

OCULAR ZYGOMYCOSIS

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Background

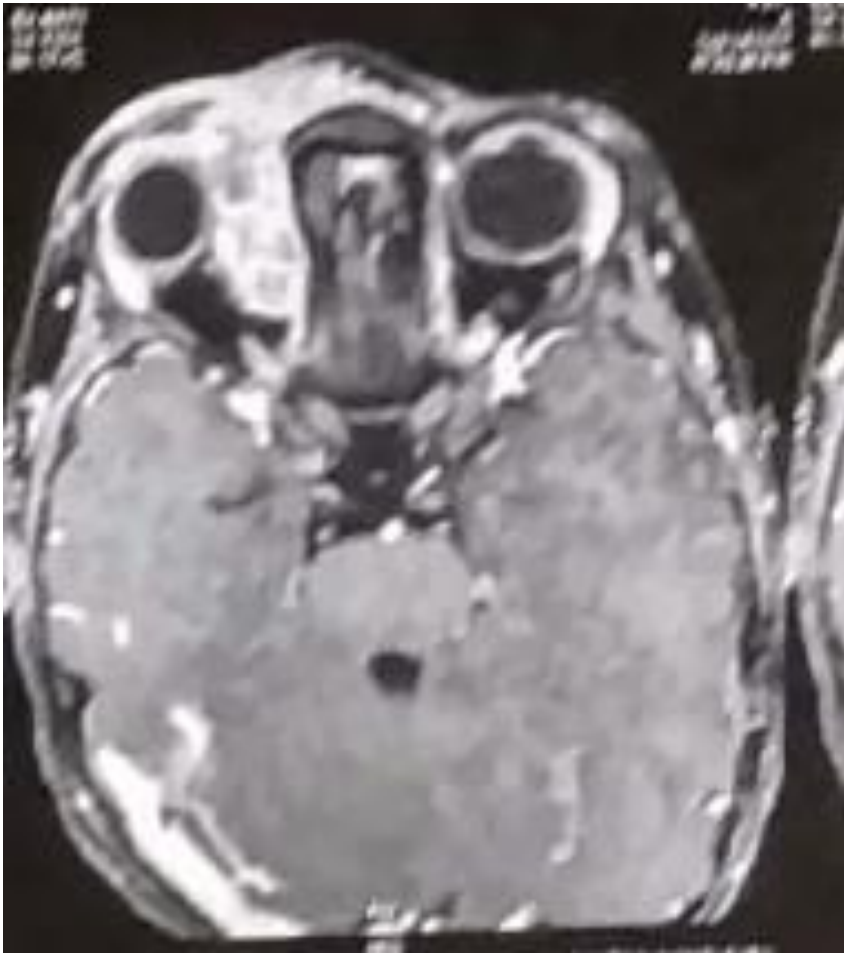
- A 2 year female toddler from Jharkhand.
- Presented with swelling over the right eye with low grade fever associated with purulent discharge - 1 month.
- The lesion started in the middle canthus and gradually progressed ,affecting the eye movements and vision.

ON EXAMINATION

- The lesion did not involve the other eye nor had any neurological signs or symptoms
- No systemic symptoms
- No significant medical illness in the past

