An Unusual case of chronic meningitis

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Date : 30/05/25

Chronology of clinical events

45 Year old male

Fever, Headache, Nausea, vomiting.

Since 15 days

Protein – 116
Glucose - 47
Cells – 118
lymphocytes

At Our Hospital

Holocranial headache
Fever – High grade
Vomiting – Non projectile.

APRIL 2024

- Admitted elsewhere for 15 days
- Treated as Meningitis
- Inj. Monocef 1gm iv BD
- Iv. Steroids
- AKT ivo suspicion of Tuberculosis

Took DAMA

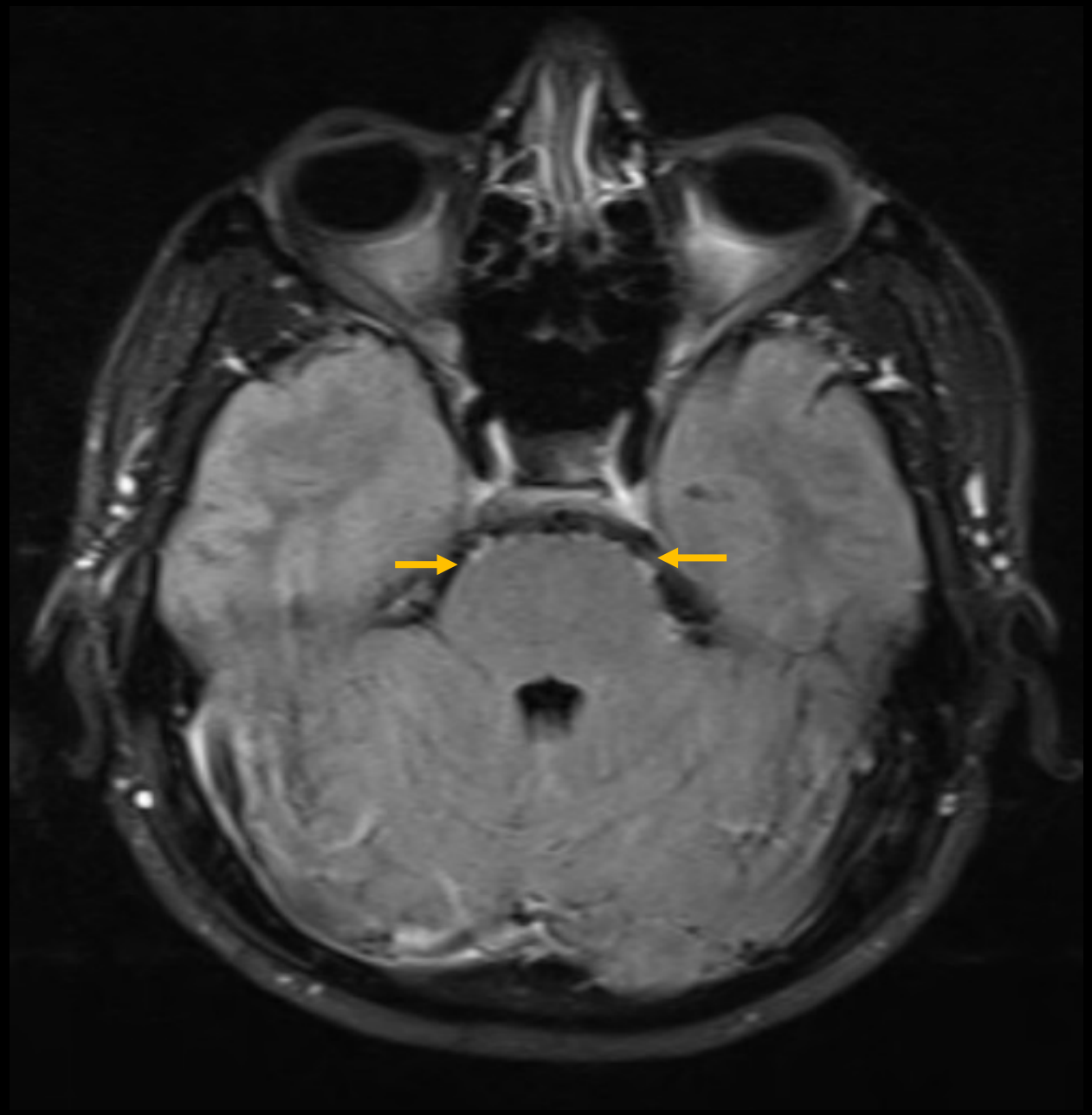
- Was asymptomatic for a while
- Continued on oral antibiotics and steroids.

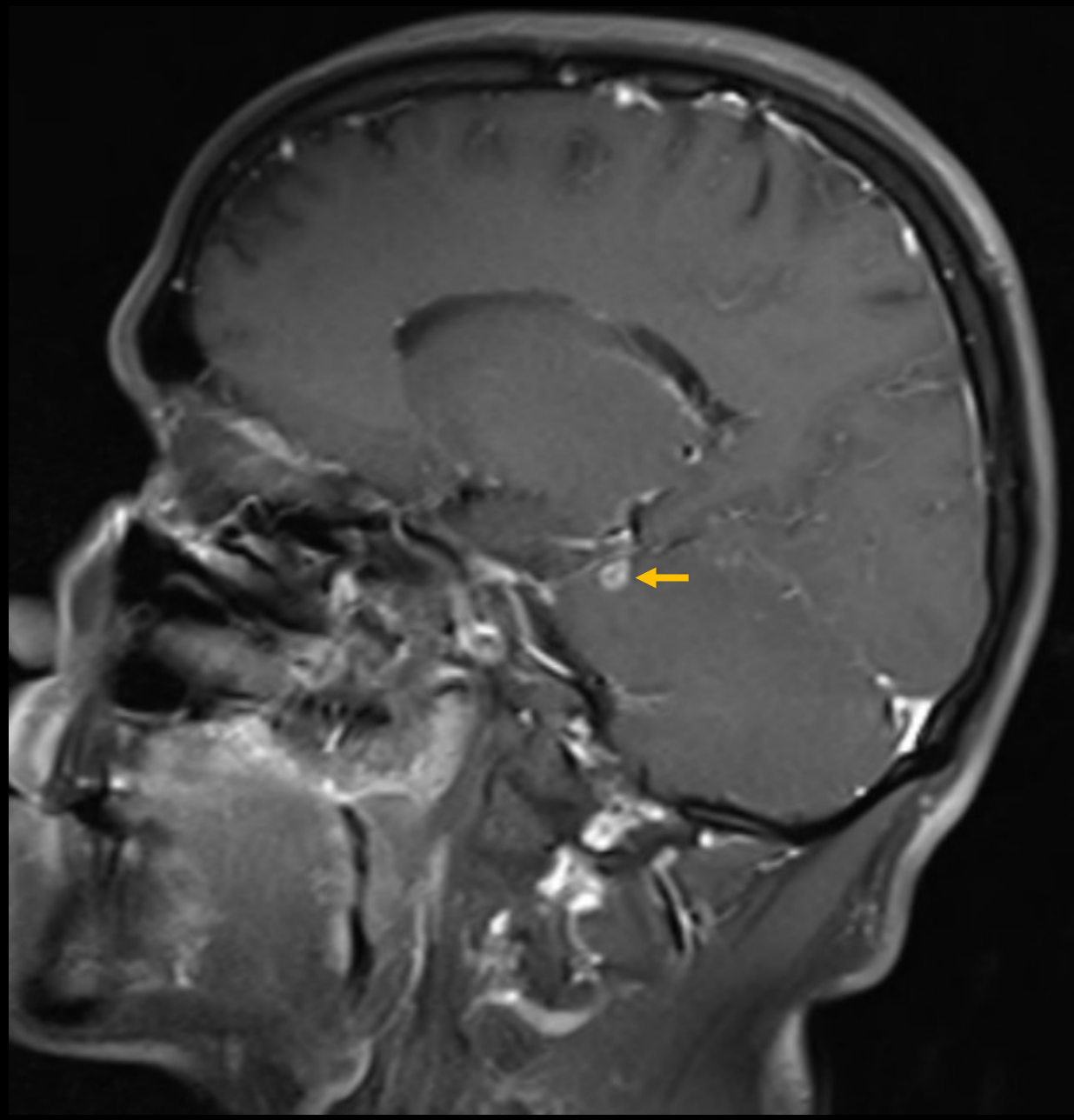
8/5/24

VITALS	GENERAL EXAMINATION	NEUROLOGICAL EXAMINATION	OTHER SYSTEMS
Pulse - 78 /min	Cachexia	Cranial Nerves Fundus - Normal	RS – Normal Breath sounds
BP - 110/70 mm of Hg	No spine tenderness	Motor – 5/5 DTRs - Normal	CVS – S1 S2 Normal
RR - 24/min	No cutaneous markers of TB /HIV	Sensory - Normal	PA - No organomegaly
Spo2 - 98 %		Bladder bowel – No involvement	
Temp - 101 F		Neck stiffness. Kernig's – Positive Brudzinski's - negative	

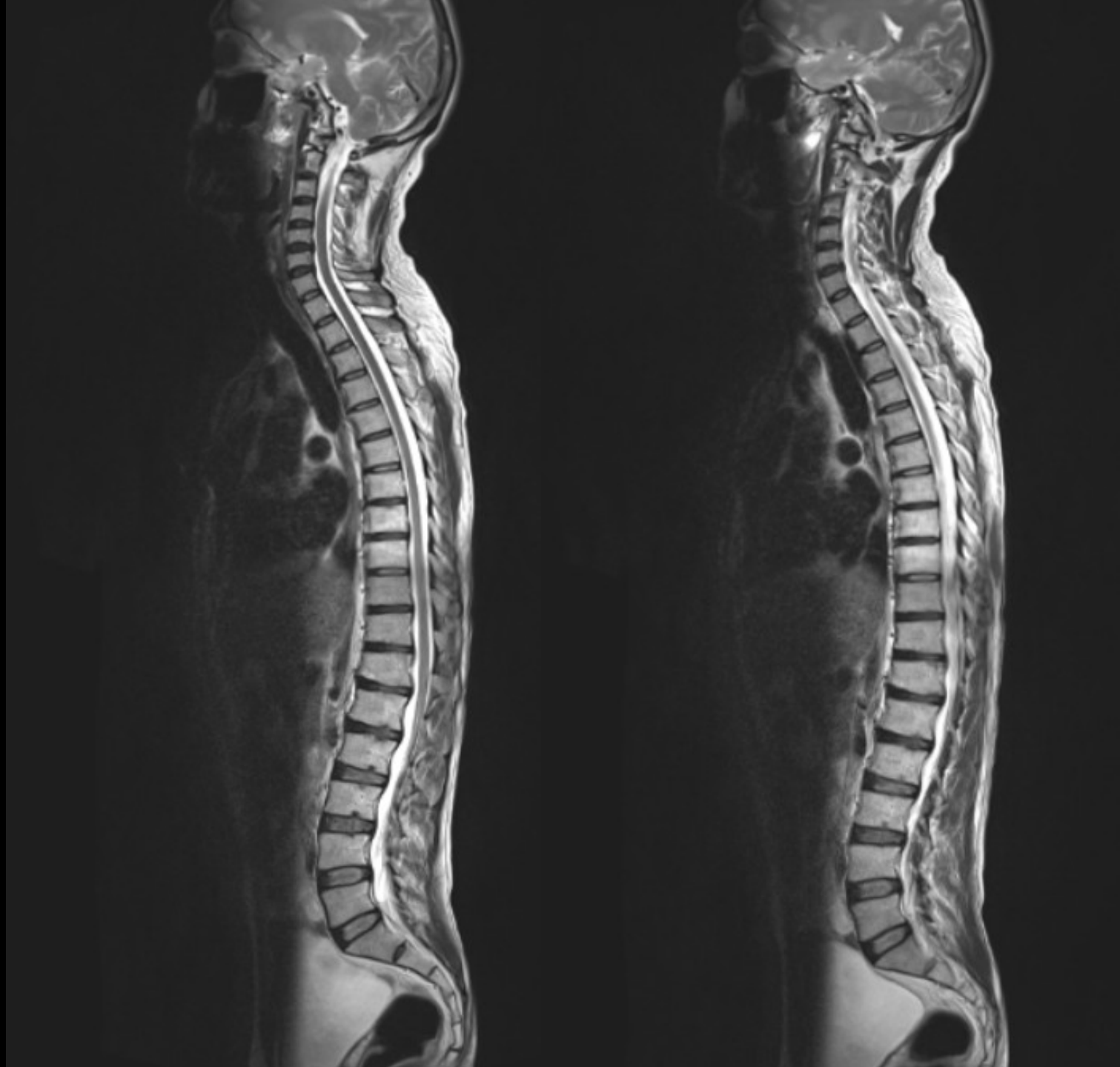
	Done Elsewhere		On Admission
CSF - Trend	16/4/24	25/4/24	8/5/24
Sugar	47	53	32
Corresponding BSL	-	-	132
Protein	116	90	139
Cells	118	98	2800
Predominance	Lymphocytes	Lymphocytes	Lymphocytes
Cob web	Absent	Absent	Absent

