A curious case of Milliary Mottling

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History

- A 43 years old gentleman, doing a desk job, living in Bharuch, had presented in November 2023 with the history of

- Fever, high grade, intermittent, with chills since 1 month
- Altered sensorium since 2 weeks

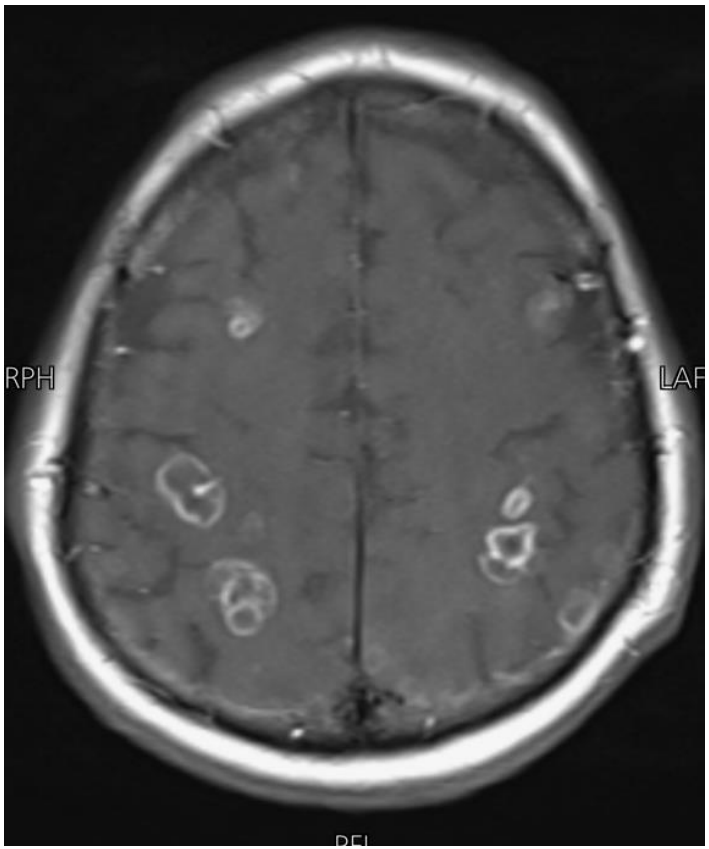
- No localizing symptoms pertaining to any other organ system

