
# Southern African HIV Clinicians Society

# 3rd Biennial Conference

13 - 16 April 2016
Sandton Convention Centre
Johannesburg

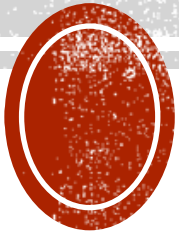
## Our Issues, Our Drugs, Our Patients

www.sahivsoc.org
www.sahivsoc2016.co.za

# WHAT A HEADACHE!

J. Nel

April 2016



# HISTORY

- 34-year-old female
- Presented with an 18-month history of headaches.
  - Bilateral, frontoparietal
  - Refractory to simple analgesia
  - Occur daily – no respite over past 18 months
- Headaches had gradually worsened over the months, to the point where the patient was in tears due to the pain.

# HIV HISTORY

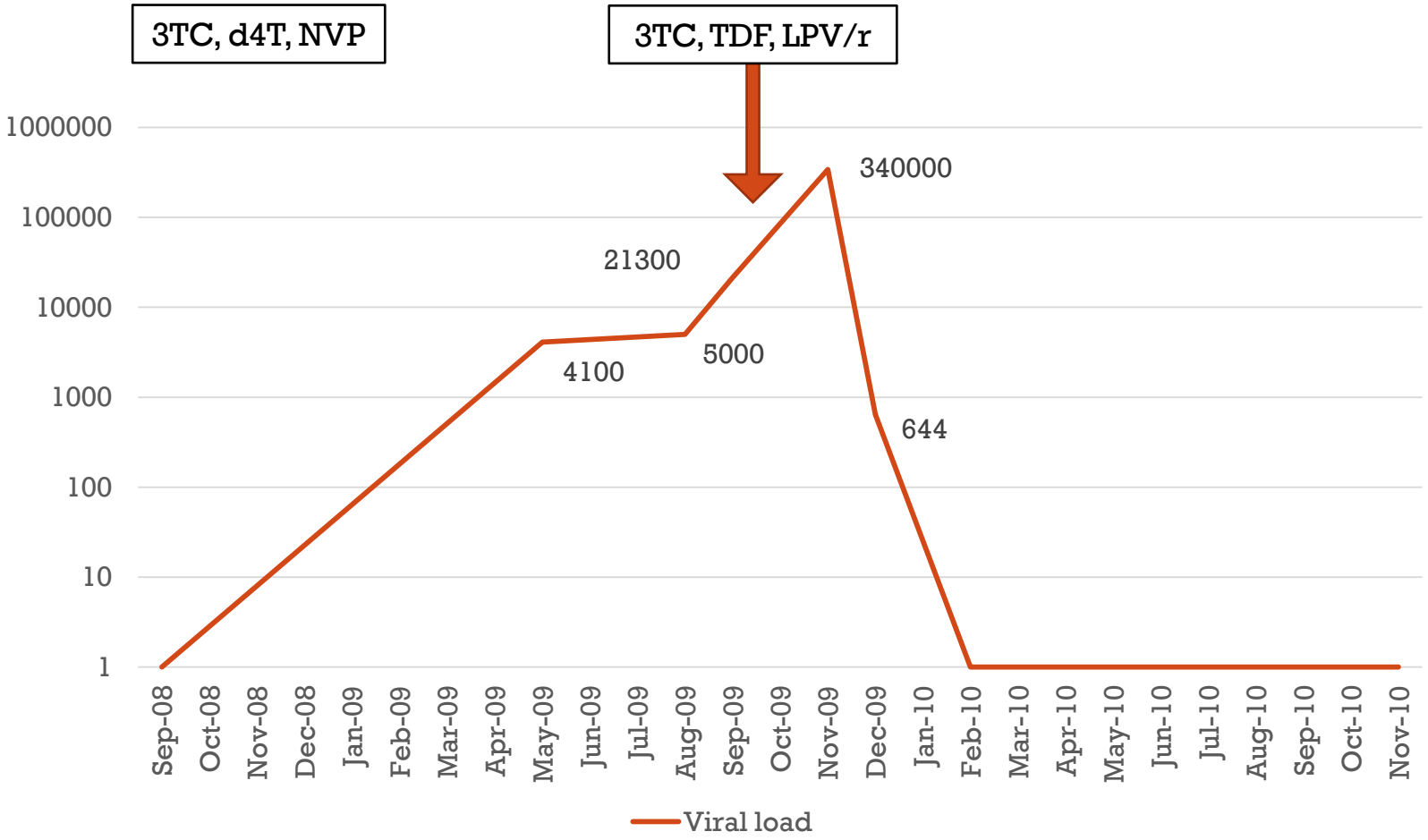
- Diagnosed with HIV in June 2006. Baseline CD4=52.
- Commenced on 3TC/d4T/EFV from June 2006.
- Defaulted ARVs after clinic visit in October 2006.

- Returned to care in April 2008. Restarted on 3TC/d4T/NVP at that time. CD4=54.
  - Unclear why NVP substituted for EFV, but probably due to EFV side-effects that patient complained of.

