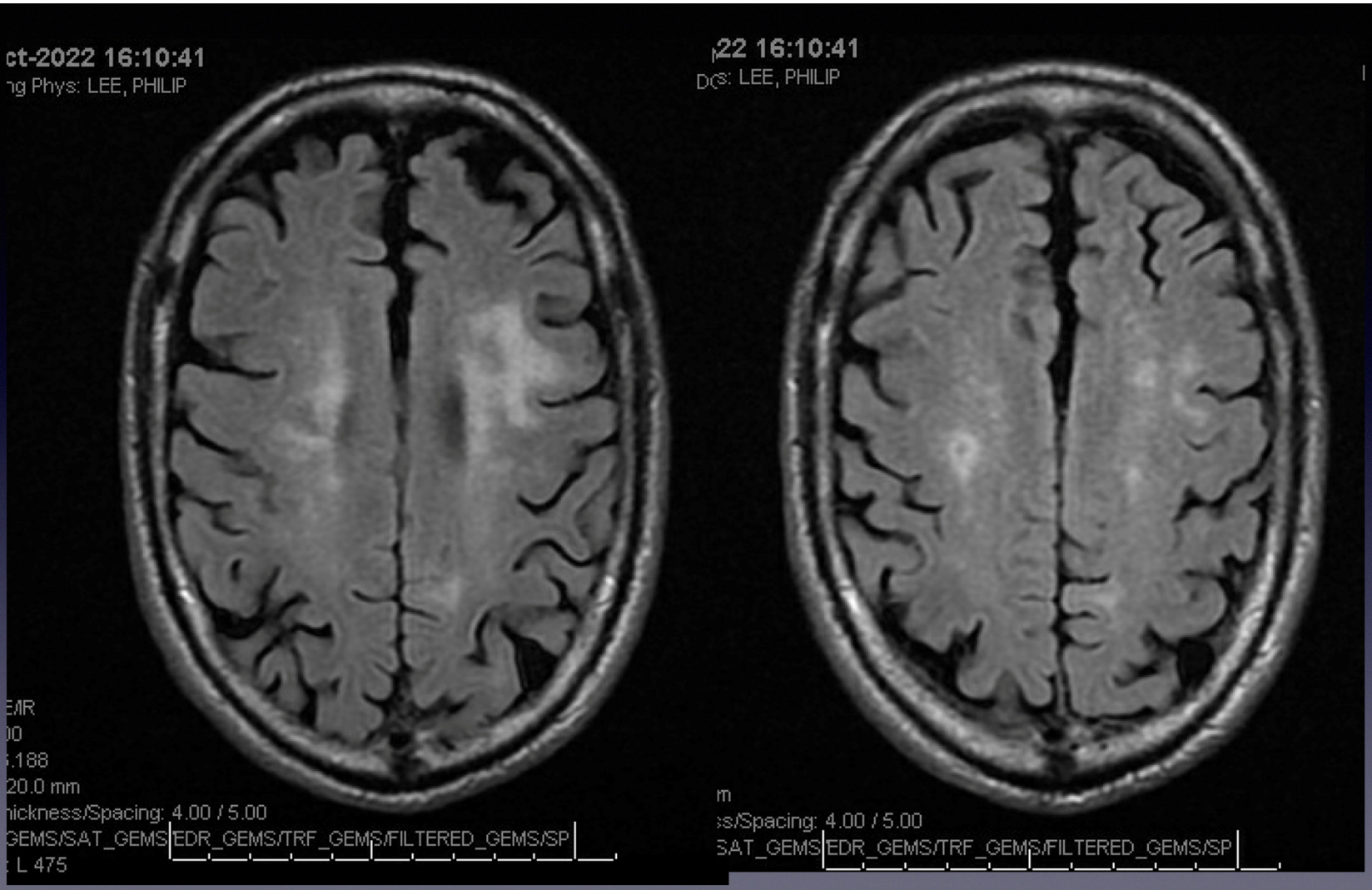
Labs and other investigations

- CBC, electrolytes including extended, GFR normal. TSH and B12 normal. CRP 0.5. Tacrolimus level normal.
- Paraneoplastic/encephalitis panel sent
- CT chest/abdo/pelvis - lungs clear, small GB stones, solid organs normal. No malignancy identified.


: 102MR220020931
-Oct-2022 16:10:41
erring Phys: LEE, PHILIP
2
R
: SE/IR
8000
116.188
v: 220.0 mm
e Thickness/Spacing: 4.00 / 5.00
ST_GEMS/SAT_GEMS
EDR_GEMS/TRF_GEMS/FILTERED_GEMS/SP
063 : L 531
MRN:
DOB:
-Oct-2022 16:10:41
erring Phys: LEE, PHILIP
12
R
SE/IR
8000
116.188
v: 220.0 mm
e Thickness/Spacing: 4.00 / 5.00
ST_GEMS/SAT_GEMS
EDR_GEMS/TRF_GEMS/FILTERED_GEMS/SP
MRN:
DOB:
Oct-2022 16:10:41
ring Phys: LEE, PHILIP
SE/IR
000
6.188
220.0 mm
Thickness/Spacing: 4.00 / 5.00
_GEMS/SAT_GEMS
EDR_GEMS/TRF_GEMS/FILTERED_GEMS/SP
08 : L 504