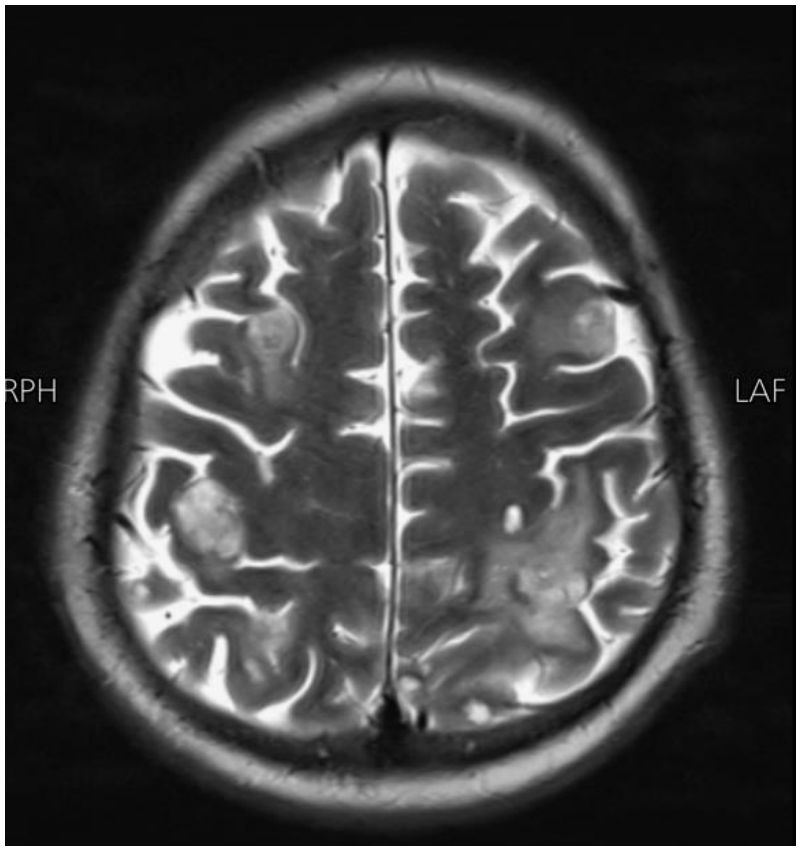
History

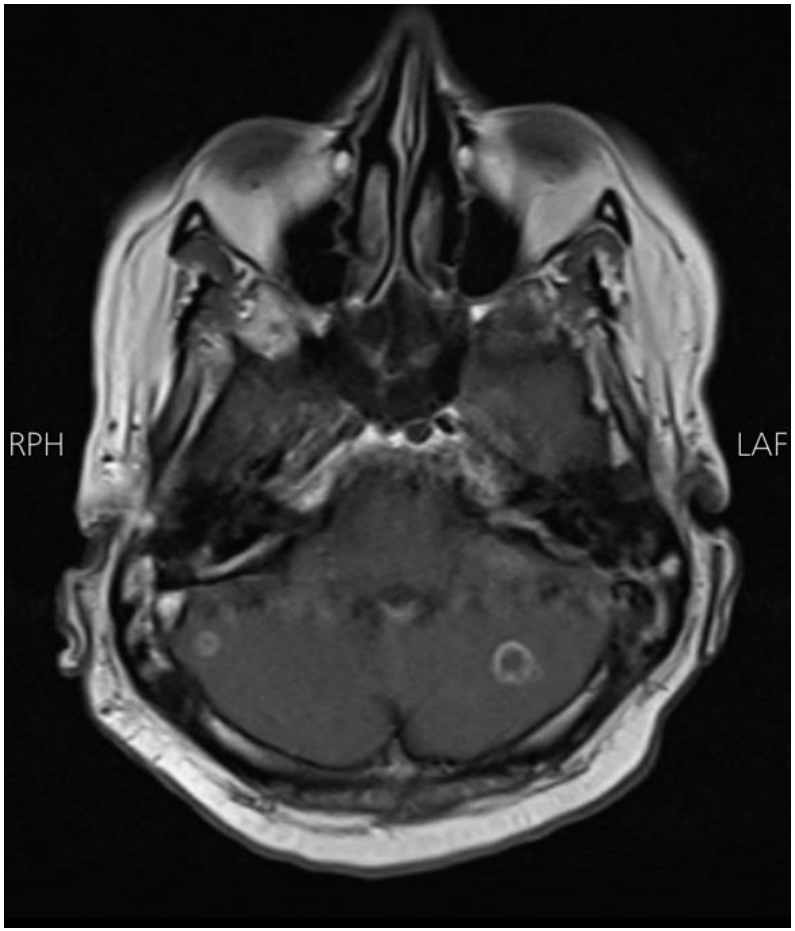
- The patient had developed bullous lesions over the skin 2 years back, for which he was evaluated and was diagnosed to have Bullous Pemphigoid.
- He was started on oral corticosteroids with Azathioprine and was continued on the same with dose escalation/tappering in between due to relapses.
- 6 months before the current presentation, he was evaluated for the prolonged dry cough lasting for more than a month and was found to have diffused milliary nodules in both the lungs.
- However, the broncoscopy and BAL didn’t reveal any etiology and hence, the patient was not started on any therapy for the same.

Previous hospital course

- Initially, the patient was evaluated elsewhere, and was found to have multiple ring enhancing lesions in both the cerebral hemisphere and left cerebellum with perilesional edema.