# HIV HISTORY

- May 2009: viral load 4100 copies/mL.
- August 2009: viral load 5000 copies/mL.
- September 2009: virological failure diagnosed and patient enrolled in CHRU Directly Observed Treatment study → changed to 3TC/TDF/LPVr in October 2009.
- Good response: viral load declined from 21 300 to LDL by Feb 2010, and remained totally suppressed until study ended in November 2010:

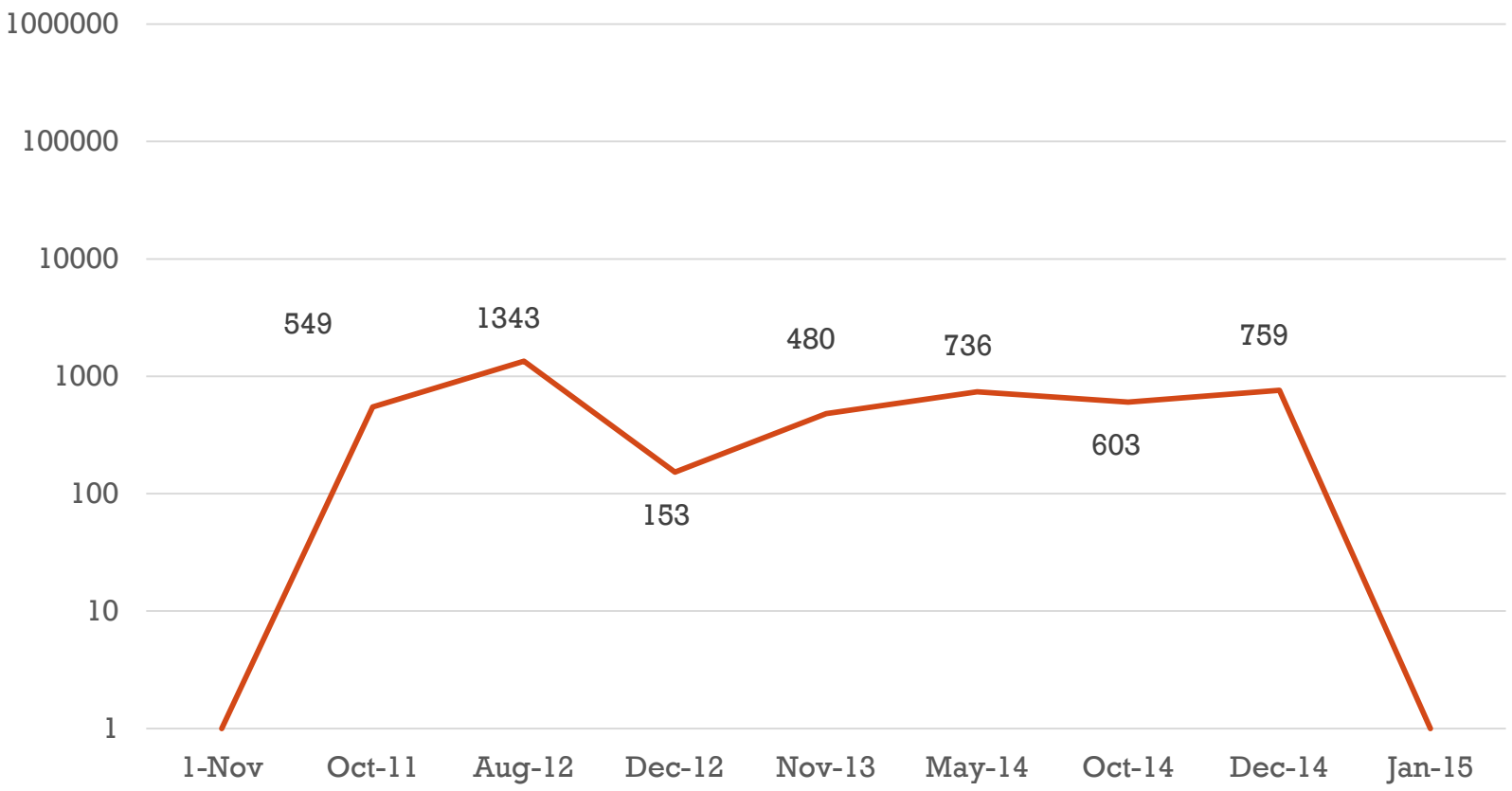
# VIRAL LOAD PATTERN



# HIV HISTORY

- Patient returned to TLC after study completion. Subsequent viral loads showed gradual deterioration of control however.
- Patient admitted to missing the evening doses of her medications, and was formally counselled and moved to the "3rd line clinic" for closer supervision.
  - Patient's mother reported that the patient had poor memory, and was forgetting to take her medications as a result.
- Viral load did improve on counselling (153 copies/mL) and the patient was moved out of 3rd line clinic again.
- Viral loads again showed upward trend over subsequent months, but had suppressed again by the time of admission.