MR220020931
-2022 16:10:41
Phys: LEE, PHILIP
A
.0 mm
kness/Spacing: 4.00 / 5.00
MS/SAT_GEMS
EDR_GEMS/TRF_GEMS/FILTERED_GEMS/SP
L_528
20931
16:10:41
LEE, PHILIP
A
Spacing: 4.00 / 5.00
T_GEMS
EDR_GEMS/TRF_GEMS/FILTERED_GEMS/SP
PEACH, DANIE
220020931
022 16:10:41
ys: LEE, PHILIP
DOB:
A
mm
ess/Spacing: 4.00 / 5.00
S/SAT_GEMS
EDR_GEMS/TRF_GEMS/FILTERED_GEMS/SP


022 16:10:41
ys: LEE, PHILIP
ss/Spacing: 4.00 / 5.00
/SAT_GEMS|EDR_GEMS/TRF_GEMS/FILTERED_GEMS/SP
)020931
2 16:10:41
LEE, PHILIP
:/Spacing: 4.00 / 5.00
AT_GEMS|EDR_GEMS/TRF_GEMS/FILTERED_GEMS/SP
:t-2022 16:10:41
g Phys: LEE, PHILIP
/R
188
0.0 mm
ickness/Spacing: 4.00 / 5.00


ct-2022 16:10:41
ng Phys: LEE, PHILIP
E/IR
00
.188
20.0 mm
hickness/Spacing: 4.00 / 5.00
GEMS/SAT_GEMS|EDR_GEMS/TRF_GEMS/FILTERED_GEMS/SP
L 475
22 16:10:41
DG: LEE, PHILIP
m
s/Spacing: 4.00 / 5.00
SAT_GEMS|EDR_GEMS/TRF_GEMS/FILTERED_GEMS/SP

MRI

- Focal area of T2 hyperintensity within the superior left frontal lobe which extends to the juxtacortical white matter with mild expansion of the gyrus.
- There is no abnormal enhancement after gadolinium.
- There is no mass effect.
- No hemorrhage.

Lumbar Puncture

- Volume 4 cc
- CSF clear and colourless
- WBC cell count, 1 x 10^6/L
- Red cell count, 2 x 10^6/L
- Glucose CSF 3.5 mmol/L
- Protein CSF 0.51 g/L (elevated)

Lumbar Puncture

- VDRL CSF negative
- Cryptococcus Ag negative
- Mycobacteria CSF negative
- **JC virus PCR positive**

Progressive Multifocal Leukoencephalopathy

- Caused by Polyomavirus 2 JC virus
- Disease of white matter
- Carried by majority of people
- Rare disease
- Occurs in patients who are immunocompromised (most commonly HIV/AIDS) or with underlying immunosuppressive therapy

Progressive Multifocal Leukoencephalopathy

- Symptoms typically are related to the area of brain involved
- Clumsiness, progressive weakness
- Visual changes, speech problems, personality changes

Diagnosis of PML

- MRI, confluent white matter lesion on T2 imaging (CT may show low-density, nonenhancing lesions but is less sensitive)
- CSF, detection of JC virus (negative test dose not rule out PML)
- Blood and urine tests not helpful
- Brain biopsy is gold standard
  - Multifocal demyelination, enlarged oligodendrocytes with nuclear inclusions, large astrocytes, reactive gliosis
  - Immunohistochemistry - JCV staining

Prognosis

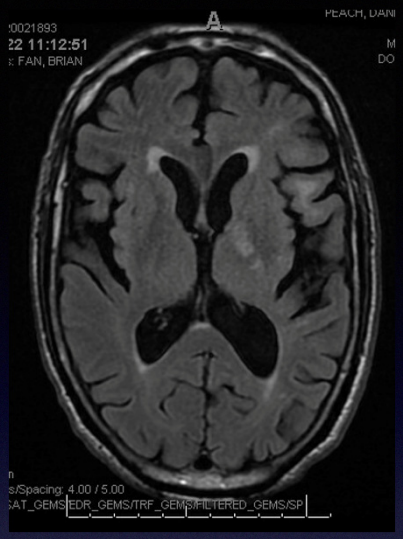
- Mortality rate 30-50% within months
- Depends of severity and treatment
- Even those who survive may be left with severe neurological disabilities