MRI Brain with contrast

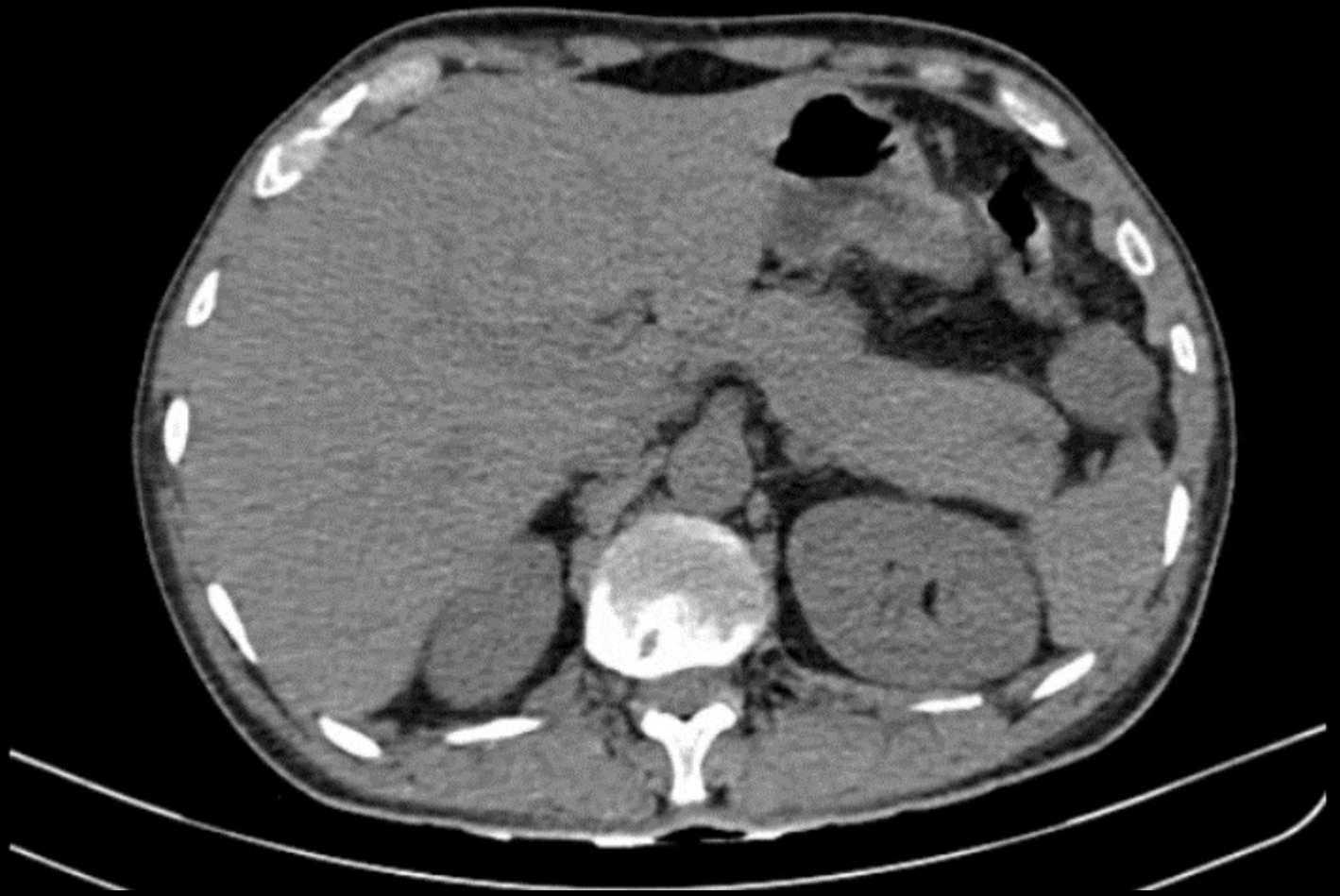




MRI Spine screening - normal



HRCT- Thorax



Past H/o

- *Patient had backache since 6 to 7 months.*
- *He received a Root block in L3 L4 epidural space.*
- *Inj Methylprednisolone 2 weeks prior.*
- *He had symptomatic benefit because of the same*

Differential diagnosis

Chronic / Subacute Meningitis

Iatrogenic meningitis

- Partially treated Bacterial meningitis
- Fungal

Meningitis due to other cause

The root block was coincidental

- Tuberculosis
- Brucella
- Carcinomatous
- Lymphoma

Initial Management

- Inj. Meropenem 2gm iv TDS.
- Inj. Vancomycin 1gm iv BD.
- Empirical AKT
- Inj. Dexamethasone 8 mg TDS.
- Inj. Mannitol TDS.
- Inj. Paracetamol 1gm SOS for pain.
- Inj. Leviteracetam 500 mg BD

CSF – *Other Investigations*

CSF opening pressure – 43

CSF Bio fire - Negative
CBNAAT – Negative

Cryptococcal Antigen Negative CSF India ink negative

TB Pyrosequencing – Negative
Bacterial Culture – No growth

KOH mount – negative.
Fungal Culture – No growth
Brucella Negative

- During the course of hospital stay patients
- Symptoms – Headache fever neck pain had worsened.
- Patient CSF was still reactive
- NO CLINCAL IMPROVEMENT

What next ?

CSF Galactomannan Positive

CSF Beta D Glycan Positive

Provisional diagnosis

- **Iatrogenic fungal meningitis**

Points in favour	Modification In treatment
Temporal evolution of symptoms after root block	Started the patient on ***Inj. Voriconazole 200 mg BD***
Worsening of symptoms on antibiotic and AKT.	Stopped Dexamethasone and AKT
CSF galactomannan and Beta D glycan positive	Continued supportive therapy

CSF - Dates	16/4/24	25/4/24	8/5/24 DAY 1	15/5/24 DAY 7
Sugar	47	53	32	36
Corresponding BSL	-	-	132	144
Protein	116	90	139	152
Cells	118	98	2800	810
Predominace	Lymphocytes	Lymphocytes	Lymphocytes	Lymphocytes
Cob web	Absent	Absent	Absent	Absent

Clinical Status – Day 14

- *Although the CSF picture improved in **terms of cell count** with empirical antifungal treatment.*
- *He had **persistent hypoglycorrhachia (low CSF Glucose)***
- *Patient was stable for a few days however he became symptomatic again.*
- *He had **persistent headaches and fever** not responding to any medications.*

Treatment modification

- Inj. Voriconazole Dose was increased to 200 mg TDS

- Voriconazole levels = 0.4. (Subtherapeutic range) {2.0 -6.0}
- Dual Antifungal regimen
- Inj. Voriconazole 200 mg TDS and
- Inj. Liposomal Amphotericin B.

CSF - Dates	16/4/24	25/4/24	8/5/24 DAY 1	15/5/24 DAY 7	28/5/24 DAY 14
Sugar	47	53	32	36	28
Corresponding BSL	-	-	132	144	129
Protein	116	90	139	152	129
Cells	118	98	2800	810	750
Predominace	Lymphocytes	Lymphocytes	Lymphocytes	Lymphocytes	Lymphocytes

Clinical Status – DAY 28

- It had been almost a month with poor clinical response to the dual antifungal regimen
- The Patient had persistent fever spike and frequent episodes of severe throbbing headache.
- Voriconazole levels were still 0.46 {2.0 -6.0} on total dose of 800mg / day.

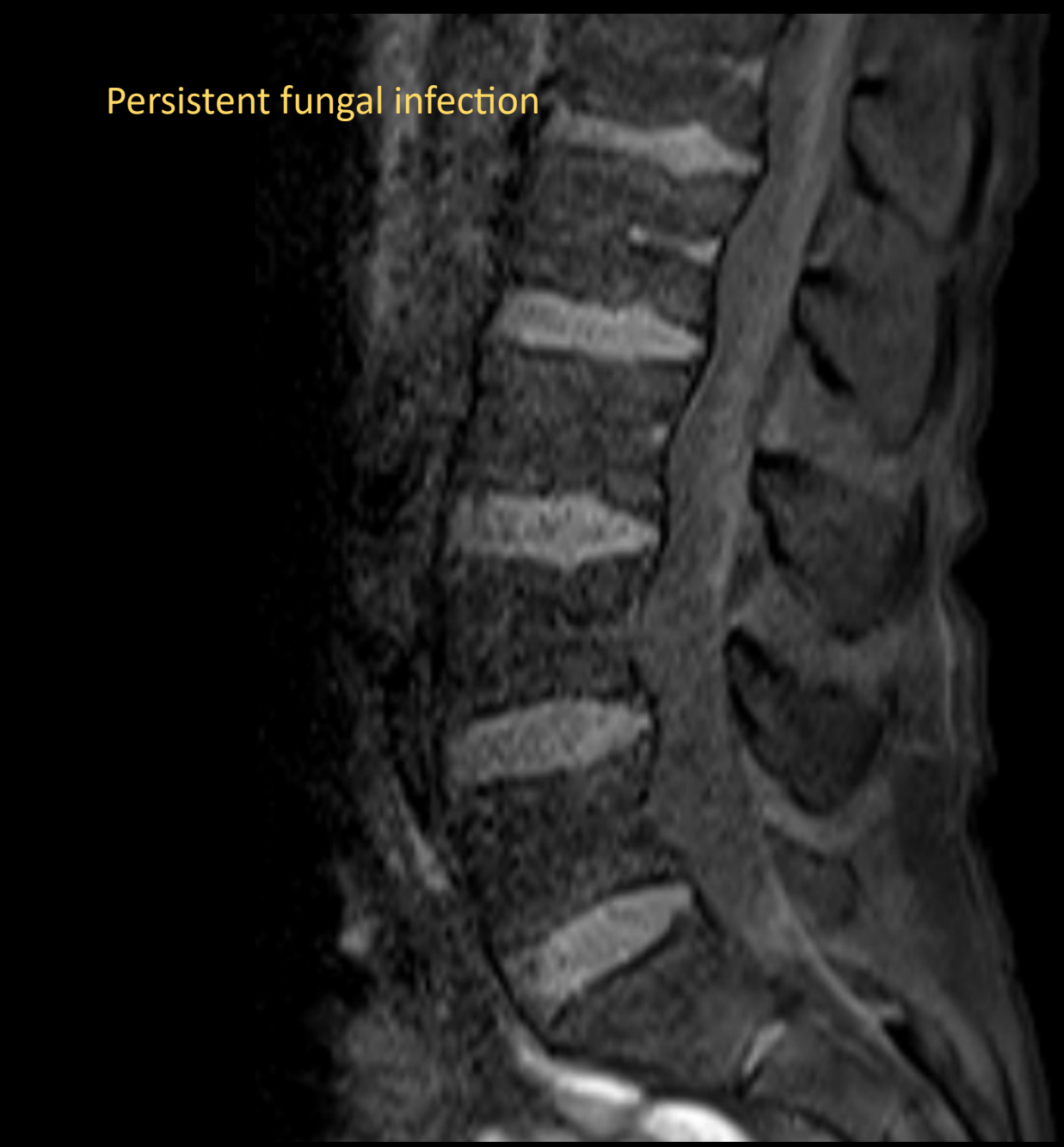
The Possibilities after1 month of treatment

