

Cerebral Abscess in Type I DM

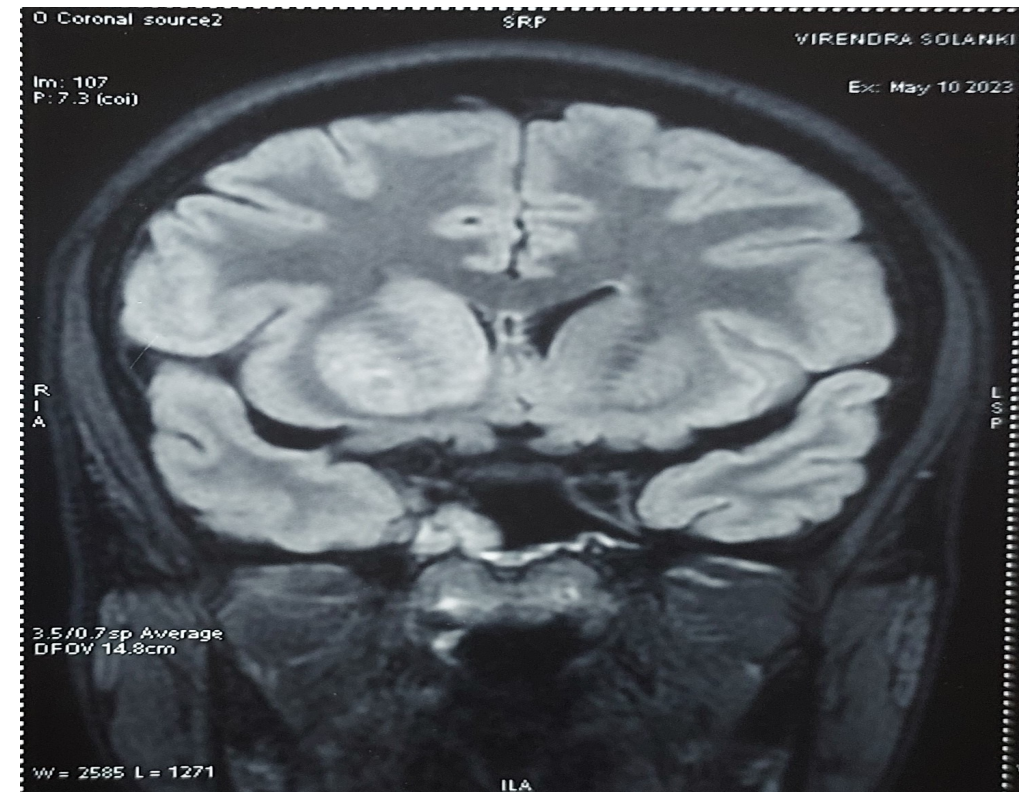
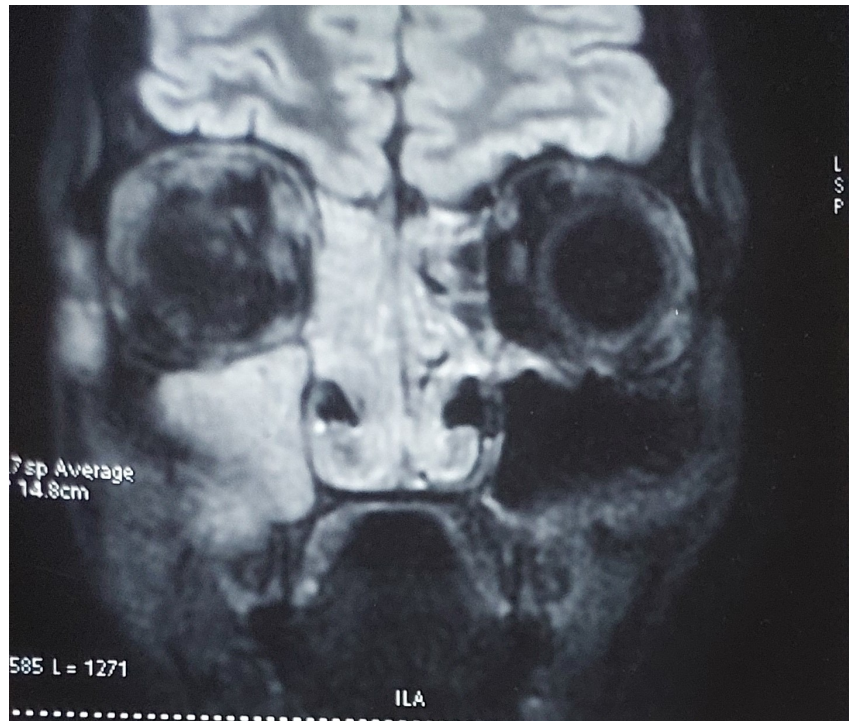
Dr. Ashish Bavishi