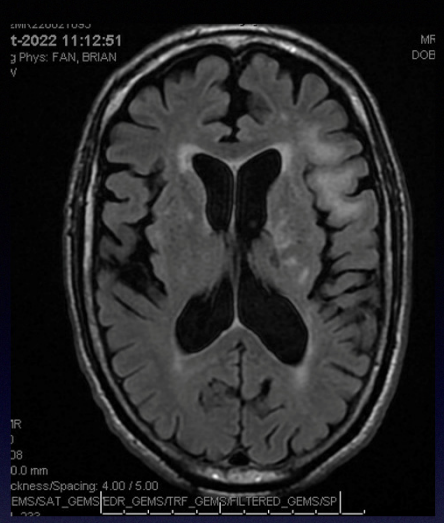
Treatment

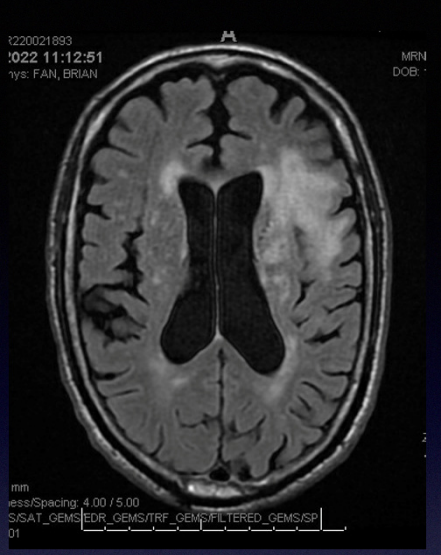
- Immunocompromised individuals - reversal of immune-deficient state
  - HIV positive - optimize ART
  - Watch for immune reconstitution inflammatory syndrome (IRIS)
- Mefloquine, filagastrim, IL-7, limited information
- Very small trial reporting some success with check point inhibitors, pembrolizumab and nivolumab

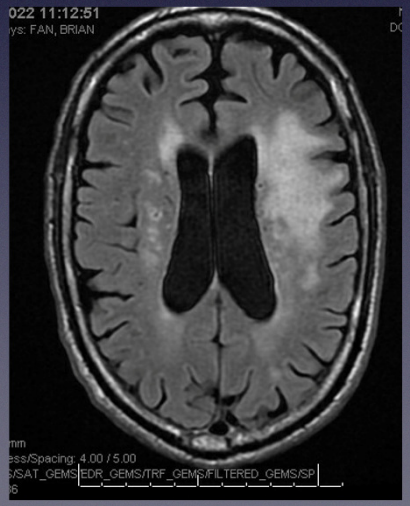
Case Presentation - Progress

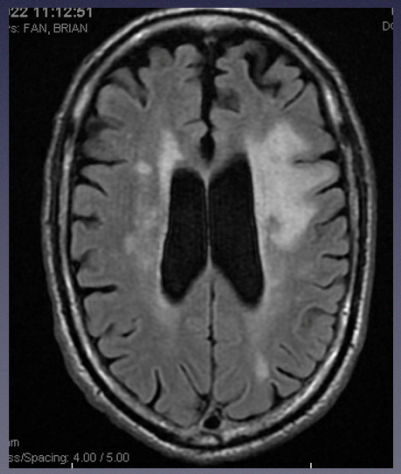
- Under guidance of Cardiology, discontinued mycophenylate.
  - Watched for IRIS.
- SLP - swallowing issues, more drooling. Decreased auditory comprehension
- Mobility - 2 WW, see by PT; A few falls in hospital
- Repeat MRI, supra and infratentorial white matter process with minimal progression over 3 weeks

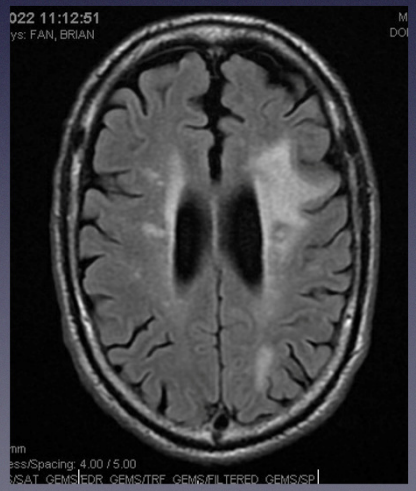

PEACH, DANI
22 11:12:51
FAN, BRIAN
Spacing: 4.00 / 5.00


t-2022 11:12:51
Phys: FAN, BRIAN
Spacing: 4.00 / 5.00


022 11:12:51
ys: FAN, BRIAN
Spacing: 4.00 / 5.00


022 11:12:51
ys: FAN, BRIAN
Spacing: 4.00 / 5.00

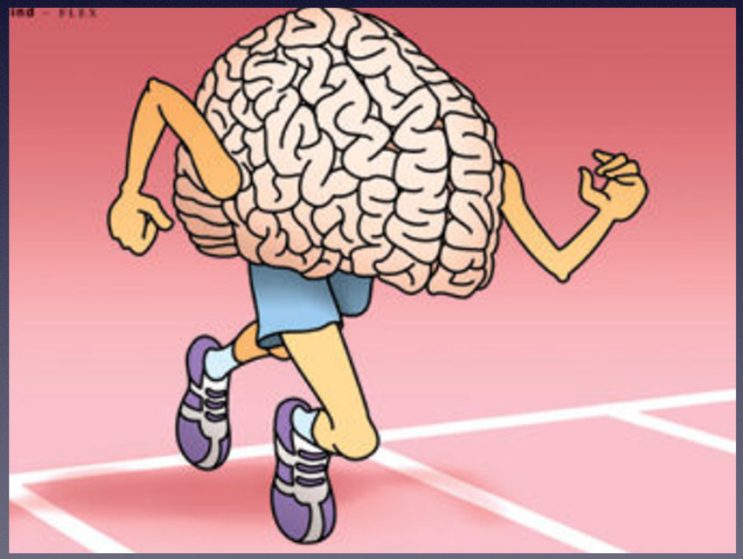

22 11:12:51
s: FAN, BRIAN
Spacing: 4.00 / 5.00


022 11:12:51
ys: FAN, BRIAN
Spacing: 4.00 / 5.00

Progress

- Goals of care discussed
- Palliative approach
- Discharge to home with supports, November 2022
- Over next month, progressive decline.
- Seizures, treated with phenobarbital/midazolam
  - Obtunded, but comfortable
- Passed away in Hospice in mid-December 2022

