From Air to Mind

DR. CHETAN PHADKE, NEPHROLOGY RESIDENT

DR. D.Y. PATIL MEDICAL COLLEGE , HOSPITAL & RESEARCH CENTRE , PIMPRI

- 34 year/ male
- Married
- Shopkeeper
- Resident of Pune

Pretransplant medical history

- CKD: 2020 May
- Hypertensive urgency, creatinine at diagnosis 3mg/dl
- ? Primary glomerulonephritis, bilateral small kidneys
- HD: October 2021
- Access: L RC AVF
- Diagnosed with hepatitis C infection in 2023, treated with sofosbuvir-velpatasvir for 3 months and achieved sustained virologic response (SVR) at 12 weeks

Transplant medical history

- Cadaveric transplant: 19 September 2023
- Induction – ATG (total dose of 150 mg)
- Maintenance immunosuppression- Tacrolimus, MMF-S, steroids
- Cold ischaemia: 8 hours 40 minutes

- Delayed graft function , one dialysis session
- Discharged on tenth post-operative day with creatinine 3.2 mg/dl
- Baseline creatinine at 1 month – 1.7 mg/dl
- DJ stent removed at 6 weeks

Post-transplant Course

- Single episode of urinary tract infection
- Improved antibiotic therapy per culture report (?)
- Uneventful monthly follow-ups

5 months post-transplantation

- Fever, cough with sputum: 3 days
- No breathlessness
- No chest pain
- No headache or other complaints

On Examination

- Pulse – 90/min,
- BP – 130/80 mm Hg,
- sPo2 – 98% on room air,
- Respiratory rate – 16 / min , Afebrile

Systemically,

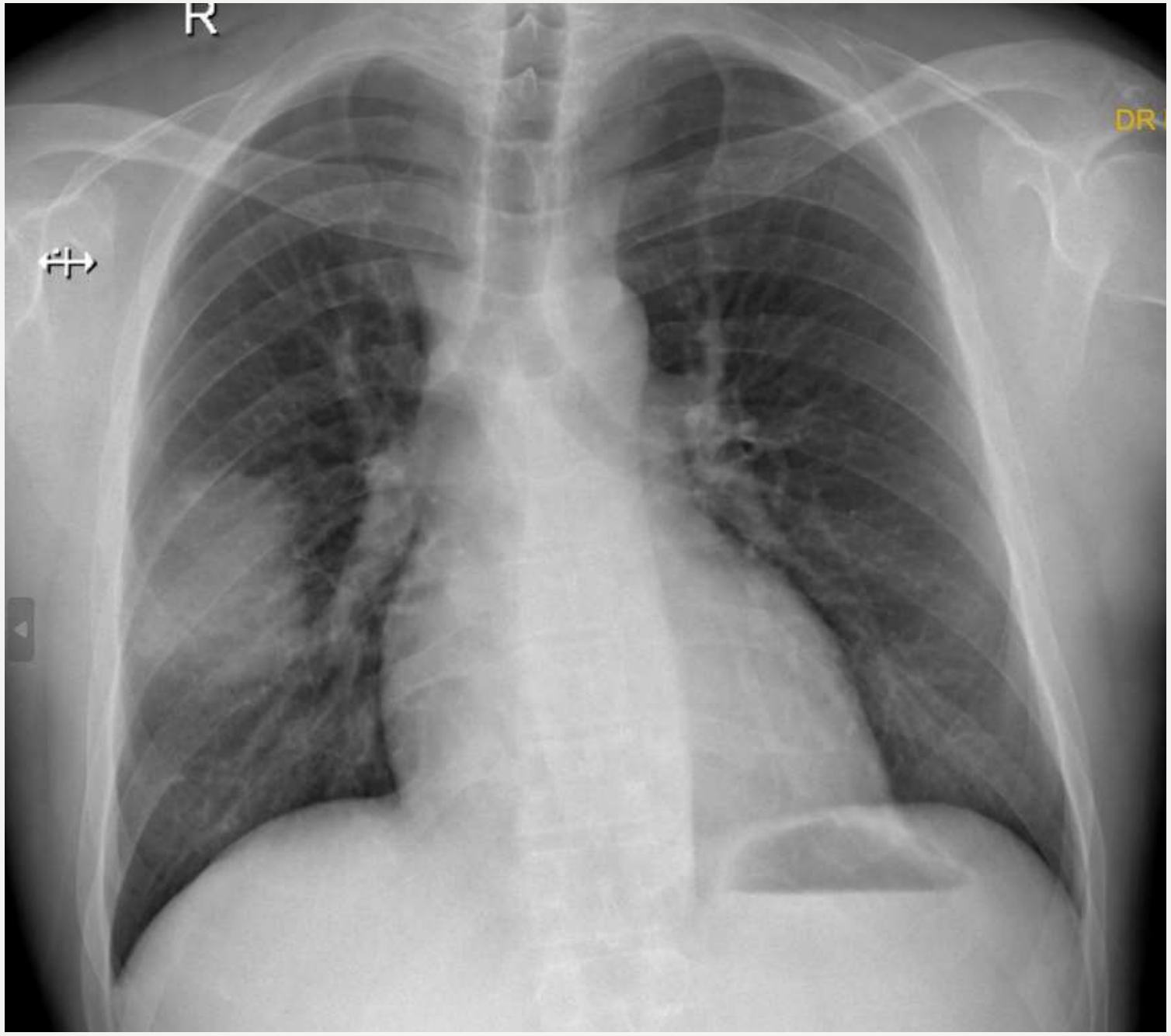
- RS- Bilateral equal air entry , fine crepts in right infraaxillary area
- CVS- S1/S2 audible
- PA –Soft , No organomegaly
- CNS – conscious , alert , oriented, no focal neurological deficit , no neck rigidity