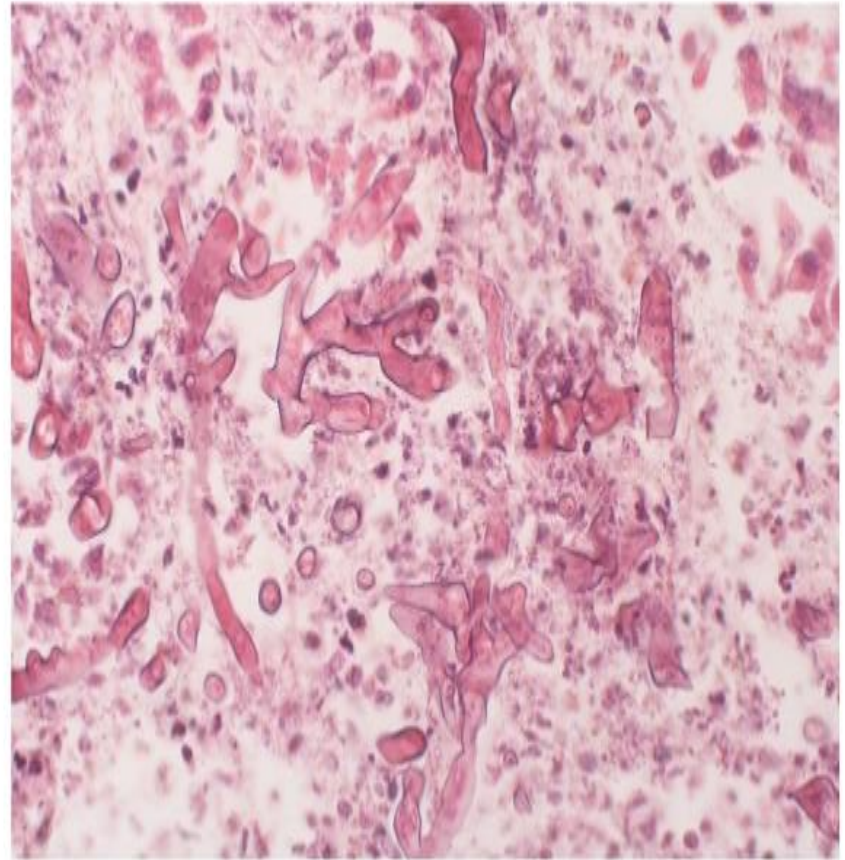


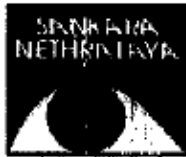
1st imaging (September 2017)



- An ill- defined hetero- genously enhancing soft tissue in the right lower eyelid, nasal bridge and the medial extra-conal space, with extension into the ethmoidal sinus.
- No significant abnormality noted in the brain parenchyma.

- Histopathology and microbiological examination
- Aseptate fungus
Mucormycosis
(zygomycosis)
with sub species
Saksenaea
erythrospora





Vision of the Millennium

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Certificate No. M-0094

Name : BABY NANDINI KUMARI

MRD No : 4201986

Age : 2 Year(s)

Sex : FEMALE

Type : Out Patient

CLINICAL MICROBIOLOGY LAB REPORT

Report ID: MIB160917909

Request No: REQ/17/09/16/0182

Location : SN MAIN

Lab No. M.NO.2727/17

Referred By : Dr. BIPASHA MUKHERJEE

Primary Specimen : OTHERS (SPECIFY)

FINAL REPORT

L401 - GRAMS STAIN

Methodology: Bright field Microscopy

Parameter Name

Grams stain

Parameter Result

: A few pus cells, RBCs, degenerated cellular material and fibrinous exudates are seen. Bacterial agents could NOT be made out.

L402 - KOH AND CALCOFLUOR STAIN

Methodology: Fluorescence Microscopy

Parameter Name

KOH and Calcofluor stain

Parameter Result

: Moderate number of sparsely septate fungal filaments ARE SEEN.

NOTE : Name of the clinical specimen: Orbital biopsy(OD)
Culture for pyogenic bacteria and fungus are put up.



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CLINICAL MICROBIOLOGY LAB REPORT

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Received By : Dr. BIPASHA MUKHERJEE

Primary Specimen : OTHERS (SPECIFY)

FINAL REPORT

TEST : CULTURE FOR FUNGUS

Methodology: Culture

Parameter Name

FUNGUS

Parameter Result

: The isolated fungus is identified as Saksenaea erythrospora.

Name of the clinical specimen: Orbital biopsy(OD)

Work-up@KKCTH

- The child was referred to us for medical management.
- Worked up for Immune-deficiency.