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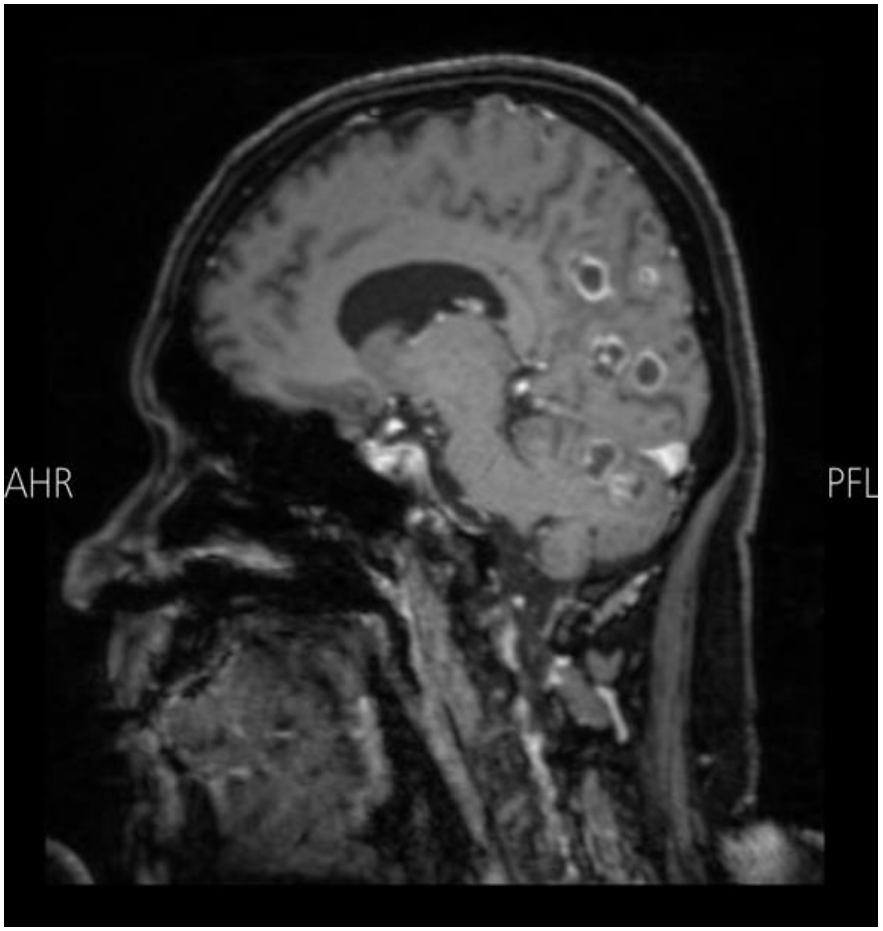
AHR
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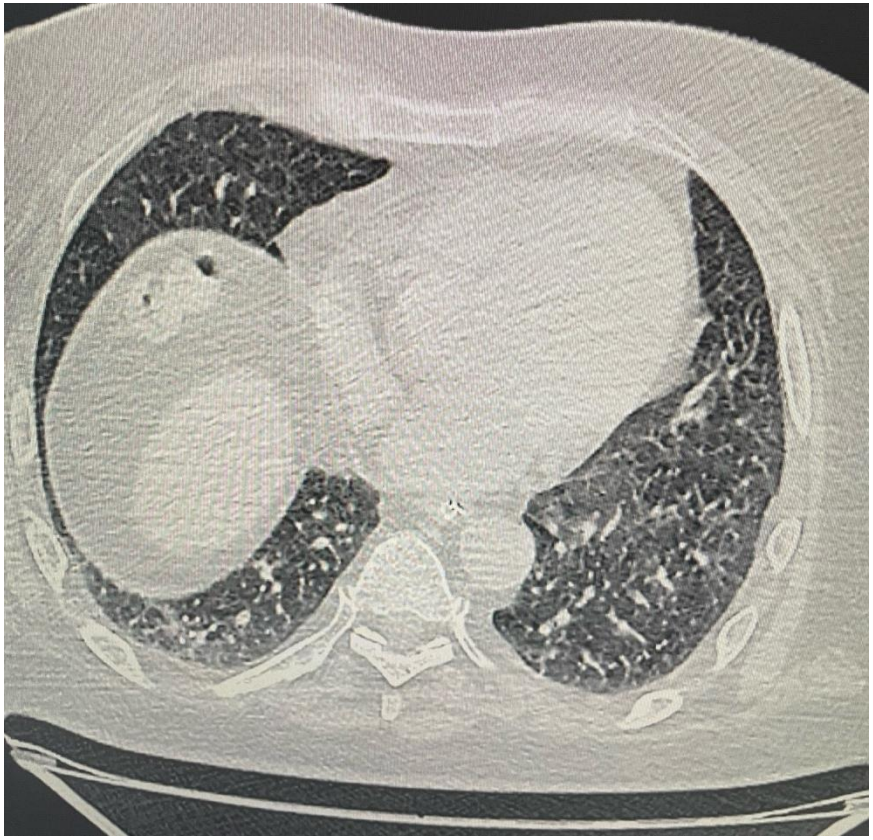
