Sero-negative Autoimmune Encephalitis: Our experience

Dept Of Neurology

- Auto immune encephalitis is relatively newly discovered illness in last one decade
- It is at least as common as viral encephalitis *.

Among persons under 30 years of age NMDAR-antibody encephalitis was more common than any individual infectious cause of encephalitis.

*Dubey D, Pittock SJ, Kelly CR, McKeon A, Lopez-Chiriboga AS,et al.Autoimmune encephalitis epidemiology and a comparison to infectious encephalitis. Ann Neurol. 2018 Jan;83(1):166-177

In AE inflammation is caused by a misdirected immune response against self-antigens expressed in the CNS

1. Autoanatibodies that target neuroglial antigens- neuronal cell surface/ion channels/receptors

Examples - NMDAR, LG1, GAD-65, IGLON-5 CASPAR 2, GABA-B R, GABA- A R. AMPA-R,GLY-R, DPPX, MOG ,NEUREXIN

- 2. Against nucleolar antigens - mostly paraneoplastic

  Examples - anti Hu,Ma-2, Yo, Ri,TA, ampiphysin

When to suspect AE ?

Subacute onset (less than 3 months)

- change in personality or level of consciousness and symptoms suggesting involvement of the limbic system including working memory deficits, psychiatric symptoms
- New onset seizures
- Movement disorders- chorea, Dystonia, dyskinesia,Myoclonus

- At least one of the following:

  EEG- epileptic/ focal slow wave activity

  CSF- mild pleocytosis/ raised proteins

- Typical MRI findings: Bilateral hyperintensities on T2-weighted /FLAIR sequence restricted to the medial temporal lobes.*

- Reasonable exclusion of alternative causes.

  CLINICAL SPECTRUM IS WIDE WITH FEW COMMON SYMPTOMS(CORE SYMPTOMS) AND FEW SPECIFIC TO THAT ANTIBODY.

* MRI brain can be normal in 80% cases

- Detection of Antibody in serum/CSF is confirmatory.
- Antibodies detection is by immunoblotting, Cell based assays
- Half of the cases may be antibody negative
- Some new antibodies have been identified whose assay is not available

Some common features which may be seen in anti NMDAR and IGLON 5 :

- Neuropsychitraic manifestations- most common- mood disturbances, delirium, frank psychosis, behaviour disturbances and catatonia
- Movement disorders- oro- facial dyskinesia, mycolonus, facio- brachial seizures, GTCS
- Autonomic dysfunctions- bladder / anhidrosis
- Bulbar symptoms – (specially in IGLON-5)

  Dysphagia, sleep disorders, central apnoea, stridor

- Anti NMDA-R antibody AE is seen both in association with or without malignancy (ovarian terratoma) . In young females chances of finding ovarian teratoma are 60%
- IgLon-5 disease is not associated with malignancy
- Therapeutic response to immuno-supressants is seen in both seronegative and seropositive AE . Paraneoplastic AE and IgLON-5 associated AE respond poorly to immunosupression.

Case 1

Case history:

- 69 year old female , with H/o Type-2 DM & Hypertension admitted on 17/9/2021 to psychiatry ward with :

-Irrelevant talking

-Excessive sleepiness during day

-Insomnia at night with frequent falls during sleep

-Suspicious behavior and confusional state

-Difficulty in swallowing (Liquids> solids).

All of the above complaints were since 5 months

- Decreased appetite and weight loss (6 kg in last 6 months)
- Insidious in onset and gradually progressive Admitted to psychiatry ward in April 2021 for similar complaints and diagnosed with organic delirium

MRI brain-white matter periventricular T2 hyperintensities (ischemic)

- On admission had breathlessness and fall in SP02 (91-95 % on room air)
- Bilateral ground glass opacities --bronchopneumonia
- HRCT thorax- CT severity score-10/25
- COVID-19 RTPCR- Negative
- Admitted to RICU , had hypercapnia (PCO2 -80 mm hg) -- type-2 Respiratory failure

Course in hospital :

- Had a stay for about 2 months
- Had hypercarbia ,gradually settled down but required long term ventilation .
- She was tracheostomised and was on ventilatory support
- She had inspiratory stridor and persistent tachypnea, episodes of central apnea
- ABG – Respiratory acidosis ,pCO2 raised (between 55-60 mm hg)
- Had frequent episodes of hypoglycemia .
- She continued to have fluctuating sensorium

- Neurology consult was obtained on 23/9/2021.
- Patient was conscious ,obeyed simple verbal commands ,but was intubated
- No neurological deficit apart from fluctuating sensorium.

- Impression :

1.Neuropsychiatric abnormalities

2.Sleep disorder

3.REM sleep behaviour disorder

4.Central apnea

5.Stridor

6.Dysphagia (Neurogenic)

Clinical impression-?Autoimmune encephalitis .?Anti NMDAR ? Iglon5

Investigations :

- Hemogram – normal
- ESR – 38
- RFT/LFT/ELECTROLYTES/AMMONIA – Normal
- Thyroid function tests – Normal
- Anti-TPO antibodies- negative
- VDRL– negative
- ABG –type-2 respiratory failure

- ANA- IFA – negative
- ANCA – Negative
- Blood ,urine culture – No growth (Done twice in view of sepsis)
- Autoimmune encephalitis panel - negative
- Serum Anti – NMDA receptor antibodies – negative
- Anti –IGLON5 – negative

Test Description	Observed Value	Biological Reference Interval
Autoimmune Encephalitis Panel, (Qualitative) (Cell Based Assay)		
Glutamate Receptor (NMDA)	**Negative**	Negative
Glutamate Receptor (AMP Type 1&2)	**Negative**	Negative
GABA-B Receptor	**Negative**	Negative
VGKC Associated Protein:		
Contactin Associated Protein 2 (CASPR2)	**Negative**	Negative
Leucine Rich Glioma Inactivated Protein 1	**Negative**	Negative
Sample Type	**Serum**	

Method : Indirect immunofluorescence
Sample type :

- CSF routine /microscopy –

-Cells -4

-Proteins -38

-Glucose- 90 (corresponding BSL- 130)

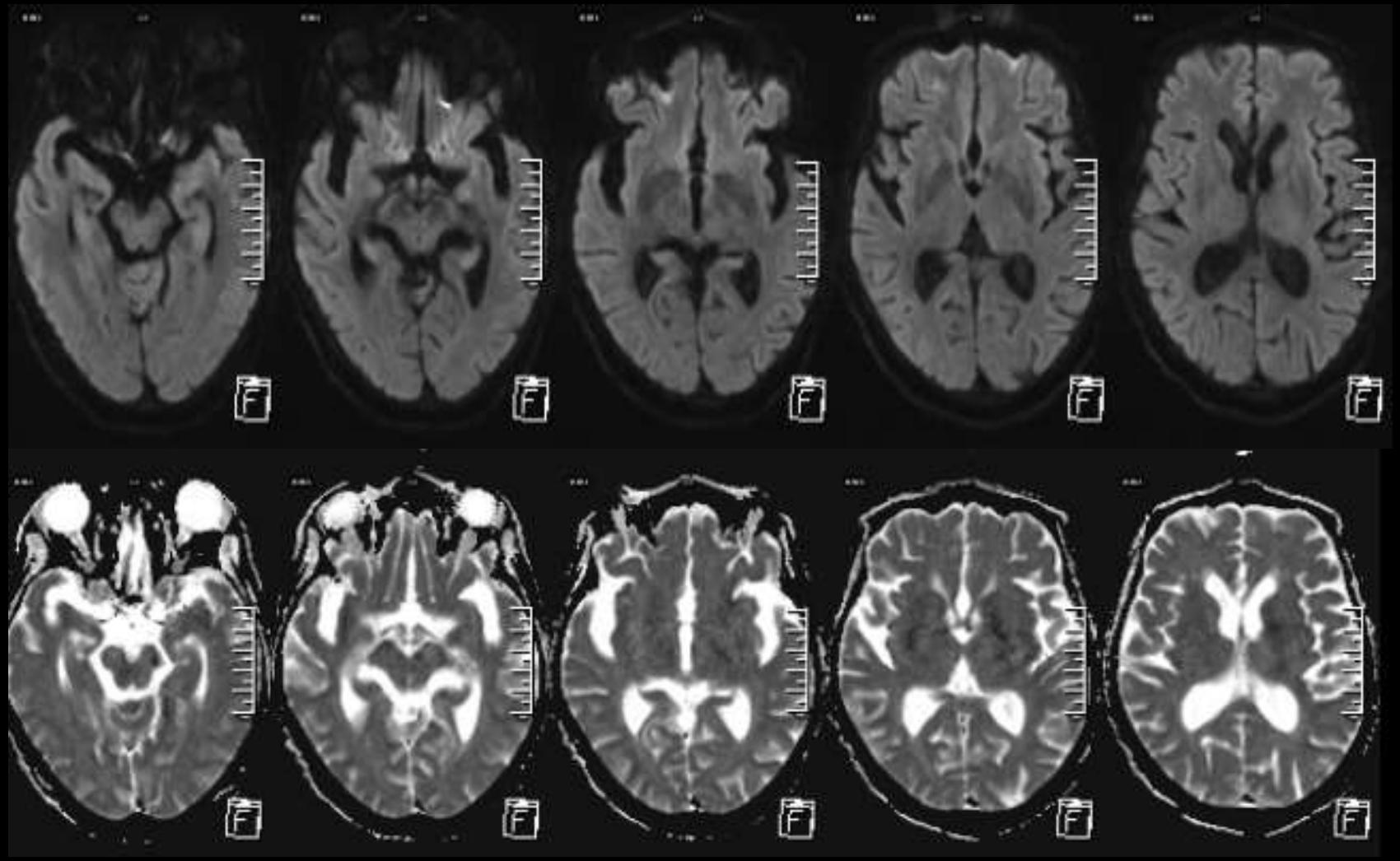
-CSF for CB-NAAT – negative

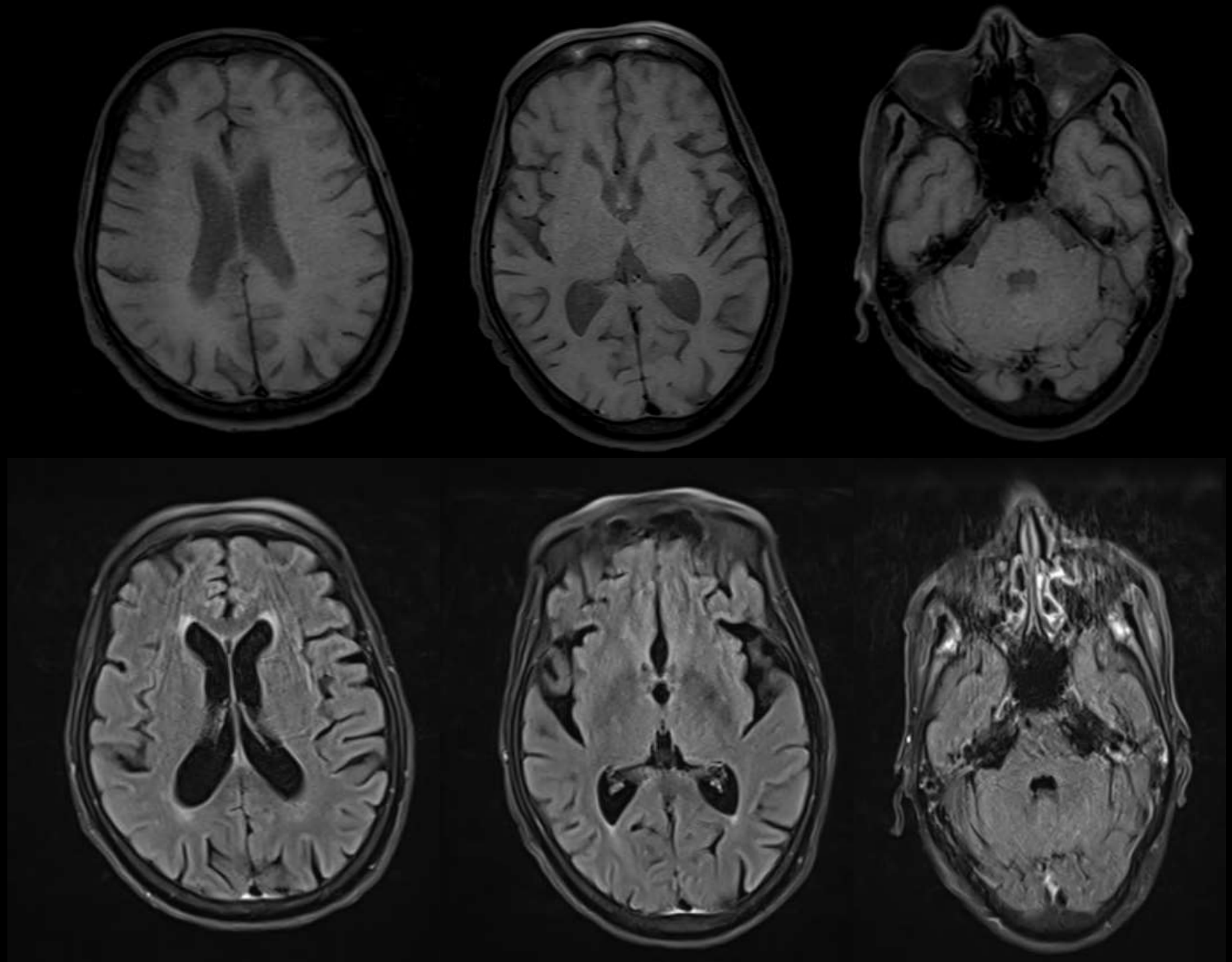
- BAL for AFB/Grams – negative
- Growth of E.Coli in BAL culture
- BAL-CBNAAT – negative
- Upper GI scopy for dysphagia-GERD

