Anti-NMDA Receptor Encephalitis; A Rare Cause of Acute Confusion in an HIV positive patient

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The Background

We present a case of anti-N-methyl-D-asparate (anti-NMDA) receptor encephalitis in a 49 year old gentleman with a known diagnosis of HIV following an admission with acutely worsening confusion and inattention.

This is the fourth reported case of anti- NMDA receptor encephalitis in an HIV positive individual, highlighting the importance of considering auto-immune conditions as a cause of acute confusion in HIV positive patients

The Patient

- 49 year old male
- MSM

- Smoker - 10 cigarettes/day
- Alcohol - 40-50 units/week
- No drug use/No chemsex
- Taxi driver
- Lived alone

- Attended GUIDe Clinic in 2015
  - Extensive cutaneous Kaposi's Sarcoma (KS)and significant oral candidiasis

- HIV +ve on serum Ab/Ag

- Nadir CD4 count - 43 cells/mm^3
- Viral Load (VL): 516,821 copies

- Resistance:
  - NRTI – no resistance
  - NNRTI – P225H
  - Protease – K20I

- Commenced on ART (2015)
  - Truvada/Darunavir/Ritonavir

- Referred to Oncology
  - Doxorubicin for KS

- Undetectable VL from 2015-2018

The Admission

- May 2018
  - X2 outbreaks of Herpes Zoster affecting upper limb dermatomes

- June 2018 - 1st seizure
  - CT Brain: NAD

- July to August 2018
  - Decline in cognition
  - Marked inattention
  - Significant change in behaviour
  - Did not attend HIV OPD appointment

- August 2018
  - Admitted with worsening confusion
  - Apyrexial, GCS 14/15 (E4V4M6)
  - Neuro Exam: PEARL, Power 5/5
    - Poor coordination, Inattentive
    - Word finding difficulties

  - CT Brain: "generalised mass effect"

  - 1st Lumbar Puncture:
    - Opening pressure 44mm/Hg
    - Protein 122 mg/dL
    - Glucose 3.74
    - RCC 104 cells/cmm^3
    - WCC 160 cells/cmm^3

The Results

- CD4: 180 cells/mm^3
- Plasma VL: 916 copies/mL
- CSF VL: 42,365 copies/ml

- Resistance pattern in plasma + CSF:
  NRTI: M184V
  NNRTI: P225H
  PI: Q58E
  Integrase: none

- Serum:
  CMV IgG - positive
  Toxoplasma IgG – negative
  Syphilis serology – negative
  EBV IgG - positive

- CSF Infection Panel:
  HSV1/HSV2 – not detected
  VZV DNA – not detected
  EBV DNA – detected (non-significant)
  JC Virus DNA – not detected
  Entero/Echo/Paraechovirus – not detected
  CMV DNA – not detected
  HHV6 PCR – not detected
  CrAg – negative
  Syphilis - negative

- CSF Autoimmune Panel:
  VGKC receptor Abs -negative
  AMPA receptor Abs – negative
  GABA receptor Abs - negative
  GAD receptor Abs – negative
  NMDA receptor Abs - POSITIVE