Risk factors

- Diabetes mellitus, particularly with ketoacidosis
- Glucocorticoids
- Hematologic malignancies (Prolonged (> 3 wk) and severe (ANC < 200) neutropenia, Monocytopenia (< 100 mm³)
- HSCT, Solid organ transplantation
- Iron overload, Treatment with deferoxamine
- HIV
- Injection drug use
- Trauma/burns
- Malnutrition

- *Mucormycosis (zygomycosis): Uptodate Feburary 2018*

Work-up

- HIV- Negative
- Hb: 8.2, TC- 37,200 (ANC- 6734), PLT- 7.8L
- Immunoglobulin levels - Normal
- NBT assay- Normal reduction of the dye
- Flow cytometry: Normal
- RBS and HbA1C: Normal

Mucor in an Immunocompetent child.....



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Isolated Renal Mucormycosis in Immunocompetent Children: A Report of Two Cases

[Sai Saran](#), [Kirti Naranje](#),¹ [Mohan Gurjar](#), [Dharmendra Bhadauria](#),² [Anupama Kaul](#),² and [Banani Poddar](#)

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Brief Communication

Esophageal mucormycosis in an immunocompetent child: A rare presentation

[Jenna Biah Bhattacharya](#)^a  , [Seema Kaushal](#)^a, [Satish Kumar Aggarwal](#)^b

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<https://doi.org/10.1016/j.bj.2015.11.001>

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Mucormycosis in immunocompetent patients: a case-series of patients with maxillary sinus involvement and a critical review of the literature

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Geographic distribution and clinical forms of mucormycosis in 212 immunocompetent/ otherwise healthy individuals described over the last 30 years

Comparison between India and all other countries in the world (Fisher's exact test, $p < 0.05$).

	Number of Patients (%)		
Country	India	94 (44.3)	
	USA	42 (19.8)	
	Australia	12 (5.7)	
	Italy	6 (2.8)	
	Brazil, Pakistan	5 (2.4)	
	Venezuela	4 (1.9)	
	Canada, China, France, Germany, UK	3 (1.4)	
	Arabia, Holland, Japan, Qatar, South Korea, Spain	2 (0.9)	
	Argentina, Belgium, Colombia, Denmark, Ecuador, Finland, Greece, Iraq, Ireland, Israel, Kuwait, Oman, Sri-Lanka, South Africa, Swiss, Taiwan, Turkey	1 (0.5)	
	Forms	Cutaneous/subcutaneous	90 (42.5)
		Rhino-orbito-cerebral	81 (38.2)
		Genitourinary	18 (8.5)
		Disseminated	10 (4.7)
		Pulmonary	7 (3.3)
		Gastrointestinal	5 (2.4)
	Years	Vascular	1 (0.5)
		2006–09	61 (28.7)
2001–05		72 (33.9)	
1996–00		25 (11.7)	
1991–95		21 (9.9)	
1986–90		18 (8.5)	
1981–85		7 (3.3)	
1978–80		8 (3.7)	

Country	OR	CI 95%	p-value
USA	3.22	2.09–4.97	< 0.0001
Australia	13.3	6.98–25.25	< 0.0001
Italy	27.35	11.62–64.37	< 0.0001
Brazil, Pakistan	32.98	13.04–83.4	< 0.0001
Venezuela	41.42	14.85–115.6	< 0.0001
Canada, China, France, Germany, UK	55.5	17.16–179.1	< 0.0001
Arabia, Holland, Japan, Qatar, South Korea, Spain	83.64	20.24–345.7	< 0.0001
Argentina, Belgium, Colombia, Denmark, Ecuador, Finland, Greece, Iraq, Ireland, Israel, Kuwait, Oman, Sri-Lanka, South Africa, Swiss, Taiwan, Turkey	168.1	23.12–1222	< 0.0001

