Unusual cases of Autoimmune Encephalitis

Date- 29/MAY/2024

Dr Pranit Khandait
Dr. D.Y. Patil Medical College, Hospital & RC.

42-year-old, male, right-handed,

Born out of 3rd degree consanguineous marriage,

Accountant by occupation,

K/c/o T2DM.

History

JUNE 2021

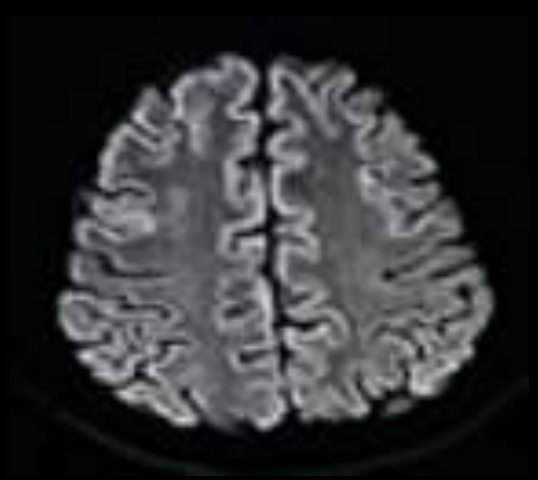
Seizure – Left upper limb focal followed by secondary generalization

Started on AED (Levetiracetam).

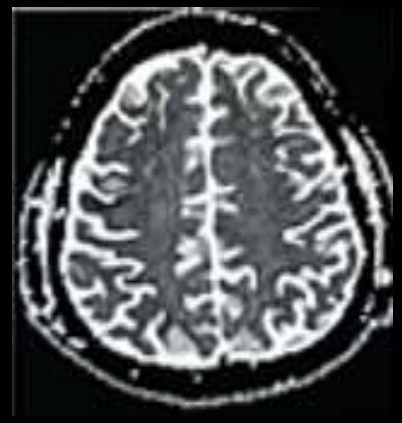
Routine lab investigation, electrolytes , calcium, magnesium – WNL

Sero-marker- Non-reactive

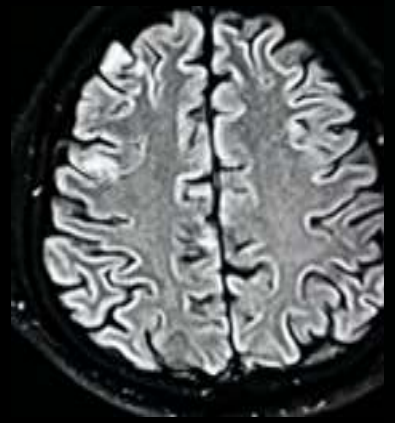
MRI BRAIN 17 JUNE 2021



DWI

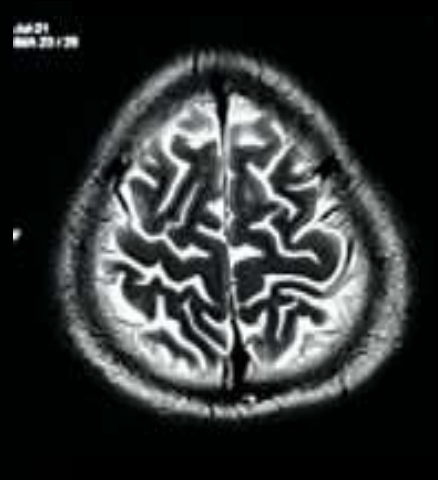


ADC



FLAIR

GRE



T2W

Antiplatelet and statin
Still in between 2-3 episodes of seizure – Dose of AED adjusted

EEG- No epileptiform activity

Insidious onset gradually progressive

JAN 2022

Forgetfulness-

Frequently misplace object
Forget recent conversations and events
Forget past personal events such as job related or places of residence.

JULY-2022

Became less attentive in office meeting.
Concentration became poor.
Planning an outing.
Patient had difficulty in using gadgets.

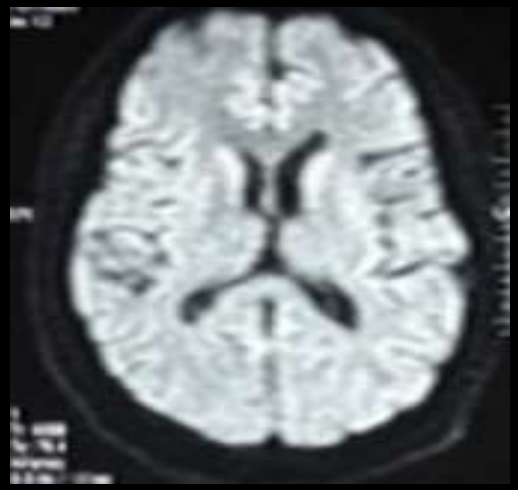
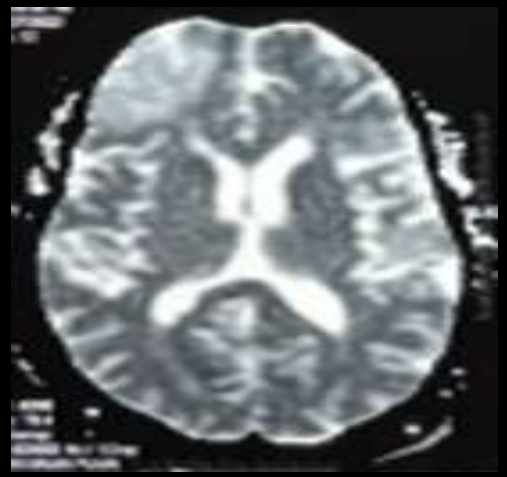
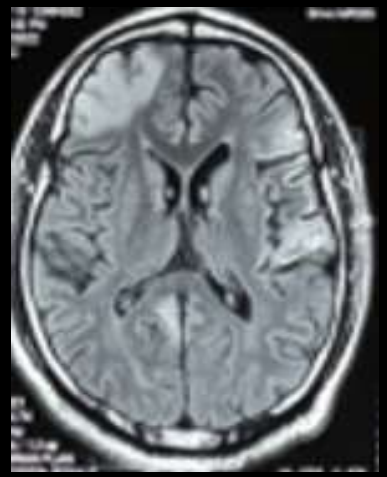
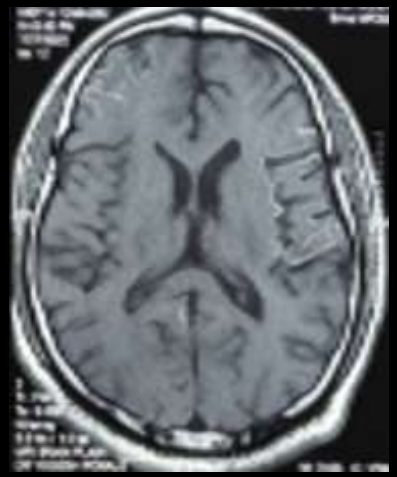
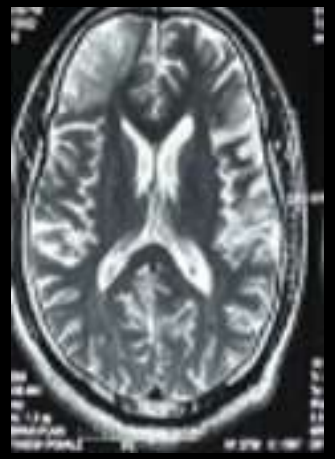
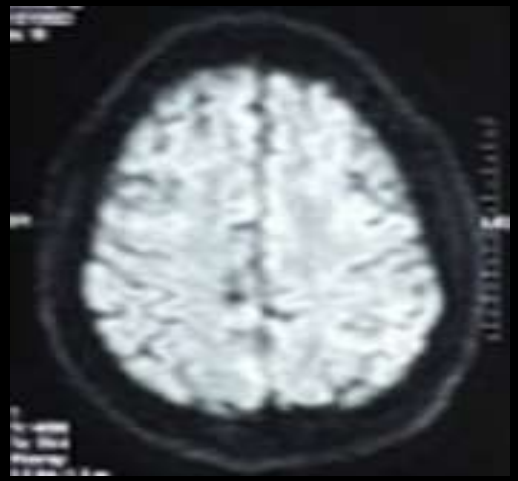
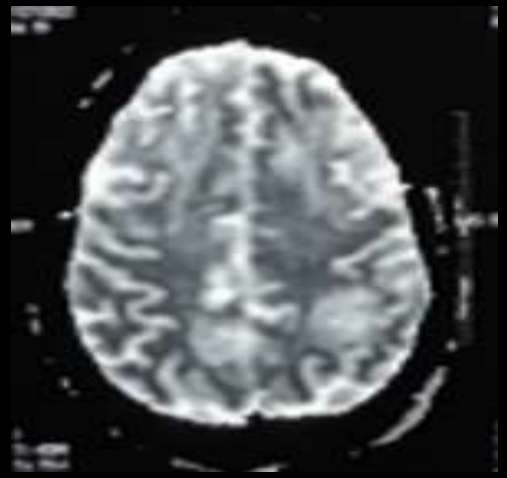
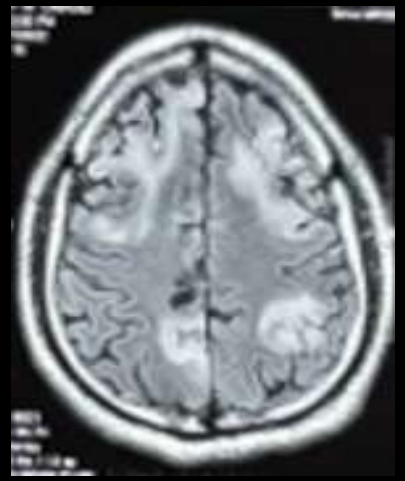
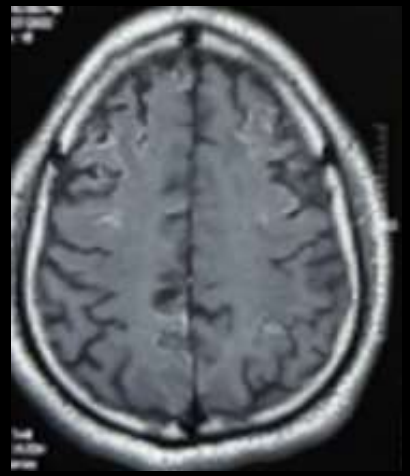
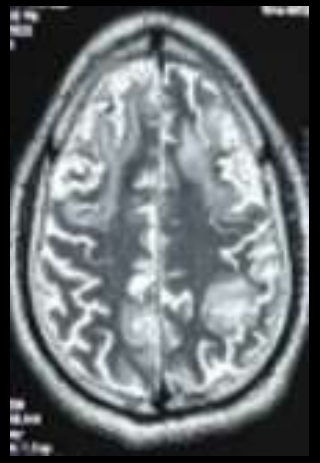
Seizure