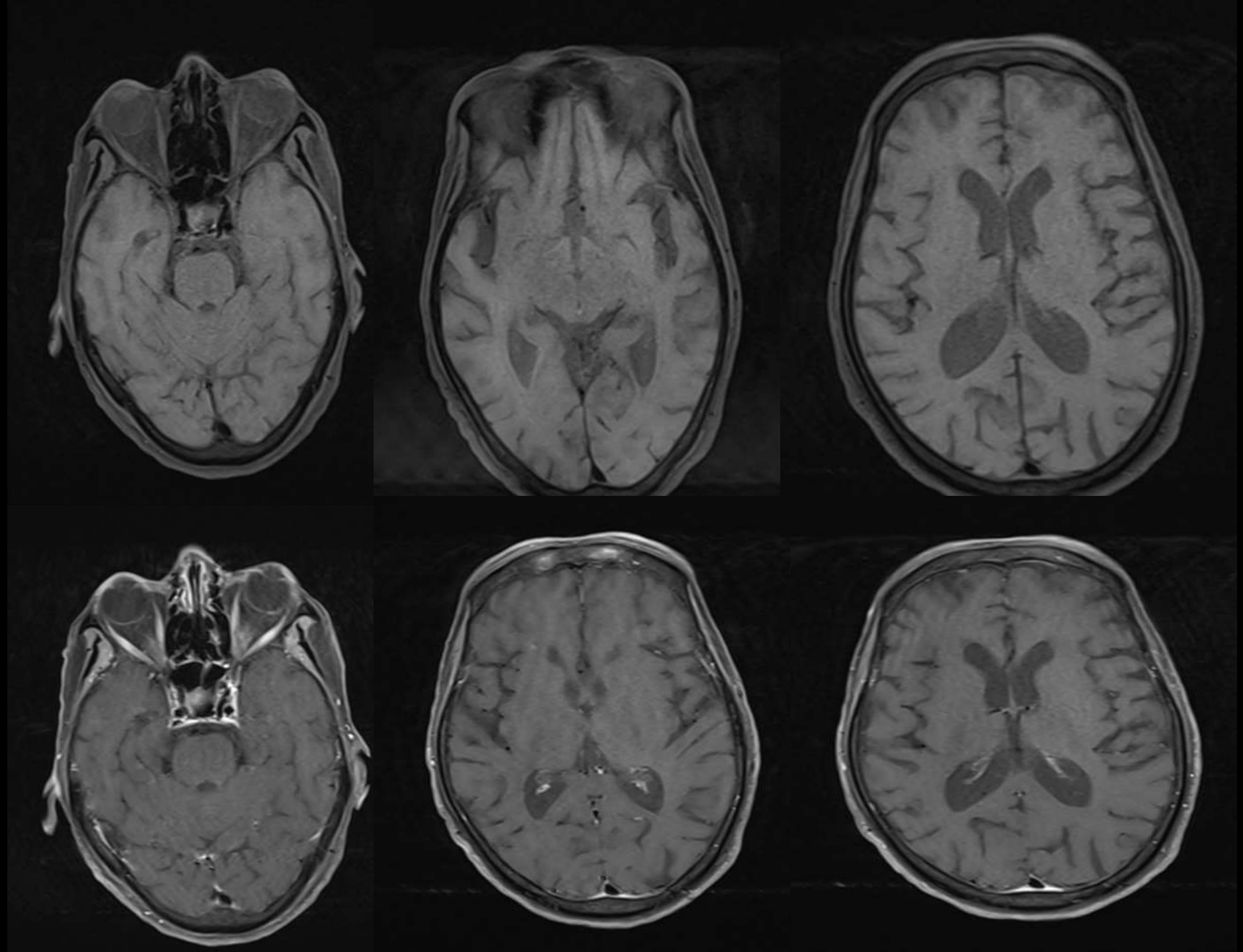
- USG abdomen /pelvis done twice to rule out malignancy – normal
- 2D-ECHO – Normal

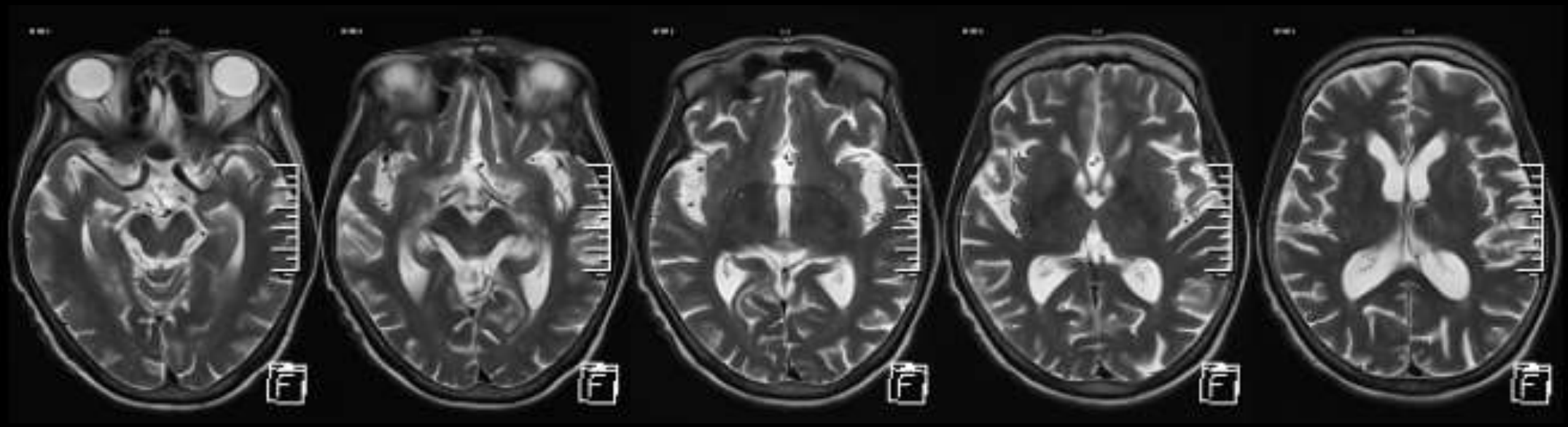
Electrophysiological studies :

- RNS – Normal
- NCV – Reduced bilateral median CMAPs (not correlating)
- EEG – Background slowing suggestive of diffuse encephalopathy









Provisional diagnosis :

- Seronegative Autoimmune encephalitis

- Initially started on Inj IV MPS , had sepsis so stopped and oral steroids started
- She had turbulent course with frequent sepsis and respiratory failure episodes
- Had one episode of NSTEMI
- Patient did not show any improvement so was started on IV-Immunoglobulins

after which she showed only mild improvement in sensorium .

Patient succumbed to sepsis and multiorgan failure on 22/10/2021

CASE 2

History:

37 year old female presented to outside hospital with history of

-Episodes of severe headache for 15 days

- Headache was severe, occipital > holocranial, throbbing type. Each episode lasting for 10-15 minutes.
- Patient used to scream in pain and often used to hold her head
- Associated with transient unresponsiveness with staring look. Multiple episodes in a day, recovered in 2 to 3 minutes.

- Patients husband reported that she had similar episodes since 2-3 weeks.
- No h/o
- focal weakness ,diplopia, blurring of vision, TVOs.
- involuntary movements.

- fever, cough, expectoration .

- TB,DM, hypertension.

- recent blood transfusion.

- weight loss.

- behavioural changes.

-any medication intake specifically anti psychotic drugs.

EXAMINATION:

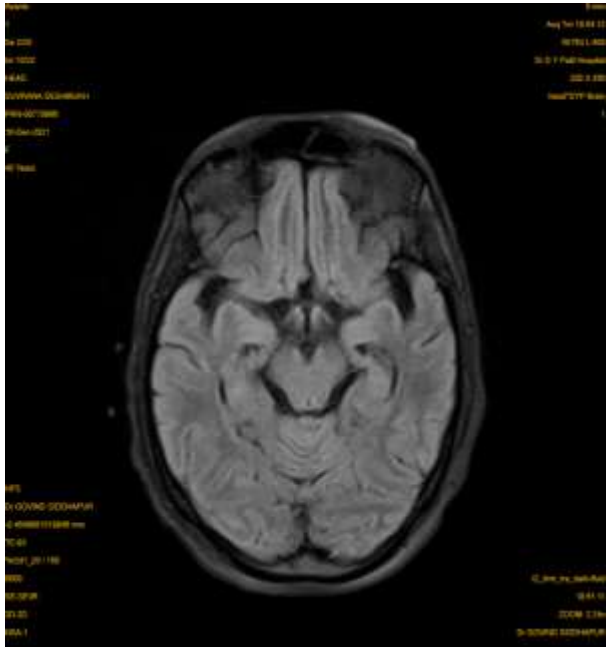
- Patient was drowsy but was following simple commands
- Vitals – stable
- No skin lesions
- Pupils - NSNR ,Extra Occular Movements- bilaterally full
- Fundus - Normal
- No focal deficit.
- No sign of meningeal irritation.
- Planters - flexors.

Differentials:

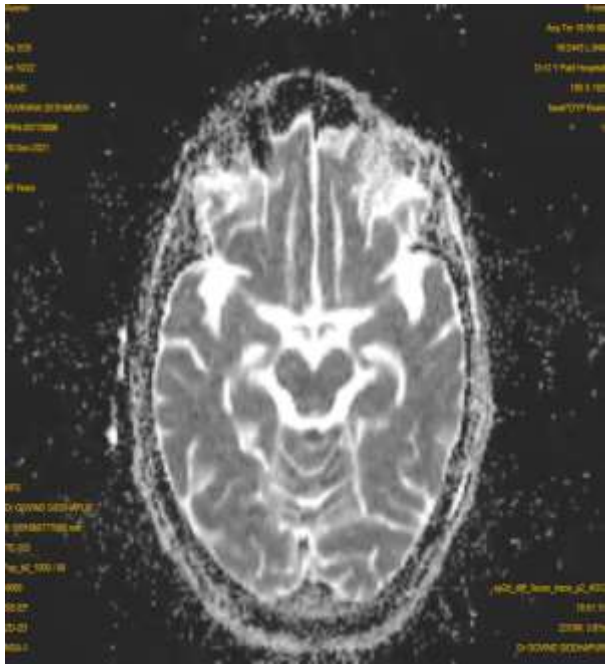
- Reversible cerebral vasoconstriction syndrome.
- Sub arachnoid haemorrhage.
- Meningitis.

MRI brain with Angiogram was done which was normal.

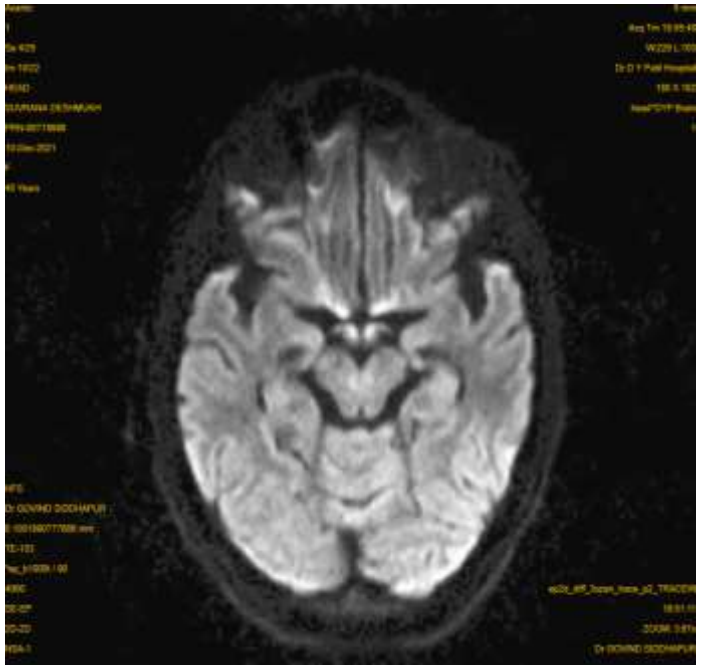
- No evidence of SAH/ beading of intracranial arteries



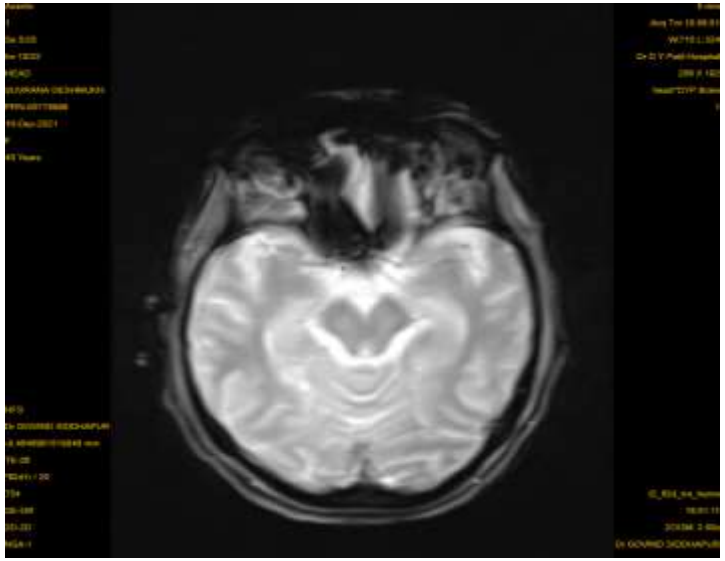
Axial FLAIR



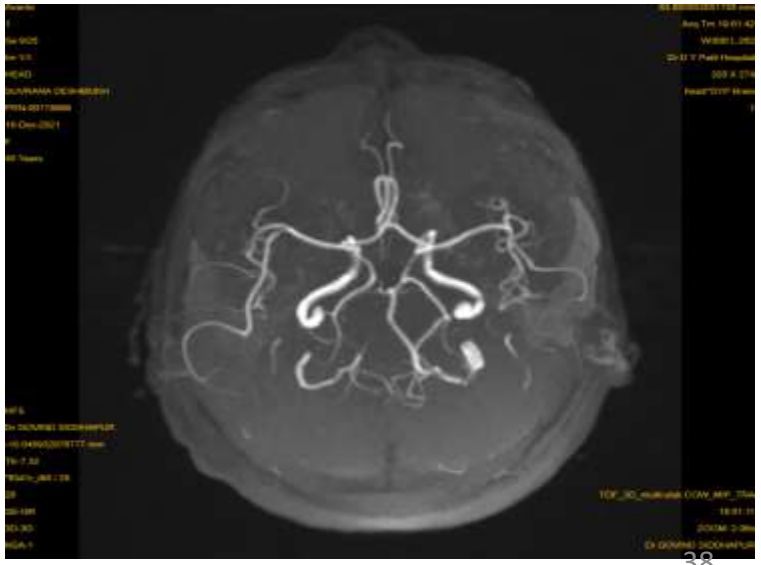
Axial ADC



Axial Diffusion



GRE



Cerebral angiogram

CSF ANALYSIS:

Opening and closing pressure- Normal.

Proteins: 65 mg/dl

Sugar : 33 mg /dl bsl:143 mg/dl

Cells:2

ADA :37

- CSF Gram Stain, KOH Mount –Negative.
- CBNAAT - Negative.
- CSF fungal culture -no growth.
- CSF aerobic culture -no growth.
- CSF malignant cytology –negative.

- Frequency and duration of episode were increasing with associated loss of conciousness lasting for 2 to 3 minutes.
- Empirically patient was started on antitubercular treatment along with antibiotics.

- On the third day of admission ,patient became unconscious ,had tachycardia & was intubated in view of low GC .
- Patient was shifted to our hospital .
- She was received with GCS E3VtM4 on pressure support.
- The episode of recurrent pupil dialation persisted.
- She was now having fever .

- Semiology of headaches ,crying spell, staring looks and pupillary dilatation could be a part of seizure .