Resistant fungal infection

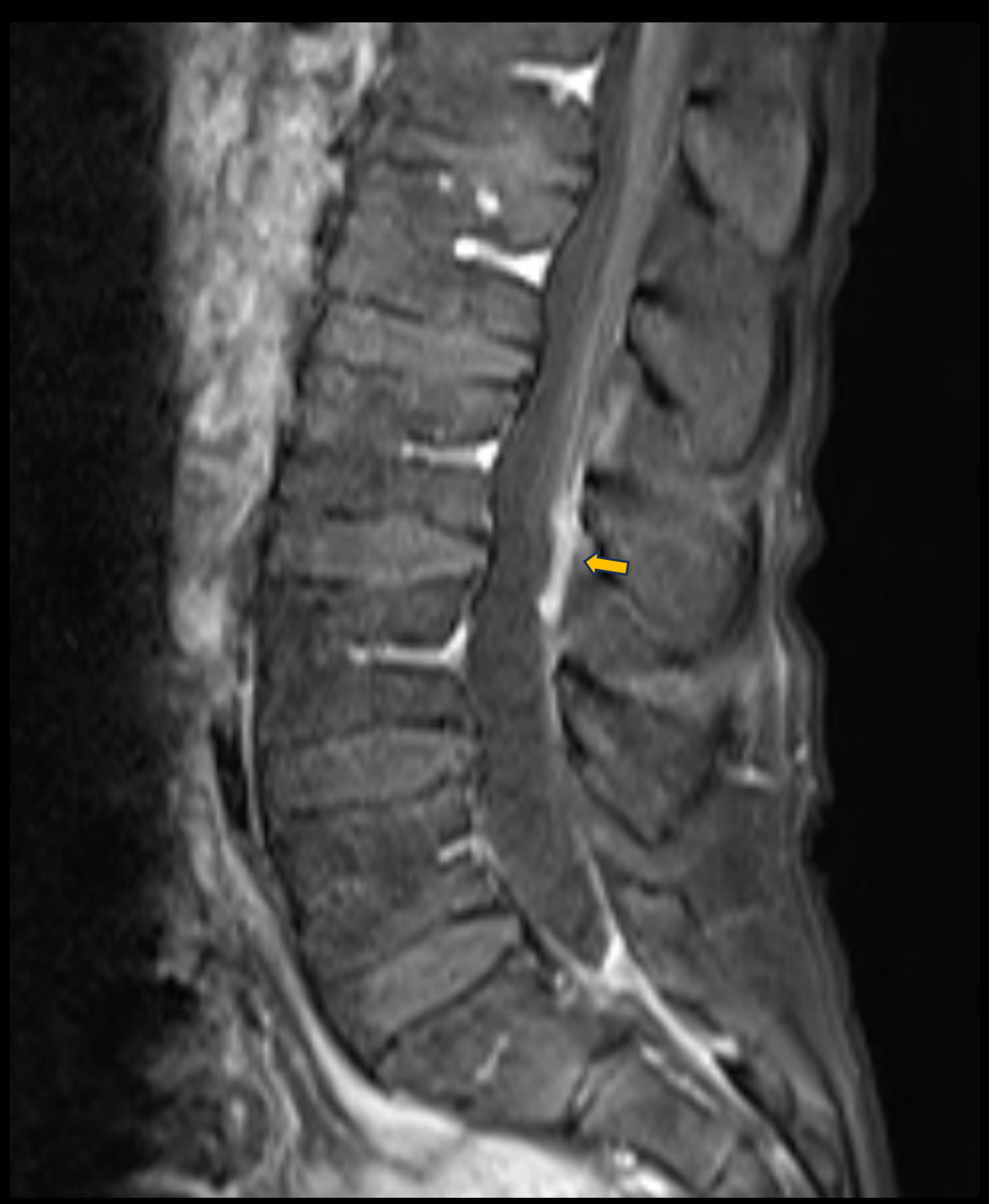
Atypical fungal infection

Any Thoughts ?

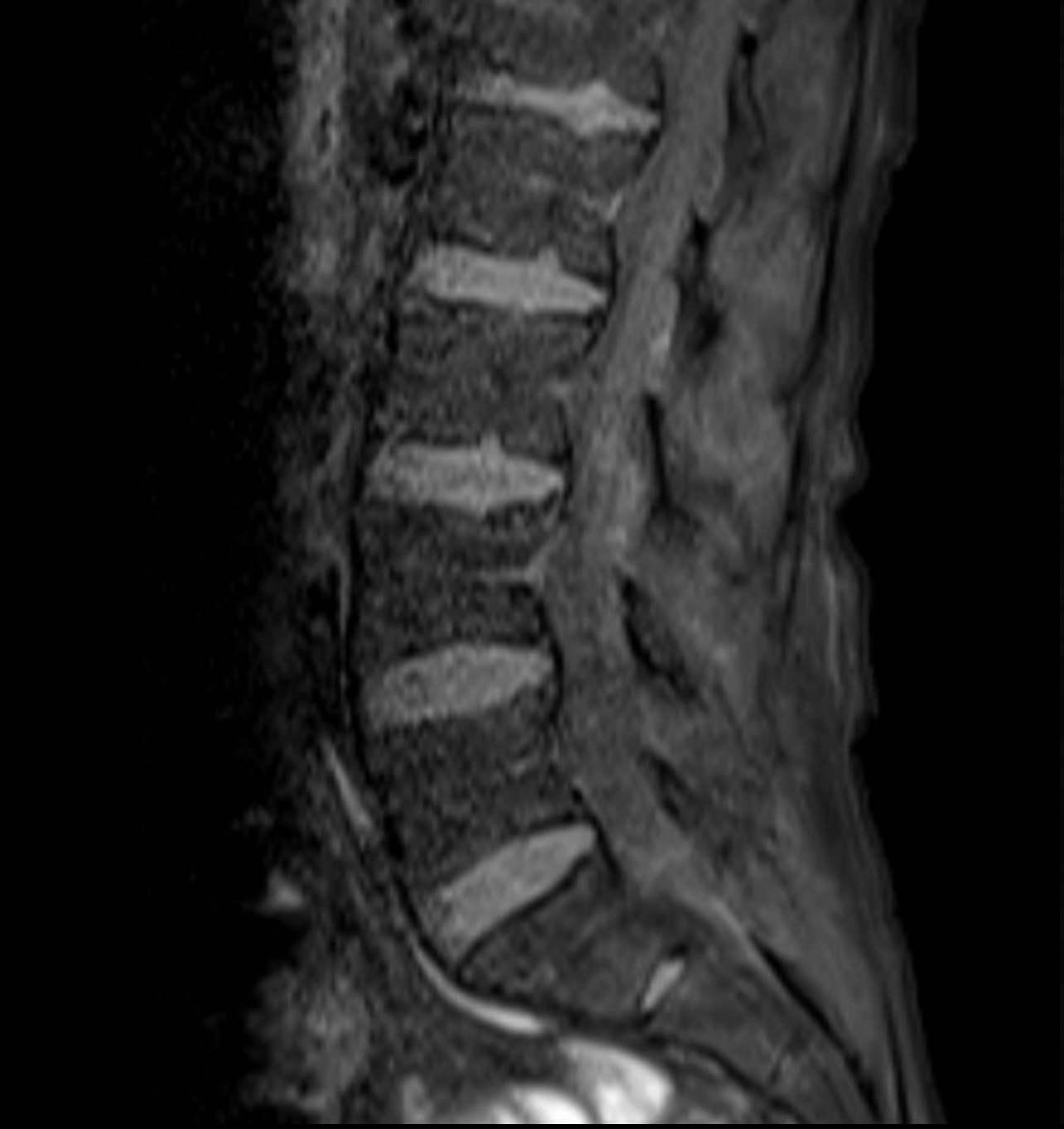
Persistent fungal infection



T1 – Pre contrast



T1 – Post contrast



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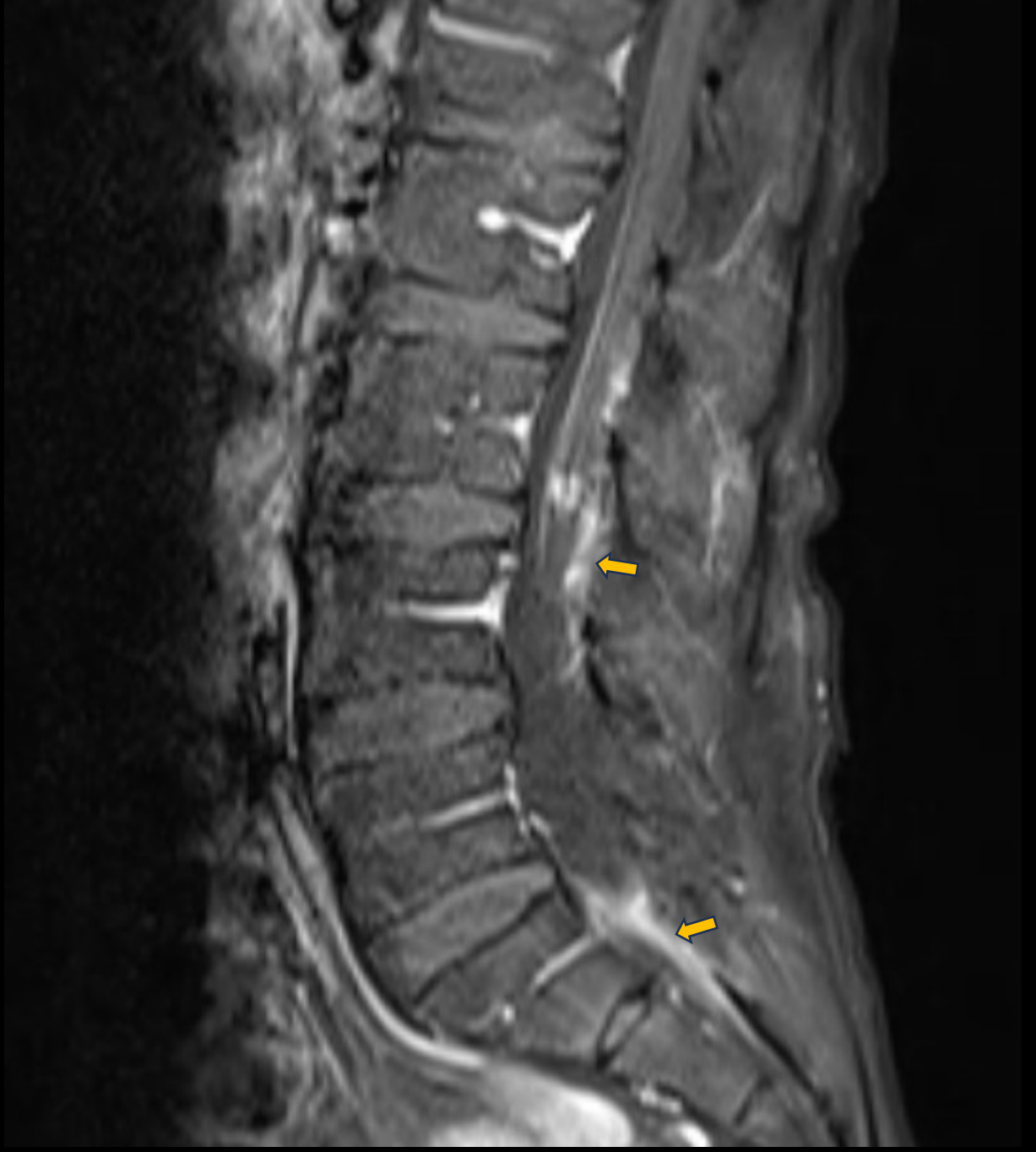
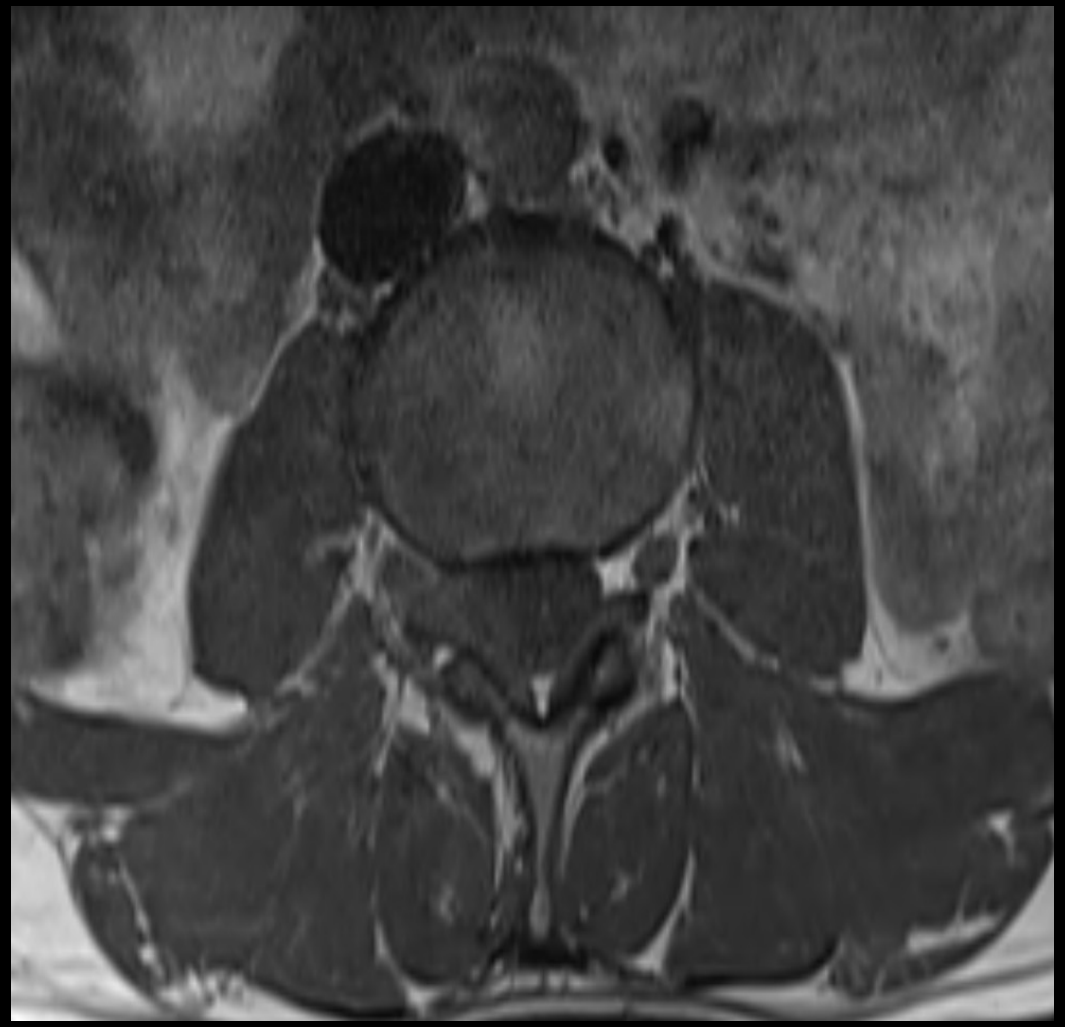
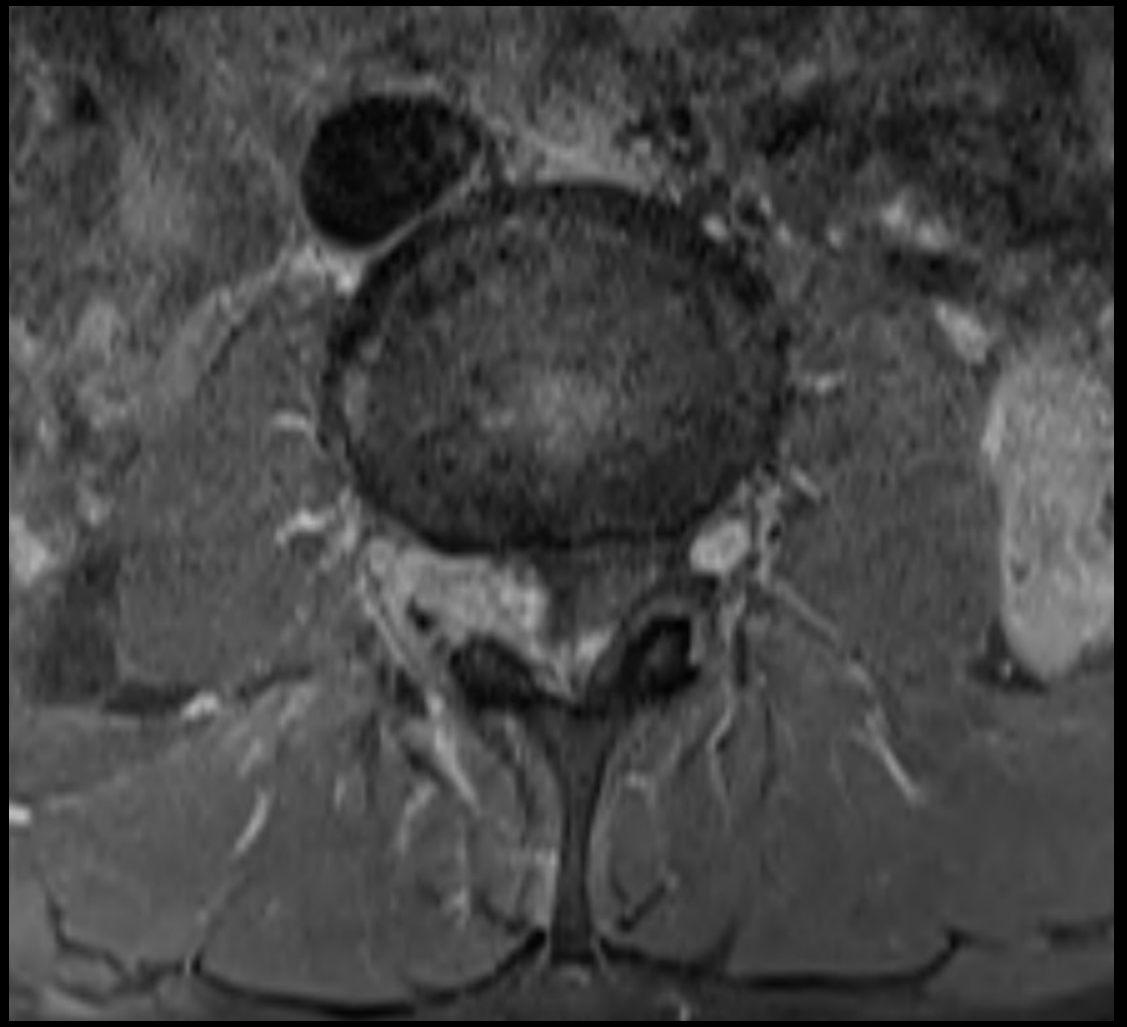