AUG-2022

Difficulty in recognising landmarks.

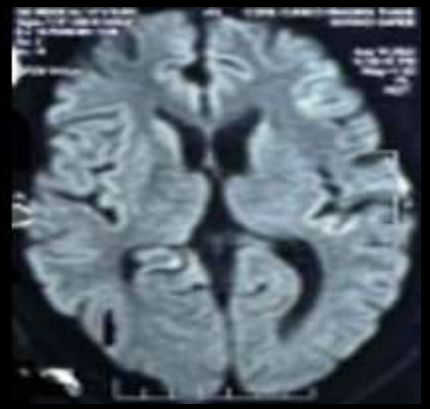
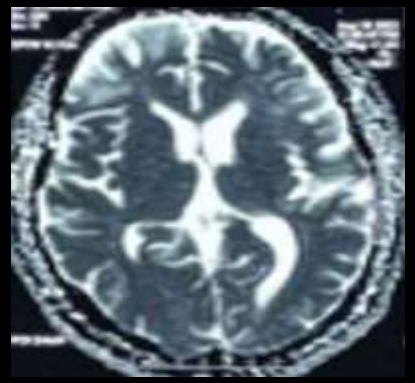
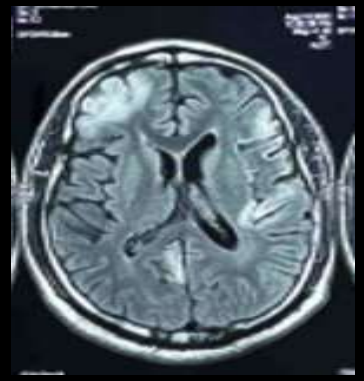
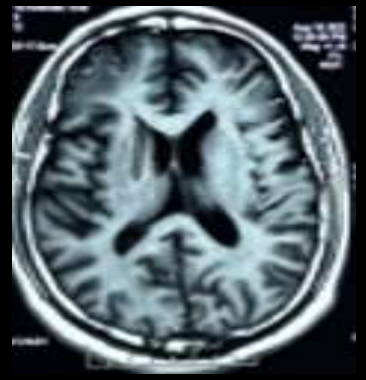
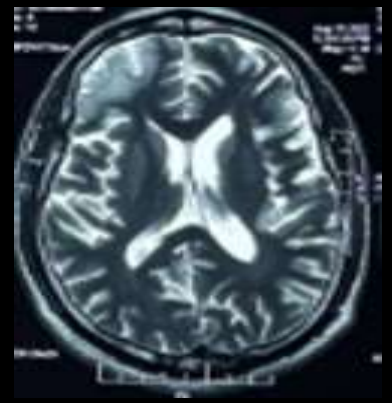
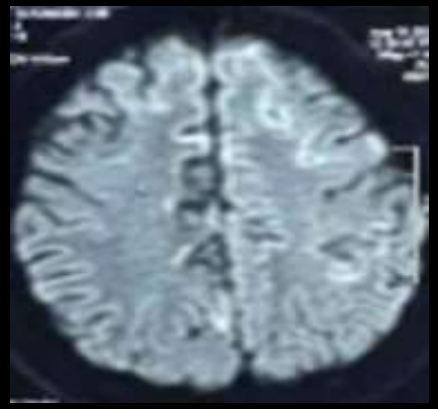
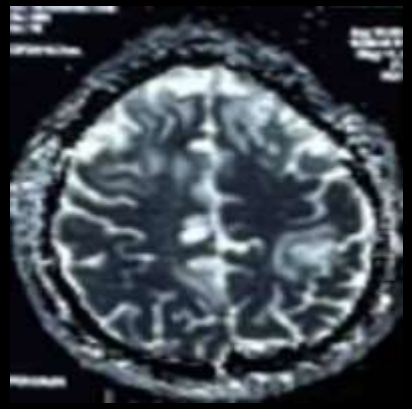
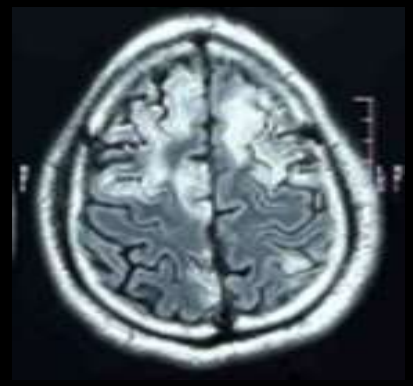
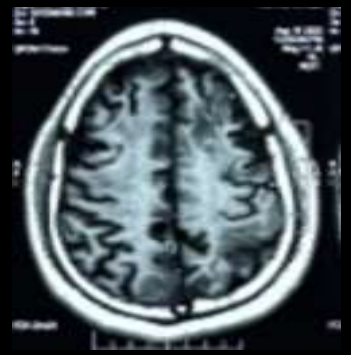
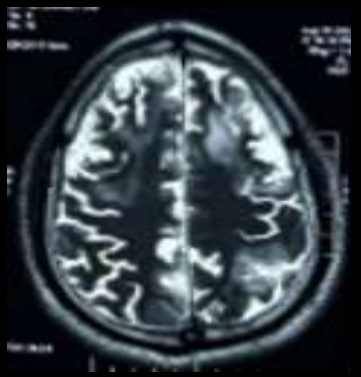
He used to forget ways back home from market