Rapidly Progressive Dementia



Rapidly Progressive Dementia

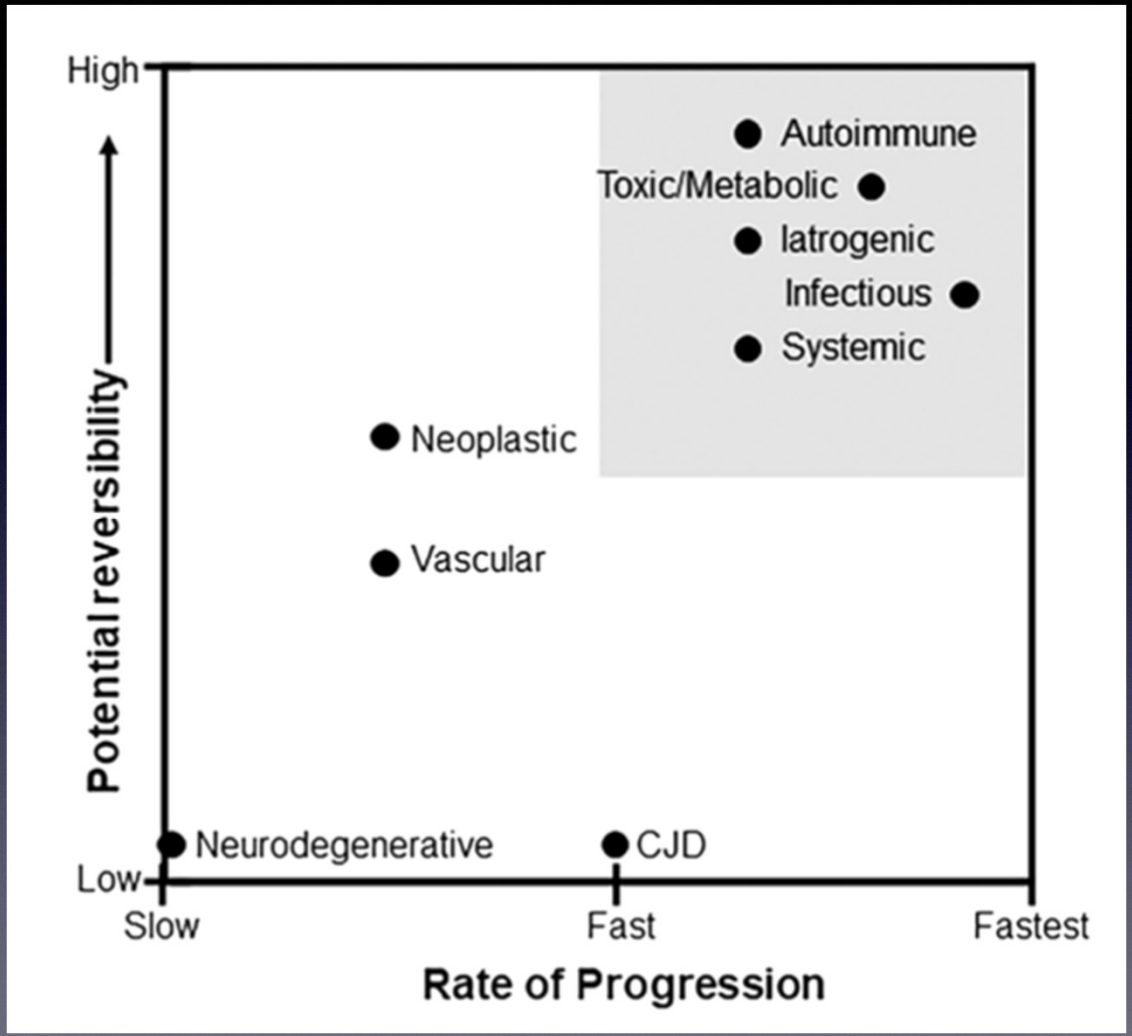
- Generally less than 1 - 2 years
  - Practically, consider when changes unfold over months
- Cognitive or behavioural decline fulfilling criteria for dementia
- Relatively “uncommon”, but it depends…

Differential Diagnosis for RPD

VITAMINS

- Vascular
- Infectious
- Toxic/metabolic
- Autoimmune
- Metastatic/neoplastic
- Iatrogenic
- Neurodegenerative
- Systemic/seizures

Geschwind MD et al. Neurologic Clinics 2007



Day GS et al. Neurodegen Dis Manag 2014

Rapidly Progressive Dementia Workup

- History and physical examination
  - Plus detailed family history, medical and travel history
- Bloodwork, routine and include infectious and autoimmune workup
  - Genetic testing, where appropriate
- Urinalysis
- Lumbar Puncture (non-specific; signs of rapid neurodegeneration like 14-3-3, RT-QuiC)
- MRI (FLAIR/DWI)
- EEG (slowing or sharp wave, seizure)
- CT or PET workup for malignancy

Improving Recognition of treatable RPD

- n=154 with RPD, 82/154 (53%) had potentially reversible causes
- Autoimmune (62.2%), vasculopathies (20.7%), psychiatric conditions (4.8%) and nutritional deficiencies (4.8%)
- Younger age (OR 1.22; 95%CI 1.11-1.36)
- Seizures (OR 6.86; 95%CI 2.27-20.68)
- CSF pleocytosis (OR 6.47; 95%CI 2.36-17.84)
- MRI features (OR 6.19; 95%CI 1.21-31.79)