T1 –Post contrast

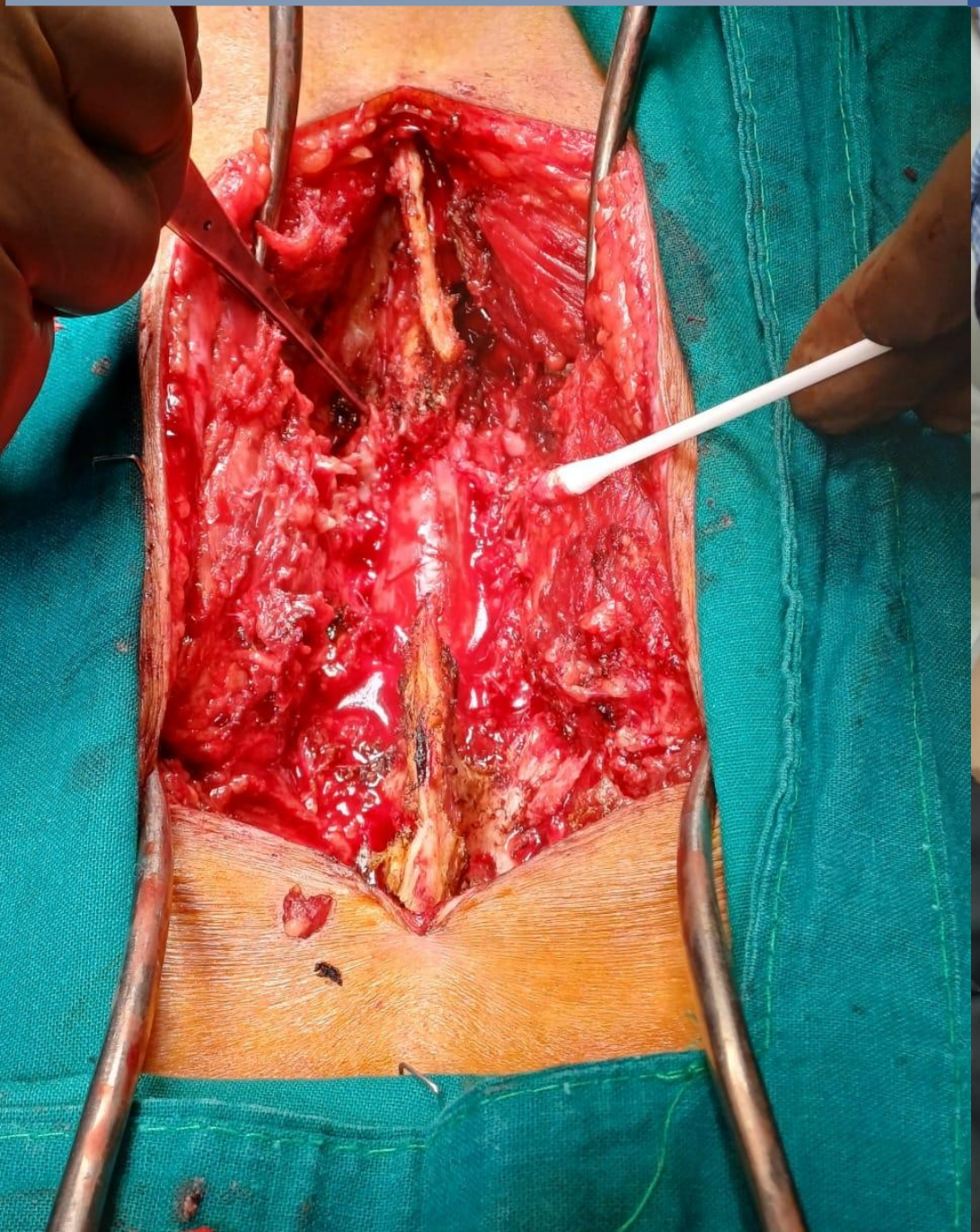


T1 –Axial Pre contrast

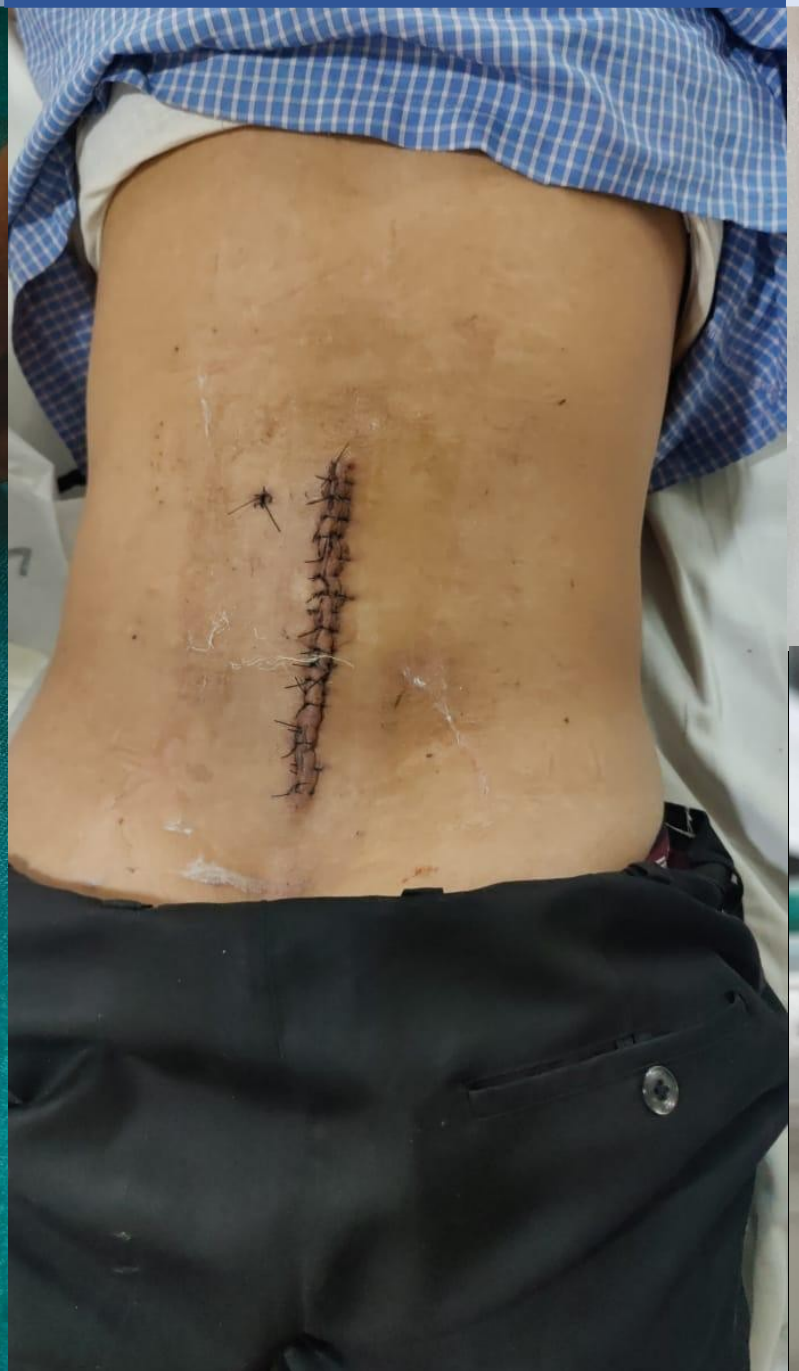


T1 –Axial Post contrast

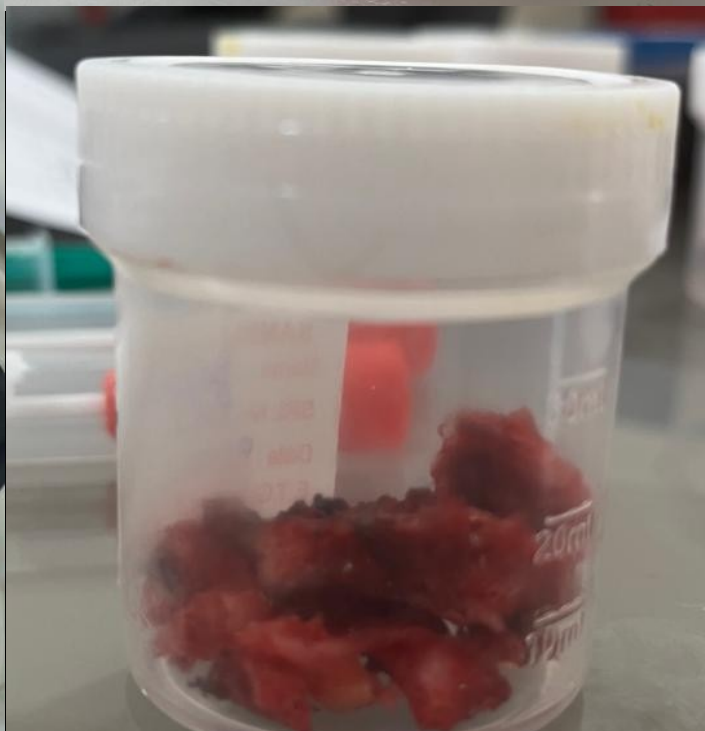
L3 – L4 Laminectomy



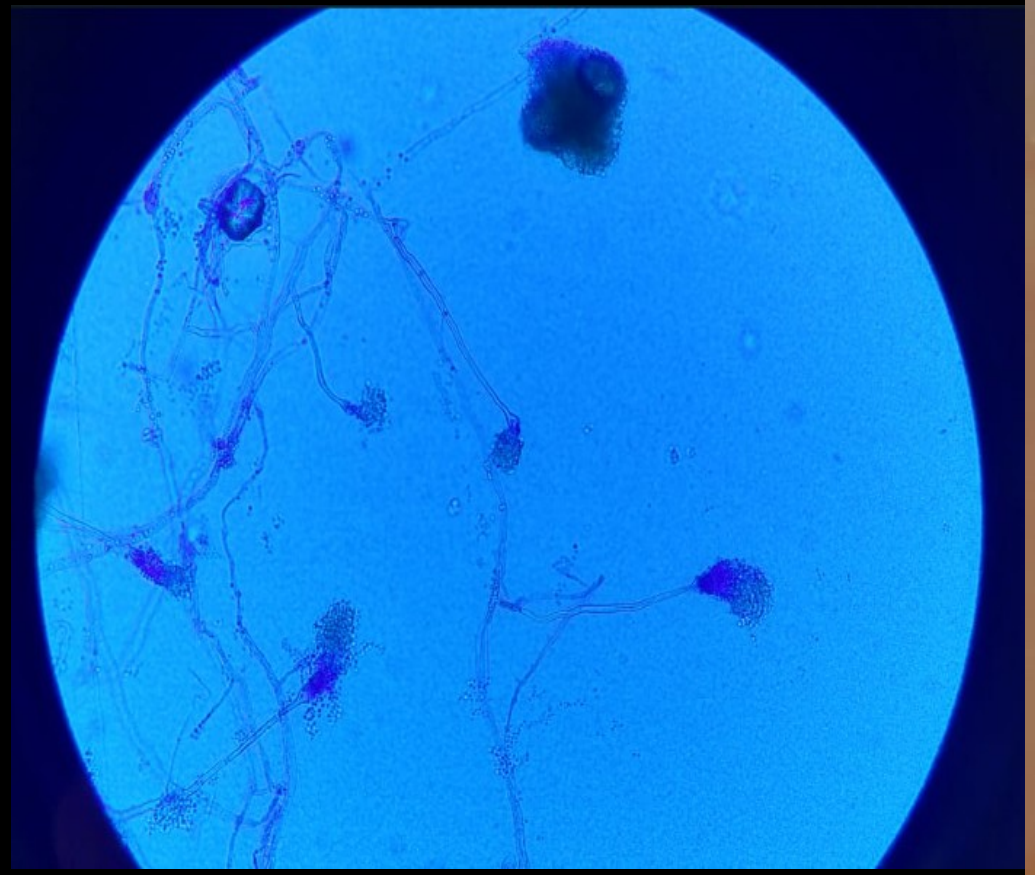
POD 12



SAMPLES



KOH mount



Fungal Culture

Other Investigations

Histopathology – Normal

Blood culture – Negative

Fungal Sequencing

Phenotype

Aspergillus Terreus.

Test: MALDI ID

Specimen: Debrided tissue (L1-L2 vertebral region)

Organisms identified: Aspergillus terreus

Score: 2.34

Note:
Test performed on MALDI-TOF-MS (Matrix Assisted Laser Desorption and Ionization - Time of Flight - Mass Spectrometry) -MALDI Biotyper SIRIUS- Bruker.

Test: MALDI ID

Specimen: Fungal isolate from Cerebrospinal fluid

Organisms identified: Aspergillus tritici

Score: 1.85

Note:
Test performed on MALDI-TOF-MS (Matrix Assisted Laser Desorption and Ionization - Time of Flight - Mass Spectrometry) -MALDI Biotyper SIRIUS- Bruker.

Cinnamon brown colored colonies on SDA

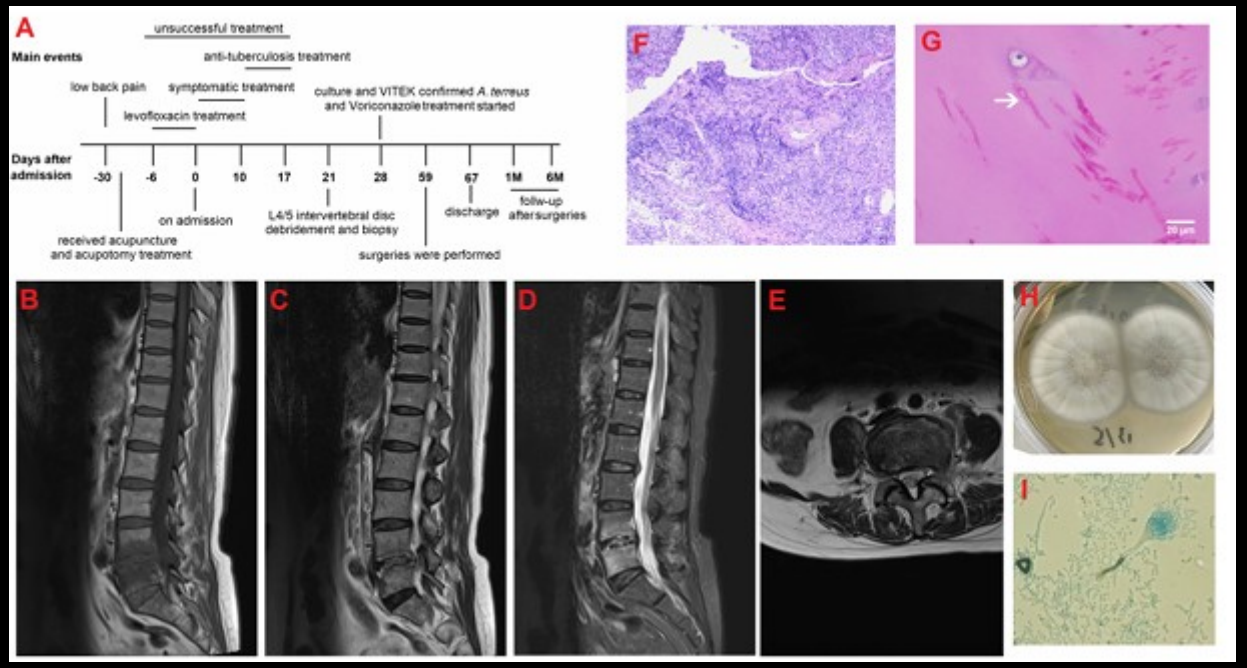
MALDI ID

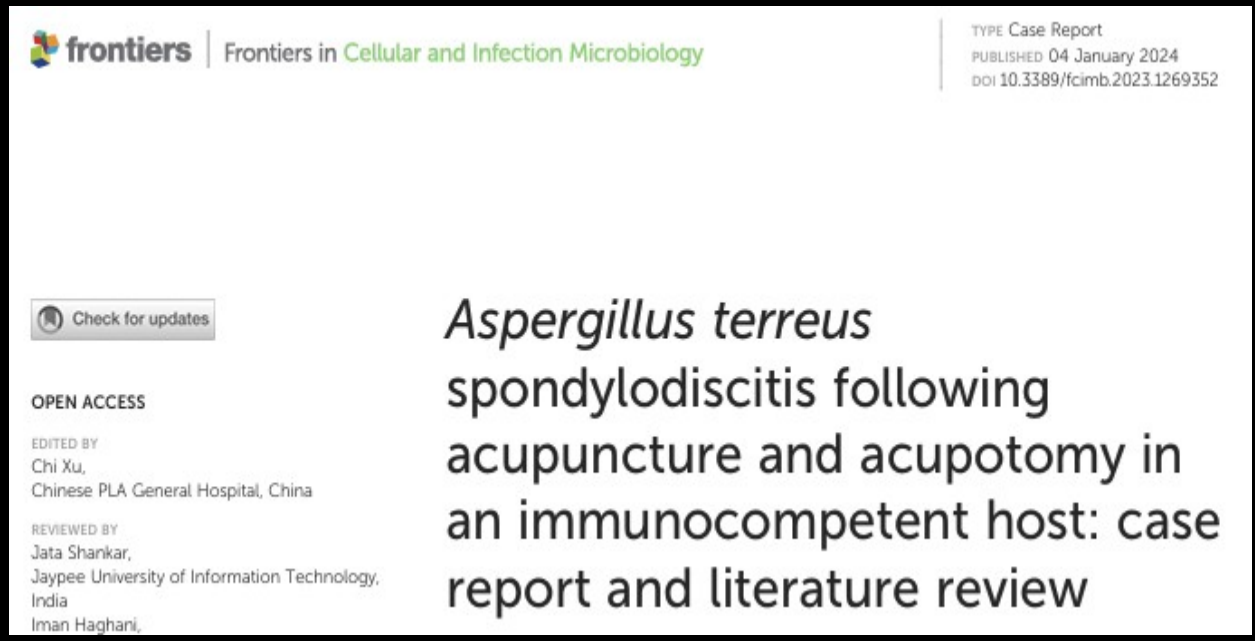
Aspergillus Terreus - Pathogenesis

- *More aggressive than of A. fumigatus.*
- *The production of **aleurioconidia** in infected tissues*
- ***The persistence in immune cells (sit-and-wait strategy)** with possible breakthrough of infections under immunosuppressive regimen.*
- ***The production of unique secondary metabolites,** such as the production of **Asp-melanin** may contribute to increased dissemination rates.*

Aspergillus Tereus