MRI BRAIN JULY 2022

DWI ADC FLAIR T1W T2W

MRI BRAIN AUGUST 2022

DWI ADC FLAIR T1W T2W

Further investigated

ANA BY IFA
Anti-DS DNA

ANCA PROFILE
P-ANCA
C-ANCA

APLA PROFILE

NEGATIVE

Sr. Lactate – WNL

Mitochondrial genetic panel- Negative

2D ECHO- 60% EF WITH NO VEGETATION OR CLOT

DSA - Normal

Came to our center for further management

JUNE- 2023

- There was a gradual decrease in speech output, eventually leading to muteness.

- Activities of daily living (bathing , eating , urine, stool passage).

- No history of
  - Myoclonic jerk
  - Stepwise progression of symptoms.
  - Constitutional symptoms (fever, weight loss)
  - Rash , joint pain, oral or genital ulcer.

Family history – Not significant

Differential diagnosis

VASCULAR – CNS vasculitis

Genetic- MELAS (Mitochondrial Encephalopathy with lactic acidosis and stroke-like episodes)

INFLAMMATORY - Autoimmune / Paraneoplastic encephalitis

INFECTIVE – Chronic HSV encephalitis

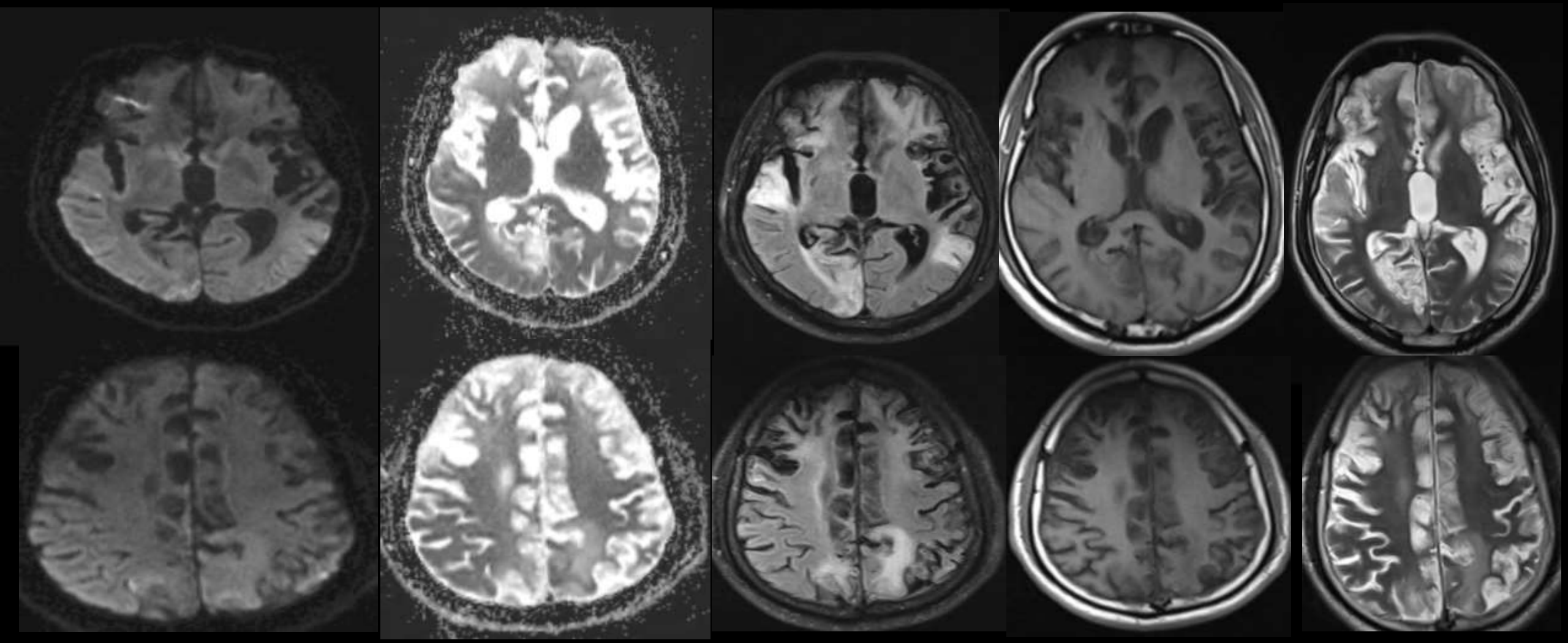
PRION – CJD (Creutzfeldt-Jakob disease)

Examination

- P- 80 /min
- BP- 130/90 mmhg

- Fundus- Normal
- Global aphasia
- Grade 2 spasticity in all 4limb with exaggerated reflex

MRI BRAIN 21 Nov 23



DWI ADC FLAIR T1W T2W

INVESTIGATIONS

Routine investigation/ TFT/ anti-TPO - Negative

CSF
PROTEIN 47 mg/dl
GLUCOSE 74 mg/dl (Corresponding bsl-102 mg/dl)
CELLS 2 (100% lymphocytes)

Serum and CSF VDRL – negative

PET Whole Body CT Scan – No FDG avid occult primary to suggest paraneoplastic syndrome

Test Name: Detection of Viruses that cause neurological disorders by Real Time PCR

Kit	**TRUPCR® NEURO PANEL KIT**		
Equipment/Machine	**Quant studio 12 K Flex**		
Specimen	**Serum**		
	Result		
Human Adenovirus	**Not Detected**	Epstein- Barr virus	**Not Detected**
Enterovirus	**Not Detected**	Varicella Zoster virus	**Not Detected**
Human Parecho virus	**Not Detected**	Human Cytomegalovirus	**Not Detected**
Herpes Simplex virus 1	**Not Detected**	Human Herpes virus 6	**Not Detected**
Herpes Simplex virus 2	**Not Detected**	Human Herpes virus 7	**Not Detected**
Human Parvo virus B19	**Not Detected**	IC (Internal Control)	**Detected (Test Valid)**
Interpretation	**Received sample found NEGATIVE for above mentioned viruses.**		

AMRITA INSTITUTE OF MEDICAL SCIENCES AND RESEARCH CENTRE

(NABH/ NABL/ ISO 9001/ 14001/ OHSAS 18001 Compliant Hospital)

Printed Date:27/11/2023 16:13:34

NEURO IMMUNOLOGY LABORATORY SERVICE REPORT

Patient Name:

MRD#: 2659599
Sex: Male
Date: 27/11/2023

Age: 42Y 1D

Sample Collected Date: 23.11.2023
Sample Received Date: 25.11.2023
Sample Received Time:4.50 PM
Reported Date:27.11.2023
Reported Time:4.12 PM

Service Order:
NMDA receptor antibody in CSF
Neuroimmunology Laboratory Service Report Reference No-28108/2023/Vol: 41
Client patient ID:Nil
Ref By Dr. Shalesh Rohatgi, Dr. Dy Patil Hospital, Pune.