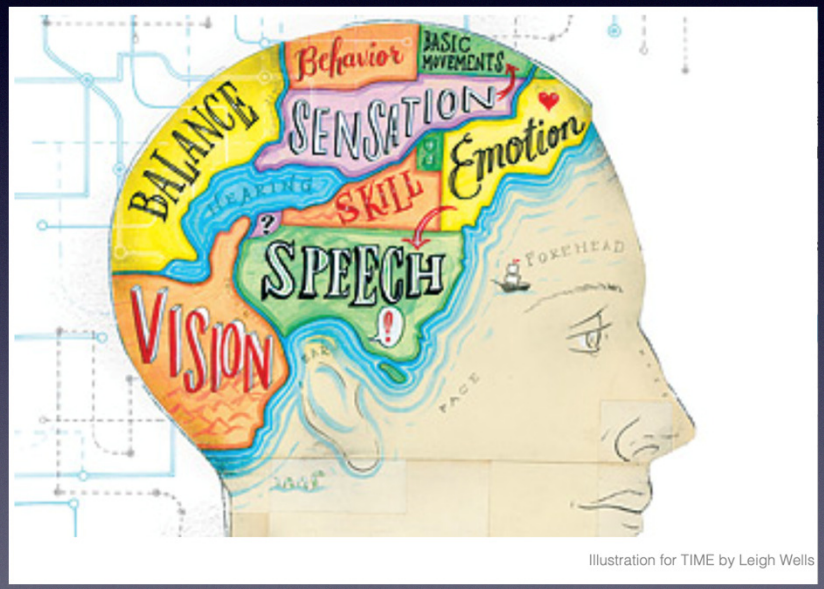
Satyadev N et al. AAN 2023

Etiology	Routine CSF tests			
	Nucleated cells	Protein	Glucose	Oligoclonal bands/ IgG index
Vascular				
Ischemic	↔	↑	↔	↔
Hemorrhagic	↑	↑	↔	↔
Vasculitis	↑↑	↑	↔	↔
Infectious				
Bacterial	↑↑↑	↑↑	↓↓	↑/↔
Viral	↑↑	↑↑	↔	↑/↔
Fungal	↑↑	↑	↓↓	↑/↔
Toxic-metabolic	↔	↑/↔	↔	↔
Autoimmune/inflammatory	↑↑	↑/↔	↔/↓	↑/↔
Metastases/neoplastic	↑/↔	↑/↔	↔	↔
Iatrogenic	↔	↔	↔	↔
Neurodegenerative	↔	↑/↔	↔	↔
Systemic/seizures/structural	↔	↑/↔	↔	↔

Day GS. Continuum. AAN 2022.

Atypical Clinical Phenotypes for Dementia

- Language
- Visuospatial
- Behavioural/Executive
- Motor



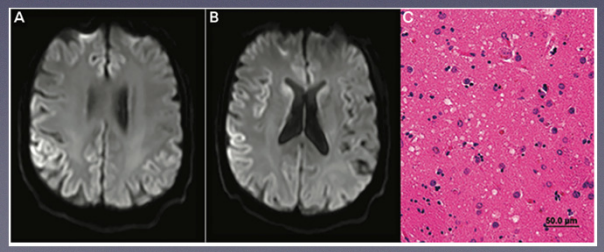
Time Magazine 2007

Prion Disease

- Sporadic CJD (85%)
  - Usually presents after age 60
  - Rapid deterioration, most die within 1 year, average about 6 months
- Genetic CJD (15%)
  - Can present rapidly or with slower progression
  - e.g., GSS or Familial fatal insomnia
- Acquired CJD (<1%)
  - Exceedingly rare
  - Iatrogenic or BSE

Sporadic CJD

- Often misdiagnosed or initially missed
  - Non-specific symptoms first (fatigue, sleep disturbance, decreased appetite, behavioural issues)
- Cognitive Impairment
- Visual, cerebellar problems, gait ataxia or incoordination
- Myoclonus
- Akinetic mutism



Real-time quaking-induced conversion

- RT-QuIC CSF assay
- Misfolded prion protein (PrP) aggregates
- Diagnosis of sporadic CJD
- Best sample, clear, colourless, low WBC and protein

Table 1
Performance Characteristics if the NML PLS CJD Assay Panel*

Marker	Sensitivity (95% CI**)	Specificity (95% CI**)
EP-QuIC (n=91)	98% (88%-100%)	96% (85%-99%)
14-3-3 (n=1000)	88% (81%-93%)	72% (69-75%)
Tau (n=1000)	91% (84%-95%)	88% (85%-90%)

* Adapted from "A guide to the cerebrospinal fluid protein marker panel and EP-QuIC testing for sporadic Creutzfeldt-Jakob disease," client email document
** 95% Confidence Interval

Autoimmune Encephalitis

- Subacute short term memory deficits
- Seizures
- Neuropsychiatric features
- MRI scan - medial temporal lobe abnormalities
- EEG and/or CSF analysis