- *Certain species of Aspergillus are known to have variable susceptibilities to different antifungal drugs.*
- *A terreus* ***is intrinsically less susceptible to amphotericin B*** *in vitro and in animal models*
- *Clinical reports suggest that outcomes are better with use of alternative drugs such as*
- ***Voriconazole or isavuconazole***

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Aspergillus terreus spondylodiscitis following acupuncture and acupotomy in an immunocompetent host: case report and literature review

Take home message

- When to suspect ?

A high suspicion of Atypical Fungal Meningitis should be suspected ***post root block.***

❖ *If it matches the* ***temporal evolution*** *of symptoms.*

❖ *No response to* ***Antibiotics and Anti tubercular drugs.***

❖ *It could also be a lab contaminant in* ***Inj. Methyl prednisolone.***

Take home message

- Drug interactions

❖ *While treating such meningitis **drug-drug interactions** should be kept in mind as they may alter the course of management.*

❖ *As in our case **Rifampicin** was continued initially as a part of AKT*

❖ *Rifampicin may decrease **Voriconazole** levels for upto one month even after discontinuing the drug.*

❖ ***Amphotericin B** is known to decrease blood levels of Voriconazole.*

Day 18

Tab Isavuconazole 200 mg BD

Clinical Status ?

A Stroke Mimic

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Dr. D.Y Patil Medical College and Research Centre, Pune

Date : 30/05/25

56-year-old female admitted with c/o

- Headache since 5 days

- Acute
- Left hemi cranial
- Continuous
- Throbbing in character
- Severe intensity

- Forgetfulness for 2 days.