Interpretation:
Undiluted CSF sample tested **negative** for NMDA receptor (Anti NR-1) antibody using recombinant, fixed transfected HEK cells by Cell Based Assay using Indirect Immunofluorescence Method.

Interpretation:
CSF sample tested for 14-3-3 test result predicts **Low risk of Creutzfeldt-Jakob Disease.** Please correlate clinically.

Result: 20,703.7 AU/ml

Reference Range:
>50,000 AU/ml- Probable diagnosis of Creutzfeldt-Jakob Disease.
>1,00,000 AU/ml- Very high risk for Creutzfeldt-Jakob Disease.

AMRITA INSTITUTE OF MEDICAL SCIENCES AND RESEARCH CENTRE

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Printed Date:28/11/2023 11:55:25

NEURO IMMUNOLOGY LABORATORY SERVICE REPORT

Patient Name:

Age: 42Y 1D

MRD#: 2659599
Sex: Male
Date: 28/11/2023

SI No	Antibody	Result	Reference
1.	ANNA-1(anti Hu)-Antineuronal Nuclear antibody -1	Negative	Negative
2.	ANNA-2(anti Ri)Antineuronal Nuclear antibody-2	Negative	Negative
3.	ANNA -3 Antineuronal Nuclear antibody -3	Negative	Negative
4.	PCA -2 Anti Purkinje Cell cytoplasmic antibody-2	Negative	Negative
5.	PCA -Tr Anti Purkinje Cell cytoplasmic antibody-Tr	Negative	Negative
6.	AGNA-1 Antiglial nuclear antibody-1	Negative	Negative
7.	CRMP-5 - Collapsin response mediator protein-5 (anti CV 2) antibody	Negative	Negative
8.	Amphiphysin antibody	Negative	Negative
9.	Ma2/Ta antibody antibody	Negative	Negative
10.	Unclassified Neuronal Antibody	POSITIVE	Negative
11.	LGI1(Leucine-rich glioma inactivated protein 1) antibody (VGKC associated)	Negative	Negative
12.	CASPR2 (Contactin-associated protein 2) antibody(VGKC associated)	Negative	Negative
13	IgLon5 antibody	Negative	Negative

Treatment

- MPS
- AED (Brivaracetam and oxcarbamazepine)
- IVIG
- Rituximab

- No further neurological deterioration
- Facial expression and interaction with family members improved.

70-year male, right-handed, educated up-to 10^{th} std, farmer by occupation

Presented with –

Insidious onset gradually progressive

- Forgetfulness – 1 year
- Postural instability - 2 month
- During sleep relative noticed sudden jerking movement of his limbs, loud vocalizations, and punching behavior, which previously injured his wife-2 month
- Slowness of activity and walking speed reduced, difficulty in turning -2months
- 2 episodes of urinary incontinence -1 & 1/2 month

- Loss of interest in day-to-day activity
- Autonomic dysfunction- postural giddiness , constipation, erectile dysfunction
- Increase daytime sleepiness
- Cognitive fluctuations

- No history of visual hallucination, psychotic behavior, socially inappropriate behavior.
- No history heavy metal exposure, drug intake, stepwise progression, trauma
- Family history – not significant

On examination

- Postural BP drop + (30/20) (Supine- 140/100 Standing-110/80)
- MMSE- 22/30, MOCA-13/30, FAB- 12/18.
- Memory – Recent , working, episodic memory affected, semantic preserved
- Language – Fluency- reduced,
  Comprehension , repetition , naming, writing- Preserved

- Frontal lobe testing – Affected
- Parietal lobe – Calculation affected , construction apraxia present
- Occipital lobe testing – Visual disorientation present

- Feature of parkinsonism:-

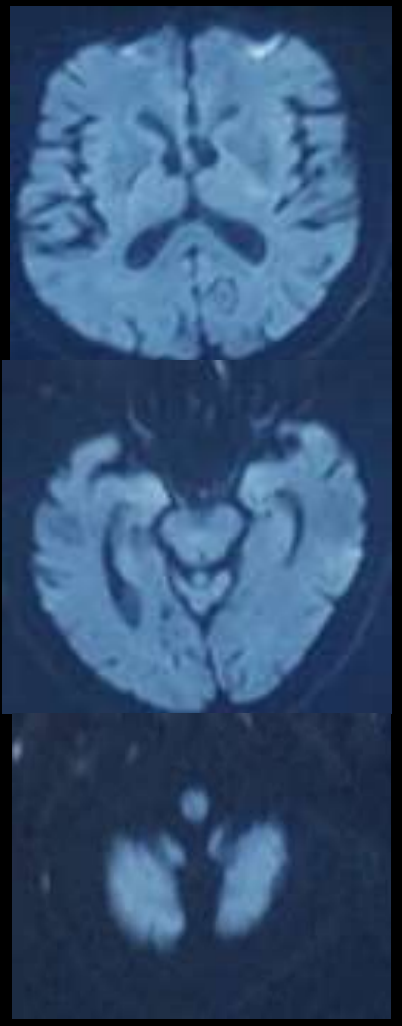
Slow hypophonic speech with word-finding pauses, mask facies, re-emergent tremor, bradykinesia, Cog-Wheel rigidity.

Pull test- negative.

No upward gaze restriction, normal saccades & pursuits and no square wave jerks.

- Routine lab investigation- WNL.
- MRI BRAIN – 4 AUG 2023

CSF- Proteins- 98.40 mg/d
Glucose- 84 mg/dl (corresponding- 118mg/dl)
TLC- 10 (100% lymphocyte)