Differentials:

1. Autoimmune Encephalitis .
2. RCVS- MRI brain did not show SAH and Angiogram was normal

Investigations:

- CBC,RFT,LFT,Electrolyte- normal
- Thyroid Profile -Normal
- ANA IFA – Negative.
- ANCA- Negative
- Anti TPO -Negative.
- VDRL-Negative.
- EEG – Generalised slowing .No spikes
- HRCT Thorax-Normal.
- Blood,Urine ,ET cultures –No growth.

CSF analysis was repeated.

Protein -30 mg /dl

Sugar-47 mg /dl bsl-152 mg /dl

Cell- 20 All lymphocyte.

- Patient was started on antiepileptics .
- IV MPS was started and given for 3 days
- Antibiotics were stepped up in view of continuous fever and antitubercular drugs were continued.
- There was little improvement in her general condition so plasmapheresis was started.

Serum Autoimmune encephalitis panel:

- NMDA(NR1 Subunit) -Negative
- AMPA(Anti Glutamate Receptor)- Negative
- GABA A/ B Receptor Antibody- Negative
- LGi1 Antibody- Negative
- CASPR2 -Negative.
- GAD 65 -Negative.

- Patient underwent three cycle of plasmapheresis with little improvement.
- During the third cycle of plasmapheresis, she had hypotension.
- She was put on ionotropic support.
- She developed sepsis along with septic shock .
- On 7th day of admission patient had cardiac arrest and we were not able to revive her.

DISCUSSION:

- In our patient one finding which was unexplained was CSF hypoglycohrrachia.
- CNS infections and malignancy was ruled out.

Other Causes of Hypoglycorrhea in CSF

1.Glut-1 deficiency- manifests with

- Abnormal developmental delay ,
- Seizures(mostly unspecified,myoclonic or absence)
- Intermittent hemiplegia
- Paroxysmal kinesogenic dyskinesia

None of this was present in our patient

Malignant Atrophic Papulosis

- Thrombo obliterative vasculopathy involving Skin,GI tract,CNS
- Skin lesions-central porcelain-white atrophy surrounding telangiectatic rim.
- 2^{nd} to 5^{th} decade
- Systemic disease develop suddenly or years after cutaneous manifestations.
- CNS manifestation in form of vasculitic infarct may develop.
- Diagnosis by biopsy

Case 3

Case of subacute cerebellar ataxia

54 year old male ,farmer by occupation presented with :

- Loss of balance while walking since 2 months
- Slurring of speech since 1 month

- No history of difficulty in walking in dark places or during night time
- Also developed smearing of face while eating and difficulty in brushing since 1 month
- H/o truncal imbalance.
- H/o Slurring of speech since 1 month.

<u>Loss of balance</u> :

- Insidious in onset since 2 months
- Gradually progressive such that he was not able to stand without support since 1month
- Increased on trying to walk in narrow passages

- No h/o Oscillopsia.

- No h/s/o Motor or sensory involvement

- No h/o Cranial nerve involvement & Bladder or bowel involvement

- No h/o behavioral abnormalities or memory disturbances, abnormal involuntary movements, loss of consciousness.

- No h/o Fever or Headache.

- No h/o Abdominal pain , diarrhea or steatorrhea.

No h/s/o :

- Thyroid disorder
- Connective tissue disorder.
- Underlying malignancy.

No h/o :

- Drug intake or toxin exposure

- Preceding viral illness

- Any vaccination prior to onset of symptoms

Personal history

- Patient was non-diabetic & non-hypertensive
- No history of any addictions
- No h/o blood transfusion
- No h/o unsafe sexual practice

Family history

- Born out of non connsanguinous marriage.

No h/o similar complaints in the family

Summary

54 year old male :

- Subacute onset rapidly progressive gait, limb and truncal ataxia and slurred speech

Possible differentials

•Immune mediated cerebellar ataxia

-AE - GAD antibody associated ataxia , Hashimotos, Paraneoplastic cerebellar ataxia

-Celiac disease (gluten ataxia)

- Sarcoidosis
- CJD – Oppenheimer variant of S-CJD

Examination findings on presentation:

- Vitals – stable
- No skin lesions/ rashes /oral ulcers/alopecia
- BMI – 28.4 kg/m2

Neurological Examination:

- Patient was conscious and well oriented
- Higher mental functions were normal(Mmse 29/30).
- All cranial nerves were normal.
- Motor and sensory examination – normal

Cerebellar signs :