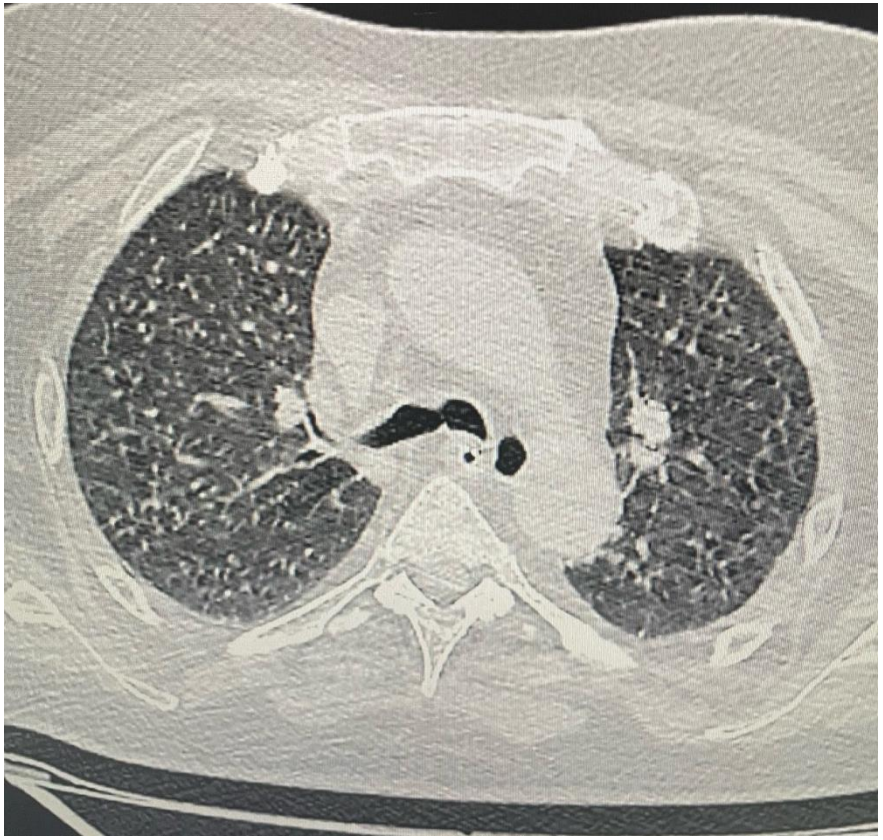
- The patient was started on empirical ATT and Dexamethasone after CSF examination and was later transferred to our centre due to persistent symptoms.