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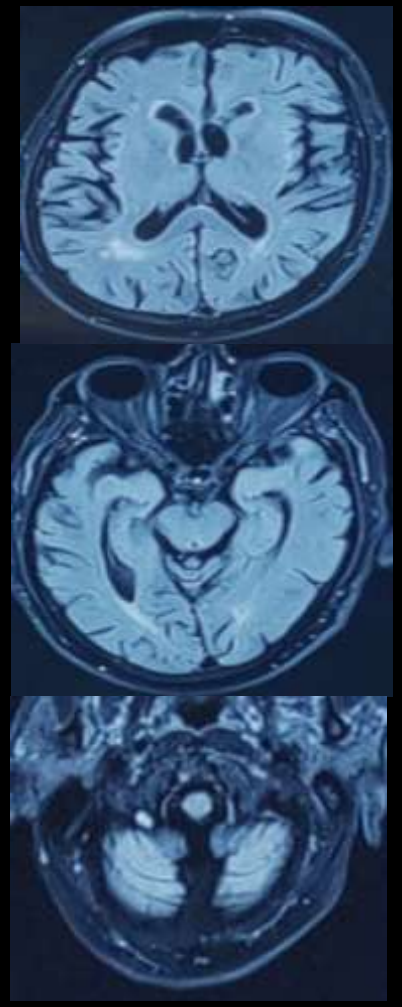
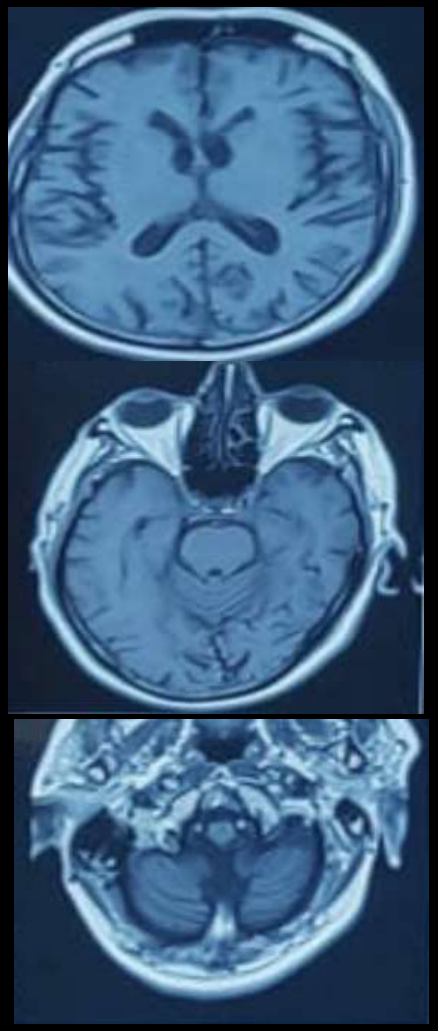
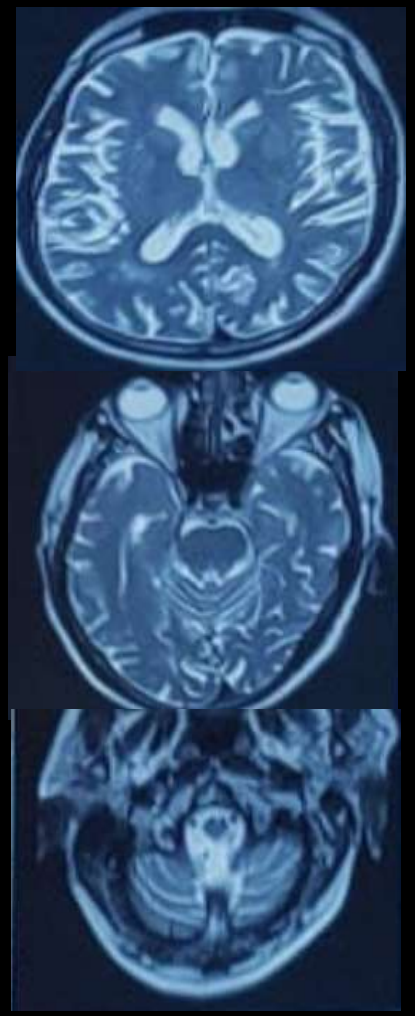


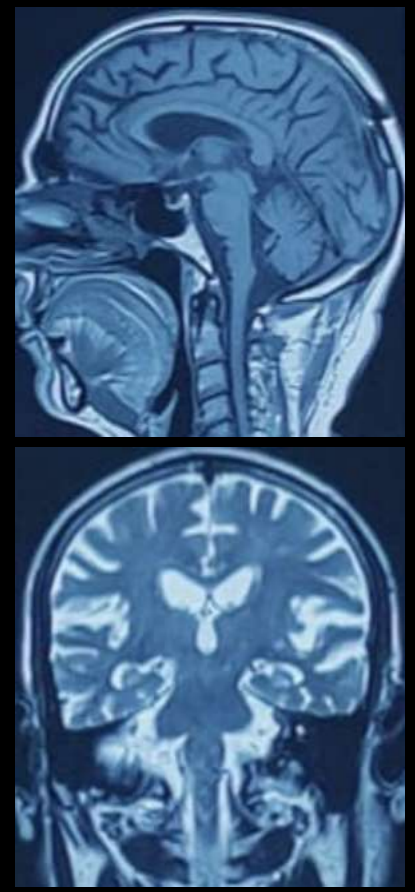
FLAIR



T1W



T2W



PET SCAN- No FDG avid occult primary to suggest paraneoplastic syndrome

AMRITA INSTITUTE OF MEDICAL SCIENCES AND RESEARCH CENTRE

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Printed Date:09/08/2023 15:00:42

NEURO IMMUNOLOGY LABORATORY SERVICE REPORT

Patient Name:

Age: 70Y 2D

MRD#: 2612217
Sex: Male
Date: 09/08/2023

SI No	Antibody	Result
1.	ANNA-1(anti Hu)-Antineuronal Nuclear antibody - 1 Conformation by Dot blot	Negative
2.	ANNA-2(anti Ri)Antineuronal Nuclear antibody-2 Conformation by Dot blot	Negative
3.	ANNA -3 Antineuronal Nuclear antibody -3	Negative
4.	PCA -2 Anti Purkinje Cell cytoplasmic antibody-2	Negative
5.	PCA -Tr Anti Purkinje Cell cytoplasmic antibody-Tr	Negative
6.	AGNA-1 Antiglial nuclear antibody-1	Negative
7.	CRMP-5 - Collapsin response mediator protein-5 (anti CV 2) antibody, Conformation by Dot blot	Negative
10.	Anti -Amphiphysin antibody ,Conformation by Dot blot	Negative
11.	Anti -Ma/Ta antibody antibody ,Conformation by Dot blot	Negative
10.	Unclassified Neuronal Antibody	**POSITIVE**	However nervous system specific autoimmunity noted in the form of an unclassified antibody, clinical significance of which is uncertain. It can be considered as significant after ruling out other etiology. If an autoimmune etiology is strongly suspected clinically, a trial of immunotherapy can be attempted after ruling out all the other alternate diagnoses.
11.	Leucine-rich glioma inactivated protein 1(LGI1) antibody	Negative	
12.	Contactin-associated protein 2 (CASPR2) antibody	Negative	
13	Anti-IgLon5 antibody detection in Serum	Negative	