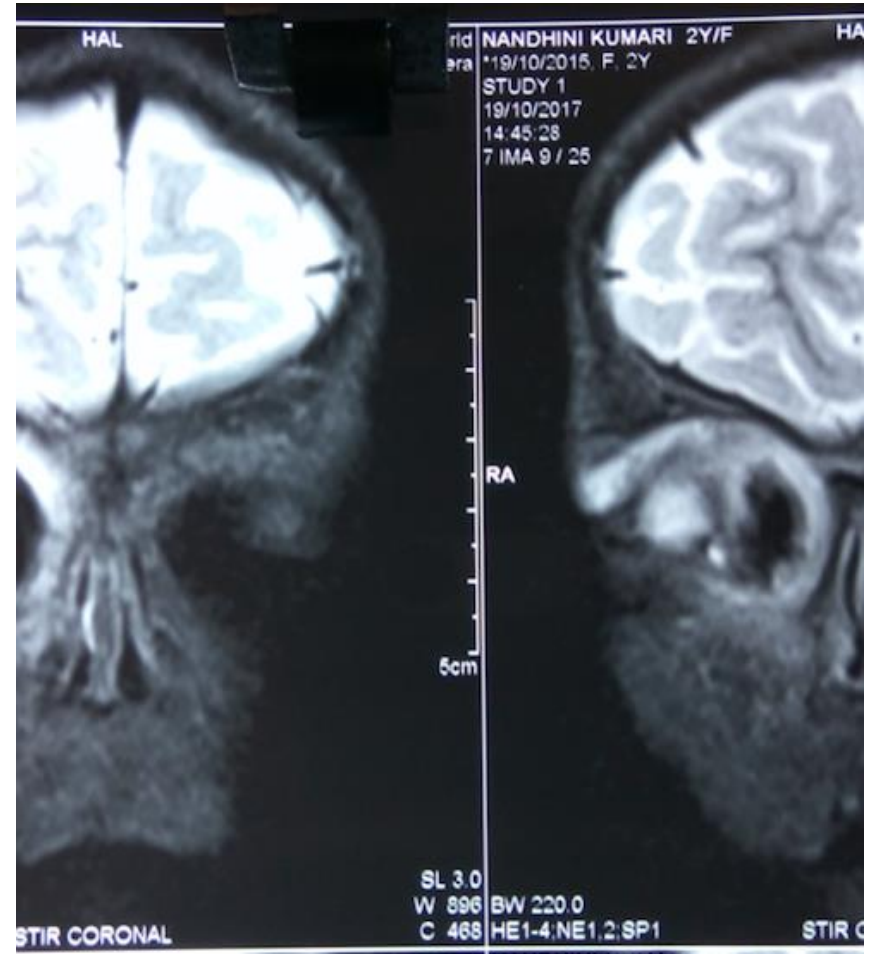
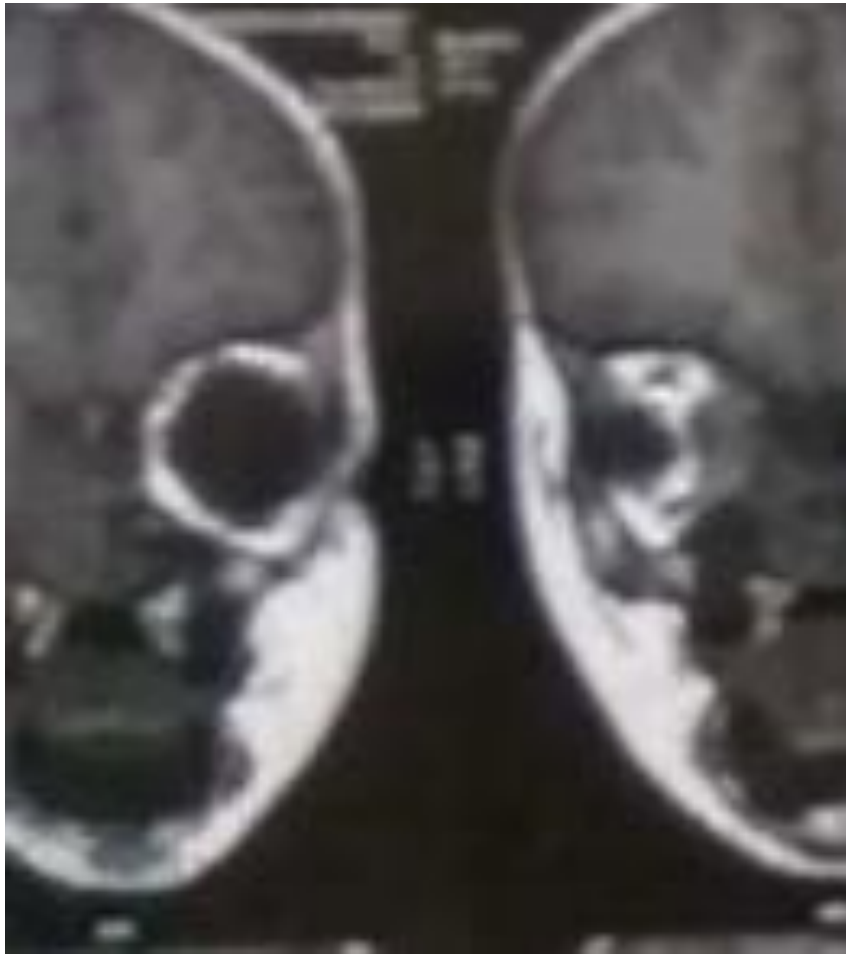
Treatment