Finger nose test – bilaterally positive

Truncal ataxia – present

Dysdiadokokinesia present

Heel shin test positive bilaterally

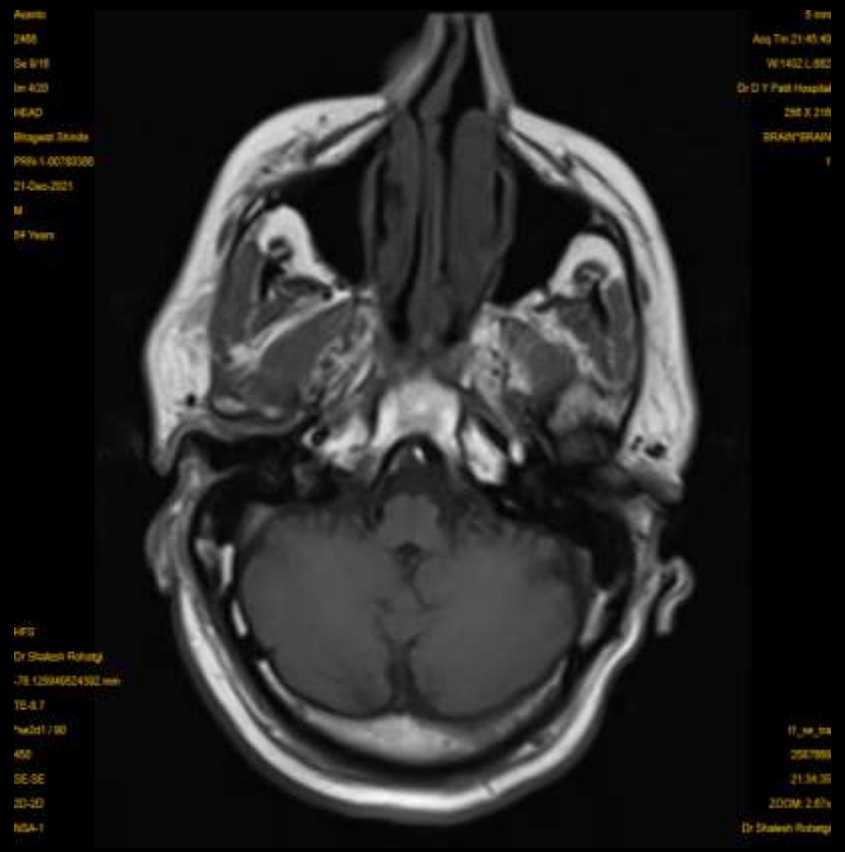
Speech - scanning

Wide base gait

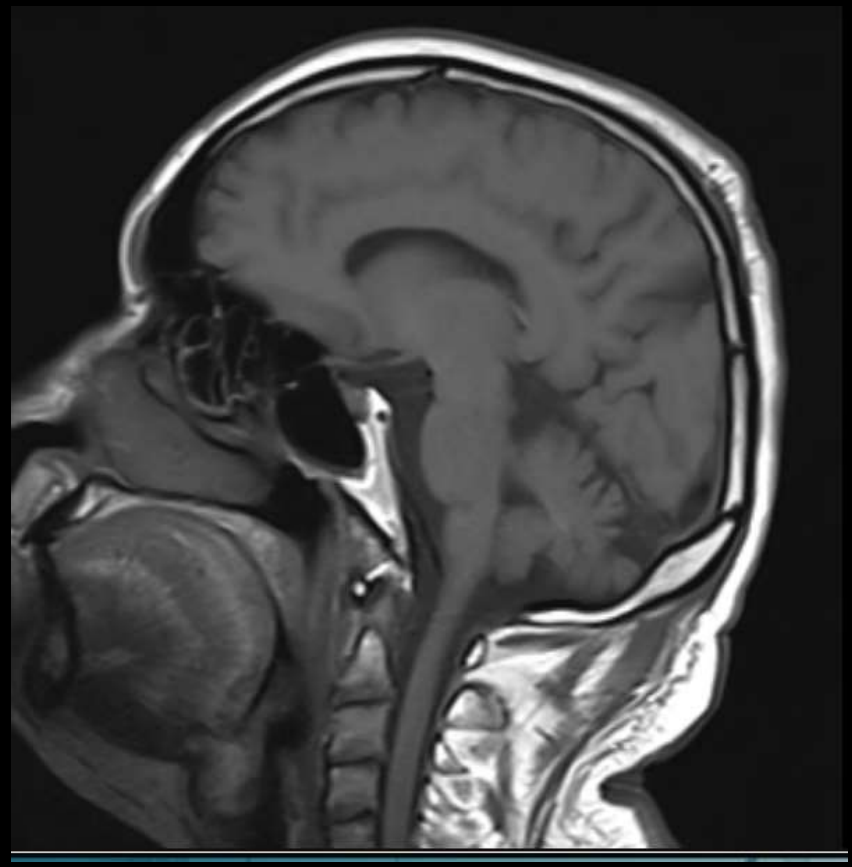
No tremors

No nystagmus

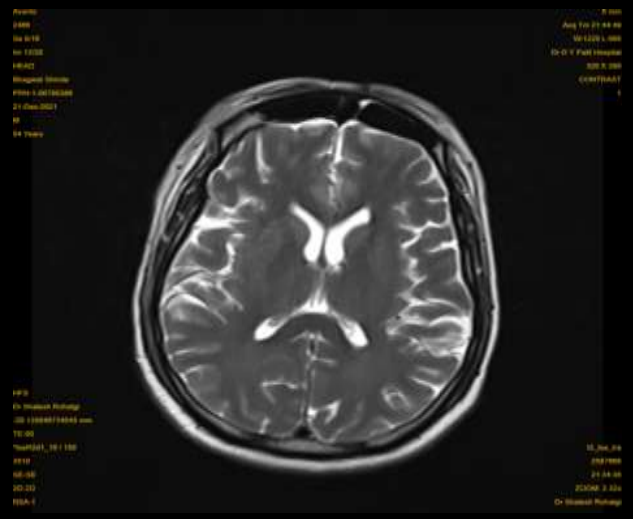
Gait at presentation



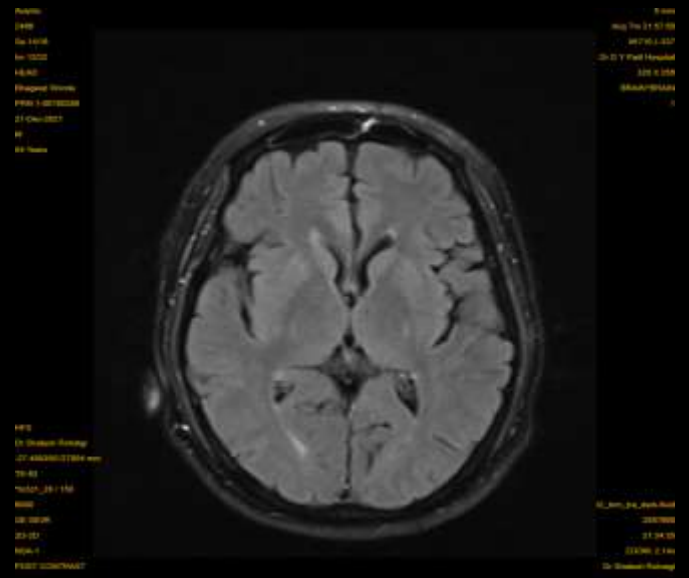
Axial T1W



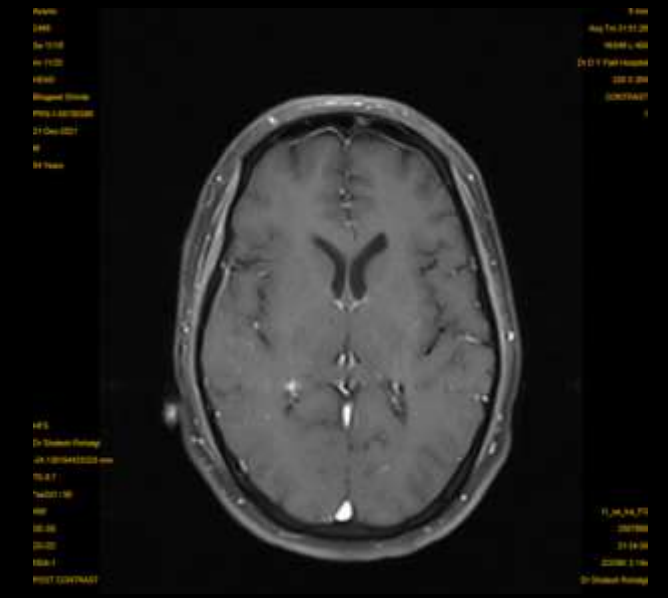
Saggital T1W



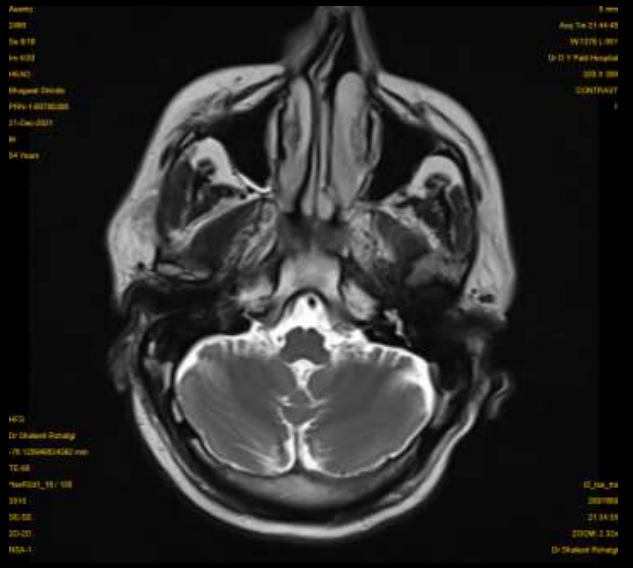
Axial T2W

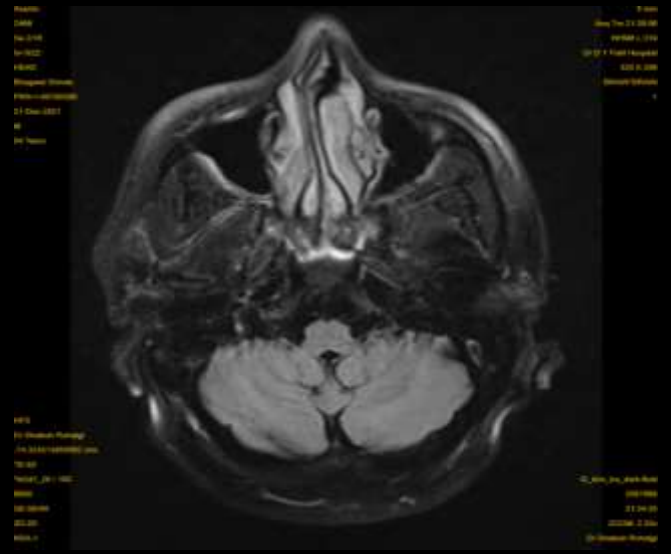


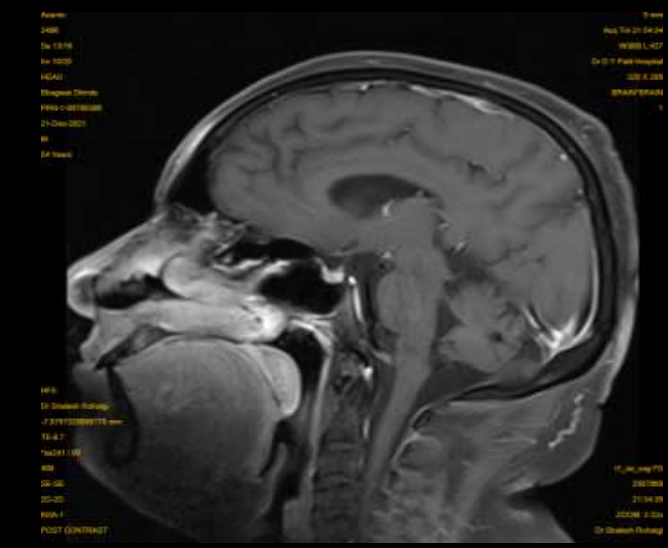
Axial T2 FLAIR

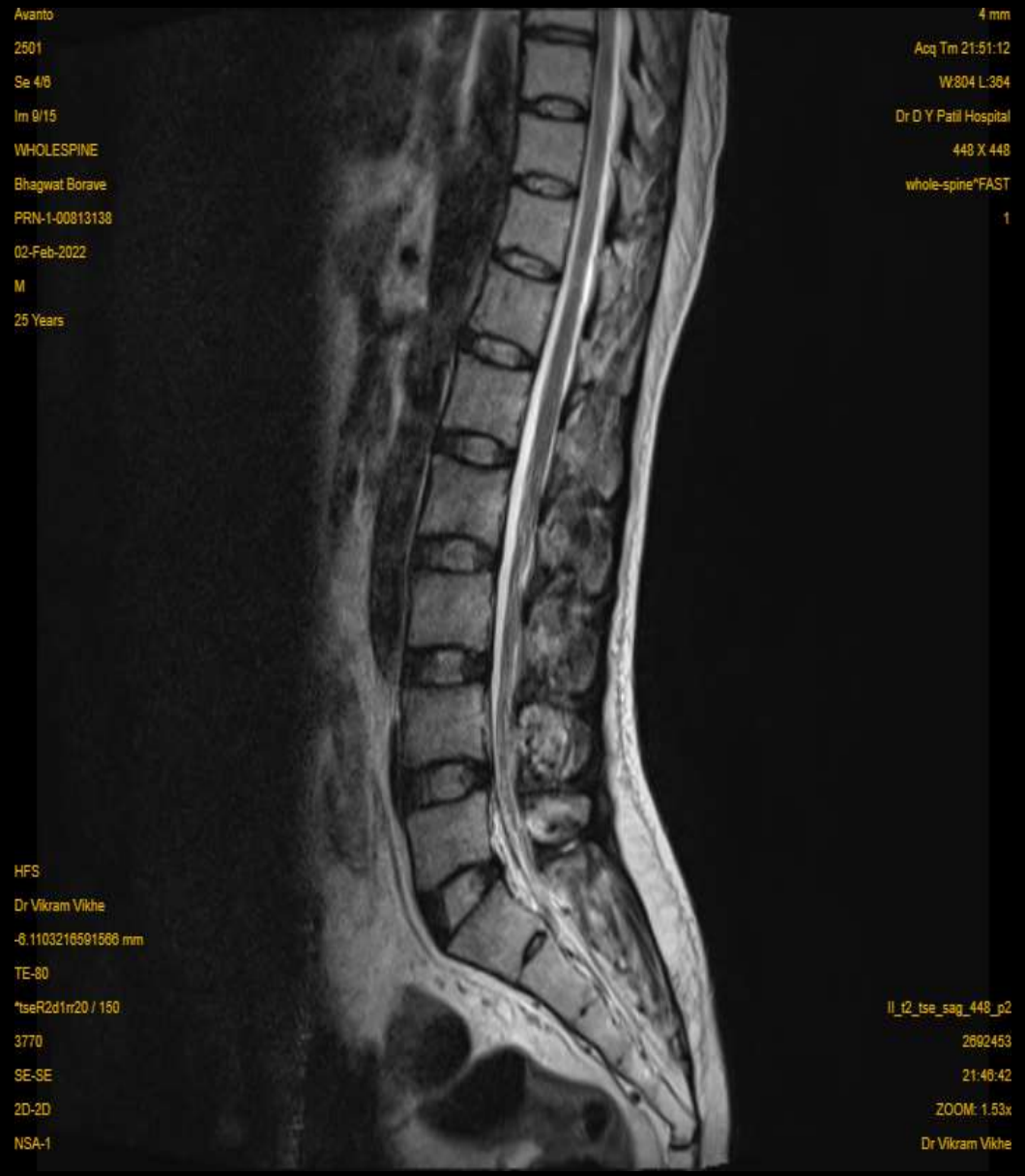


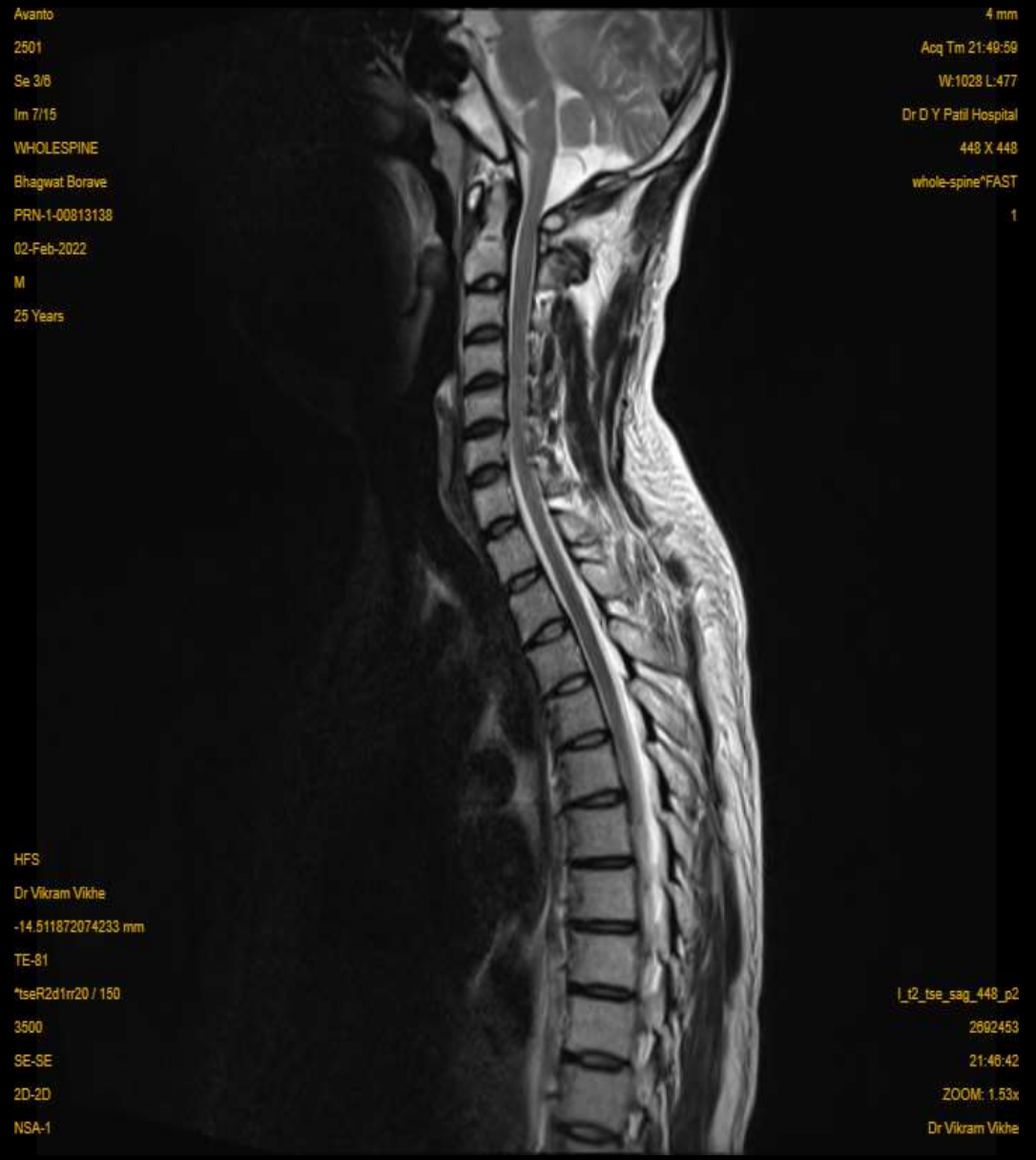
T1W POST CONTRAST











MRI WHOLE SPINE

INVESTIGATIONS:

- Hemogram- normal
- ESR levels –15
- Thyroid function tests – normal
- HIV/HBsAg/HCV- negative
- Blood sugar levels - normal
- Renal function and liver function test – normal

- ANA – IFA – Negative
- ANCA Profile – Negative
- Vitamin B12 / Vitamin E levels – Normal
- Serum ACE levels : Normal
- Anti –TPO levels : normal
- Anti-TTG / anti – gliadin : Negative

CSF analysis:

- Protein - 49.3mg/dl
- Glucose – 68 mg/dl (corresponding bsl-142 mg /dl)
- Cells - 02 (All lymphocytes)

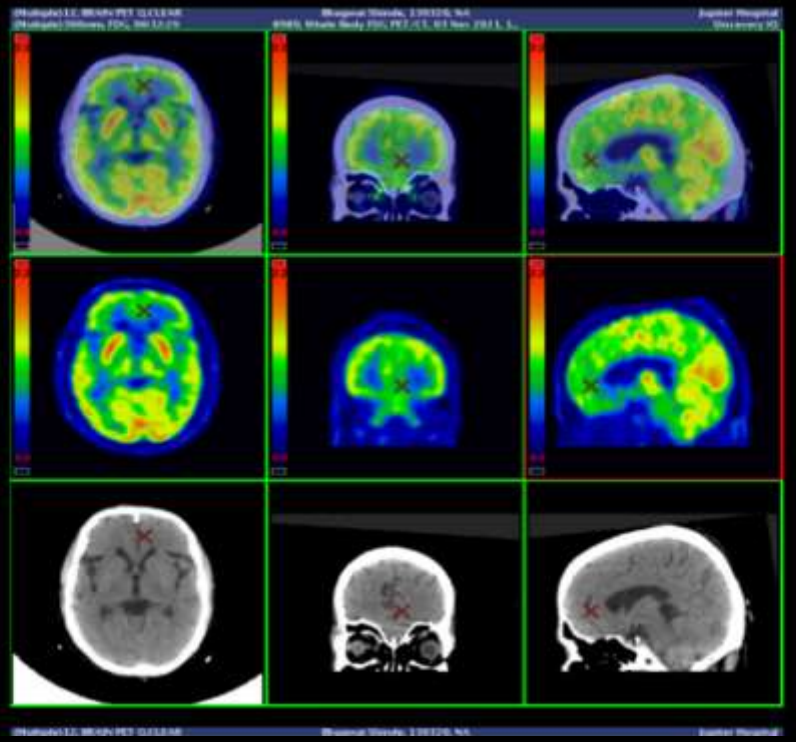
EEG Brain - Normal study

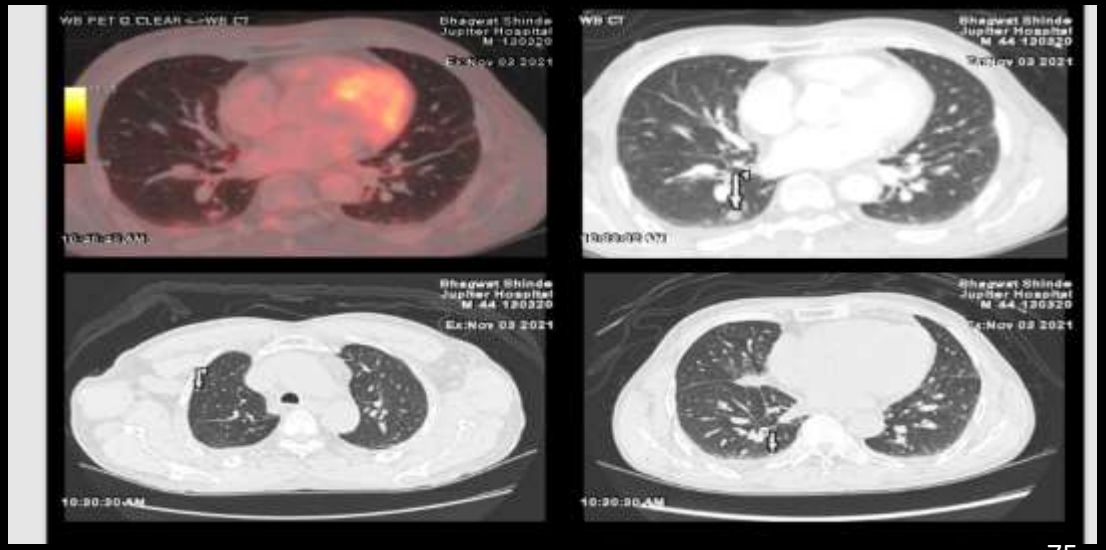
Serum autoimmune encephalitis profile

Investigation	Observed Value	Biological Reference Interval
Autoimmune encephalitis panel 1 (Serum,Immunofluorescence)		
NMDA (anti-glutamate receptor against NR1 subunit)	Negative	Negative
AMPA(anti-glutamate receptor) - GluR1	Negative	Negative
AMPA(anti-glutamate receptor) - GluR2	Negative	Negative
GABA-B receptor antibody	Negative	Negative
LGi-1 antibody (VGKC type)	Negative	Negative
CASPR2 antibody (VGKC type)	Negative	Negative

Serum paraneoplastic profile

	Observed Value	Reference Range
Anti - Amphiphysin	Negative,3	Negative
Anti - CV2/CRMP5	Negative,3	Negative
Anti - PNMA2 (Ma 2 / Ta)	Negative,1	Negative
Anti - Ri/ANNA - 2	Negative,4	Negative
Anti - Yo/PCA - 1	Negative,1	Negative
Anti - Hu/ ANNA - 1	Negative,1	Negative
Anti Recoverin	Negative,7	Negative
Anti SOX1	Negative,4	Negative
Anti Titin	Negative,4	Negative
Anti Zic4	Negative,3	Negative
Anti GAD65	Negative,1	Negative
Anti Tr(DNER)	Negative,2	Negative





Whole body PET-CT did not reveal any occult malignancy

SUMMARY

54 years/male with Sub-acute onset progressive gait , limb and truncal ataxia with dysarthria.