# VIRAL LOAD PATTERN (CONT.)



# OTHER HISTORY

- Previous pulmonary TB:
  - Diagnosed April 2006. Completed 6 months of standard TB treatment.
- Herpes zoster Feb 2014.
  - No residual neurology.
- Chronic hepatitis B
  - First diagnosed in September 2009

# OTHER HISTORY

- Lives in Meadowlands, Soweto in a house with full amenities. Lives with uncle, grandmother, daughter, cousin and brother.
- Employed as a cleaner since 2010. Highest education level attained: Grade 11. Dropped out due to financial difficulties.
- No obvious animal exposures.
- No allergies.
- No illicit drug usage.
- Smoker: 10 pack year history

# EXAMINATION

- BP 124/73
- P 103
- RR 16
- Temp 36.3°C

- Miserable-looking, in pain.
- BMI 28.9 kg/$m^2$

# EXAMINATION

- **Chest**: clear, normal vesicular sounds, no distress
- **CVS**: JVP normal, normal heart sounds, not in failure
- **Abdo**: SNT, no masses, no HSM, normal bowel sounds

# EXAMINATION

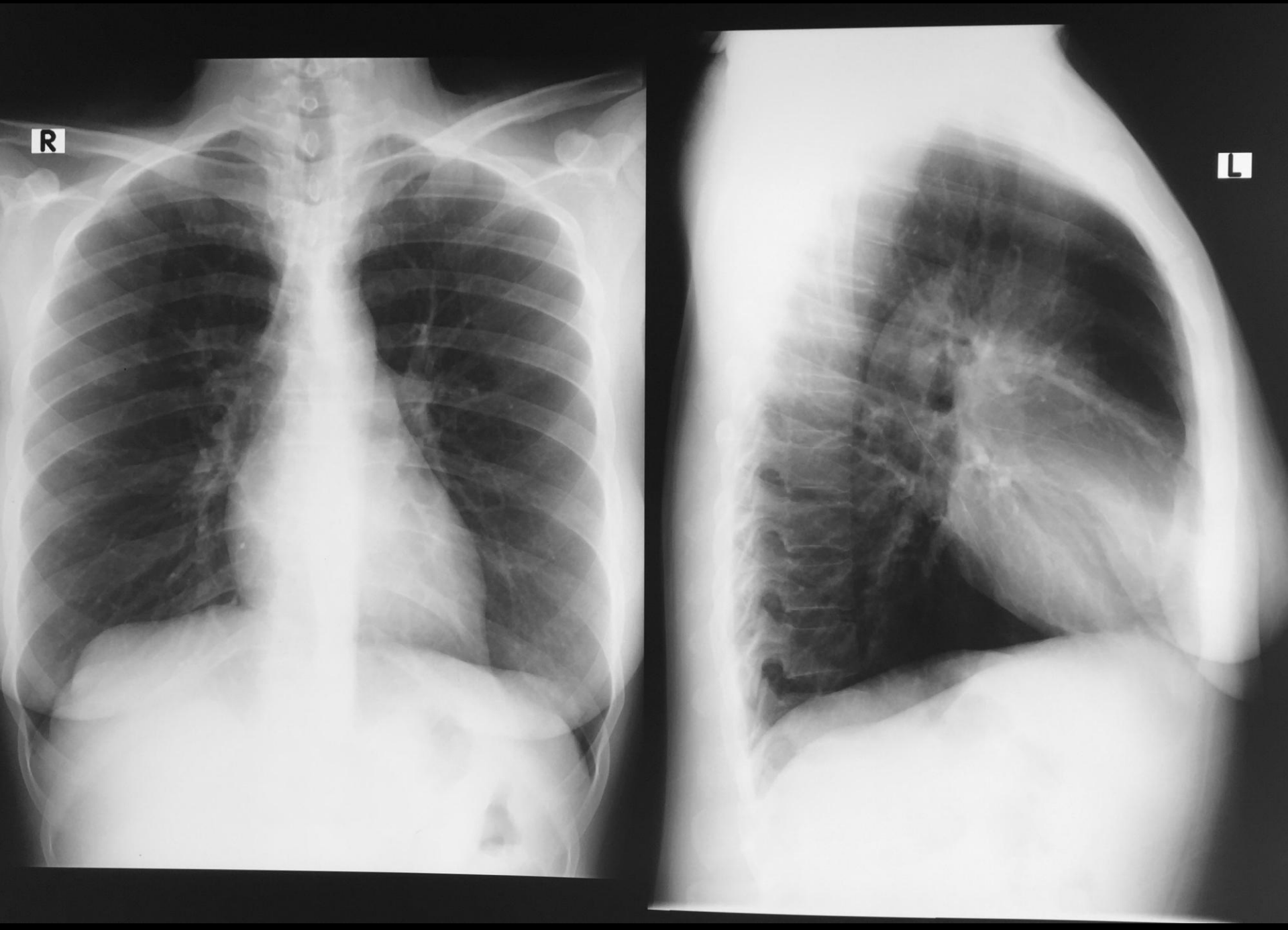
- **Neuro**:
  - GCS 15/15
  - Tearful, unhappy
  - Sometimes slightly irrelevant answers to questions
  - Slow to respond
  - Cranial nerves normal
  - Cerebellar exam normal
  - Motor and sensory exams normal

# BASIC BLOODS

| | | | |
|---|---|---|---|
| WCC | 3.38 | Sodium | 141 |
| Hb | 12.7 | Potassium | 3.7 |
| MCV | 91.5 | Chloride | 105 |
| Platelets | 297 | Bicarbonate | 24 |
| Viral load | 759 | Urea | 4.3 |
| CD4 | 439 | Creatinine | 39 |
| Viral load | LDL | CRP | < 5 |