- Child was started on conventional Amphotericin B
- It was very difficult to gauge the degree of improvement in the lesion without detailed ocular examination.
- Intermittent surgical debridement gave us a clinical clue that the lesion was receding .

Treatment- duration

- After 4 to 5 weeks of treatment with IV Amphotericin B, child was improving clinically and also had radiological reduction of the mass.
- Hence stepped down to Oral Posaconazole as an add on

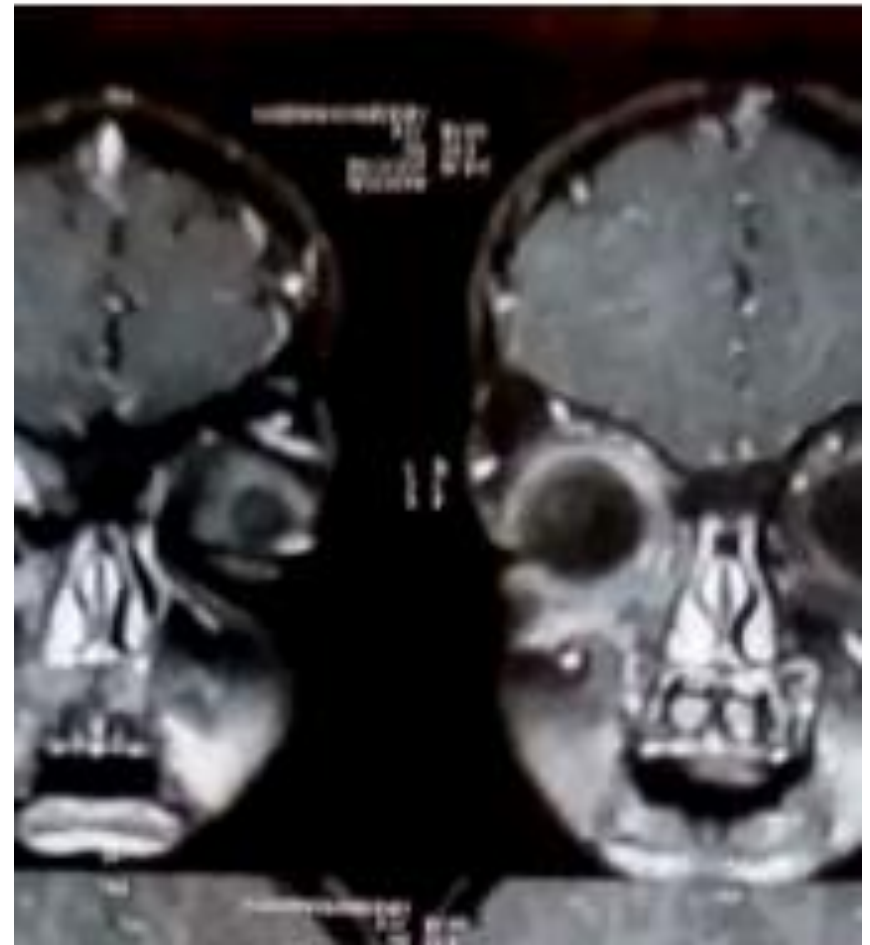
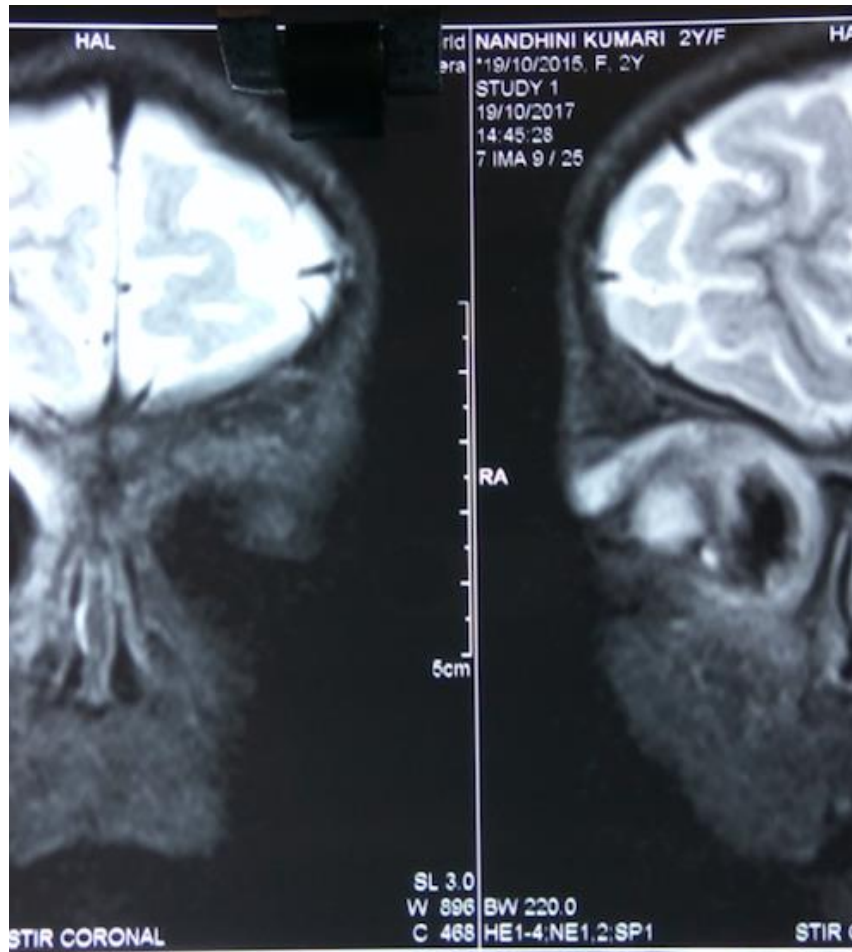
1st and 2nd MRI (1.5 months interval)



Treatment- duration

- Posaconazole was given for a total duration of 16 weeks.
- After 6 weeks of oral Posaconazole, a repeat MRI showed further reduction of the mass and healing by fibrosis.