Diagnosis-? Seronegative AE

- Started on high dose IV MPS followed by 7 cycles of weight based plasmapheresis.
- Post plasmapheresis → improvement in the ataxia.
- Induction therapy → Rituximab
- Remarkable improvement in ataxia.
- Walks without support.

Post treatment gait

Subacute onset rapidly progressive cerebellar ataxia

Most common causes :

- AE - GAD antibody associated ataxia , Hashimotos, Paraneoplastic cerebellar ataxia
- Celiac disease (gluten ataxia)
- Sarcoidosis
- CJD – Oppenheimer variant of S-CJD
- Post infectious cerebellar ataxia

Newly detected antibodies with pure cerebellar ataxia :

1. Neurochondrin
2. Septin-5
3. Metabotropic glutamate receptor 2 (mGluR2)

Thank you

Case 4

Case of subacute cerebellar ataxia

60 year old/ male presented with :

- Loss of balance while walking since 1 1/2 months
- Slurred speech since 20 days

- Loss of balance was insidious, progressive such that not able to stand without support and was associated with truncal imbalance.

- Increased on walking in narrow passages.

- Slurred speech since 20 days.

- No h/o spillage of food while eating/involuntary movements on reaching objects.

- No h/o suggestive of motor or sensory involvement
- No h/o suggestive of cranial nerve involvement/ bladder and bowel disturbances
- No h/o neuropsychiatric disturbances/ memory disturbances/ loss of consciousness/ abnormal movements
- No h/o fever/ headache

- No h/o native or ayurvedic drug intake/ toxin exposure
- No h/o suggestive of thyroid disorder
- No h/o suggestive of connective tissue disorder
- No h/o suggestive of underlying malignancy
- No h/o preceding viral illness/ vaccination

Personal history

- Patient was non-diabetic & non-hypertensive
- No history of any addictions
- No h/o blood transfusion
- No h/o unsafe sexual practice

Family history

- Not born out of consanguinous marriage
- No h/o similar complaints in the family members

Summary

Subacute onset rapidly progressive gait and truncal ataxia with slurred speech.

GENERAL EXAMINATION

- Vitals –stable
- No skin rash or ulcers
- No goitre
- Spine – normal

Possible differentials

•Immune mediated cerebellar ataxia

-AE - GAD antibody associated ataxia , Hashimotos, Paraneoplastic cerebellar ataxia

-Celiac disease (gluten ataxia)

- Sarcoidosis
- CJD – Oppenheimer variant of S-CJD

Neurological examination-

- Patient was conscious and well oriented
- Higher mental functions were normal.(MMSE 30/30)
- Cranial nerves - normal

Motor system

Tone – grade 1 spasticity (Ashworth's) in lower limbs

Power - 4/5 in both lower limbs, 5/5 in upper limbs

All reflexes - brisk

Planter - B/L extensor

Sensory examination - normal

Cerebellar signs

Truncal ataxia - present

Finger nose test – positive bilaterally.