Treatment

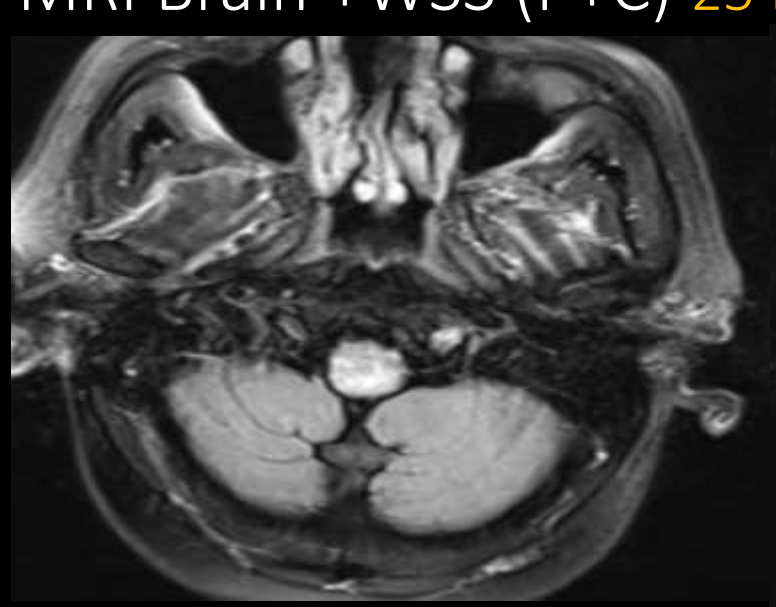
IV MPS * 5 days f/b Oral steroid

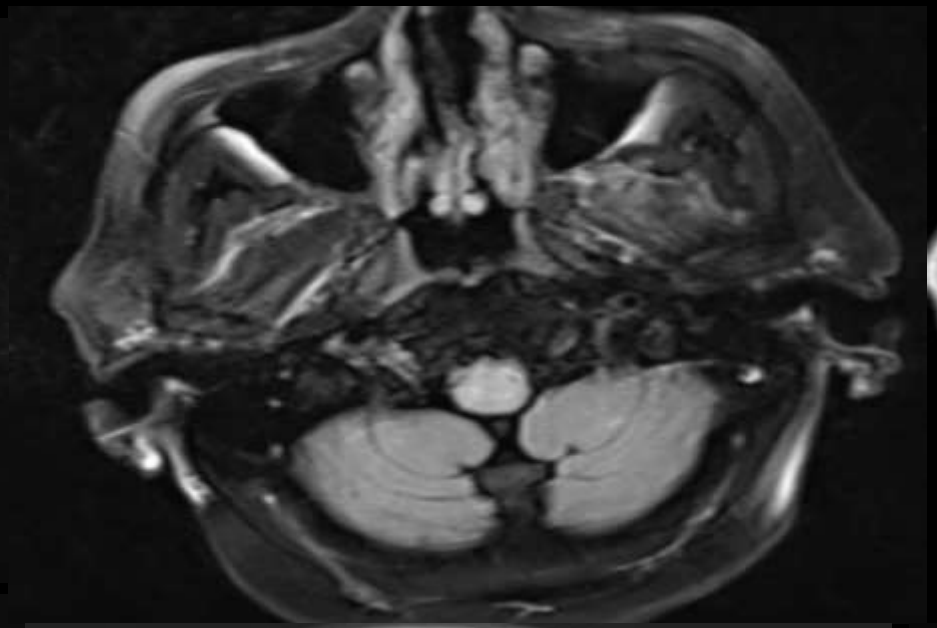
Significant improvement in symptoms

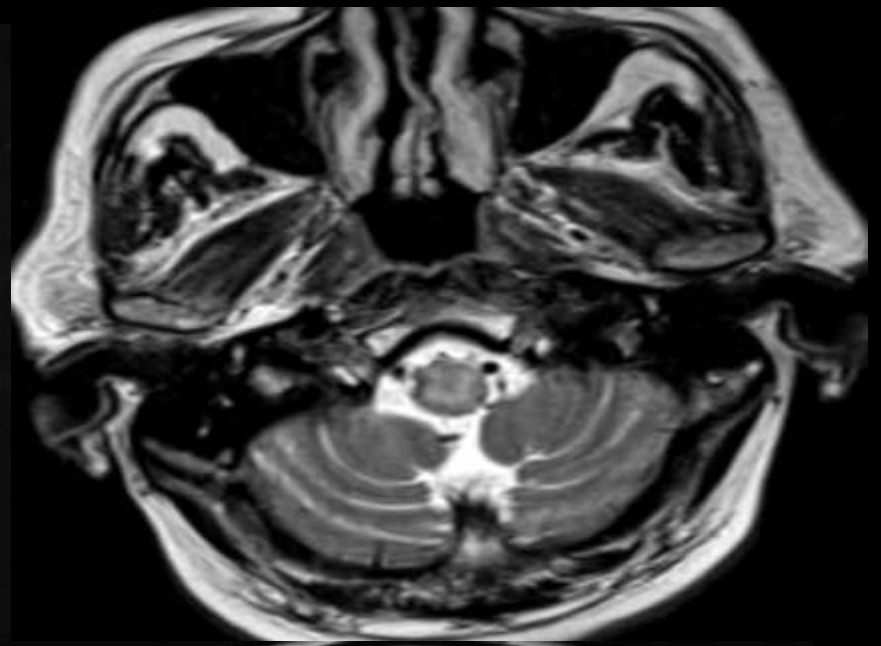
(25 Dec 2023)

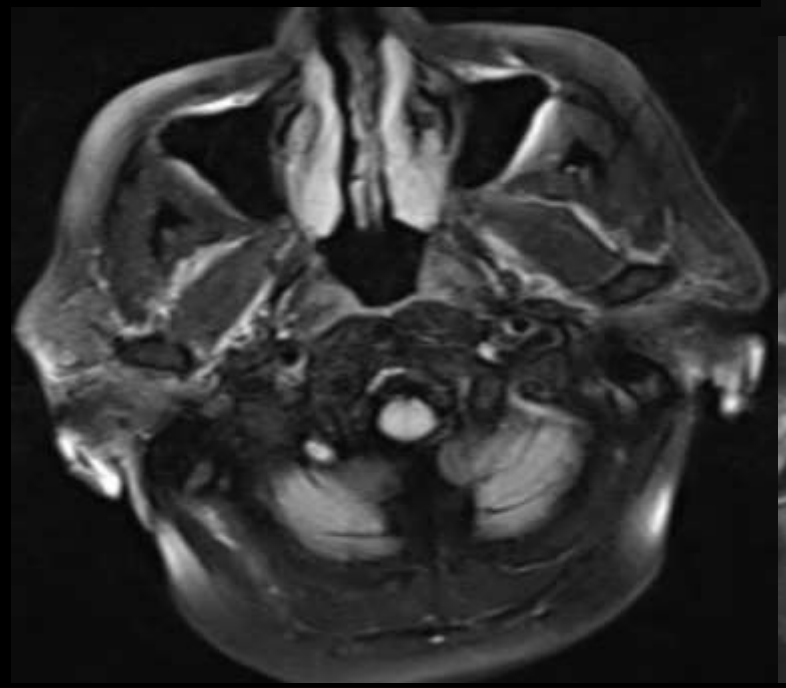
- Worsening of symptoms post fever
  - RBD
  - Increase forgetfulness
- MMSE-23/30
- FAB-9/18