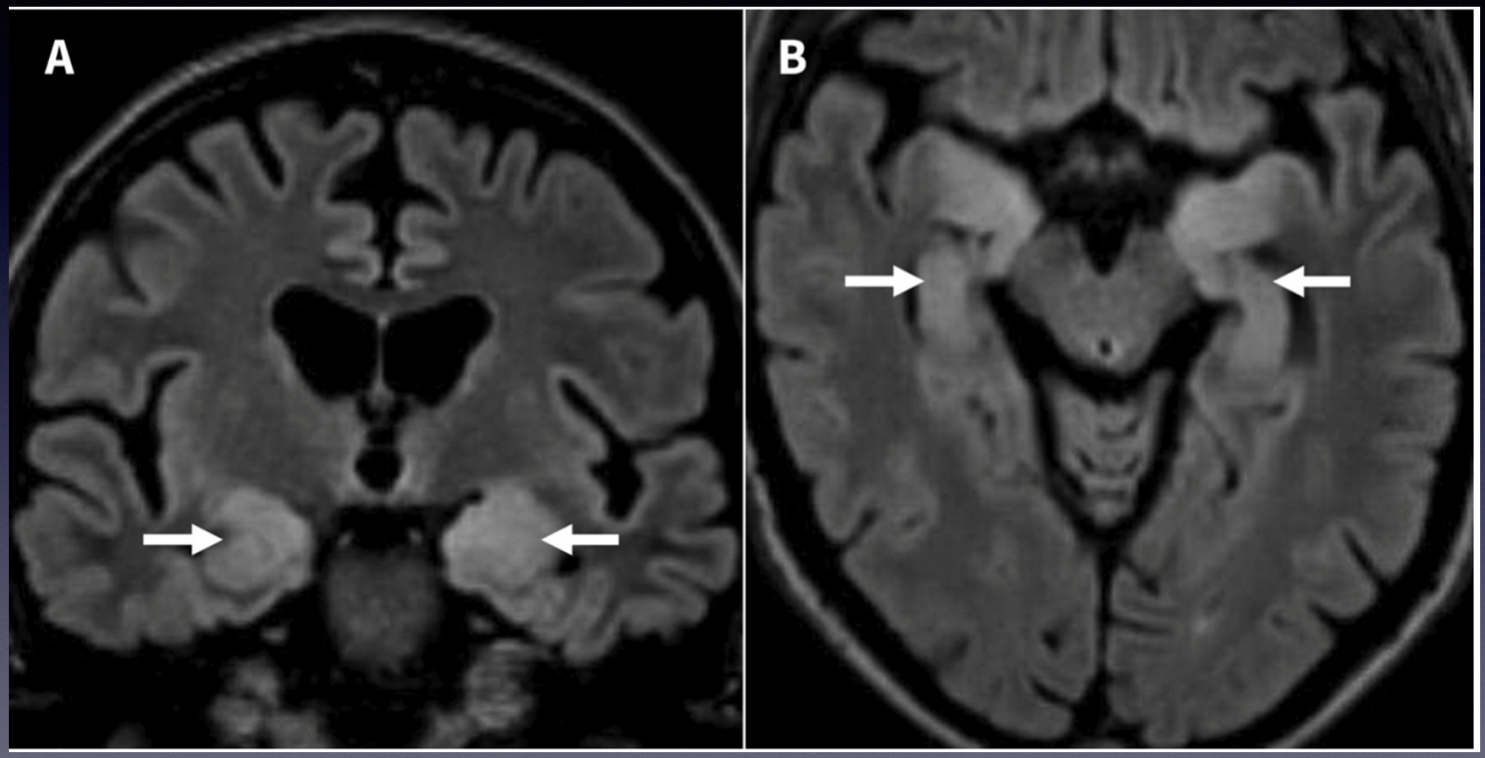
Budram A., et al. CMAJ May 2019

Box 2: Diagnostic criteria for definite autoimmune limbic encephalitis[4]

Diagnosis can be made when all 4* of the following criteria have been met:

- Subacute onset (rapid progression of less than 3 mo) of working memory deficits, seizures, or psychiatric symptoms suggesting involvement of the limbic system.
- Bilateral brain abnormalities on T_2-weighted fluid-attenuated inversion recovery MRI highly restricted to the medial temporal lobes†
- At least one of the following:
  - CSF pleocytosis (white blood cell count of more than 5 cells per mm^3)
  - EEG with epileptic or slow-wave activity involving the temporal lobes
- Reasonable exclusion of alternative causes

Budram A., et al. CMAJ May 2019


A
B

Autoimmune Encephalitis

- Autoantibodies detectable in CSF or serum
  - Classic paraneoplastic syndromes which target intracellular proteins
  - <1% with cancer and may preceded diagnosis of cancer by years
  - Cell-surface neuronal receptors or synaptic proteins
    - 5 times more common than intracellular
    - More treatable

Table 1: Antibodies that may be found in autoimmune limbic encephalitis, and their tumour associations