- M/18. K/C/O- Type I DM
- Presented in casualty on Jan 2, 2024 with C/o:
 - Lt. hemiparesis x 8 hrs
 - Rt. Facial swelling with drooping of eyelid x 1 day

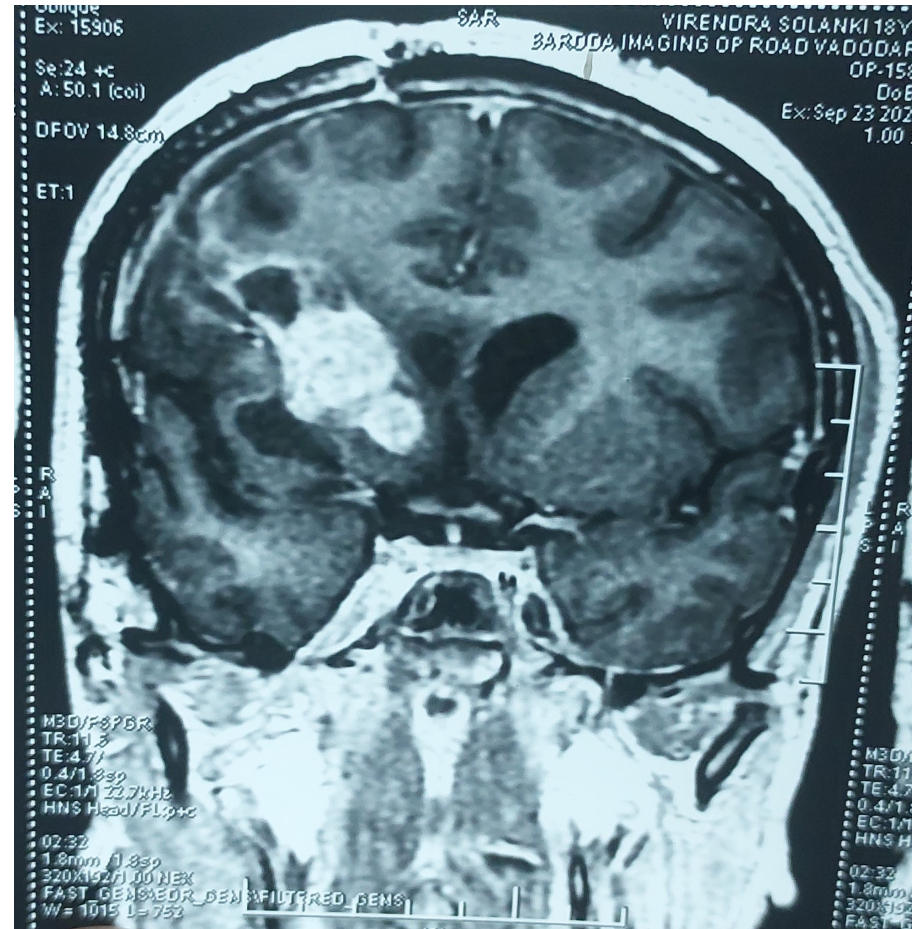
- Past History/Clinical course:

1. May 2023-

- Diagnosed ROCM at Civil hospital, Vadodara. (Tissue- sinus and Rt. Basal ganglia. Smear- broad aseptate hyphae. Fungal C/s- No growth)
- Received 24 doses of Lyophilized AmB 50 mg f/b Posaconazole 300mg 12hrly x 1 day then 300 mg OD x 3 months



2. September 23rd, 2023- Repeat MRI- Reduction in lesion size.
Asymptomatic. Posaconazole prescribed for 3 months by neurologist.