Examination

- At the time of admission
- Conscious, irritable
- Febrile
- P: 100/m
- BP: 130/70 mmhg
- No central venous access
- Rest of the general and systemic examination was unremarkable
- Baseline CBC, RFT, LFT, Urine routine :WNL

- In view of prior history of Miliary pulmonary nodules, CECT thorax was done, which showed persistent miliary nodules.





Syndrome

- A middle aged gentleman on long term immuno suppresents, presented with prolonged fever, multiple ring enhancing lesions in the cerebral and cerebellar hemispheres and bilateral pulmonary nodules with miliary pattern.

Differential diagnosis

- Disseminated Tuberculosis
- Disseminated Cryptococcal infection
- Nocardiosis
- Endovascular infections with secondary dissemination (Doesn’t produce miliary nodules however)
- Rare possibilities such as Brucellosis, Melioidosis

CSF Examination

	Day 2
WBC counts (PMN/Lymphocytes)	360 (82/18)
Protein	96 mg/dl
Sugar	11 mg/dl
Stains (Gram stain/AN/Modified ZN)	Negative
Gene xpert MTB RIF	MTB Not detected
Culture	No growth

- Blood culture : No growth

Broncoscopy, TBLB and BAL

- Gene xpert MTB RIF: MTB not detected
- Gram stain: many pus cells, no organisms
- KOH: negative
- Culture: Klebsiella Pneumoniae, ESBL
- Fungal culture: no growth
- Biofire respiratory panel: CMV
- HPE: Acute on chronic inflammation, no granuloma.

Hospital course

- Continued ATT and Dexamethasone
- Started on Meropenem by the primary team for growth of ESBL in BAL culture.
- Showed clinical improvement.
- Fever was persistent but reduce in intensity and frequency.

CSF

	Day 2	Day 10
WBC counts (PMN/Lymphocytes)	360 (82/18)	207 (44/56)
Protein	96 mg/dl	82 mg/dl
Sugar	11 mg/dl	30
Stains (Gram stain/AN/Modified ZN)	Negative	
Gene xpert MTB RIF	MTB Not detected	Neg
Culture	No growth	No growth

- CSF and Serum cryptococcal Antigen, Toxoplasma IgG : Negative
- CSF biofire meningitis/encephalitis panel: CMV detected
- Further evaluation was deferred and the patient was discharged after 10 days of hospitalization with ATT and oral dexamethasone.

Readmission

- On day 3 post discharge, the patient presented after an episode of generalized seizures and altered sensorium.
- Repeat CT brain: Increased peri-lesional edema involving all the lesions with obstructive hydrocephalus.

- Possible causes?
  - Paradoxical worsening of Tuberculosis (Dexamethasone was changed to oral formulation on discharge)
  - Insufficient Drug levels
  - An undiagnosed and untreated infection other than TB

- Dexamethasone IV was started along with other anti edema measures.
- Pick serum levels for INH and Rifampicin were low, the doses were adjusted accordingly.
- However, the sensorium kept worsening over the next 48 hours.

Surgical intervention

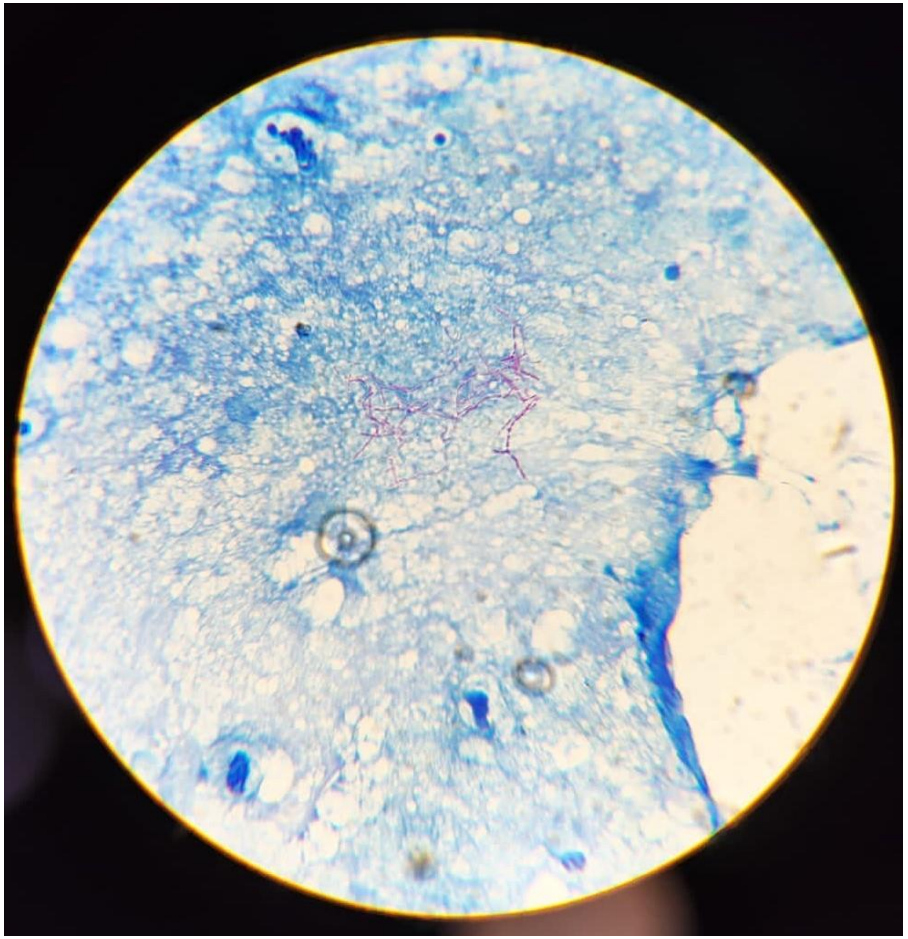
- Finally, the patient underwent Extra ventricular drain insertion along with drainage and biopsy from the superficially located lesion.
- Intra operative tissue and pus:
  - Gene xpert MTB RIF : Negative
  - AFB and Gram stain : negative
  - Culture at 24 hours : no growth
  - Preliminary HPE: Abscess formation with no evidence of Granuloma