# BASIC BLOODS

| | |
|---|---|
| Total bilirubin | 7 |
| Conj. bilirubin | 3 |
| Protein | 73 |
| Albumin | 35 |
| ALP | 84 |
| GGT | 30 |
| ALT | 14 |
| AST | 14 |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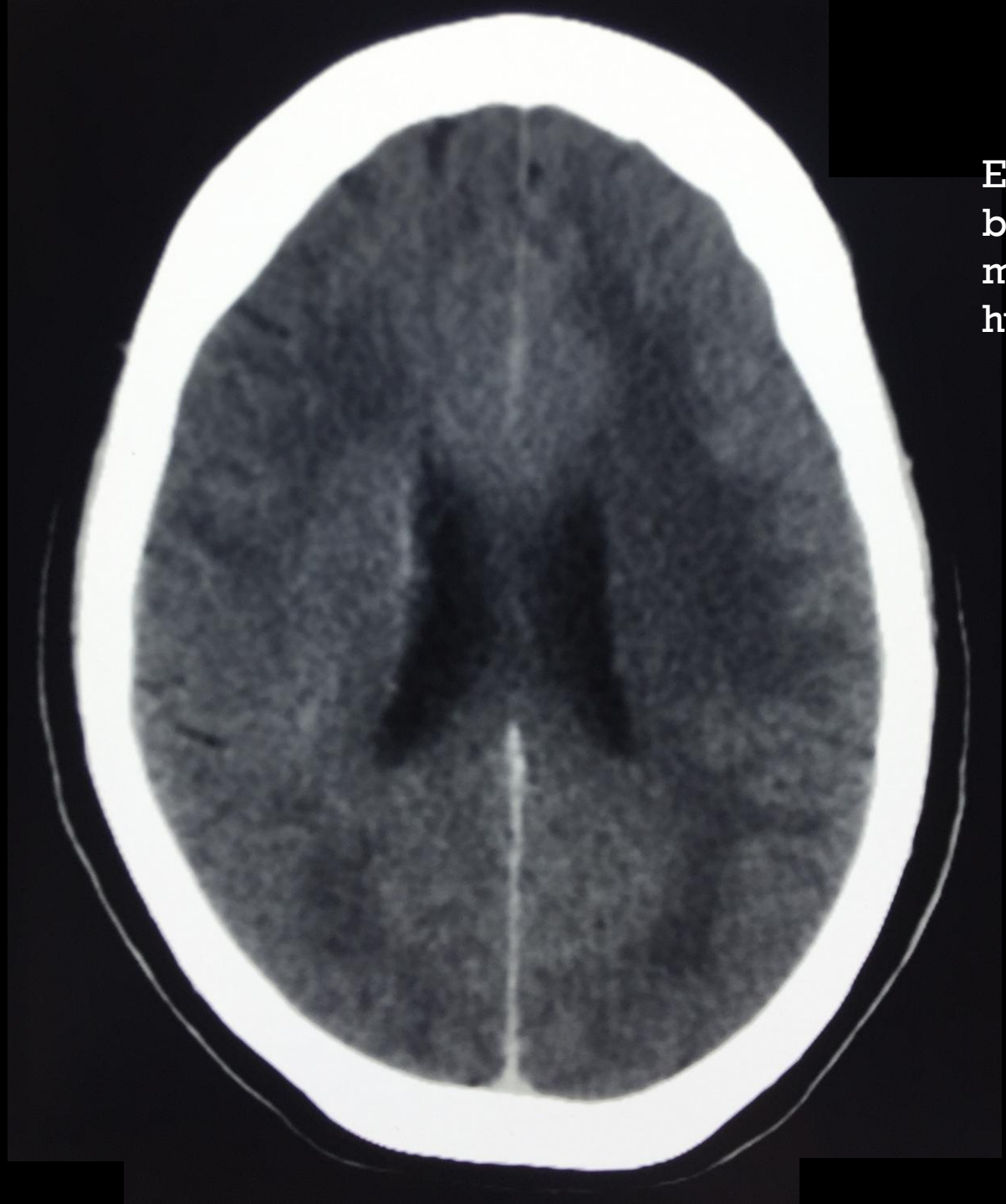
# LUMBAR PUNCTURE RESULTS

| | Aug 2014 | Sep 2014 | Oct 2014 | Dec 2014 |
|---|---|---|---|---|
| Protein | 0.81 | 0.66 | 0.98 | 0.70 |
| Glucose | 2.4 | 2.7 | 2.3 | 2.5 |
| Polymorphs | 8 | 0 | 7 | 0 |
| Lymphocytes | 126 | 42 | 109 | 6 |
| Erythrocytes | 1 | 33 | 2 | 492 |
| CLAT/India Ink | Negative | Negative | Negative | Negative |
| Fungal culture | (N/A) | (N/A) | No growth | (N/A) |
| Bacterial culture | No growth | No growth | No growth | No growth |
| GeneXpert | (N/A) | (N/A) | (N/A) | Negative |