Antibodies*	Main tumour association	Approximate tumour frequency, %
Antibodies to extracellular cell surface or synaptic proteins		
LGI1[12,14]	Various (thymoma, breast, thyroid, colon, pancreatic and other cancers)	10
CASPR2[10,14]	Thymoma	20†
$GABA_BR$[6,17]	SCLC	50
AMPAR[18,19]	SCLC, thymoma	60
NMDAR[20]	Ovarian teratoma	40‡
mGluR5[21]	Hodgkin's lymphoma	50
Neurexin-3-α[22]	None identified	NA
Antibodies to intracellular proteins		
Hu[8,23]	SCLC	> 90§
Ma2[24]	Testicular tumour	> 90¶
GAD[25]	SCLC, thymoma	25**
Amphiphysin[26]	SCLC, breast cancer	> 90
CV2/CRMP5[27]	SCLC, thymoma	> 90
AK5[28]	None identified	NA

Budram A., et al. CMAJ May 2019

Outside of Alberta Test Requisition Form

Clear Form

MITOGENDx

Lab Use Only	
Date rec'd:	
Sample Frozen:	Yes No
All Required Information Provided:	Yes No

Tests not yet approved by Health Canada for diagnostics are labeled as Research Use Only (RUO). See Page 2 for a list of Diagnostic Tests. Please mark ALL tests to be done. Patient Information, Referring Physician, and Referring Laboratory, and Billing Options are ALL REQUIRED for samples to be processed without delay.

PATIENT INFORMATION

Patient Name (Surname, First name)

Gender Female Male Other

Personal Health Number

Date of Birth (dd/mm/yy)

Address (for non-Alberta Residents)

REFERRING PHYSICIAN INFORMATION

Physician Name (Surname, First name)

Phone Number

Fax Number

Email address

Comments

REFERRING LABORATORY INFORMATION

Laboratory Name

Address

Phone number

Fax number

Email address

SAMPLE INFORMATION

Sample Type Serum Cerebrospinal Fluid (CSF)

Time and Date Collected (dd/mm/yy)

Comments

BILLING OPTIONS

Invoice to be sent to (choose only one):

Referring Physician

Referring Laboratory

Other: Name **Address** **Phone #**

Self-Pay*

*Must be prepaid in full prior to the test(s) being performed. Payment may be made by credit card. Please call 403-800-8852 (ext. 1) for more information.

British Columbia Reciprocal Billing

SAMPLE COLLECTION

Sample Collection Procedure: **Serum** samples should be obtained from blood collected in a Serum Separator Tube (SST). Serum obtained from a single SST tube is preferred. Cerebrospinal fluid (**CSF; 3mLs)** samples should be sent in a small sterile tube and/or a polystyrene tube. Serum samples may be refrigerated and shipped with ice packs. CSF samples should be frozen and shipped on dry-ice if possible. If both serum and CSF are to be shipped together, samples may be shipped with ice packs (4°C).

SHIPPING INFORMATION

Please ensure your samples are scheduled to arrive **before 3pm on Friday** of any desired workweek. Please do not send samples on weekends or holidays as Mitogen will be closed and SAMPLES WILL NOT BE RECEIVED UNTIL THE FOLLOWING WORKWEEK. Shipments from any shipping company are accepted (including Purolator and FedEx). Tracking numbers should be retained for delivery confirmation. If problems arise or your package is not delivered promptly please email us at lab@mitogendx.com

Shipping--See Intra-Canada Shipping Guide/International Shipping Guide. Please send properly labeled and packaged samples with this requisition to:
Mitogen Diagnostics Laboratory, HRIC 3A26, 3330 Hospital Dr. NW Calgary, AB T2N 4N1

RECEIVING RESULTS

Results typically follow 7-10 days after receipt of sample, depending on the test(s) requested. Please visit our website for turnaround times for specific tests (www.mitogendx.com).

Outside Alberta – Results/reports will be faxed to **referring laboratories only**. If you have not received your results, please contact the laboratory that sent your sample. For missing or delayed reports, please contact us.

NOTE: This requisition form is **ONLY** for labs outside of Alberta. Please note that MitogenDx only sends paper reports to **referral labs**, with the exception of cytokine and cytokine antibody orders. For cytokine, cytokine antibodies, and ADAMTS-13 orders please use our separate requisition forms online at **www.mitogendx.com.**

CONTACT US

MitogenDx Laboratory
Cumming School of Medicine, University of Calgary
3330 Hospital Drive NW, HRIC 3A26
Calgary, AB, T2N 4N1
Phone: 403-800-8851 Fax: 403-800-8852
Email: lab@mitogendx.com
Visit our website: www.mitogendx.com

ENCEPHALITIS

Anti-NMDA (NR1) Receptor
Anti-glutamate receptor (type NMDA)

Anti-DPPX (dipeptidyl aminopeptidase-like 6)
Anti-Dipeptidyl aminopeptidase-like protein 6

Anti-VGKC (Voltage gated potassium channel) LGI1 & CASPR2
Anti-Contactin-associated protein 2 (CASPR2) & Anti-Leucine-rich glioma-inactivated protein 1 (LGI1)

Anti-$GABA_B$ Receptor
Anti-γ-amino-butyric acid Receptor ($GABA_B$)

Anti-AMPA Receptor
Anti-glutamate receptor (type AMPA1/2)

NEURO

Neurological Disease Test Panel (IgG +IgM) (Serum only)
Anti-GM1, GM2, GM3, GD1a, GD1b, GT1b, GQ1b

Neuromyelitis Optica Spectrum Disorder (NMOSD) (Anti-Aquaporin 4 & MOG)
Anti-Aquaporin 4 (AQP4 / NMO) / Anti-Myelin Oligodendrocyte Glycoproteins (MOG)