- About day-to-day events
- Names of family members

- **Past history**

- Cataract surgery 3 weeks back

No H/O

- Loose stools , vomiting , dehydration
- Transient visual obscursions
- Visual blurring
- Fever
- Neck stiffness
- Weight loss
- Appetite loss
- Other cognitive symptoms
- Cranial nerve involvement
  Motor deficits
- Sensory symptoms
- Urinary , bowel complaints

On Examination

HMF

- **Nominal aphasia**
- Recent memory – impaired
- Rest WNL

Cranial nerves

- **Fundus**- normal
- **Vision**->6ft B/L
- Other - Normal

Motor examination

- Tone- normal
- Power R L
- U/L 5 5
- L/L 5 5

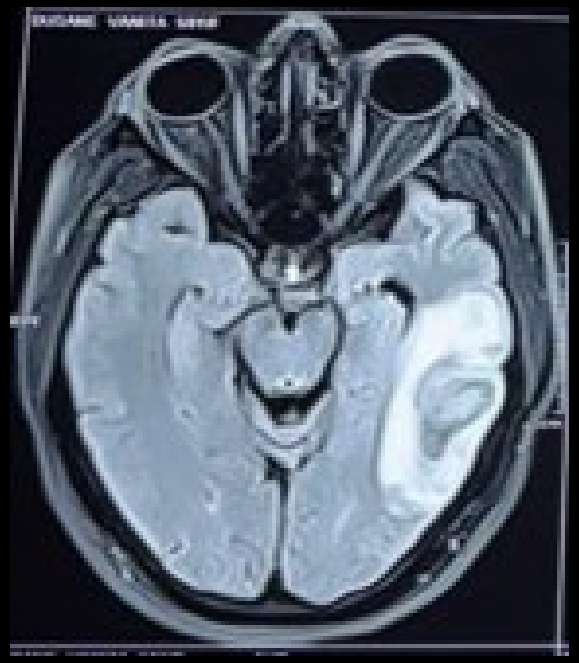
- DTRs +2 B/L
- Planters flexors B/L

Sensory examination

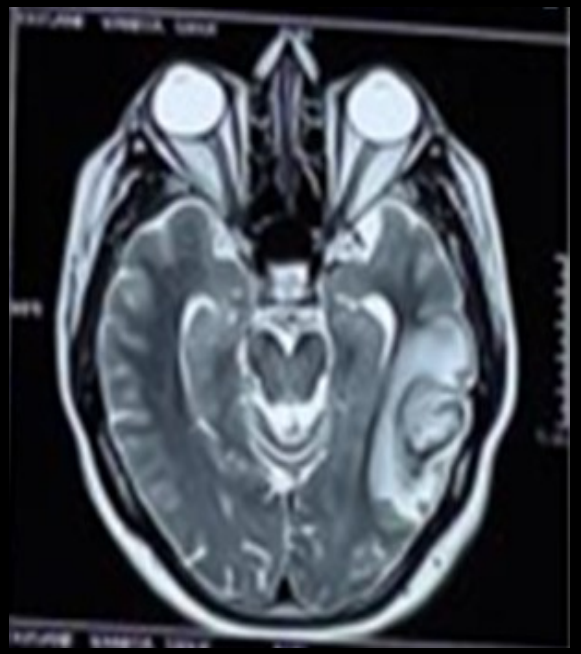
- Normal

Cerebellar signs

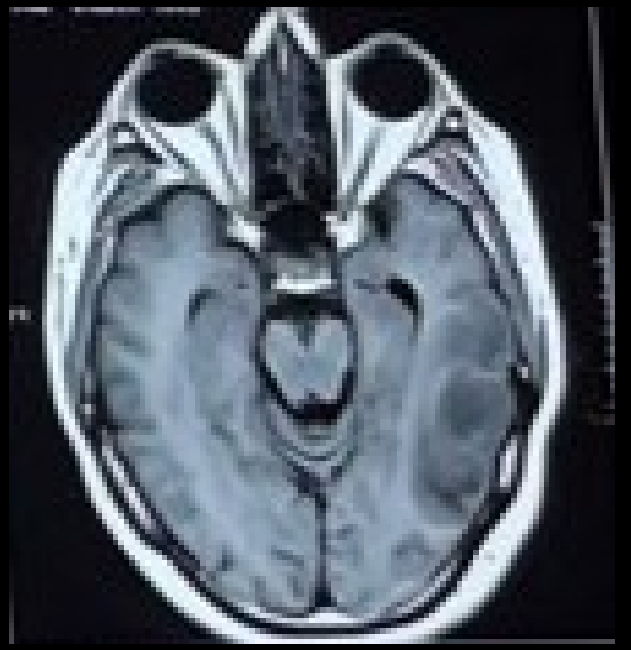
- Absent



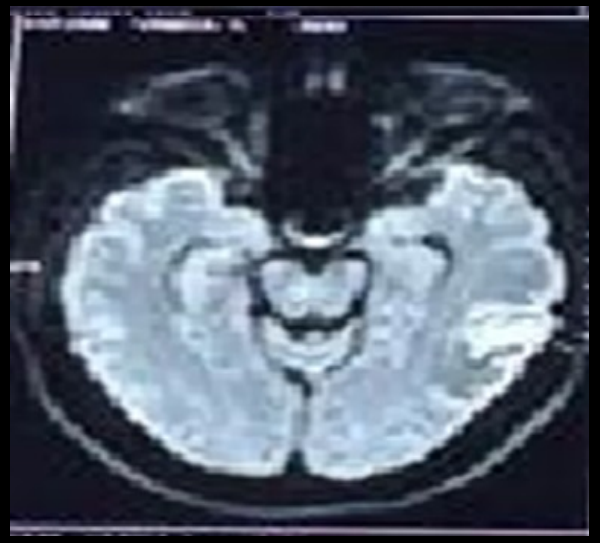
FLAIR



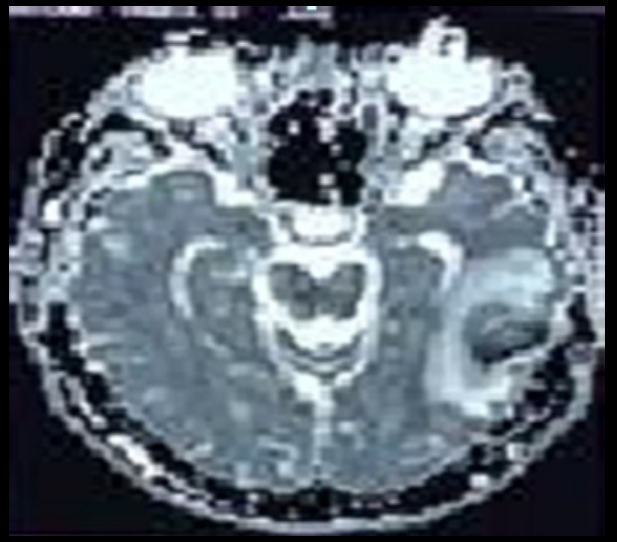
T-2W



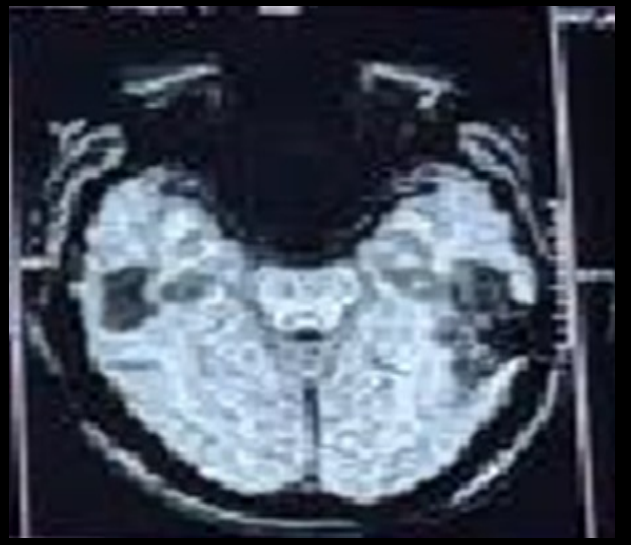
T-1W



DIFFUSION

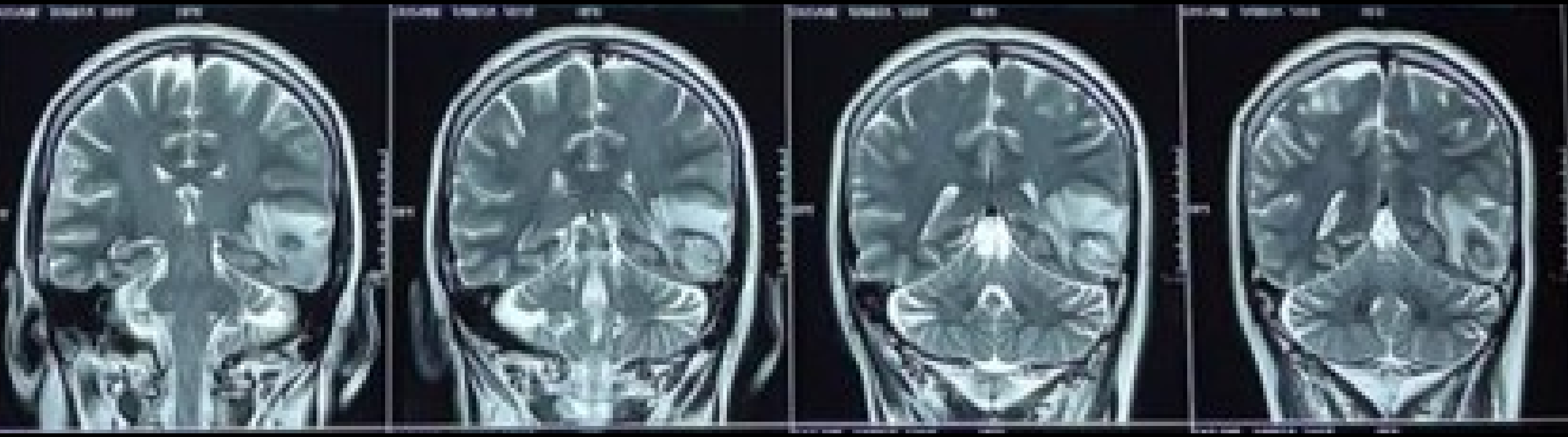


ADC

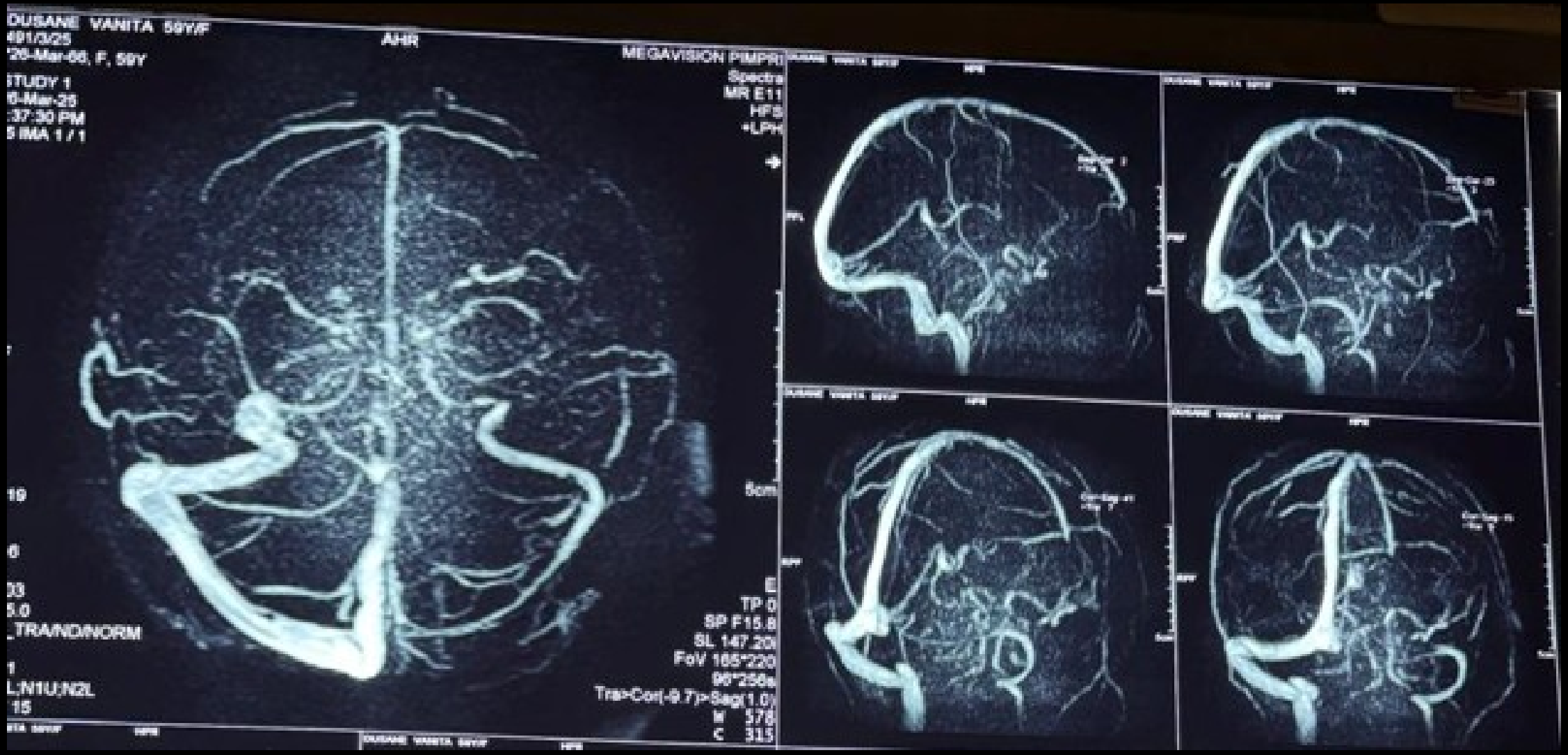


SWI

- T2 W CORONAL



MR- Venogram



Provisional diagnosis

Cortical Vein of Labbe and Transverse venous sinus thrombosis with venous infarct.