Dysdiadokokinesia present

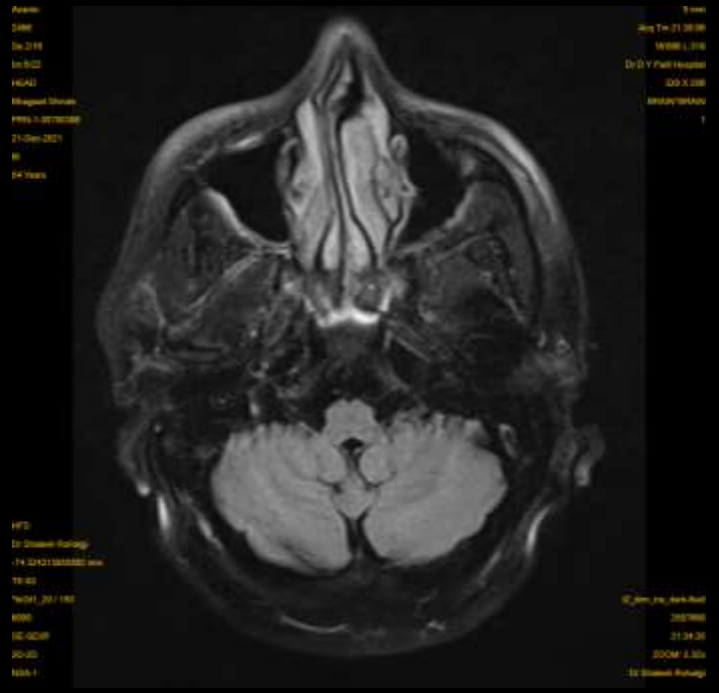
Scanned Speech

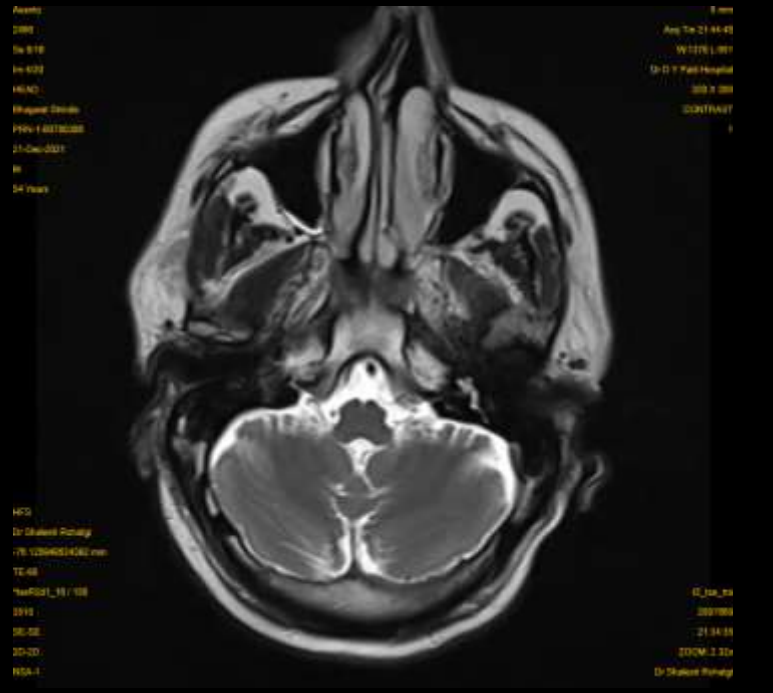
Gait – wide based gait

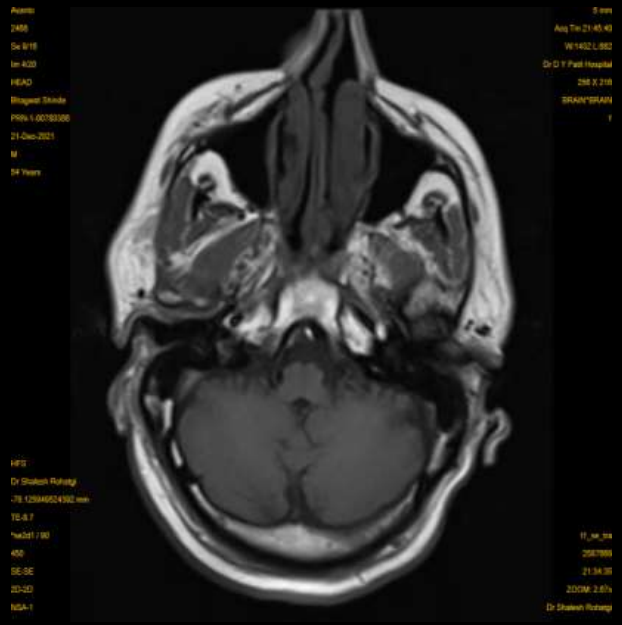
No nystagmus

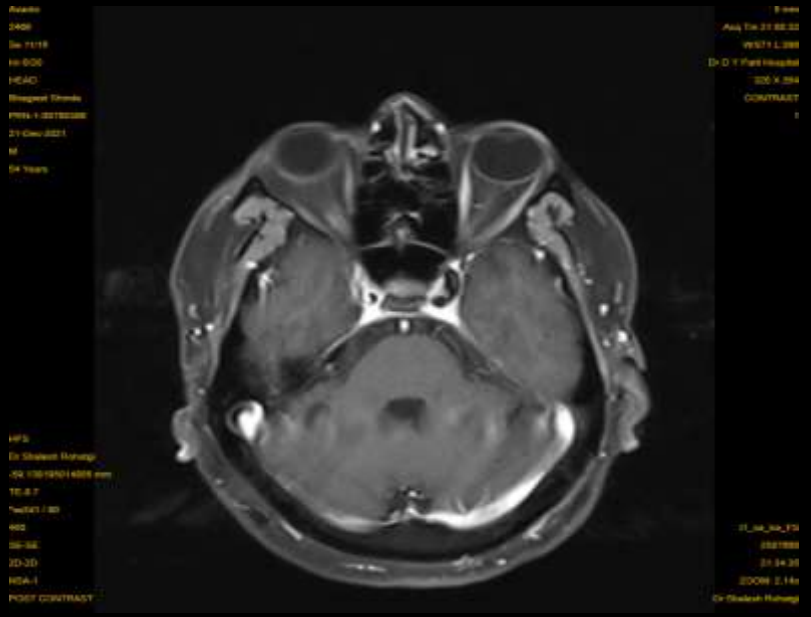
No tremors

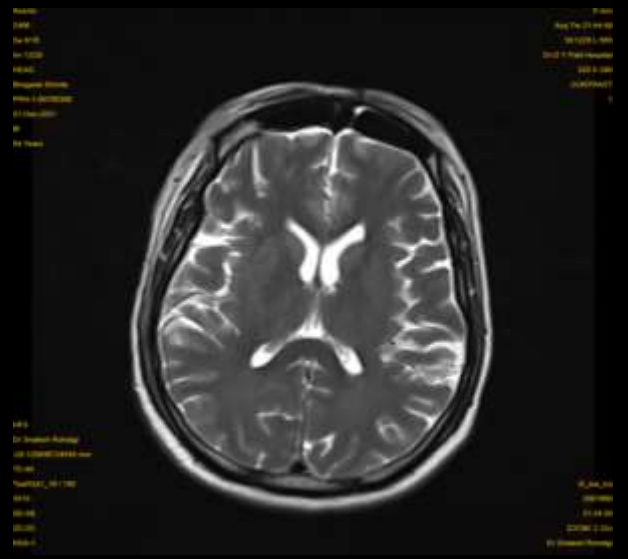
Gait at presentation

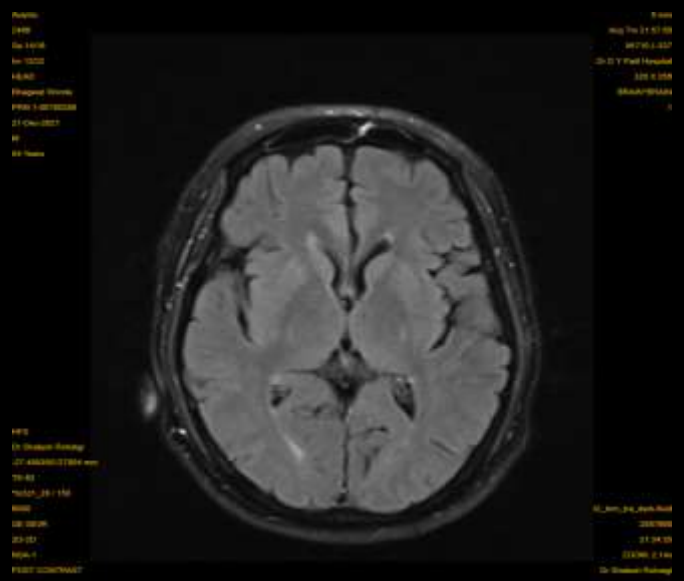


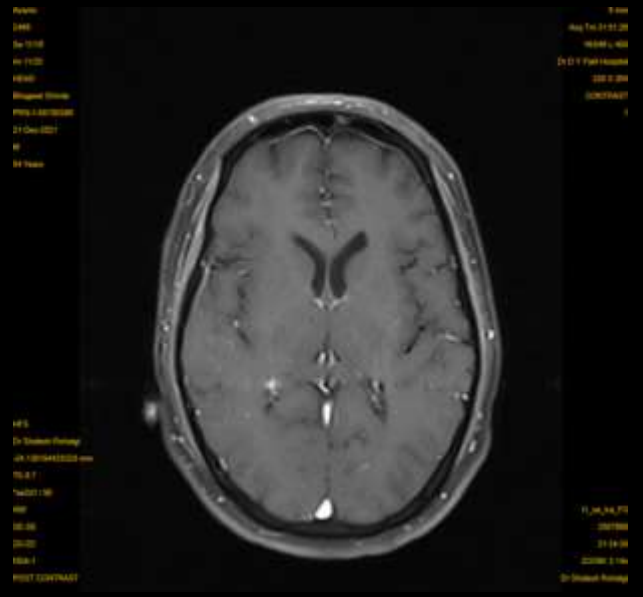


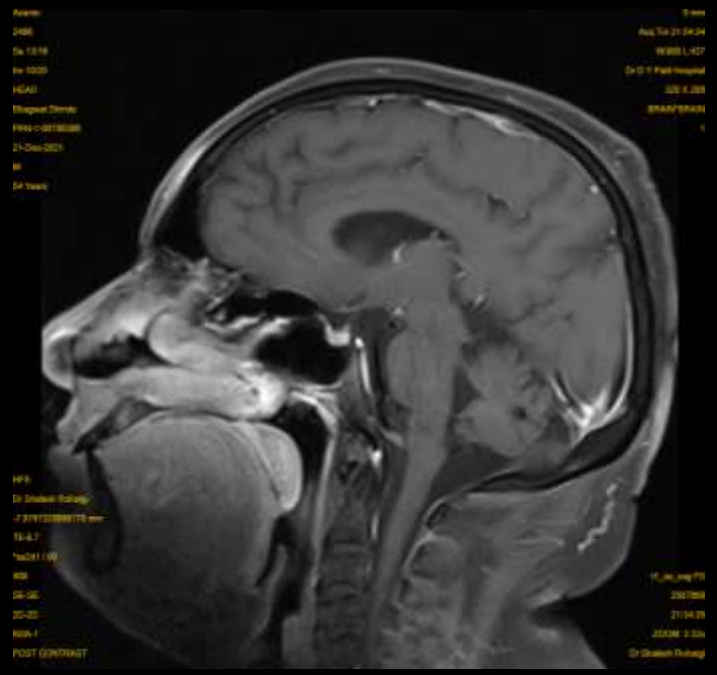


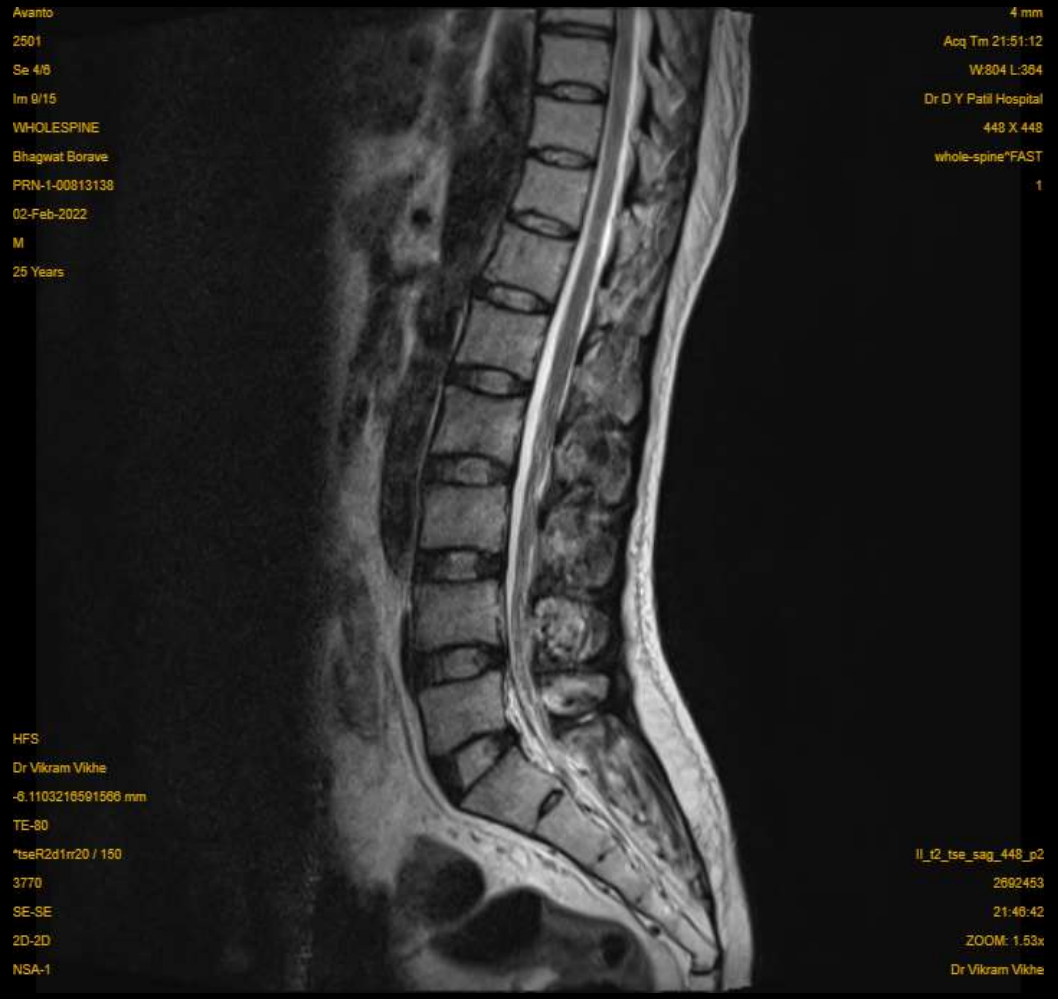








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PRN-1-00813138
02-Feb-2022
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Dr D Y Patil Hospital
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whole-spine^FAST
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Dr Vikram Vikhe
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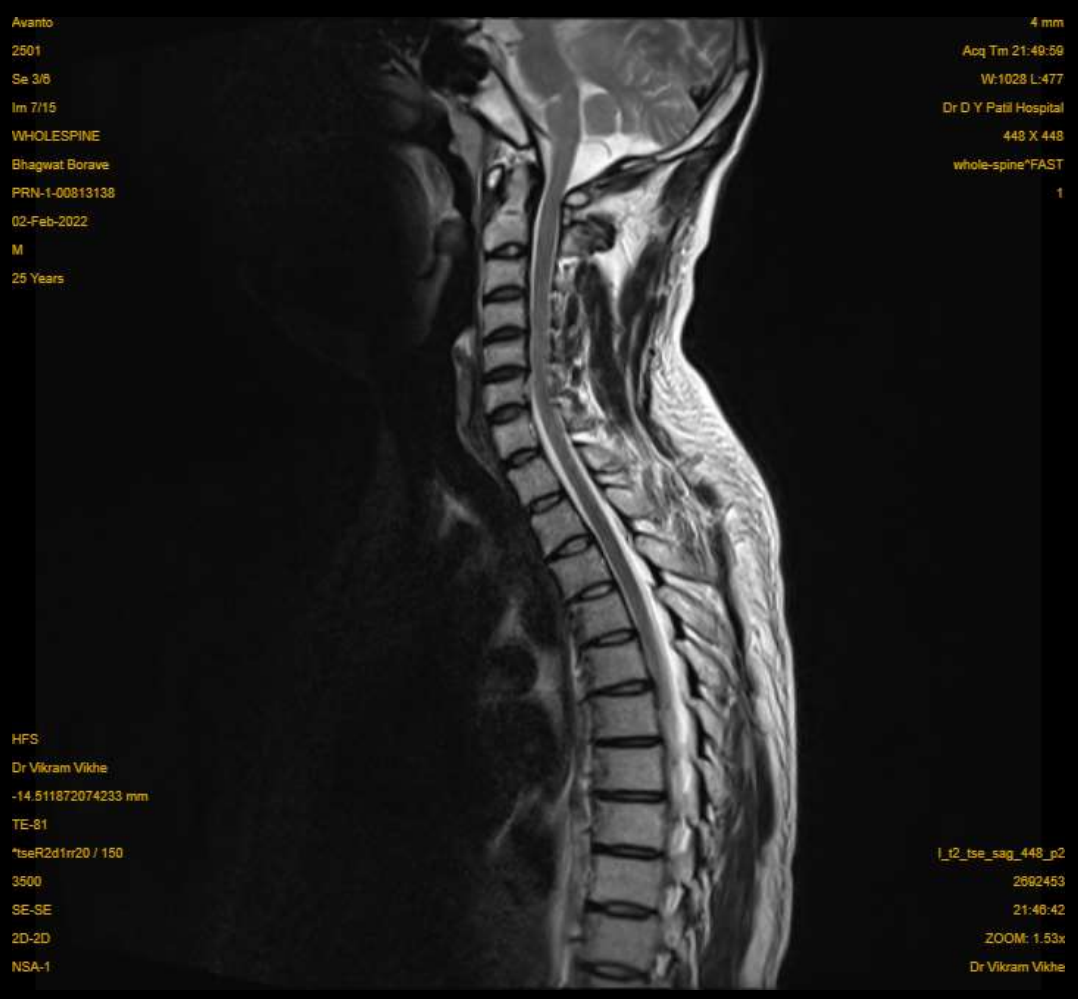
Dr Vikram Vikhe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ZOOM: 1.53x
Dr Vikram Vikhe

INVESTIGATIONS:

- Hemogram- normal
- ESR levels –24
- Thyroid function tests – normal
- HIV/HBsAg/HCV- negative
- Blood sugar levels - normal
- Renal function and liver function test – normal

- ANA – IFA – Negative
- ANCA Profile – Negative
- Vitamin B12 / Vitamin E levels – Normal
- Serum ACE levels : Normal
- Anti –TPO levels : normal
- Anti-TTG / anti – gliadin : Negative

CSF analysis:

- Protein – 64mg/dl
- Glucose – 94 mg/dl (corresponding bsl-142 mg /dl)
- Cells - 02 (All lymphocytes)
- CBNAAT – Negative
- Gram stain/AFB – Negative

EEG Brain - normal study

SERUM AUTOIMMUNE ENCEPHALITIS PANEL

Investigation	Observed Value	Biological Reference Interval
Autoimmune encephalitis panel 1 (Serum,Immunofluorescence)		
NMDA (anti-glutamate receptor against NR1 subunit)	Negative	Negative
AMPA(anti-glutamate receptor) - GluR1	Negative	Negative
AMPA(anti-glutamate receptor) - GluR2	Negative	Negative
GABA-B receptor antibody	Negative	Negative
LGi-1 antibody (VGKC type)	Negative	Negative
CASPR2 antibody (VGKC type)	Negative	Negative

SERUM PARANEOPLASTIC PROFILE

	Observed Value	Reference Range
Anti - Amphiphysin	Negative,3	Negative
Anti - CV2/CRMP5	Negative,3	Negative
Anti - PNMA2 (Ma 2 / Ta)	Negative,1	Negative
Anti - Ri/ANNA - 2	Negative,4	Negative
Anti - Yo/PCA - 1	Negative,1	Negative
Anti - Hu/ ANNA - 1	Negative,1	Negative
Anti Recoverin	Negative,7	Negative
Anti SOX1	Negative,4	Negative
Anti Titin	Negative,4	Negative
Anti Zic4	Negative,3	Negative
Anti GAD65	Negative,1	Negative
Anti Tr(DNER)	Negative,2	Negative

PET CT Scan


WB PET Q.CLEAR <->WB CT
Ashok Ghatmallu
Jupiter Hospital
M 147209
Ex:Apr 07 2022
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WB CT
Ashok Ghatmallu
Jupiter Hospital
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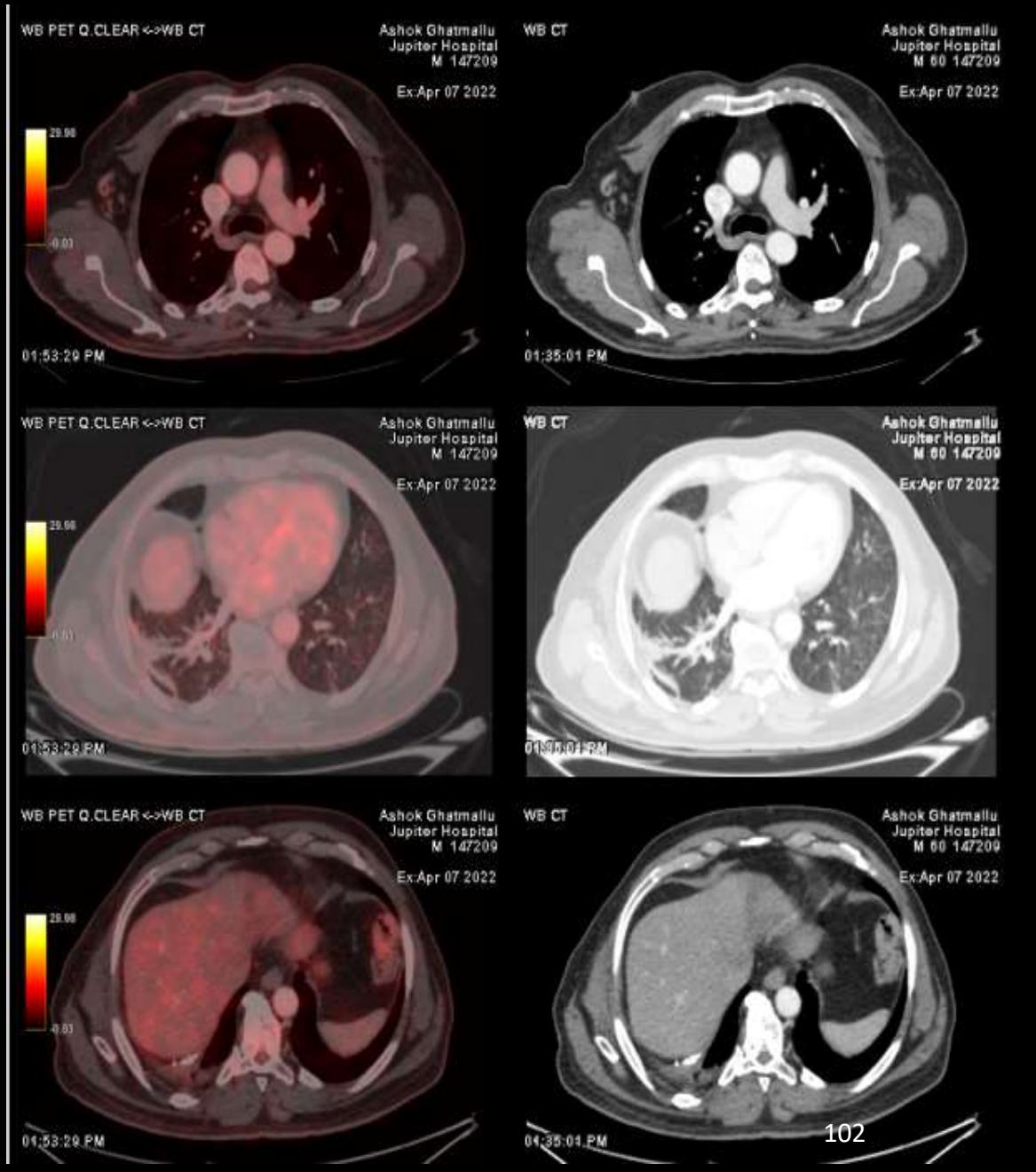
WB PET Q.CLEAR <->WB CT
Ashok Ghatmallu
Jupiter Hospital
M 147209
Ex:Apr 07 2022
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WB CT
Ashok Ghatmallu
Jupiter Hospital
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SUMMARY

60 years male with Subacute onset progressive predominant gait and truncal ataxia with dysarthria

Diagnosis-? Seronegative AE

Treatment:

- Patient was started empirically on iv MPS for 5 days followed by 7 cycles of plasmapheresis.

- After completion of plasmapheresis patient showed significant improvement in ataxia.

POST PLASMAPHERESIS

“We have an unknown distance yet to run, an unknown river to explore. What falls there are, we know not; what rocks beset the channel, we know not; what walls ride over the river, we know not. Ah, well! we may conjecture many things.”

John Wesley Powell

Case 5

A RARE CASE OF ENCEPHALOPATHY

Dr Sravya kotaru

A 74 yrs old female presented with complaints of

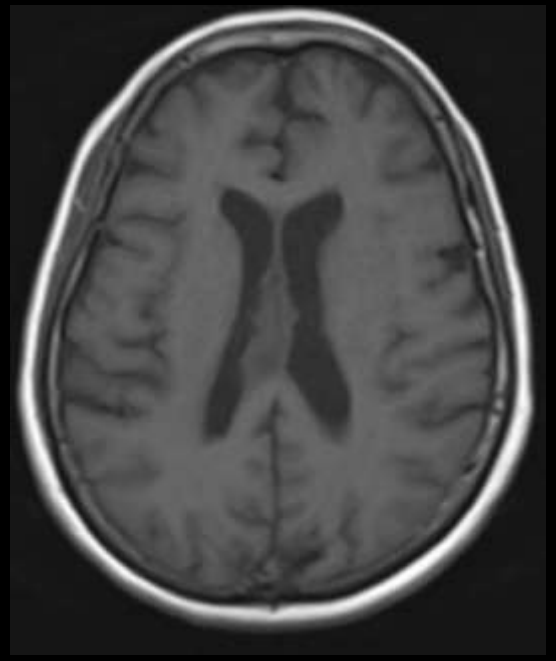
- Irrelevant talking since 25 days which was associated with excessive sleepiness and delayed verbal response

- No h/o fever/rash
- No h/o seizures/headache /vomitings
- No h/o weakness of limbs
- No h/o hypothyroidism, kidney disease
- No h/o similar complaints in the past.