2nd and 3 MRI (2 months interval)



Zygomycosis

- Mucormycosis (Zygomycosis) is manifested by a variety of different syndromes in humans, particularly in immuno-compromised patients and those with diabetes mellitus
- *Mucormycosis (zygomycosis): Uptodate February 2018*

Clinical presentation

- Rhino-cerebral-ocular
- Pulmonary
- GI
- Isolated CNS disease
- Cutaneous
- Renal
- Disseminated

- *Mucormycosis (zygomycosis): Uptodate Feburary 2018*

Rhino-cerebral-ocular

- The most common is rhino-orbital-cerebral infection, which is presumed to start with inhalation of spores into the para-nasal sinuses of a susceptible host.
- The infection usually presents as acute sinusitis with fever, nasal congestion, purulent nasal discharge, headache, and sinus pain.
- *Mucormycosis (zygomycosis): Uptodate February 2018*

Rhino-cerebral-ocular

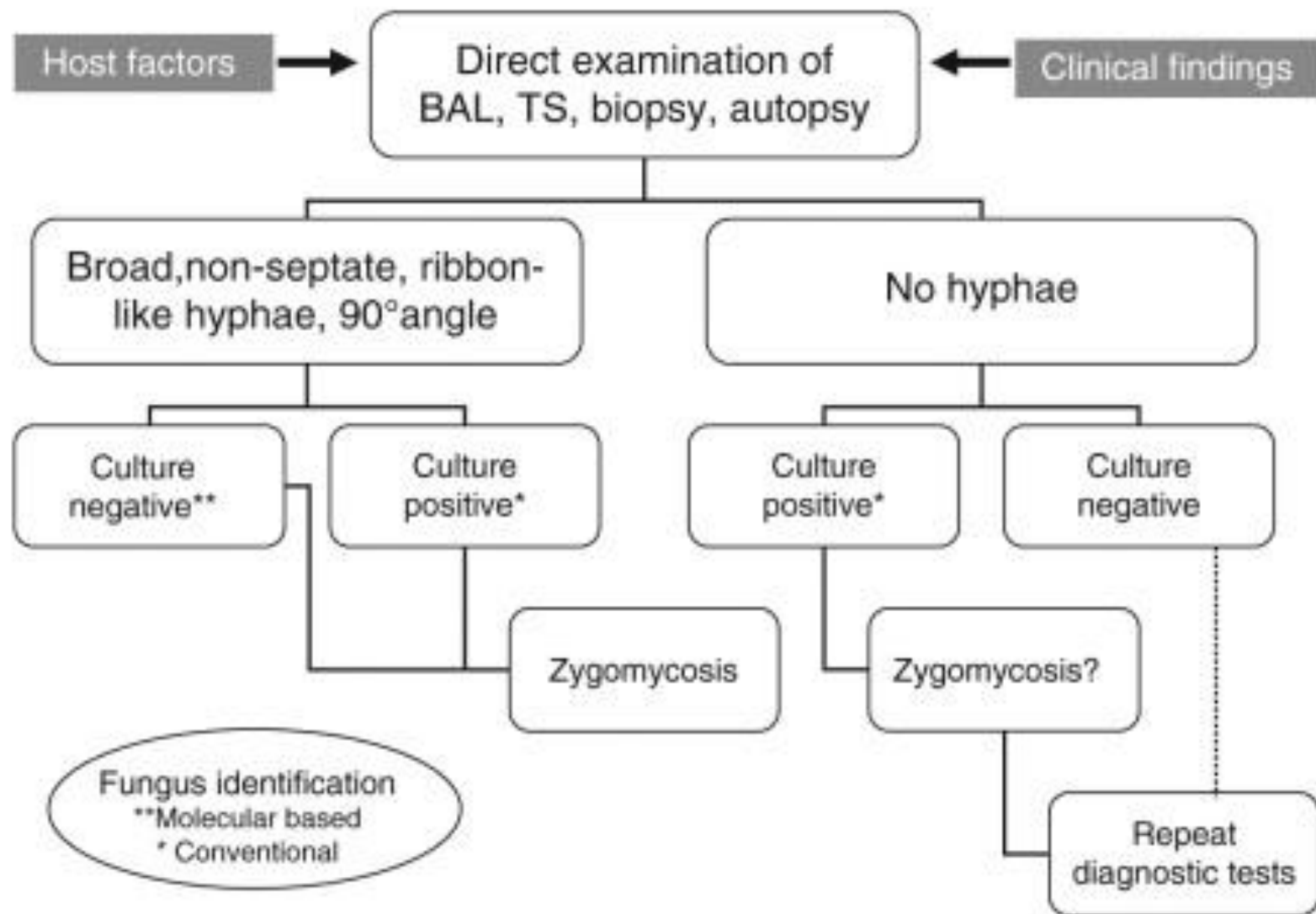
- All of the sinuses become involved, and spread to contiguous structures, such as the palate, orbit, and brain usually progresses rapidly.