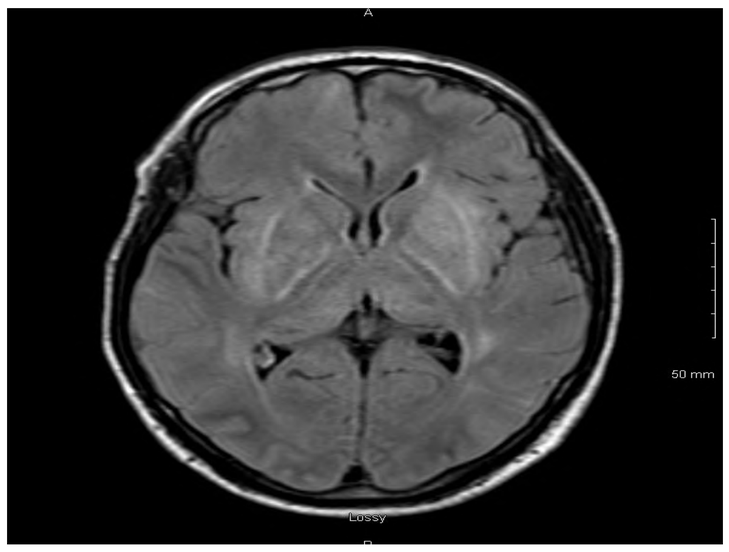

Image 1. MRI showing signal change at the basal ganglia

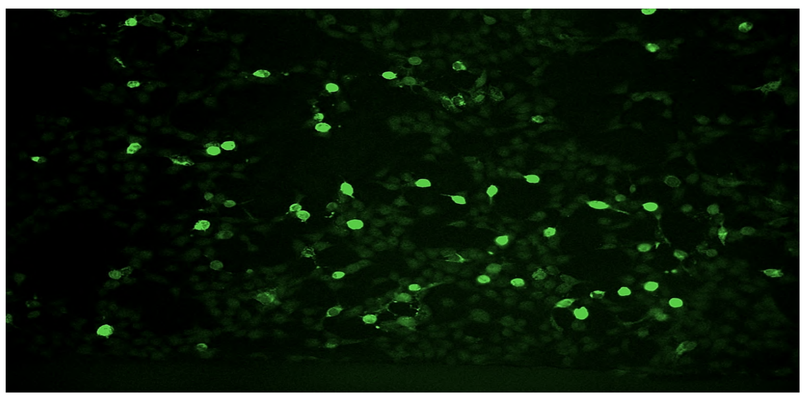

Image 2. Positive CSF sample following immunofluorescence

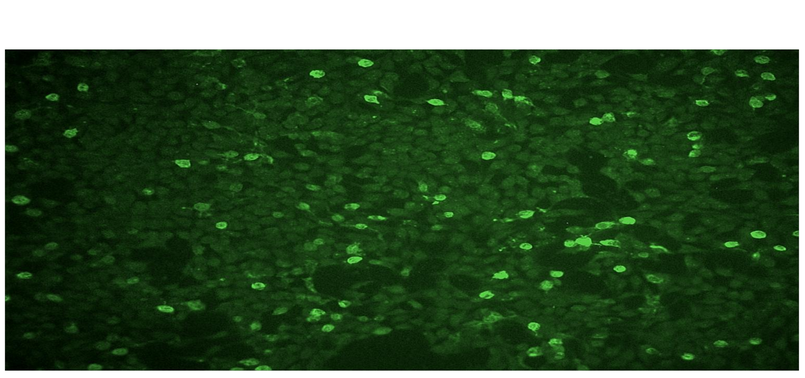

Image 3. Positive serum sample following immunofluorescence

The Management

- On admission, broad spectrum cover for bacterial and HSV meningoencephalitis

  Cefotaxime - 2g 4 hourly IV
  Vancomycin – 1.25g BD IV (titrated)
  Aciclovir – 10mg/kg TDS IV

- Extended for Listeria and Cryptococcus:

  Amphotercin B 300mg OD IV
  Flucytosine 2.5g QDS IV
  Amoxicillin 2g 4 hourly IV

- High-dose Pabrinex (I+II)x2

- Neurology review:
  likely focal seizures
  commenced on Keppra 500mg BD
  Locosamide added in as seizures ongoing

- Following positive NMDAR result:

  Methylprednisolone 500mg IV OD for 3/7
  (reduced dose due to ARV booster effect)
  +
  IVIG 40g, for 5/7 (x 2 courses)

- ARV switch to Truvada/Dolutegravir
  for increased CNS penetration

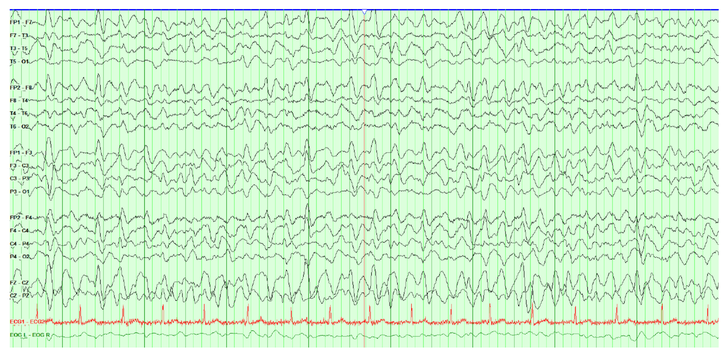

Image 4. EEG showing triphasic and delta brush waves

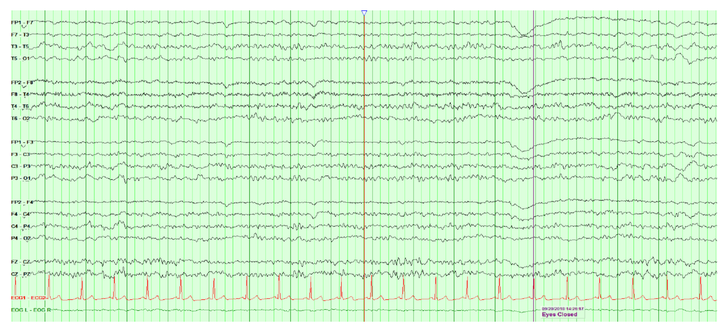

Image 5. EEG following treatment with AEDs and steroids

The Follow Up

- HIV clinic - January 2019
  - CD4 375 (25%), VL undetectable
  - ARV: Truvada/Dolutegravir
  - Meds: Dapsone 50mg OD

- Neurology OPD - January 2019
  - AEDs: Keppra + Locosamide tapering
  - Returned to work
  - Returned to driving
  - MOCA improved from 11/30 to 22/30

The Conclusion

Anti-NMDA encephalitis is a rare cause of encephalitis in patients with HIV.

A growing number of cases are being reported in the literature, and autoimmune encephalitis is not only becoming an increasingly apparent cause of acute confusion in HIV patients, but a potentially reversible one if identified early.

With greater availability and increased efficiency of testing this trend in diagnosis is likely to continue.

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