Treatment

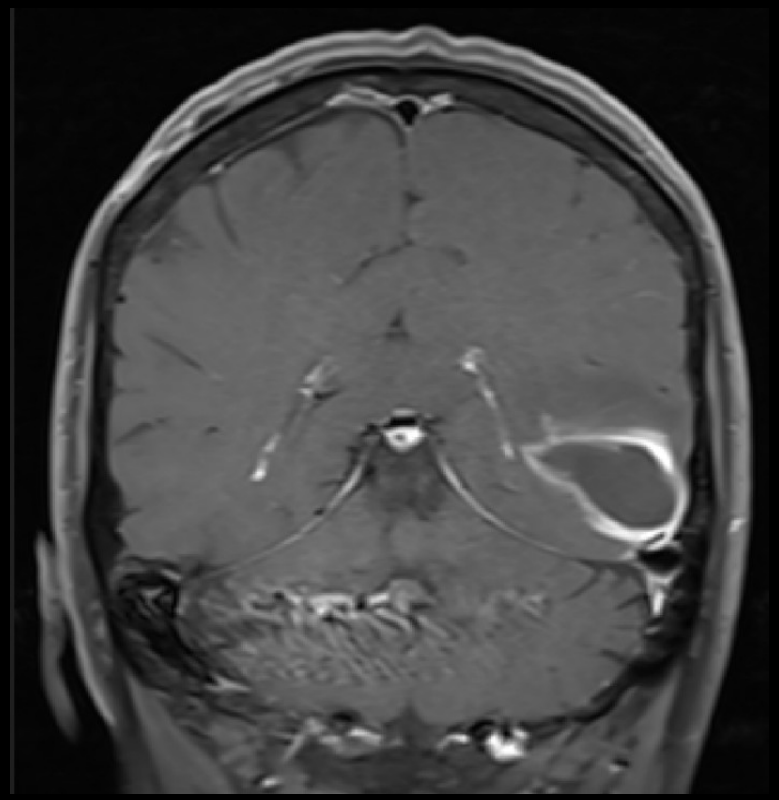
- Anticoagulation
(LMWH)

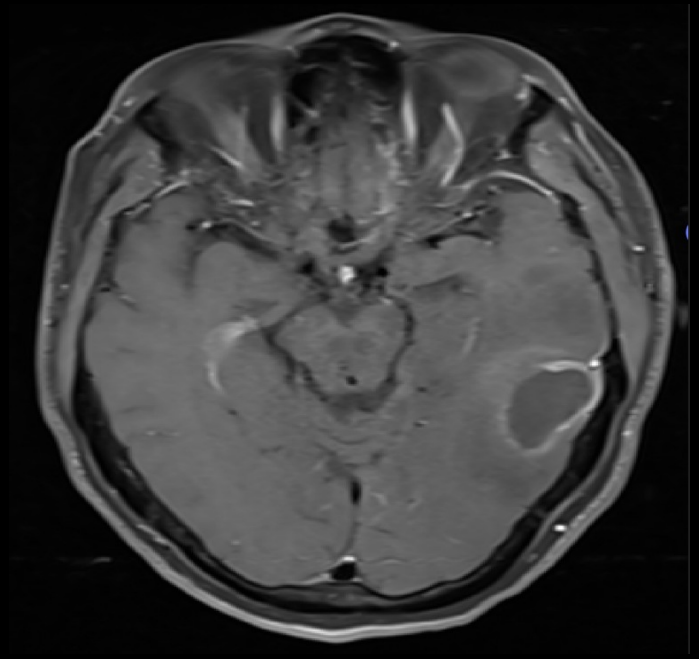
- Anti-edema measures
(Mannitol)

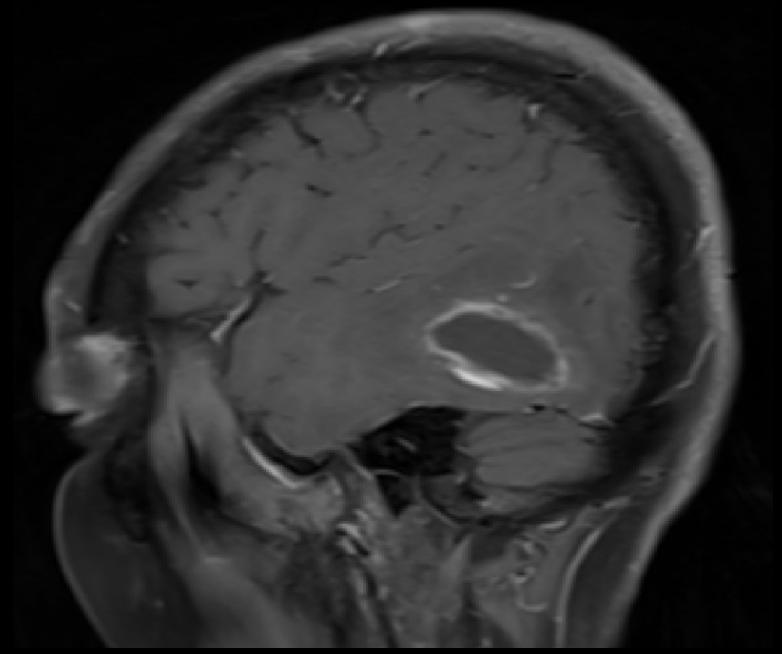
Opinion of senior radiologists

- Radiologist 1 – Cortical Vein thrombosis
- Radiologist 2 – Tumoral bleed (advised contrast)

MR Spectroscopy showing Increased choline peak







Differential Diagnosis

- Hemorrhagic metastasis
- Neoplasm with intra-tumoral bleed
- Resolving hematoma
- Abscess

Whole body PET scan

Peripheral enhancing soft tissue lesion in left temporal lobe with peripheral ring of hypermetabolism with no FDG avid lesion elsewhere.

Treatment started &Response Dexa 8mg iv tds

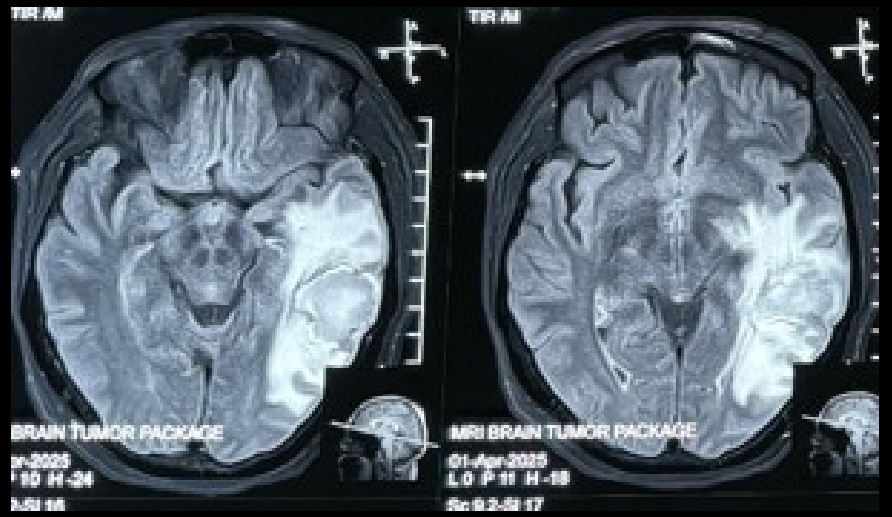
•No relief of symptoms despite treatment

What next ?

1. **Operate** and excise
    1. If SOL – good decision
    2. If thrombosed cortical vein – high risk

2. Continue **medical** management

3. **Repeat imaging** and take 3rd opinion


TR/M
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BRAIN TUMOR PACKAGE
MRI BRAIN TUMOR PACKAGE
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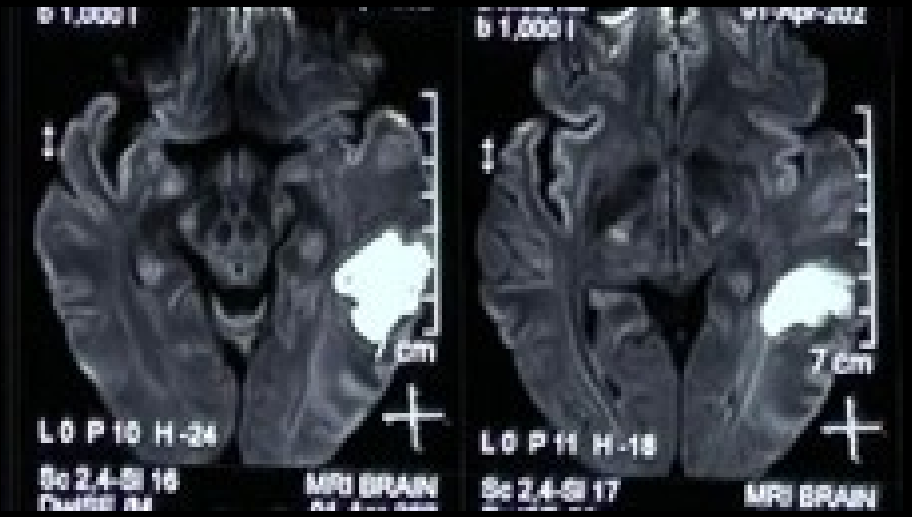
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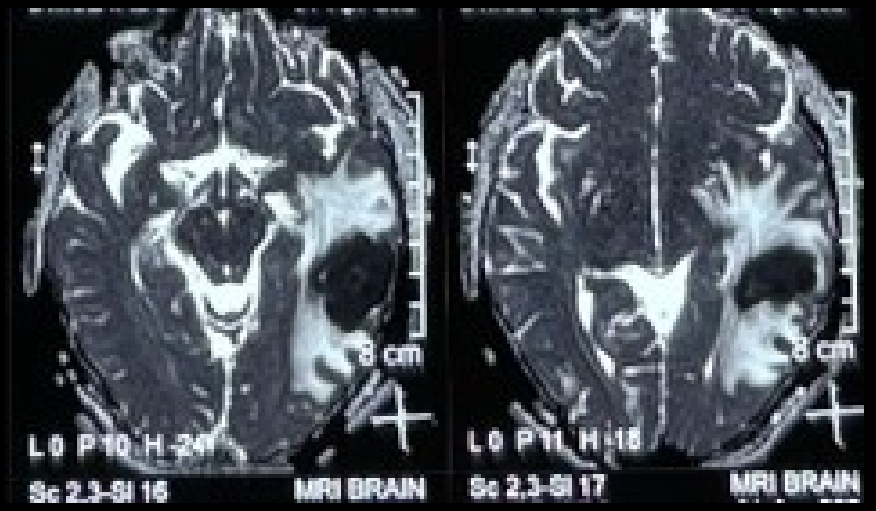
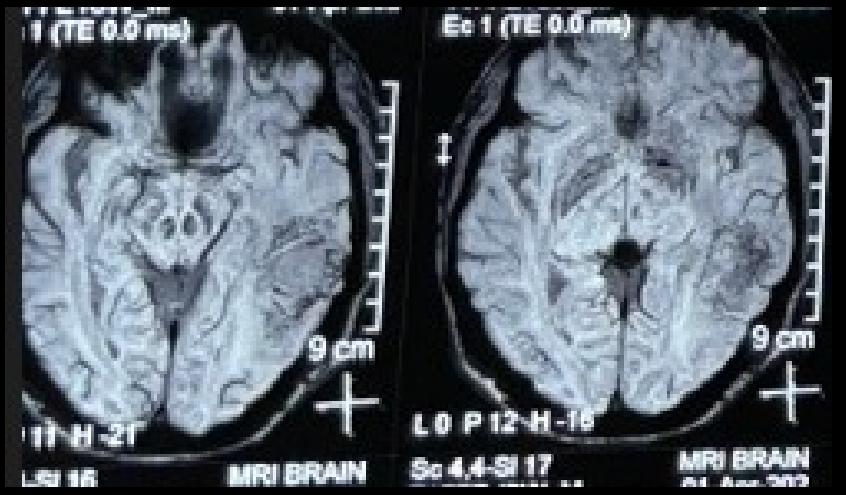
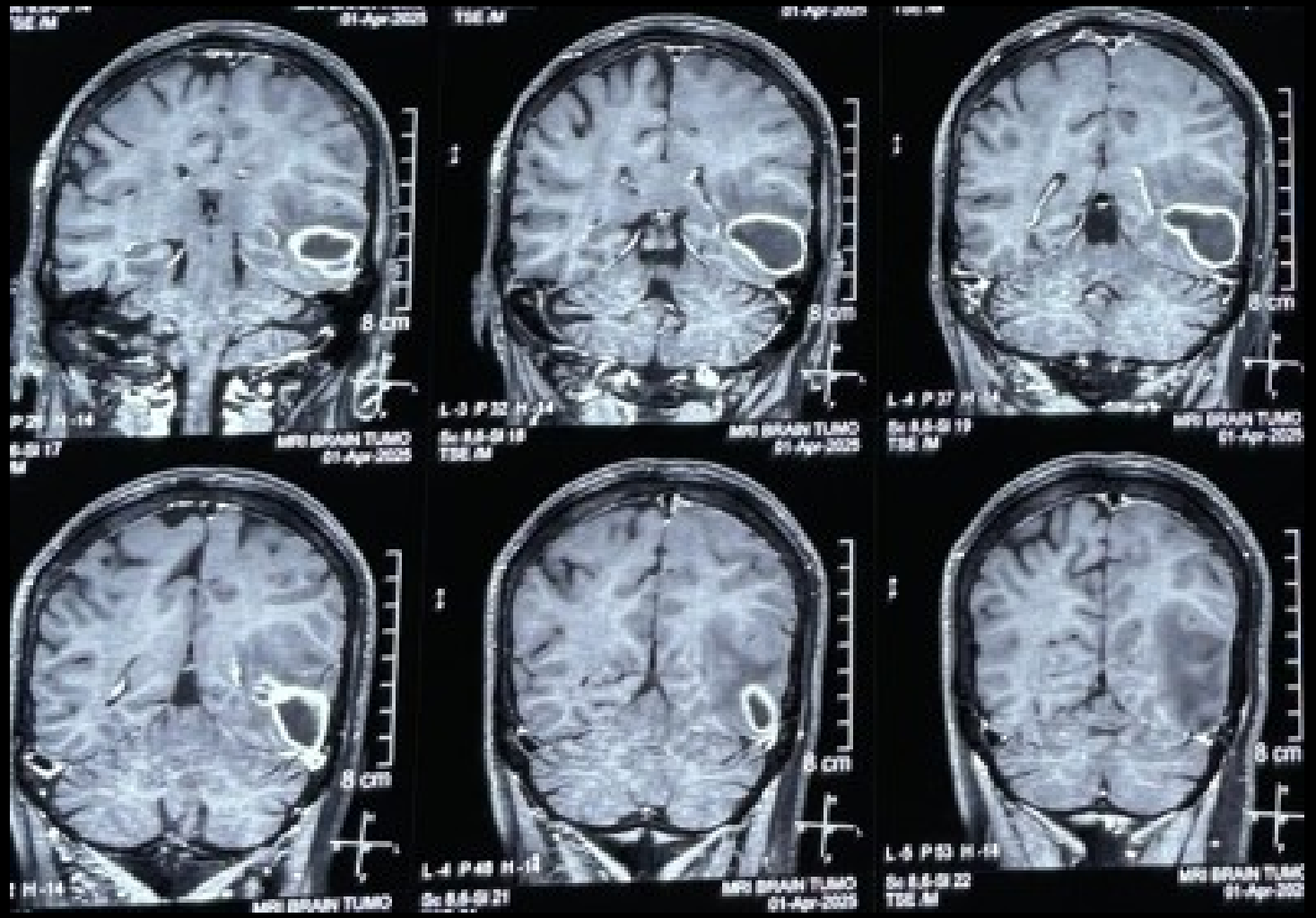
b 1,000 I
7 cm
7 cm
L 0 P 10 H -24
L 0 P 11 H -18
Sc 2,4-SI 16
Sc 2,4-SI 17
MRI BRAIN
MRI BRAIN