# CT

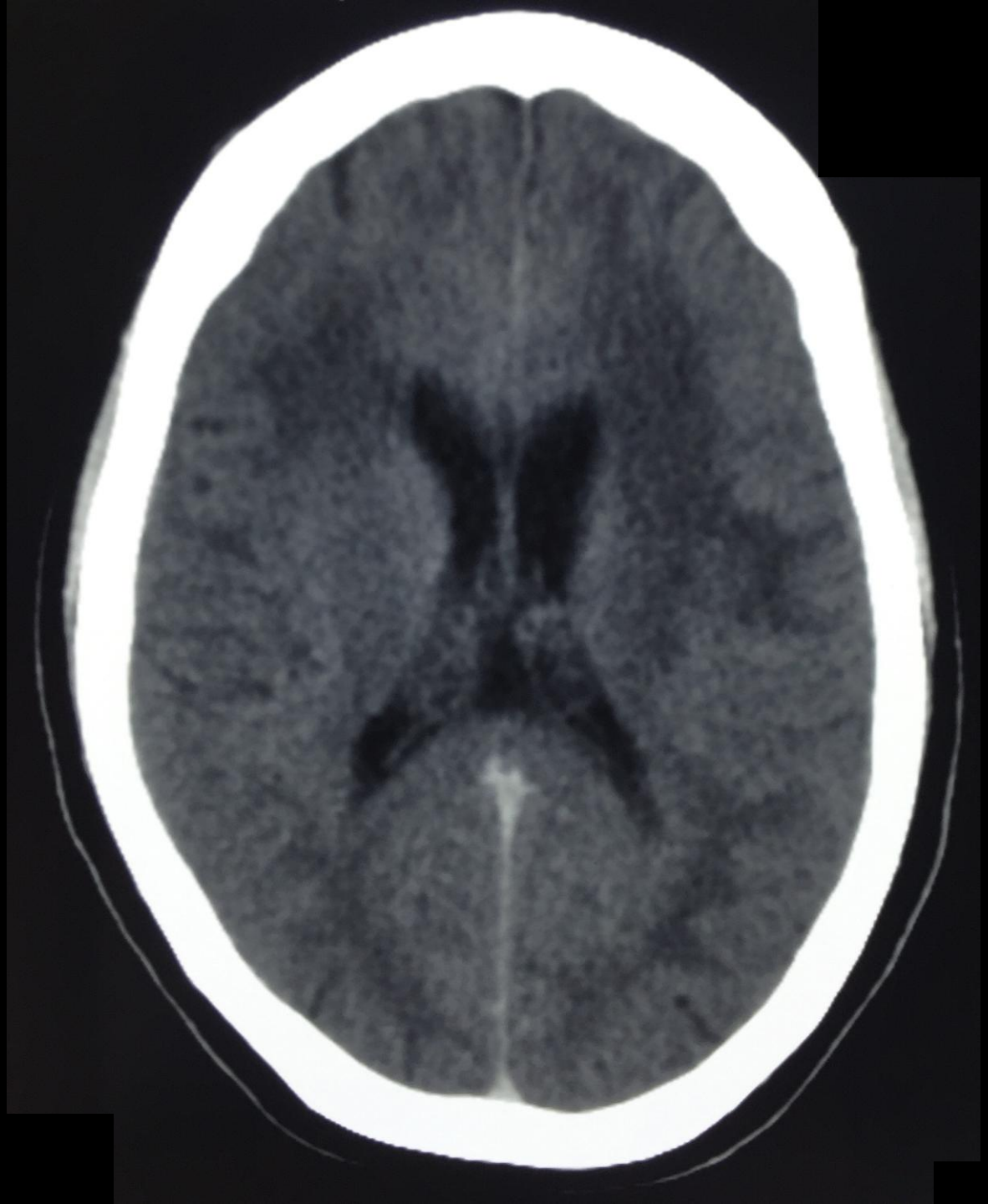
w/ contrast



Extensive bilateral white matter hypodensities

# CT

w/ contrast



# NEUROPSYCHOLOGICAL TESTING

- Objectively and subjectively **depressed.** Teary at times.
- **Worked steadily but extremely slowly** and needed a lot of prompting and encouragement.
- **Deficits in sustaining attention** for simple processing tasks, difficulty with divided attention, and an inability to encode information for further processing. **Limited mental flexibility.**
  - This implies that she might have difficulty focusing her attention for long periods at a time and should be given clear and precise instructions while making sure she understands.

# NEUROPSYCHOLOGICAL TESTING

- Difficulty with sequential processing, short term acquisition, retaining and retrieval of information. Poor immediate and delayed **memory**. Very little information gets consolidated and stored in her long term memory.
- Deficits in **spatial abilities**, **non-verbal concept formation**, simultaneous processing, perceptual abilities, construct abilities non-verbal problem solving and **fine motor abilities**.
- Deficits in **frontal lobe functioning** that may influence ability to respond to social cutes. Needs a lot of encouragement to start and complete tasks.

# NEUROPSYCHOLOGICAL TESTING

**MOCA** – cognitive screening device designed to assess for mild cognitive impairment.

- Tests memory, attention, abstraction, visuo-contruction skills and orientation.
- Cut-off score is 26/30.