Chest Xray

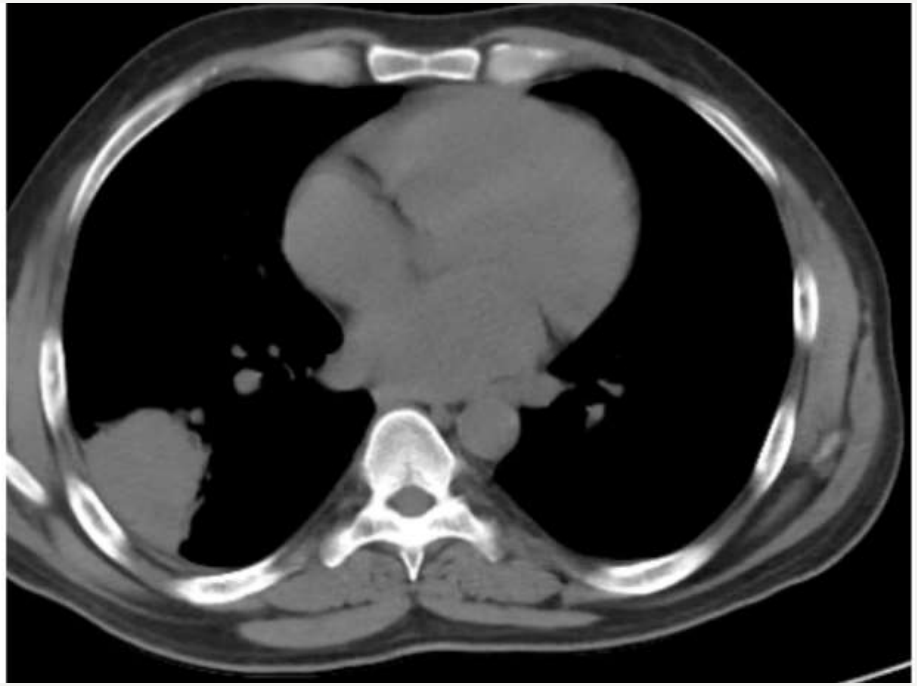
Well-demarcated round consolidation in right midzone

Bilateral costophrenic angles are clear

Cardiac size normal



HRCT Chest



Focal consolation in subpleural right lower lobe with peripheral groundglass halo
No air bronchogram, no calcification , no cavity
No extrapleral fat invasion/ rib erosion

Laboratory parameters

Hb – 9 gm/dl
TLC -12400 /ul
Platelets – 2.6 lacs/ ul
Urea 47 mg/dl
Creatinine 2.5 mg/dl
Sodium 132 mmol/L
Potassium 5 mol/L

Urine
Protein – Absent
RBC – Absent
Pus cell – 1 to 2 /HPF
UPCR – 0.7 gm/gm
Culture – No growth

Tacrolimus - 10 ng/ml
pH – 7.33
Bicarbonate – 18 mEq/L

Procalcitonin - < 0.05
CRP – 55 mg /L
ESR – 58 mm/hr
Serum galactomannan - Negtaive