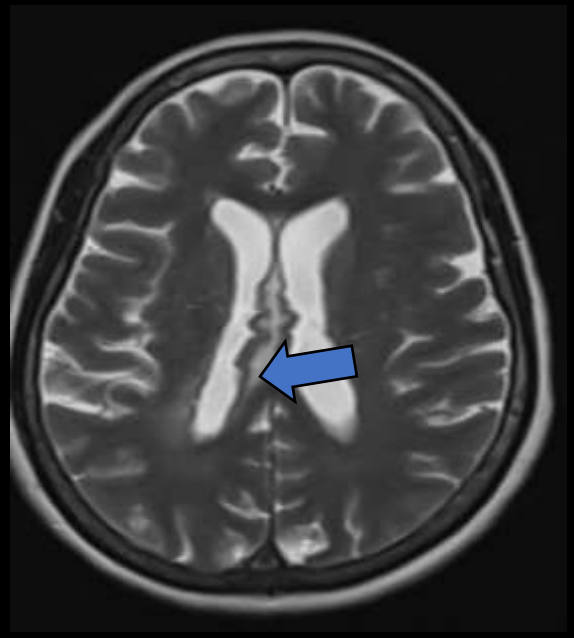
- Admitted outside for hyponatremia.
- Mildly Improved.
- Readmitted for altered sensorium after 3 days .

On examination:

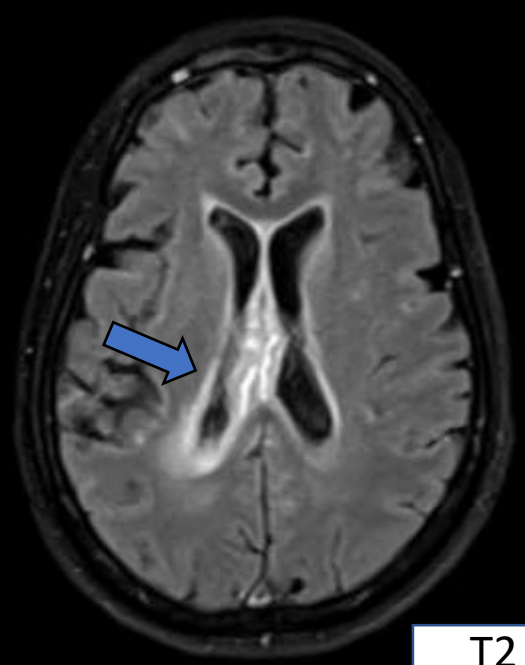
- Drowsy but arousable
- Obeying simple verbal commands.
- No signs of meningeal irritation.
- No focal neurological deficit.