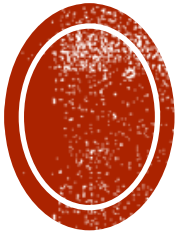
- Our patient: 17/30. Lost points on each subdivision of the test – globally weak.

# NEUROPSYCHOLOGICAL TESTING

**Becks Depression Inventory (BDI)**

- 21 items assessing the patient's feelings and symptoms of depression over a one week period.
- Maximum points = 63. Higher is worse. Scores of > 30 indicate severe depression.

- Our patient: 50/63: severe depression



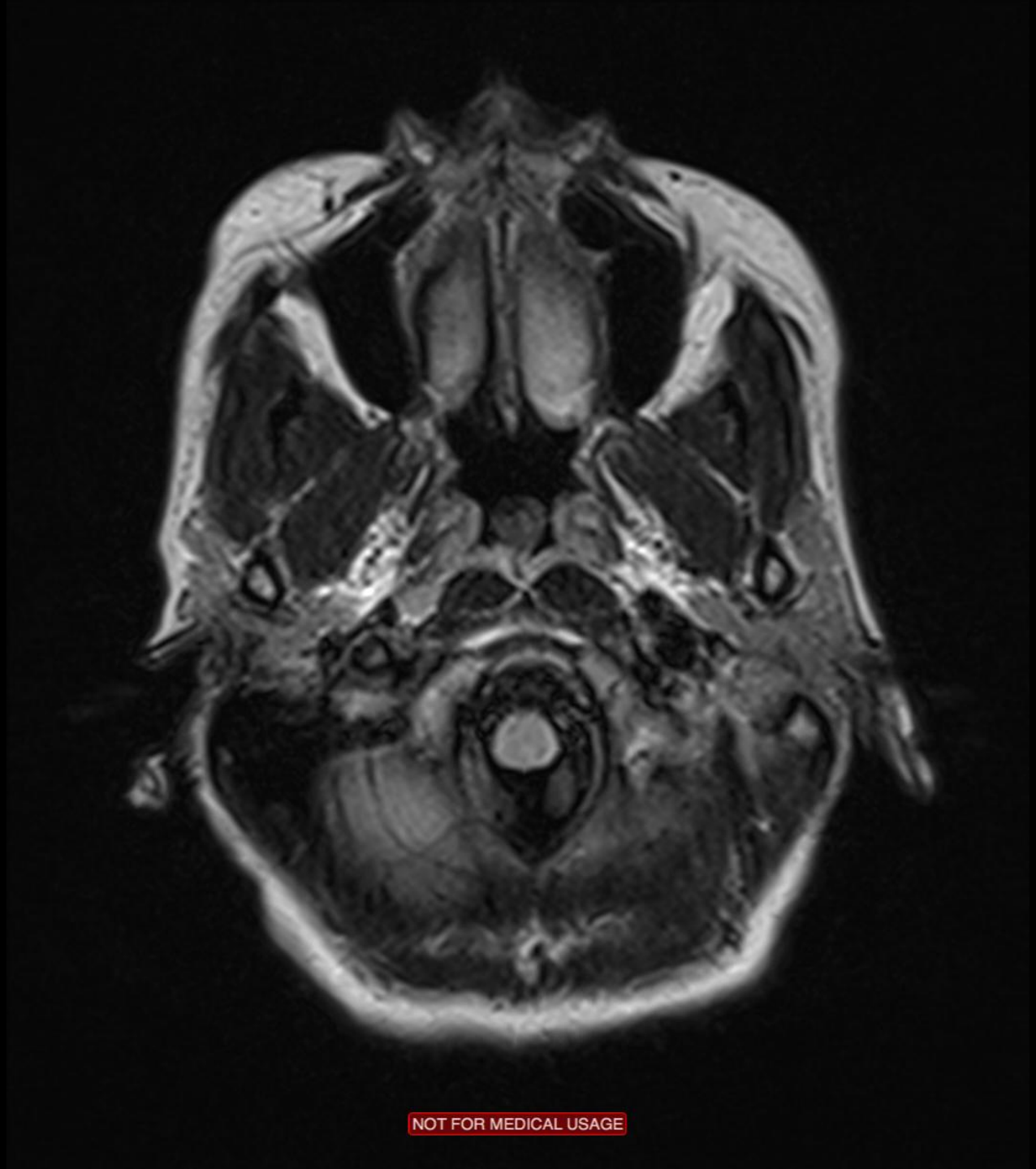
# STOP AND THINK

# FURTHER BLOOD RESULTS

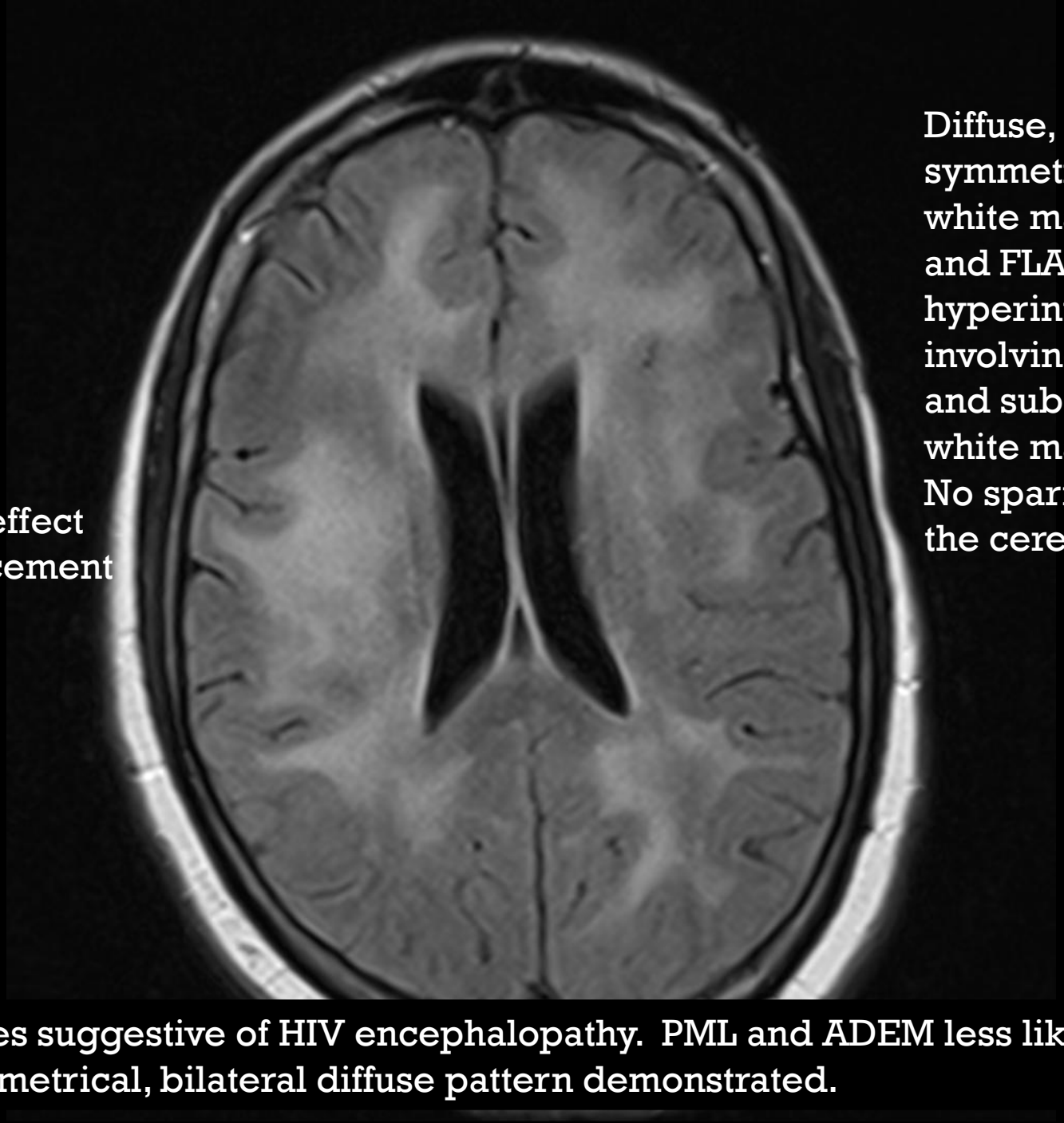
- TB Bactec (blood): Negative
- TB culture (sputum): Negative
- ANA: Negative
- RF: Negative
- ANCA: Negative
- TPHA (serum): Negative

# FURTHER CSF RESULTS

- CSF TPHA: Negative
- CSF VDRL: Negative
- CSF cytology: no malignant cells
- CSF ADA: 0.6
- TB culture: Negative
- JC virus PCR: Negative
- HSV-1 and -2 PCR: Negative



# MRI



Diffuse, bilateral, symmetrical white matter $T_2$ and FLAIR hyperintesities involving deep and subcortical white matter. No sparing of the cerebellum.

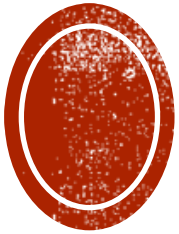
No mass effect or enhancement

Features suggestive of HIV encephalopathy. PML and ADEM less likely due to symmetrical, bilateral diffuse pattern demonstrated.