- O/E:
 - PR-84/m
 - BP- 120/80 mm Hg
 - RR- 18 cycles/m
 - T- 98.8°F
 - SpO2- 98% on RA

- S/E:
 - CNS:
 - Conscious, obeying VC. No e/o neck rigidity.
 - Power- Rt UL/LL- 5/5. Lt UL/LL- 2/5
 - Plantars-↓

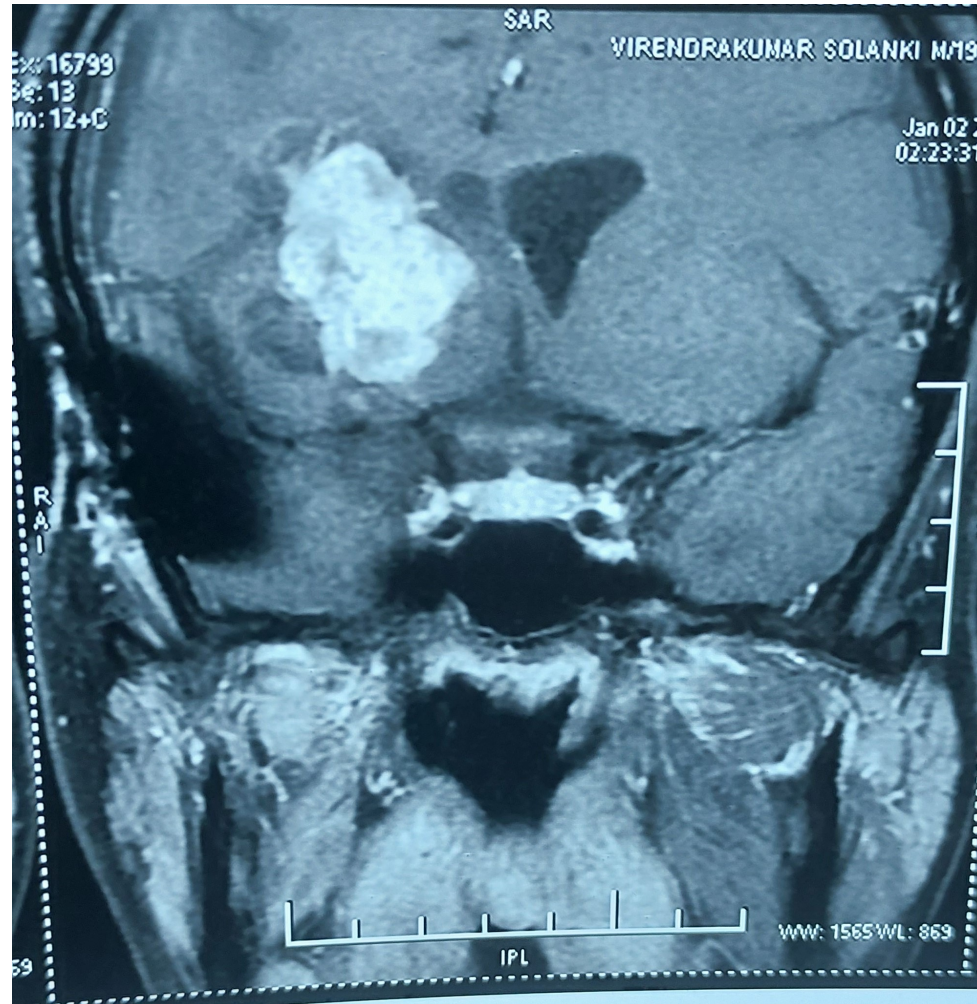
 - RS- BS B/L +
 - CVS- S1S2+, No murmurs
 - P/A- Soft. No e/o organomegaly

- L/E: Rt. Infraorbital swelling and erythema+. Rt. Ptosis.