8 cm
8 cm
L 0 P 10 H -24
L 0 P 11 H -18
Sc 2,3-SI 16
Sc 2,3-SI 17
MRI BRAIN
MRI BRAIN


Ec 1 (TE 0.0 ms)
9 cm
9 cm
L 0 P 12 H -18
MRI BRAIN
MRI BRAIN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01-Apr-2025
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MRI BRAIN TUMO
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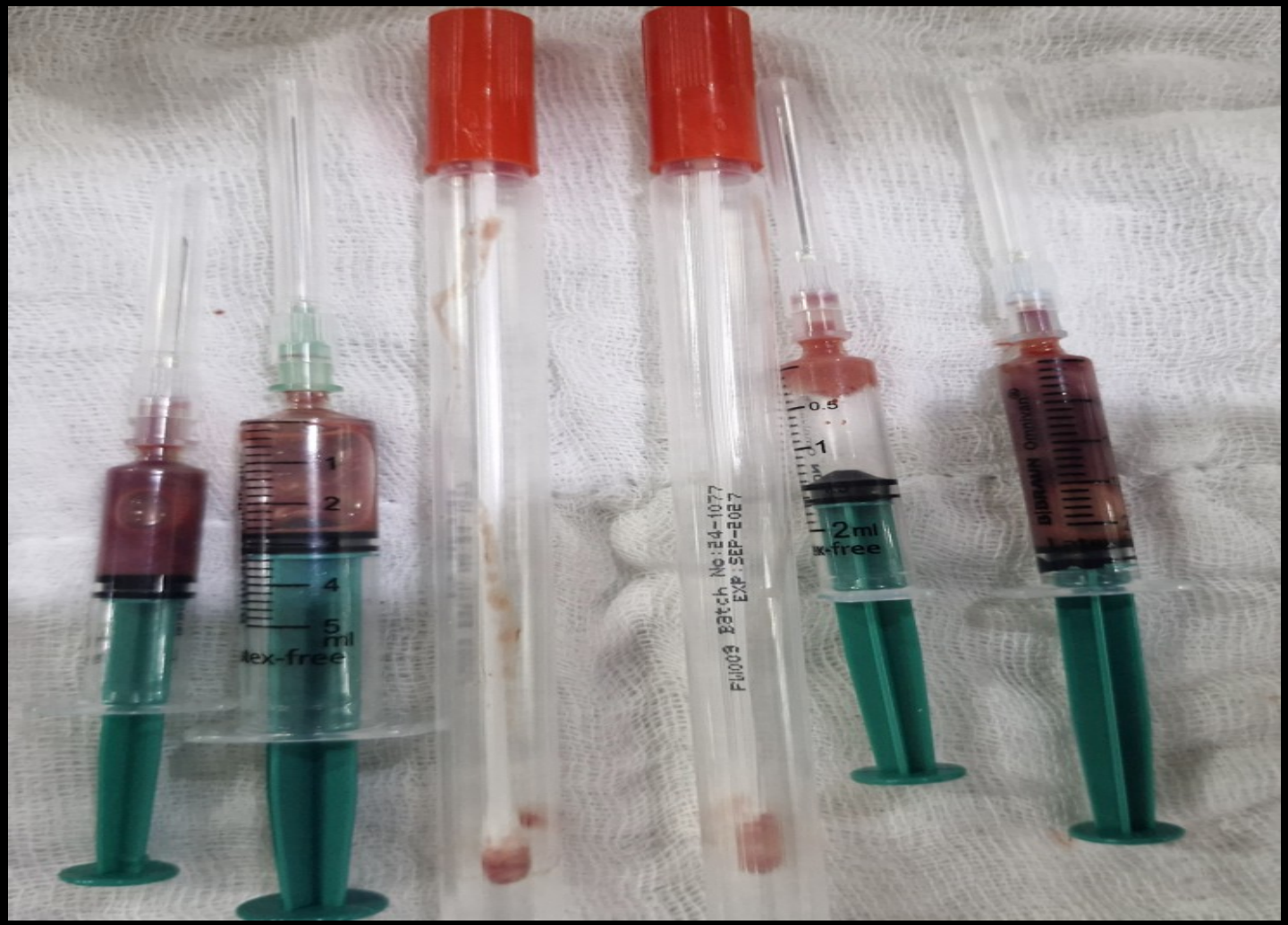
8 cm
MRI BRAIN TUMO
01-Apr-2025

Surgical exploration of the SOL done



Laboratories

Next generation sequencing

(**NGS**)

Pus **culture** sensitivity

} **Streptococcus intermedius**

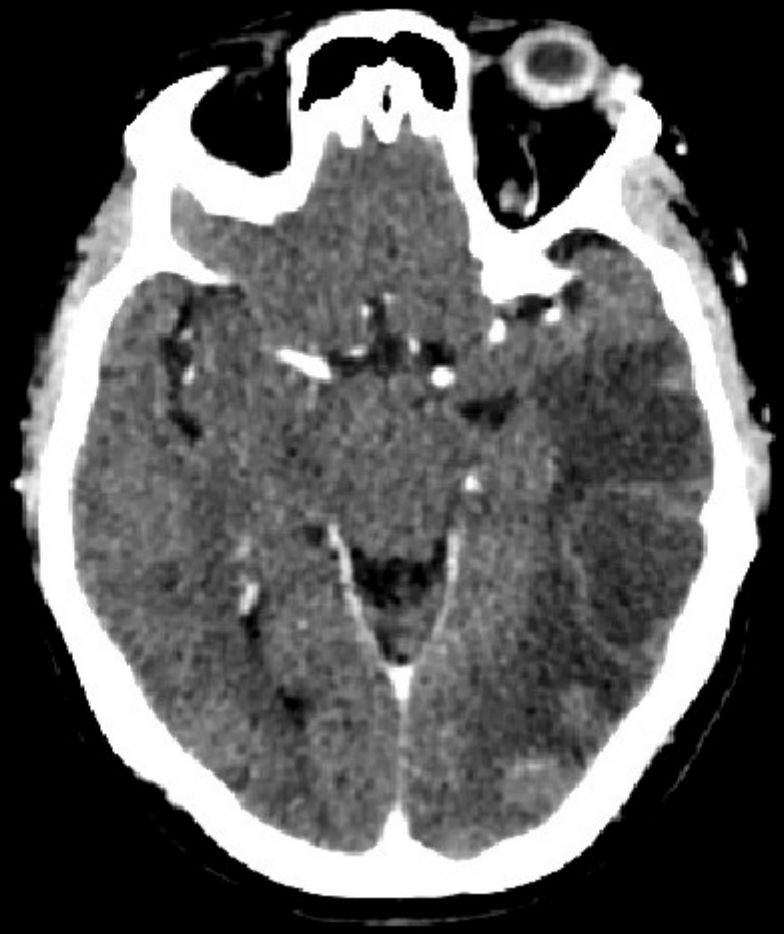
Histopathology report- Suppurative inflammation

(abscess) with no evidence of granulomas , fungal elements , parasites or neoplastic cells

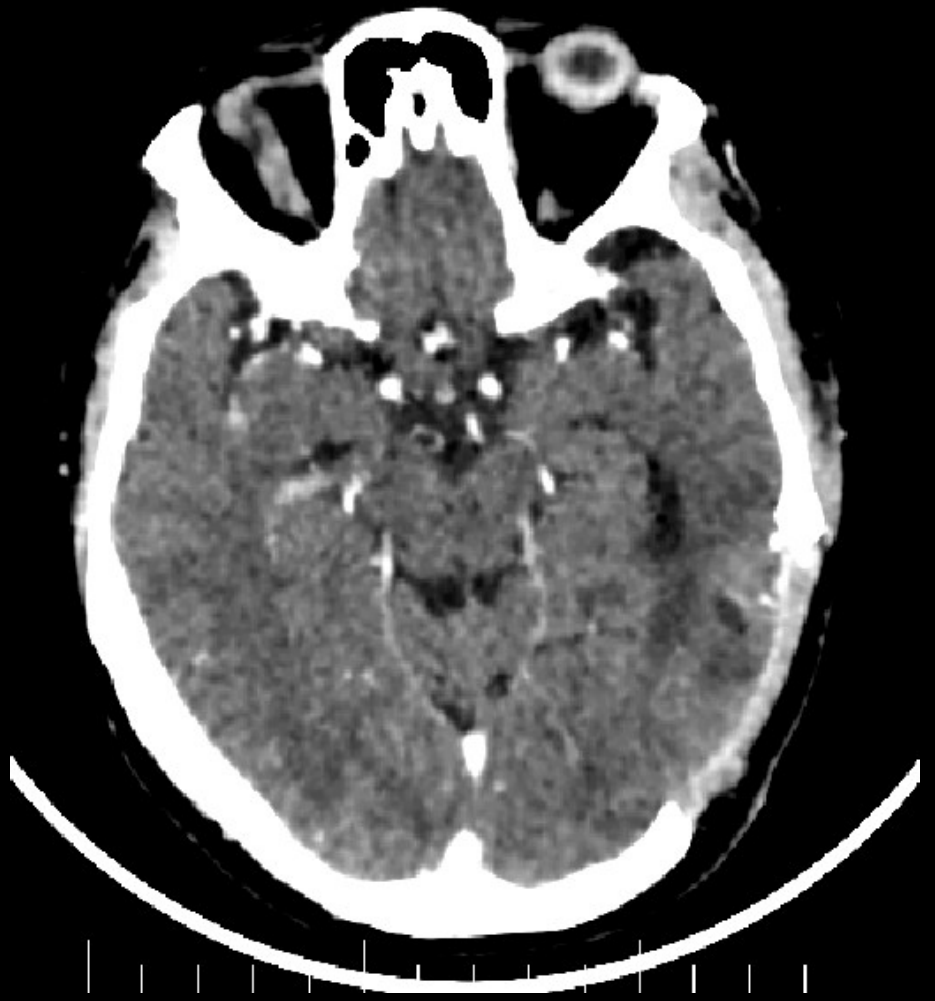
Treatment

- Inj Ceftriaxone 2gm iv bd
- Inj Metronidazole 1gm iv bd

Day 2



Follow up CT



Take home message

- Keeping a broad differential diagnosis helps

- **Pyogenic abscess may present as an acute bleed/CVST without fever**

- When unsure, take multiple opinions and revisit your management plan

Thank you