# THE ANSWER

- **HIV viral load <u>on CSF</u>**: 14 000 copies/mL
- **Serum viral load** *lower than detectable limit*.

## CSF HIV viral escape



# SO NOW WHAT?

Compartmentalised viral escape of HIV within the CSF

# DECISIONS, DECISIONS

- The patient was currently on **3TC, TDF and LPV/r**.
- The serum viral load was suppressed.
- The CSF viral load was 14 000.

What can be done?

# CSF PENETRATION OF ART

| Agent type | CNS penetration–effectiveness score | | | |
|---|---|---|---|---|
| | *4 (very good)* | *3 (good)* | *2 (fair)* | *1 (poor)* |
| NRTI | Zidovudine | Abacavir<br>Emtricitabine | Didanosine<br>Lamivudine<br>Stavudine | Tenofovir<br>Zalcitabine |
| NNRTI | Nevirapine | Delavirdine<br>Efavirenz | Etravirine | |
| PI | Indinavir/r | Darunavir/r<br>Fosamprenavir/r<br>Indinavir<br>Lopinavir/r | Atazanavir<br>Atazanavir/r<br>Fosamprenavir | Nelfinavir<br>Ritonavir<br>Saquinavir<br>Saquinavir/r<br>Tipranavir/r |
| Entry inhibitors | | Maraviroc | | Enfuvirtide |
| Integrase inhibitors | | Raltegravir | | |

*NNRTI: Non-nucleoside reverse transcriptase inhibitor; NRTI: Nucleoside reverse transcriptase inhibitor; PI: Protease inhibitor.*
*Data taken from* [91].