CSF

	Day 2	Day 10	CSF from EVD
WBC counts (PMN/Lymphocytes)	360 (82/18)	207 (44/56)	16 (60/40)
Protein	96 mg/dl	82 mg/dl	9 mg/dl
Sugar	11 mg/dl	30	95 mg/dl
Stains (Gram stain/AN/Modified ZN)	Negative		
Gene xpert MTB RIF	MTB Not detected	Neg	Neg
Culture	No growth	No growth	

Breakthrough

- While discussing the case with the microbiologist, requested a modified ZN stain, despite of gram stain being negative.
- Showed, thin filamentous structures, suggestive of Nocardia spp.



Treatment

- Started High dose Meropenem and Cotrimoxazole
- Amikacin was continued
- ATT was discontinued.
- Dexamethasone: tappered.

TEST	RESULTS
Identification By MALDI TOF (Mass Spectrometry)	
Specimen	Growth plate
Identification By Maldi TOF (Mass Spectrometry)	Nocardia cyriacigeorgica
Note	Score: 1.90

Non-Tuberculosis Mycobacteria (NTM/MOTT) or Aerobic Actinomycetes Drug Ser	
Specimen	Pure growth of Nocardia received in Blood agar plate
Organism	Nocardia cyriacigeorgica
Linezolid (1 - 32)	S (1)
Trimethoprim / Sulphamethaxole (0.25/4.75 - 8/152)	S (2/38)
Ciprofloxacin (0.12 - 4)	R (4)
Imipenem (2 - 64)	S (2)
Moxifloxacin (0.25 - 8)	I (2)
Cefepime (1 - 32)	S (8)
Cefoxitin (4 -128)	R (128)
Augmentin (2/1 - 64/32)	I (16/8)
Amikacin (1 - 64)	S (1)
Ceftriaxone (4 - 64)	S (8)
Doxycycline (0.12 - 16)	S (1)
Minocycline (1 - 8)	S (1)
Tigecycline (0.015 - 4)	S (0.12)
Tobramycin (1 - 16)	S (1)
Clarithromycin (0.06 - 16)	R (16)

- Final diagnosis:

  Disseminated Nocardia Cyriacigeorgica infection (Pulmonary and CNS) in a patient on prolonged systemic corticosteroids.

Further course

- The patient was later transferred to another centre due to the financial constrains, where after a week of treatment, unfortunately, the patient had succumbed to probable sepsis and multi organ failure.

Discussion

- Nocardia is an aerobic actinomycete, known to cause opportunistic infections in immunocompromised individuals, especially in those on prolonged corticosteroid therapy.
- Classical sites of infection : Lungs, Skin and CNS.
- N. Cyriacigeorgica is thought to be a rare occurrence in the Indian subcontinent, and has a favorable antimicrobial susceptibility profile.
- Milliary lung nodules is a very rare presentation for nocardiosis and has been described in a few case reports.
- It is very important to go for tissue diagnosis as the early identification and treatment can prevent the undue mortality and morbidity.

Acknowledgements

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THANK YOU