- Labs

- CBC- 8.8/6,300/2.73x10⁶ (N- 50%, L-45%, E-2%, M-3%)
- Na⁺- 132 meq/l, K⁺- 3.9 meq/l
- Creatinine- 1.3 mg/dl, Urea- 25 mg/dl
- Bilirubin T- 0.8 mg/dl, ALT- 11 U/L, AST- 22 U/L, ALP-298 U/L
- Fundoscopy- N
- RBS- 390 mg/dl
- HbA1c- 15.2%
- S. Ketones- Neg
- CSF-
 - Proteins- 62 mg/dl, Glucose- 52 mg/dl (S. Glucose-108 mg/dl), WBC- 0
 - Gram stain/ ZN stain- neg.
 - KOH- neg

- MRI Brain (2nd Jan, 2024)- Increase in size of the lesion with microabscesses in capsulo-ganglionic area.



- Diagnostic aspiration of the lesion carried out. Histopathology and Culture is as below:

SURGICAL PATHOLOGY REPORT

Specimen :
Tissue sample in case of recurrent fungal infection in basal ganglion region.

Gross Findings :

1. Received, a gray-white mass measuring 1.5x1.5 cm. Representative sections were subjected to H.P. examination (00243,A).
2. Received, a mass measuring 1.2x1.0 cm. Representative sections were subjected to H.P. examination (B,C).

Microscopic Findings :
The sections show multiple granulomas with necrotic and suppurative core. Some of them show presence of broad and branching aseptate fungal hyphae.

Comments :
The features are those of suppurative granulomatous reaction to fungal infection, most compatible with mucor spp.

----- End Of Report -----

Patient's Name Virendra Solanki		Please fill out separate form for each investigation		Certificate number: 0-4644	
Age 119 Y/M/D	Sex:	CR. No.	Ward/OPD	Bed No.	
Clinical Diagnosis Fungal granuloma in Brain? mucormycosis Juvenile Diabetes.	Previous results, if any		Antimicrobial Therapy oral posaconazole x 3 months		
	Collection Date : 6/1/24 Time :		Consultant		
Specimen Tissue	Investigation Required Fungal culture		Signature of Resident		
Site Rt. Basal ganglia region.	AFST, PCR				
Report					
Direct microscopy/smear		Culture			
Smear Report		CULTURE SHOWS NO GROWTH OF PATHOGENIC FUNGUS AFTER 25 days INCUBATION.			
Epithelial Cells _____					
Pus Cells _____					
Yeast Cells _____					
Pseudohyphae _____					
Hyphae _____					
Cryptococcus _____					
RBC _____					
Bacteria _____					
Technologist		Resident		Consultant	
Micro No.	Division No.	Receipt Date :	Despatch Date :		
	P-3961	Time:	Time:		
	13/1/24				

Factors to consider

- Posaconazole monotherapy for cerebral mucormycosis requires frequent TDM to optimize outcome.

H. Ruth Ashbee, Rosemary A. Barnes, Elizabeth M. Johnson, Therapeutic drug monitoring (TDM) of antifungal agents: guidelines from the British Society for Medical Mycology, Journal of Antimicrobial Chemotherapy, Volume 69, Issue 5, May 2014, Pages 1162–1176

- Culture negative, histopathological diagnosis may miss an alternative differential.
- Lyophilized AmB is inferior as an initial treatment for cerebral mucormycosis.
Maertens J, Pagano L, Azoulay E, Warris A. Liposomal amphotericin B-the present. J Antimicrob Chemother. 2022
- Isavuconazole may be considered as a viable alternative owing to better pk/pd characteristics.
- Uncontrolled Type I DM is a major risk factor for recurrence/relapse of mucormycosis

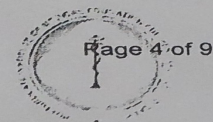
- Citing the above factors, following steps were taken:
 1. Serum Posaconazole trough levels were sent.
 2. IV Meropenem + Vancomycin was added for possibility of bacterial brain abscess (although laboratory features and CSF study were not suggestive of bacterial infection, uncontrolled DM was considered as an important risk factor)
 3. Brain tissue was sent to PGI Chandigarh for molecular identification.
 4. Liposomal Amphotericin B was started at dose of 5mg/kg. Isavuconazole was advised but declined owing to financial considerations.
 5. Strict glycemetic control was commenced and maintained.