- *Mucormycosis (zygomycosis): Uptodate February 2018*

Symptoms

- Fever
- Nasal ulceration or necrosis
- Periorbital or facial swelling
- Decreased vision
- Ophthalmoplegia
- Sinusitis
- Headache

Diagnosis of zygomycosis



Approach to treatment

Treatment of Mucormycosis involves a combination of :

- Surgical debridement of involved tissues.
- Early initiation of appropriate antifungal therapy.
- Elimination of predisposing factors
- *Mucormycosis (zygomycosis): Uptodate February 2018*

Antifungal treatment

- Polyene group– Amphotericin B
- Azole group- Posaconazole, Isavuconazole
- Echinocandins (alternative therapies)-
Caspofungin, Micafungin (Variable activity in vitro)
- *Mucormycosis (zygomycosis): Uptodate February 2018*

Posaconazole

- Posaconazole is a second-generation triazole.
- It is closely related to itraconazole, is fungicidal in vitro against *Aspergillus*, and has activity against mucormycosis, which is an advantage over Voriconazole .
- Posaconazole has been best studied as antifungal prophylaxis, including a large randomized controlled trial in patients with acute myelogenous leukemia or myelodysplastic syndrome.

Posaconazole

FDA approved in children > 12 years and adults :

- Invasive Aspergillosis, Candidiasis.
- Used as prophylaxis or salvage therapy.
- Fungal prophylaxis in HSCT recipients, AML, MDS (open label use in pediatric population)
- *Posaconazole: UptoDate 2018*

Posaconazole

- Dose: 4 to 5 mg/kg/dose q6-8 hrly (syrup/Capsule)
- Advantages of Posaconazole: It covers almost all fungal elements (*Candida spp*, Opportunistic molds, Dimorphic fungi) as a single drug which is superior than other Azoles (Fluconazole, Voriconazole, Itraconazole)
- Studies have demonstrated its superiority for salvage therapy for invasive mold infection
- *Sarah Long: Pediatric Infectious Diseases 5th edition*

Toxicities and Tests

- Periodic Liver function test monitoring is essential (once every 2 to 3 weeks).
- Literature mentions testing of drug levels to maintain the therapeutic range.
- Levels of $>1\text{mcg/ml}$ are needed for therapeutic action.
- *Sarah Long: Pediatric Infectious Diseases 5th edition*

Treatment

- Initial therapy: Amphotericin B (Lipid or deoxycholate) either alone or in combination with Posaconazole.
- Switch/step-down: Once patient improves can stop IV Amphotericin B (minimum 3 to 4 weeks IV) and continue with Posaconazole (oral)
- *Mucormycosis (zygomycosis): Uptodate Feburary 2018*

End-point

- Clinical resolution , and radiographic (MRI) evidence that the lesion has come down and not spreading.
- Usually takes several weeks (6-8 weeks).
- For immuno-compromised patients , restoration of immunity along with other parameters before stopping antifungal therapy.

Clinical dilemmas?

Invasive fungal infection with no compromised immunity??

End point of treatment is not definitive.



TAKE HOME MESSAGE

- (1) Rapid initiation of effective antifungal therapy and concomitant aggressive attempts for diagnosis.
- (1) Extensive “early” surgical debridement of necrotic lesions
- (2) Rapid control of underlying medical condition, when feasible.

Gratitude and thanks to

- Shankar Nethralaya
- Parents and relatives
- ID team@KKCTH