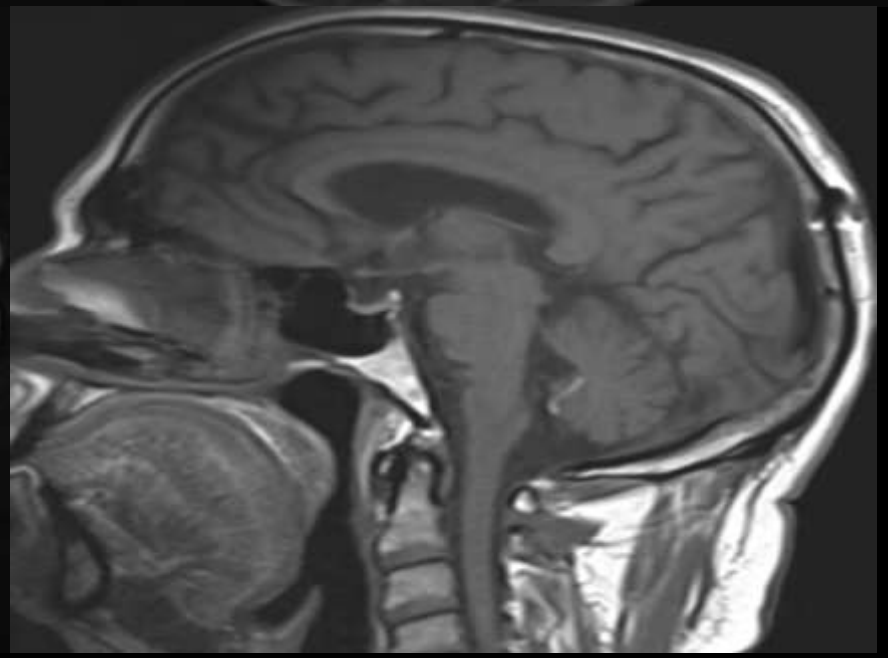
MRI Brain +WSS (P+C) 25 Dec 23

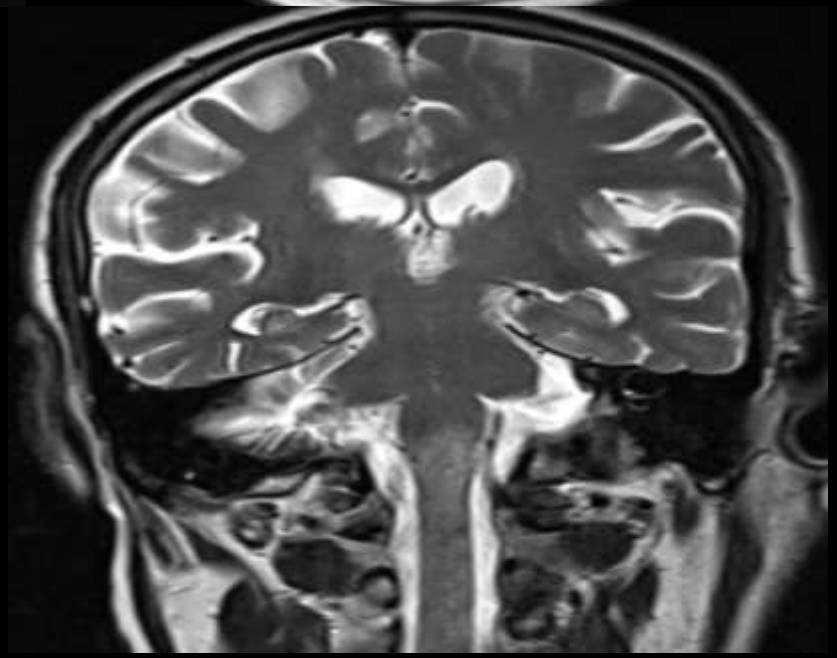










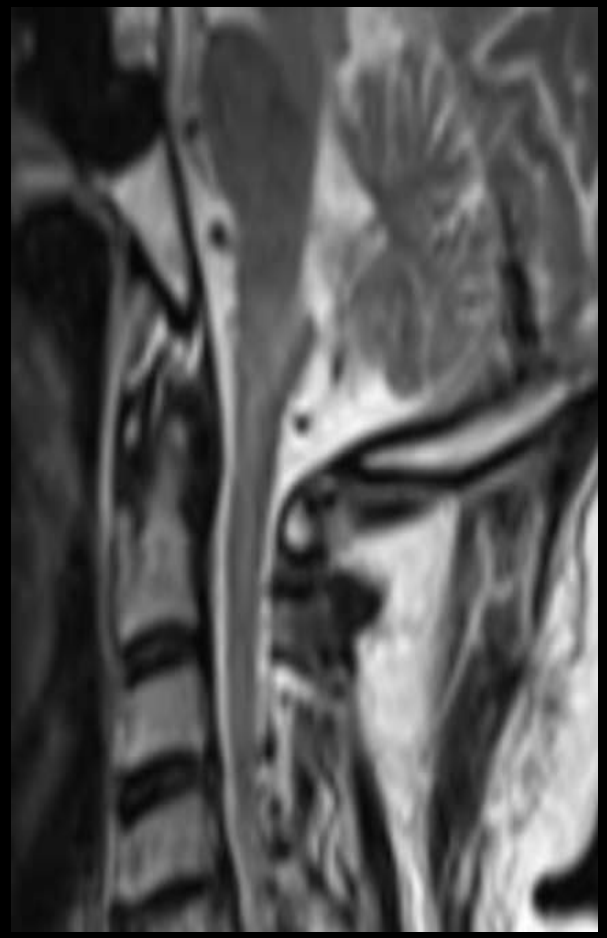


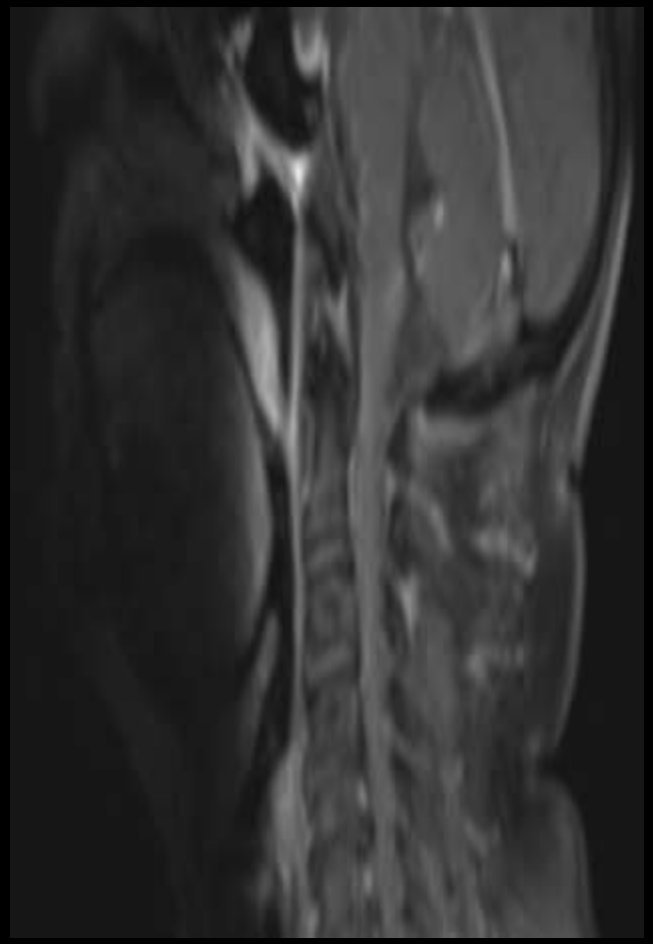
FLAIR

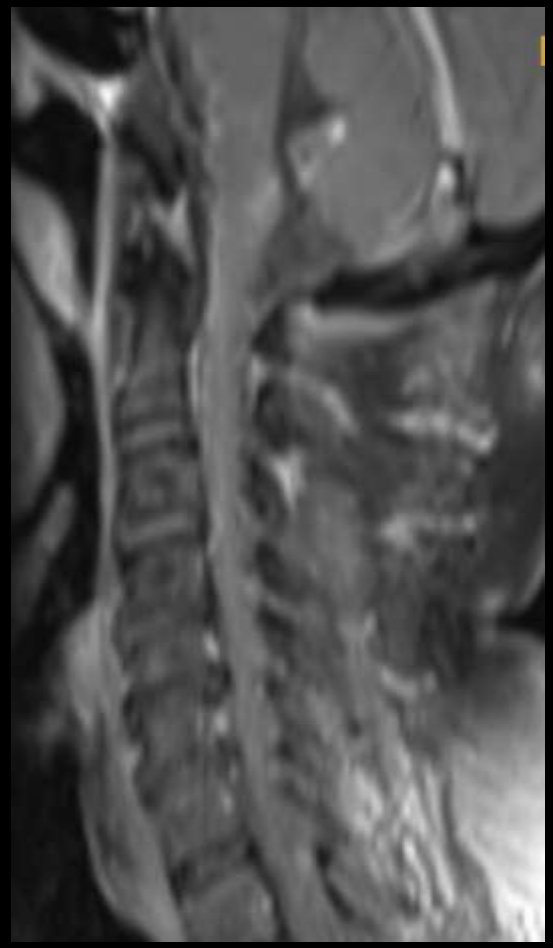
T1W

T2W

MRI Brain +WSS (P+C) 25 Dec 23







Sr. NMO/MOG- Negative

Treatment

- IV MPS * 5 days f/b Oral steroid
- Plasmapheresis
- Rituximab

MMSE- 25/30 (Improvement in recall 2 Point)