# SO WHAT REGIMEN WOULD YOU CHOOSE FOR THIS PATIENT?

Currently: virally suppressed

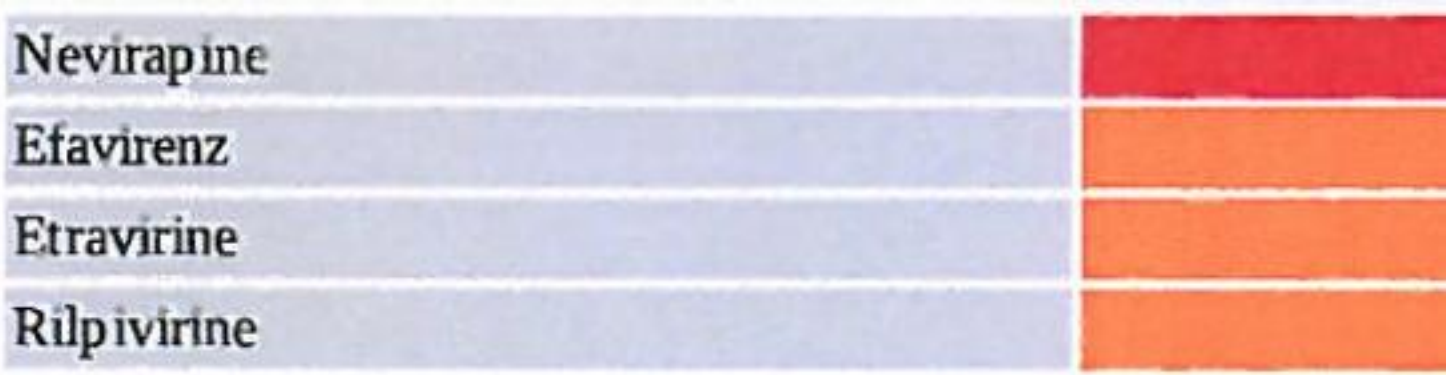
on 3TC / TDF / LPV/r

# CSF HIV GENOTYPE

Major NRTI mutation: M184V

# CSF HIV GENOTYPE

Major NRTI mutations: Y181C, K219N



# CSF HIV GENOTYPE

Significant PI mutations: L10F, M46I, T74S, L76V

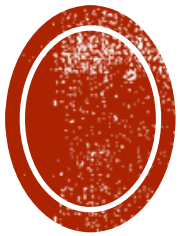
# SO, LET'S TRY THIS AGAIN…

2nd time lucky…

| Drug | CSF Penetration | CSF susceptibility |
|---|---|---|
| 3TC/FTC | | |
| TDF | | |
| AZT | | |
| ABC | | |
| d4T | | |
| EFV | | |
| NVP | | |
| ETR | | |
| LPV/r | | |
| ATV/r | | |
| DRV/r | | |
| RAL | | |

# BUT WHAT IF THE *SERUM* HIV VIRUS STRAIN IS DIFFERENT?

Patient suppressed on 3TC/TDF/Aluvia



# SO, LET'S TRY THIS ONE MORE TIME…

3rd time's the charm!

# SO, THE BEST COMBINED REGIMEN:

For The CSF:

| Drug | CSF Penetration | CSF susceptibility |
|---|---|---|
| AZT | | |
| LPV/r | | |
| RAL | | |
| *and a little help from:* | | |
| 3TC/FTC | | |

For the serum:

3TC, LPV/r, RAL *and maybe* AZT

# WHAT ARE WE MISSING?

OK, 4th time lucky…

# FINAL REGIMEN

**For the chronic hep B:**

- 3TC, TDF

**For the HIV in the CSF:**

- AZT, LPV/r, RAL ± 3TC

**For the HIV in the serum:**

- 3TC, TDF, LPV/r, RAL ± AZT

Final regimen: 3TC, AZT, TDF, LPV/r, RAL

Patient ended up on DRV/r instead of LPV/r due to intolerance (diarrhoea). Easy swap because same CSF effect and CSF susceptibility, and likely same or better serum susceptibility.

# FINAL LP – 4 MONTHS LATER

| | July 2015 |
|---|---|
| Protein | 0.08 |
| Glucose | 3.0 |
| Polymorphs | 0 |
| Lymphocytes | 3 |
| Erythrocytes | 0 |
| CLAT/India Ink | Negative |
| Bacterial culture | No growth |

# HIV CONTROL

- Ever since the CSF-penetrating ARVs given:
  - Depression cleared
  - Headaches gone
  - Neurocognitive issues improved
- Patient's serum viral load has been undetectable ever since switching regimens, despite having to take 5 ARVs.
  - This is the first time since the DOT trial that she has ever maintained viral suppression.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