Anti-Myelin Associated Glycoproteins (MAG)
Anti-Myelin Associated Glycoproteins (MAG)

Anti-GAD 65 (Glutamate Decarboxylase)
Anti-Glutamate Decarboxylase

High-Sensitivity Neurofilament (heavy chain)
Neurofilament Heavy Chain (pNf-H)

High-Sensitivity Neurofilament (light chain) (RUO)
Neurofilament Light Chain (pNf-L)

Idiopathic Ataxia/ Peripheral Neuropathy Anti-MPP-1 (Laboratory Developed Test)
Anti-MPP1

VASCULITIS

ANCA (PR3, MPO)
Anti-neutrophil cytoplasmic antibody (ANCA): perinuclear ANCA (MPO), cytoplasmic ANCA (PR3)

Atypical ANCA: Anti-LAMP2, Anti-Elastase (Laboratory Developed Test)
Anti-LAMP2, Anti-Elastase

CANCER

Cancer-Associated Autoantibody Panel (Laboratory Developed Test)
Anti-CENP-F1, CENP–F4, p53

Paraneoplastic Disease Panel PLUS
Anti-Amphiphysin, Ri (NOVA-1), Yo, Hu, PNMA2 (Ma2/Ta), CV2.1, Recoverin, SOX1, Titin, Zic4, GAD65, Tr (DNER)

Treatment for Rapidly Progressive Dementia

- Depends on the underlying cause
- Many conditions are supportive management only, but certain ones can be treatable
- Sometimes, a treatment trial is warranted – but follow up required
- Can be worked up as outpatient, but often requires collaborative consultation and ready access to investigations best organized in an inpatient setting

Rapidly Progressive Dementia

By Gregory S. Day, MD, MSc, MSCI, FAAN

ABSTRACT

PURPOSE OF REVIEW: **This article presents a practical approach to the evaluation of patients with rapidly progressive dementia.**

RECENT FINDINGS: **The approach presented in this article builds upon the standard dementia evaluation, leveraging widely available tests and emergent specific markers of disease to narrow the differential diagnosis and determine the cause(s) of rapid progressive decline. The discovery of treatment-responsive causes of rapidly progressive dementia underscores the need to determine the cause early in the symptomatic course when treatments are most likely to halt or reverse cognitive decline.**

SUMMARY: **A pragmatic and organized approach to patients with rapidly progressive dementia is essential to mitigate diagnostic and therapeutic challenges and optimize patient outcomes.**

INTRODUCTION

Cognitive impairment in patients with rapidly progressive dementia (RPD) develops faster than expected for a known dementia syndrome. Although the definition of *rapid* varies in practice, it is generally accepted that the interval from first symptom to dementia onset is measured in weeks or months, with the majority of patients with RPD progressing from independence to complete (or near-complete) dependence within 1 to 2 years. Patients meeting these criteria are rare, accounting for 3% to 4% of dementia cases in clinical practice.[1-3] Yet, despite their rarity, patients who are rapidly declining present a disproportionately great clinical challenge owing to the breadth of potential causes, the plethora of available tests to consider, and the need to complete the assessment with an urgency that matches the rate of decline. The importance of timely evaluation is further exemplified by increasing recognition of eminently treatable autoimmune or inflammatory causes of RPD.[2,4-6]

The practical approach to RPD builds upon the standard dementia evaluation, as discussed throughout this *Continuum* issue, with modifications intended to optimize the speed of evaluation and improve early recognition of patients with potentially reversible causes of RPD. A timely assessment begins with timely referrals and triage of appropriate patients. Although most patients with RPD can be efficiently evaluated in the outpatient setting, a timely assessment may require patients to be added onto busy clinic schedules. Selected patients may benefit from referral to a specialty center with dedicated resources and clinic

REVIEW ARTICLE

CONTINUUM AUDIO INTERVIEW AVAILABLE ONLINE

VIDEO CONTENT AVAILABLE ONLINE

CITE AS:
CONTINUUM (MINNEAP MINN) 2022;28(3, DEMENTIA):901-936.

Address correspondence to Dr Gregory S. Day, Mayo Clinic, Department of Neurology, 4500 San Pablo Rd S, Jacksonville, FL 32224, day.gregory@mayo.edu.

RELATIONSHIP DISCLOSURE:
Dr Day has received personal compensation in the range of $500 to $4999 for serving as an editor, associate editor, or editorial advisory board member for DynaMed (EBSCO Industries, Inc), as a presenter at the Annual Meeting (CME) of the American Academy of Neurology, as a grant reviewer (honorarium) with the Pennsylvania Department of Health, and for CME content and delivery for PeerView and Continuing Education Inc. Dr Day has received personal compensation in the range of $5000 to $9999 for serving as a consultant for Parabon NanoLabs, Inc and personal compensation in the range of $10,000 to $49,999 for serving as an expert witness for Barrow Law. Dr Day has a noncompensated relationship as a clinical director for the Anti-NMDA Receptor Encephalitis Foundation Inc that is relevant to American Academy of Neurology interests or activities.

Continued on page 936

UNLABELED USE OF PRODUCTS/INVESTIGATIONAL USE DISCLOSURE:
Dr Day reports no disclosure.

Day GS. Continuum. 2022 Jun 1;28(3):901-936.

Questions?