NATIONAL CULTURE
COLLECTION OF PATHOGENIC FUNGI

Department of Medical Microbiology, Mycology Division
National Culture Collection of Pathogenic Fungi (NCCPF)
WHO Collaborating Centre

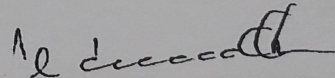
Post-Graduate Institute of Medical Education & Research,
Chandigarh



MOLECULAR IDENTIFICATION REPORT

Patient Name : Virendra Solanki
Age/Gender : 19/M
Referred By : Dr Nirav Pandya
Date of receiving : 14-01-24
Date of reporting : 07-02-24
Sample Type : Tissue
Lab ID :
Method used : P-3961/23(IL6032/23)
Gene target : Zygo-mucor Specific Primer
Final Identification : *Rhizopus arrhizus*

Technologist


Dr M.R. Shivaprakash
Professor & In-charge
Mycology Division
Department of Medical Microbiology

Unique characteristics of *R. arrhizus* (aka *R. oryzae*)


- Less susceptible to host defenses as compared to other zygomycetes due to higher content of chitin which stimulate TNF α and IL-6 by mimicking mononuclear cells.

Roilides E, Kontoyiannis DP, Walsh TJ. Host defenses against zygomycetes. Clin Infect Dis. 2012 Feb;54 Suppl 1:S61-6.

- ERG11, the gene responsible for lanosterol 14 α demethylase synthesis, which is the major target site for triazole antifungals, are duplicated throughout its genome resulting in multiple copies. Hence, associated with variable susceptibility and increased virulence.

*Ma LJ, Ibrahim AS, Skory C. Genomic analysis of the basal lineage fungus *Rhizopus oryzae* reveals a whole-genome duplication. PLoS Genet. 2009 Jul;5(7):e1000549.*

Serum Posaconazole levels

LABORATORY REPORT				
Name : VIRENDRAKUMAR M SOLANKI	Sex/Age : Male / 19 Years			
Ref. By : DR.ASHISH BAVISHI	Dis. At : lab	Case ID : 40200204612		
Bill. Loc. : Labcore spec lab baroda		Pt. ID : 3357431		
Reg Date and Time : 16-Feb-2024 14:12	Sample Type : Serum	Pt. Loc : Lab Collection		
Sample Date and Time : 16-Feb-2024 14:12	Sample Coll. By : non	Mobile No. : 9265240411		
Report Date and Time : 17-Feb-2024 16:06	Acc. Remarks	Ref Id1 : -		
		Ref Id2 : -		
TEST	RESULTS	UNIT	BIOLOGICAL REF RANGE	REMARKS
Posaconazole	0.006	µg/mL	Therapeutic level: >0.7	
----- End Of Report -----				
<p># For test performed on specimens received or collected from non-NLCL locations, it is presumed that the specimen belongs to the patient named or identified as labeled on the container/test request and such verification has been carried out at the point generation of the said specimen by the sender. NLCL will be responsible Only for the analytical part of test carried out. All other responsibility will be of referring Laboratory.</p>				

Clinical course

- IV Meropenem and Vancomycin were stopped i/v/o negative Blood, CSF and Tissue cultures.
- LAMB (5 mg/kg) was given for 4 weeks with Posaconazole (Gastro resistant tab).
- Posaconazole was continued in therapeutic doses with weekly TDM.
- Clinical improvement was noticed- weight gain, reduction in focal neuro deficit, optimal glycemc control and improved gait.
- Patient was advised to take Posaconazole tablets after meals. Compliance to treatment was ensured.
- Patient was discharged after 4 weeks on Posaconazole monotherapy and is currently on weekly follow up.

Final Diagnosis

- ✓ Proven Rhino-Orbital-Cerebral mucormycosis (EORTC-MSG criteria) in uncontrolled Type I Diabetes Mellitus.

Learning Points

- Liposomal Amphotericin B (LAMB) is initial drug of choice for Rhino-orbital-cerebral mucormycosis.
- Posaconazole (delayed release or gastro resistant tablet formulation) is an acceptable alternative to LAMB, provided regular TDM, compliance and follow up is ensured.
- Molecular diagnosis provides an unequivocal evidence of Invasive Fungal Infection and is a valuable aid to diagnosis.
- Adequate redressal of risk factors is essential to improve clinical outcomes and prevent relapse.

Thank You