No RBD

Discussion

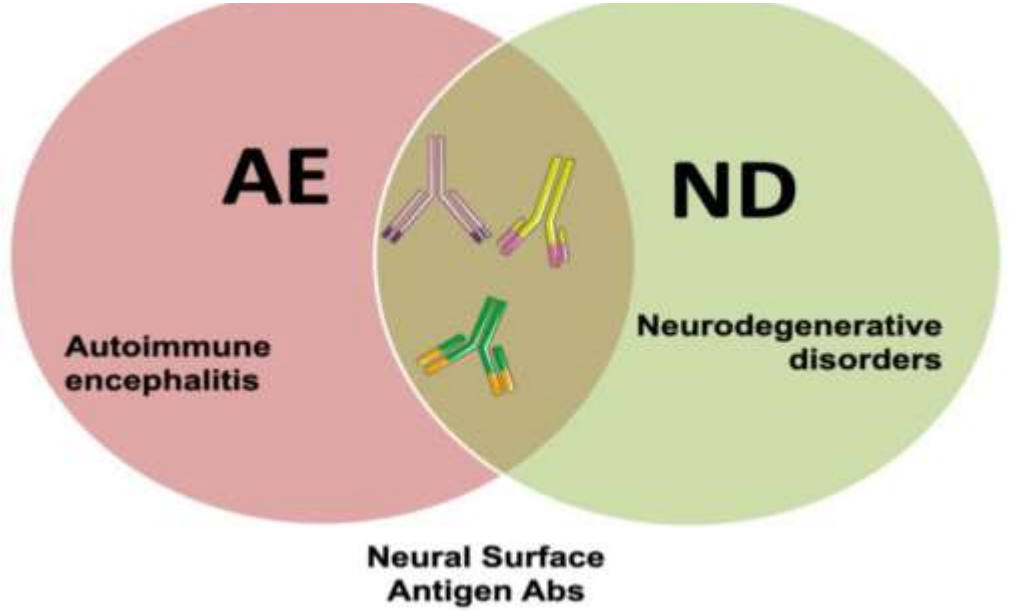
When to suspect autoimmune encephalitis ?

Neural Surface Antibodies and Neurodegeneration: Clinical Commonalities and Pathophysiological Relationships

by Maria Pia Giannoccaro [1,2,*], Federico Verde [3,4], Luana Morelli [2], Fortuna Ricciardiello [1] and Rocco Liguori [1,2]

MDPI

biomedicines



Core features :

- Subacute onset of cognitive impairment, behavioural and psychiatric changes +/- focal CNS signs/ seizure +/- Movement disorder
- +/- Brain MRI
- +/- Reactive CSF

THE LANCET Neurology

Panel 2: Criteria for probable antibody-negative autoimmune encephalitis

1. Rapid progression (<3 months) of working memory deficit (short-term memory loss), altered mental status, or psychiatric symptoms
2. Exclusion of well defined syndromes of autoimmune encephalitis (limbic encephalitis, acute disseminated encephalomyelitis, Bickerstaff's brainstem encephalitis)
3. Absence of well characterised autoantibodies in serum and CSF, and at least two of the following*:
   - MRI abnormalities suggesting autoimmune encephalitis†
   - CSF pleocytosis, CSF-specific oligoclonal bands, or elevated CSF IgG index†
   - Brain biopsy showing inflammatory infiltrates and excluding other disorders (eg, vasculitis or tumour)
4. Reasonable exclusion of alternative causes (table)

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Autoimmune atypical parkinsonism — A group of treatable parkinsonism

Sudheeran Kannoth • Anandkumar Anandakkuttan • Annamma Mathai • Anuja Nirmala Sasikumar • Vivek Nambiar

No.	Age/sex	Clinical diagnosis	Clinical features	CSF	Antibody	Response to treatment	Cancer	Levo-dopa trial
1	75/M	Probable multiple system atrophy	Autonomic dysfunction × 4 months. Parkinsonism × 3 months Cerebellar dysfunction × 3 months	Normal	VGKC complex antibody–LGI1 antibody	Improved with Intravenous Methyl Prednisolone (IVMP)	Whole body PET CT negative.	No levodopa trial
2	53/F	Possible progressive supranuclear palsy (PSP)	Tremors × 13 years Slowness and rigidity × 10 years	Normal except mildly elevated protein 52.3 mg/dl	Uncharacterized neuronal antibody	Improved with IVMP	Whole body PET CT negative.	Poor response to levodopa
3	66/M	Probable PSP	Parkinsonism × 6 months	Normal except elevated protein 51.2 mg/dl	Uncharacterized neuronal antibody	Improved with IVMP	Whole body PET CT negative.	No levodopa trial
4	51/M	Probable multiple system atrophy (MSA)	Bladder symptoms × 3 years Cerebellar and parkinsonian symptoms 1 year. Vocal cord involvement × 4 months.	Normal	Uncharacterized neuronal antibody	Improved with IVMP	Limited cancer work up no cancer.	No response to L Dopa
5	75/M	Probable PSP.	PSP feature 3 months Encephalopathy 1 months	Normal except elevated CSF protein 117.5 mg/dl	LGI1 antibody with an uncharacterized neuronal antibody.	Improved with IVMP	Whole body PET CT — early carcinoma lung	No levodopa trial
6	73/M	Atypical parkinsonism	Parkinsonism, ataxia, falls × 4 months	Normal	Uncharacterized neuronal antibody	Improved with IVMP	Limited cancer work up no cancer.	No levodopa trial
7	49/M	Atypical parkinsonism	Parkinsonism with psychosis × 7 years	Normal	Uncharacterized neuronal antibody	Improved with IVMP	Limited cancer work up no cancer.	Total daily dose of 1100 mg levodopa with carbidopa in combination. Now dose reduced to 100 mg/day.
8	61/M	Atypical parkinsonism	PSP with cerebellar signs × 6 months.	Normal	Uncharacterized neuronal antibody	Improved with IVMP	Whole body PET CT No malignancy	Syndopa trial was given, no response.
9	70/M	Probable PSP	Parkinsonism, fall × 1 year	Normal	Uncharacterized neuronal antibody	Improved with IVMP	Limited cancer work up no cancer.	No levodopa trial
10	64/M	Atypical parkinsonism.	Cortico basal syndrome with cerebellar signs × 1 year.	Pleocytosis 28 cells/cmm, 100% lymphocytes, normal glucose, protein 47.5 mg/dl	Uncharacterized neuronal antibody	Improved with IVMP	Limited cancer work up no cancer.	No levodopa trial

Thank You