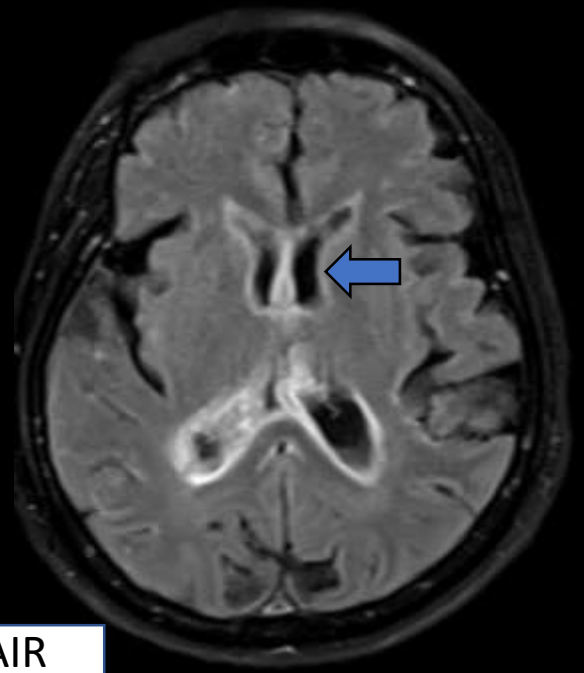


T1W

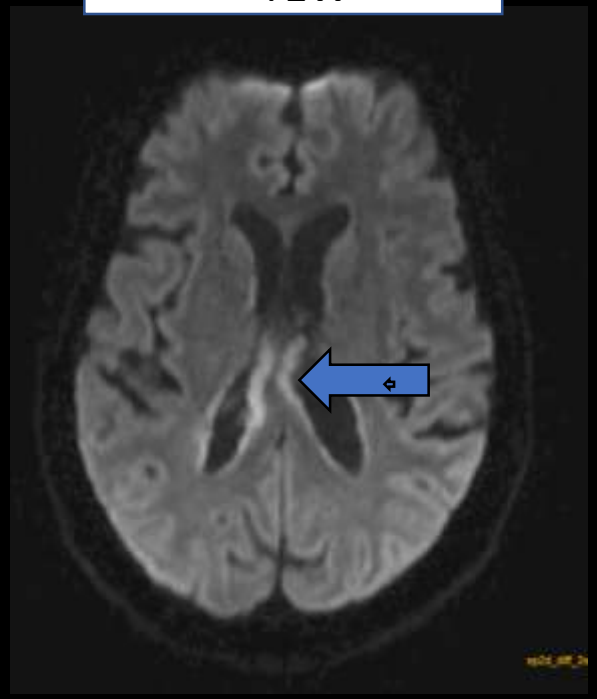


T2W

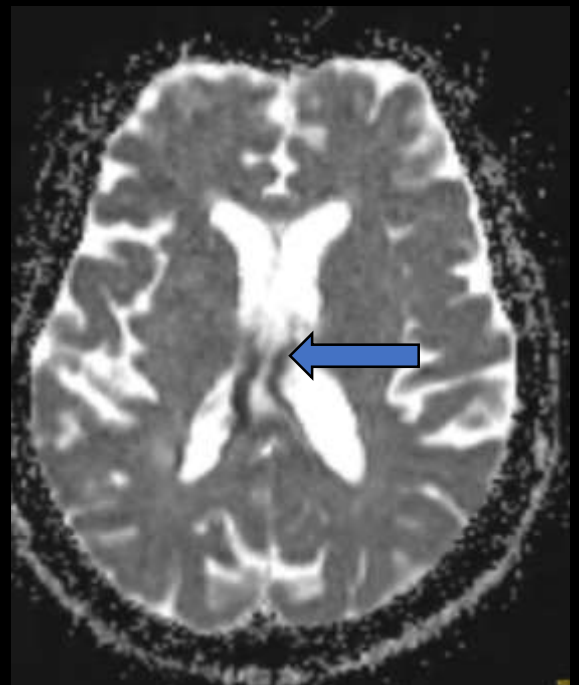


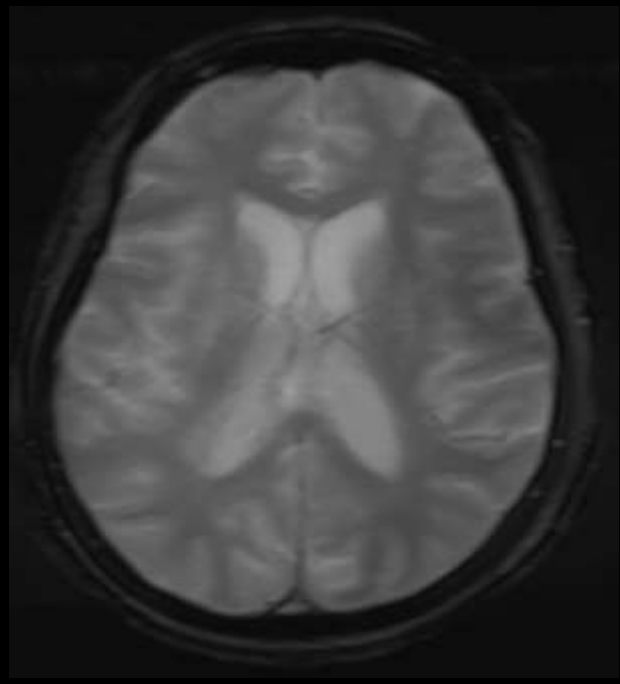


T2 FLAIR

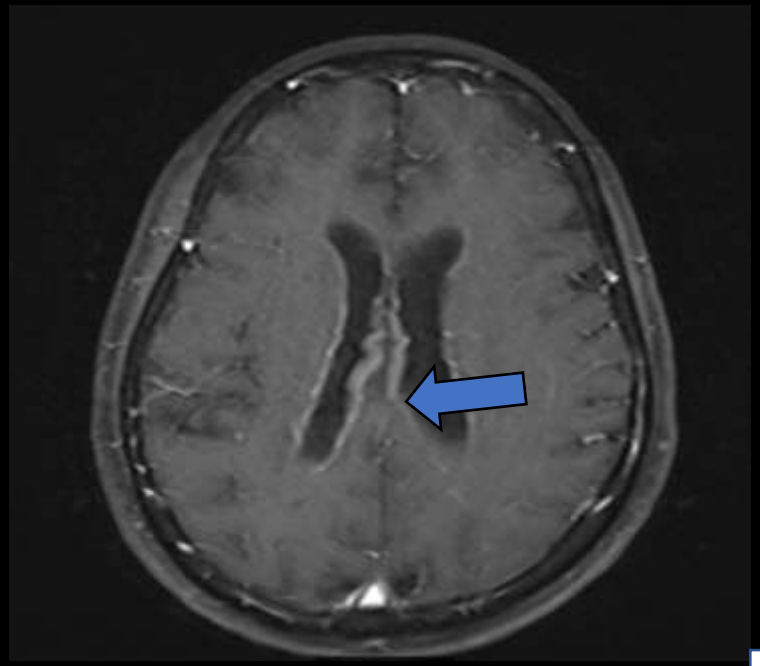


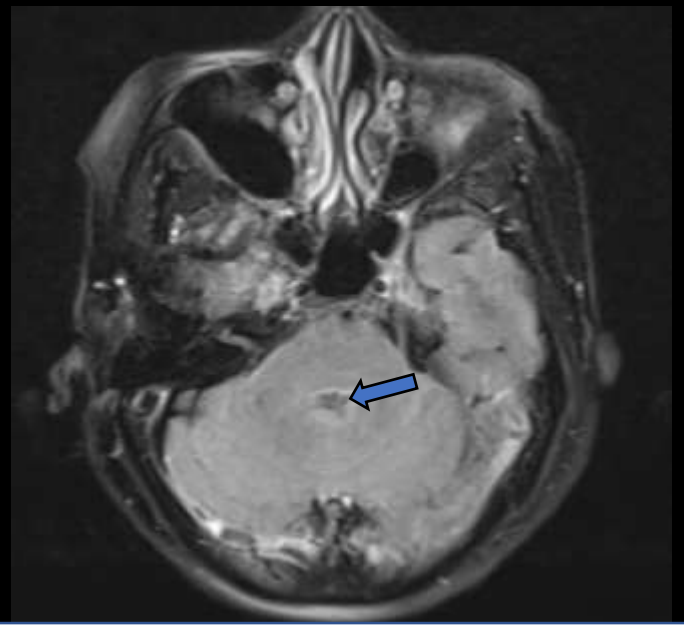
DWI &
ADC

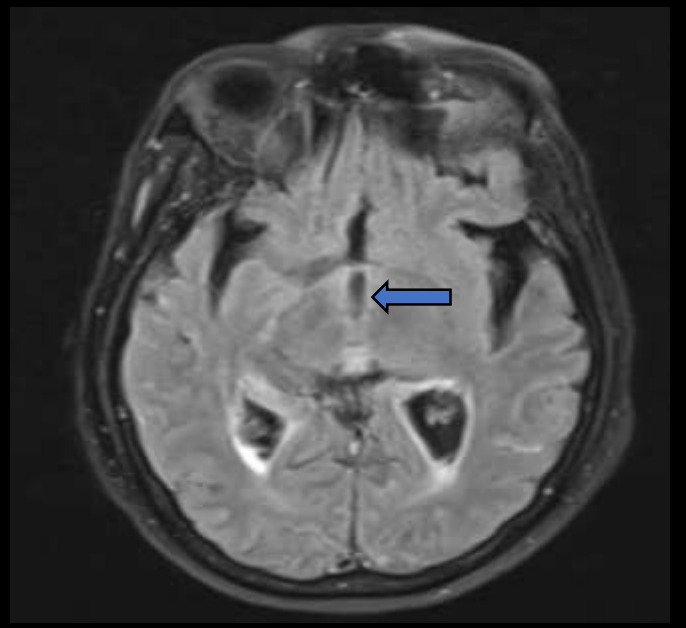




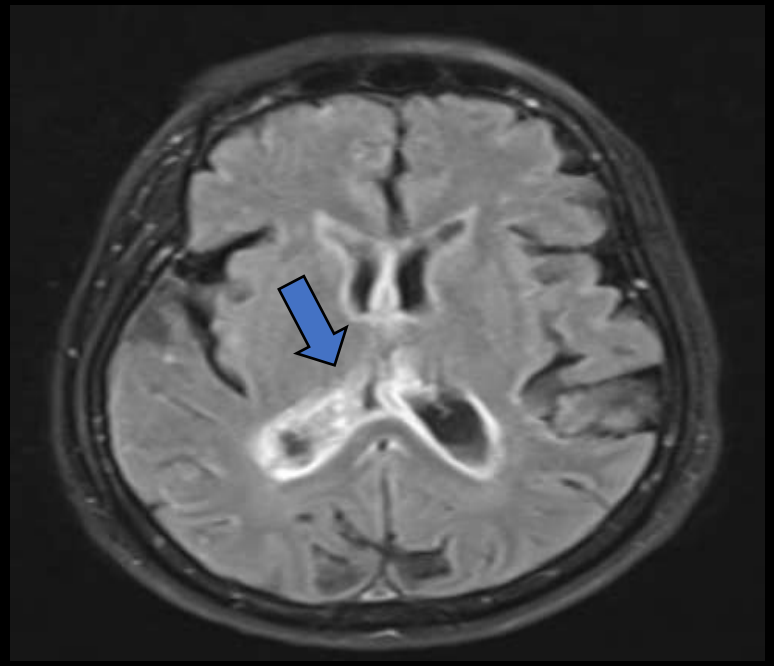
GRE

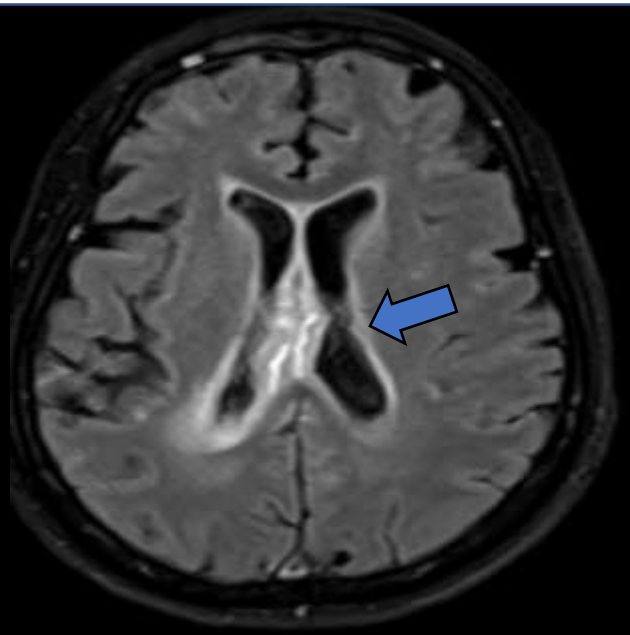


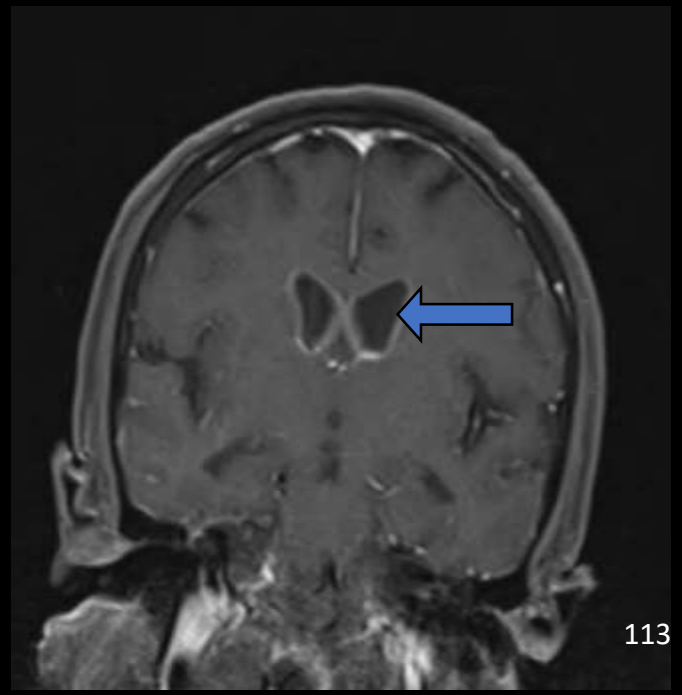




POST CONTRAST T1W







- CSF Neurotropic viral panel: Negative
 (EBV, VZV, HSV1, HSV2, CMV PCR)

- CSF CBNAAT: Negative

- HRCT Thorax : normal

- USG abdomen : normal

- Based on this clinical and MRI findings
- Infective causes of meningitis with ventriculitis like

??Tubercular Meningitis with ventriculitis

?? Pyogenic (STAPHYLOCOCCUS)

?? Viral (CMV)

?Primary CNS lymphoma

- Routine lab investigations: normal, mild leukocytosis present
- HIV/HbsAG/HCV : negative
- ESR: **65**
- CSF manometry : 18 cms
- CSF Protein: **235**mg%, Glucose:**7**mg%, cells:2
- CSF KOH mount: negative
- CSF culture : no growth

- Based on these investigations patient was started on

Inj Dexa 8mg TDS

Inj Acyclovir 500mg IV TDS

Inj Vancomycin 1gm IV TDS

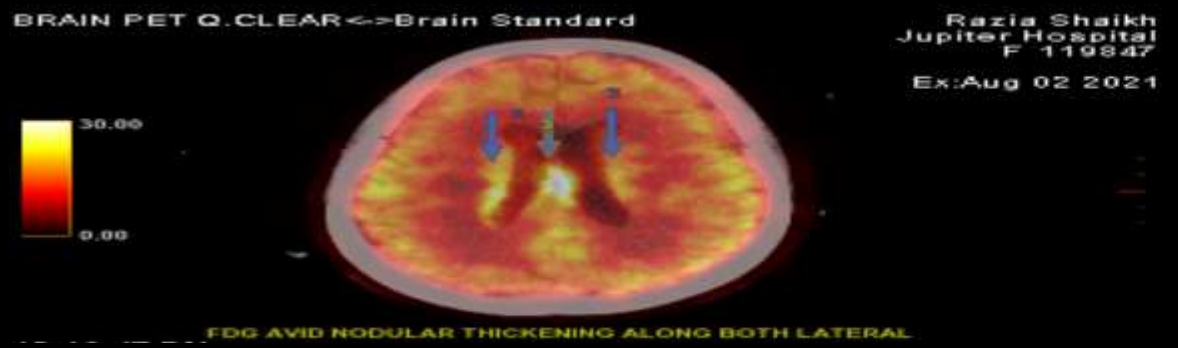
Inj Monocef 2gm IV BD

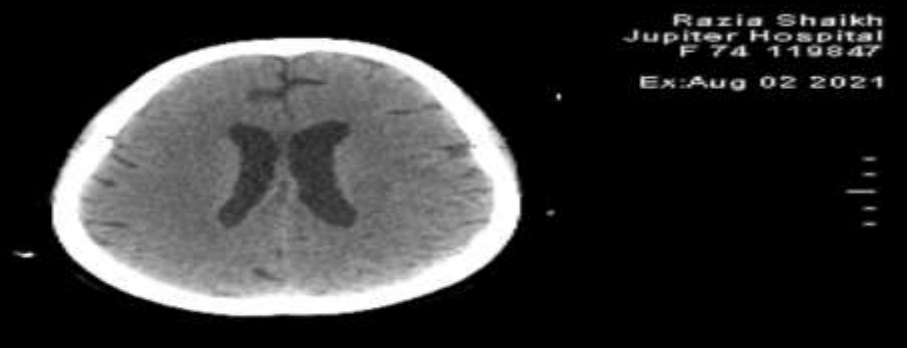
- After 14 days of treatment→ minimal improvement

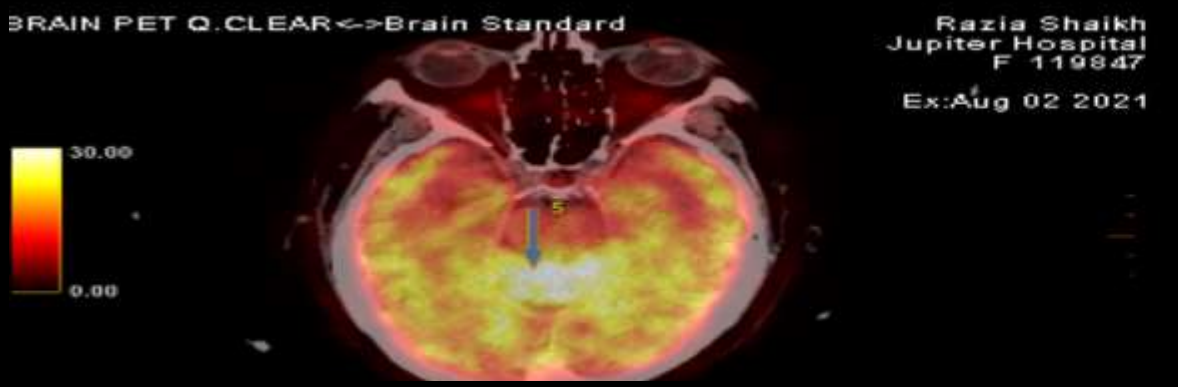
- Repeat CSF showed raised protein(114mg/dl), very low sugar20mg/dl with cells count of 200cells/UL(predominant lymphocytes)

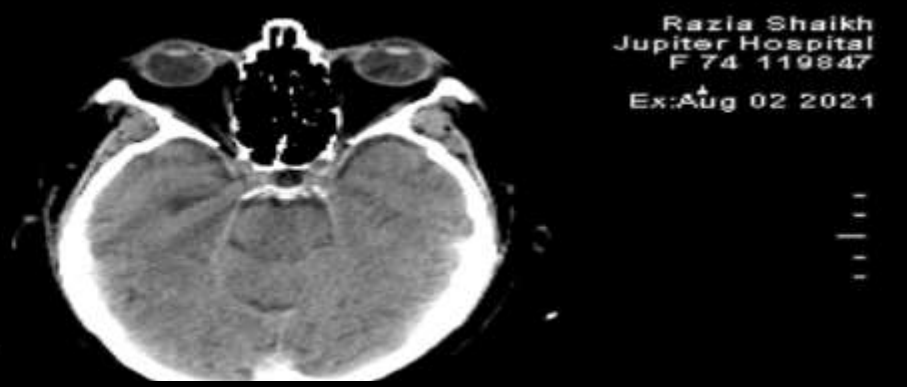
- CSF for malignant cells : negative

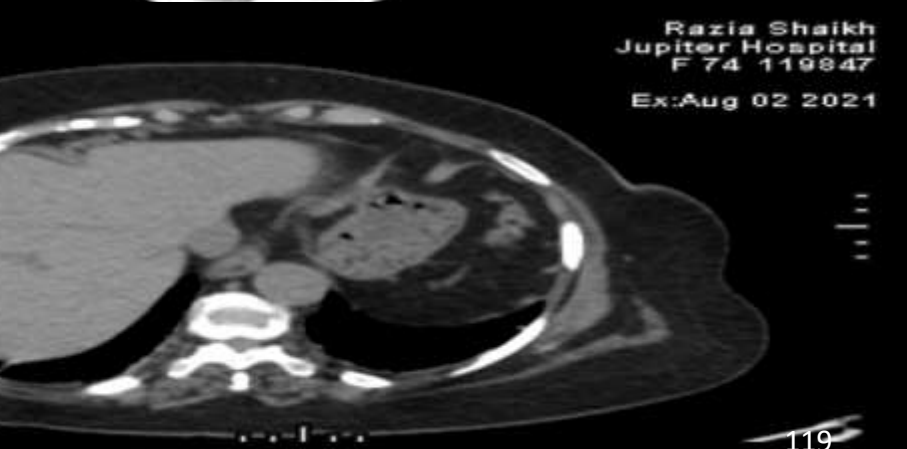
PET CT scan showed hypermetabolic nodular thickening in interventricular region and along the ventricles.











- Patient was readmitted for further workup
- CSF flowcytometry done

Lata Mangeshkar Medical Foundation's
DEENANATH MANGESHKAR HOSPITAL AND RESEARCH CENTER
Erandawane, Pune - 411 004. Tel.: 49153000 / 40151000 / 66023000. Email : info@dmhospital.org Website : www.dmhospital.org

DEPARTMENT OF PATHOLOGY
TEST REPORT

Printed Date: 07/08/2021 17:33:45

Patient Name: Smt. SHAIKH RAZIYA AYUB
Age: 74Y 3M 7D
Visit Code: OP0001

MRD#: 1151300
Sex: Female

Referred by: Dr. CMO .
Sample Suitability: Suitable
Report status: RC
Sample ID: 0266HM210806
Receiving Date/Time: 06-08-2021 12:11
Collection Date/Time: 06-08-2021 12:11
Result Date/Time: 06-08-2021 18:24

CLPD

Sample: CSF

Expression of markers and their percentages from gated cells.

Markers	%	Intensity	Markers	%	Intensity
CD19	50.7	Dim positve	**CD23**		
CD20	55.7	Moderate positive	**CD79b**		
CD5	-	Negative	**FMC-7**		
CD10	57.4	Dim positive	**CD43**		
CD4	-	Negative	**CD200**		
CD8	-	Negative	**TCR (alpha/beta)**		
TCR (Gamma/Delta)			**CD7**	-	Negative
sCD3, cCD3, Kappa, Lambda, CD117, CD13, CD33, CD15, CD11b, CD34, CD64	-	Negative	**CD2**		

Result:
* cCD79a - Moderate positive (59.4%)
* CD22 - Dim positive (60.9%)
* HLA-DR - Dim partial positive (35.3%)

Flow cytometry analysis of CSF reveals 38.7% atypical lymphoid cells with dim CD45 and low SSC on CD45 Vs SSC gating.
These cells are characterized by expression CD19, cCD79a, CD22, CD20, CD10, HLA-DR but are negative for cCD3, sCD3, CD7, CD5, CD4, CD8, CD34, CD117, CD13, CD33, CD64, CD15, CD11b, Kappa, Lambda.
37.7 % T lymphocytes are also present.

Morphology:
CSF examination shows 50% large atypical lymphoid cells with 1-2 nucleoli and moderate amount of deep blue cytoplasm.

Myeloperoxidase (MPO), by cytochemistry: Large atypical lymphoid cells are MPO negative.

Impression:
Flow cytometry analysis of CSF is suspicious of involvement by 'B' cell Non-Hodgkin's lymphoma. However, biopsy and immunohistochemistry is necessary for confirmation and subtyping.

Intrument: BC Cytoflex.

Sample: CSF.

Method: Flow cytometry.

End of Report:

DR. RAVIBHUSHAN GODBOLE
M.D.(Pathology)
Consultant Hematopathologist
Reg. No: 2000/02/0729

Signed By: 16199

Final diagnosis

B cell non Hodgkin primary CNS Lymphoma

- Medical oncologist opinion was taken patient was started on rituximab and high dose methotrexate regimen with rescue leucovorin .
- Patient was lost to follow up.

Discussion

- Primary CNS lymphoma (PCNSL) is a highly aggressive non-Hodgkin lymphoma confined to the CNS, including the brain, spine, cerebrospinal fluid (CSF), and eyes.
- PCNSL in immunocompetent patients is rare and represents 4% of all intracranial neoplasms and 4% to 6% of all extranodal lymphomas.
- PCNL involving ventricular system is very rare and accounts only for 1% of all primary CNS tumours. Only 2 cases of simultaneous involvement of lateral and fourth ventricles have been reported in literature

Asian Journal of Neurosurgery

Asian J Neurosurg. 2020 Jan-Mar; 15(1): 126–127.

Published online 2020 Feb 25. doi: 10.4103/ajns.AJNS_94_16

PMCID: PMC7057909

PMID: 32181185

Primary Central Nervous System Lymphoma Involving Entire Ventricular System

Hemant Kumar, Achal Sharma, Vinod Sharma, and Shashi Singhvi[1]

▸ Author information ▸ Article notes ▸ Copyright and License information Disclaimer

Diagnosis-

- Stereotactic biopsy is recommended for intracerebral lesions with intraoperative rapid cytology and review of frozen sections.
- CSF cytology and flow cytometry may be used in cases where a biopsy is not possible.

Treatment of primary CNS lymphoma

- Chemotherapy-HD-MTX,
- Immunotherapy- rituximab and an orally administered alkylating agent within an established protocol.
- Radiotherapy – whole brain radiotherapy.
- Surgery -Role is restricted to stereotactic biopsy.

Prognosis – 5 yr survival rate 30% with treatment

Thank you