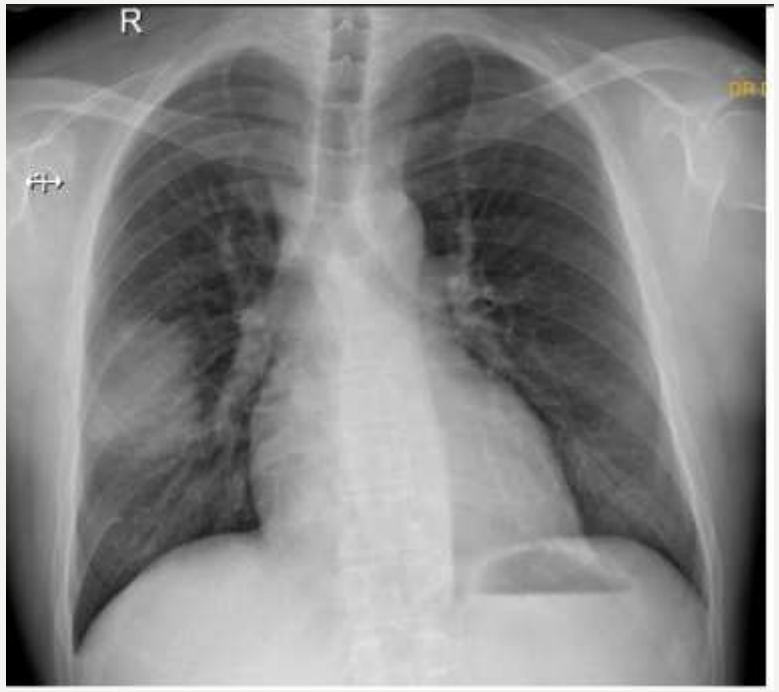
Provisional diagnosis and treatment

Post transplant pneumonia

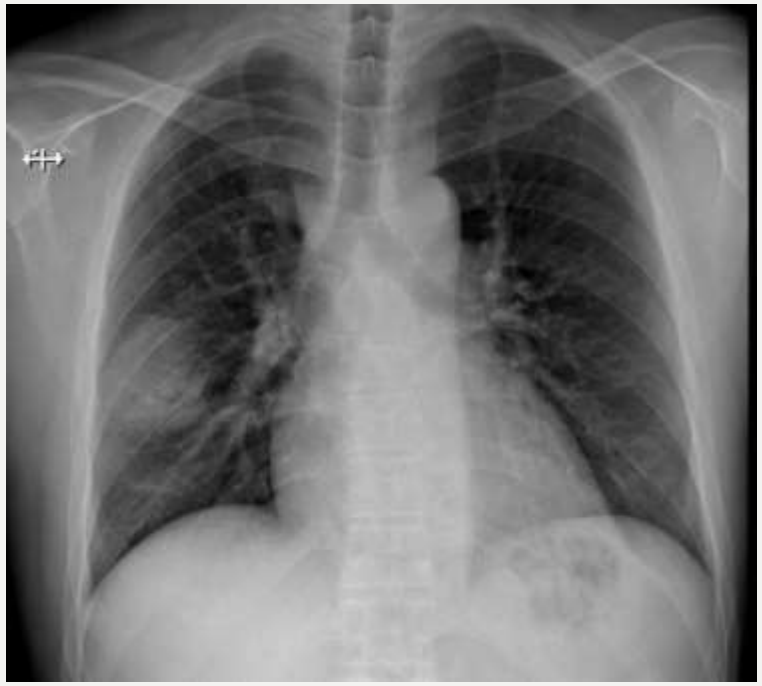
Empirical therapy – IV Meropenem x 6 days converted to oral Minocycline

Oral Cotrimoxazole SS (400/80) alternate day

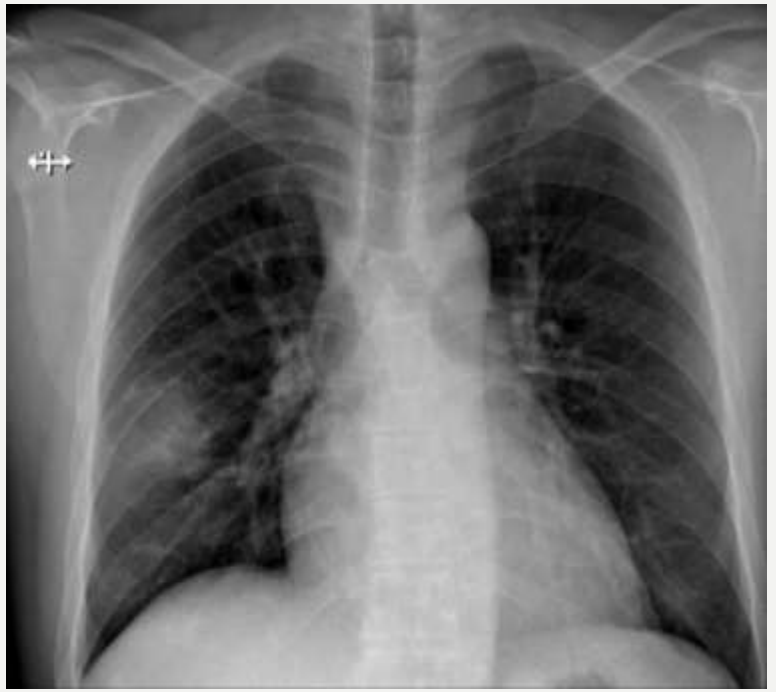
Serial Chest Xray



Day 1

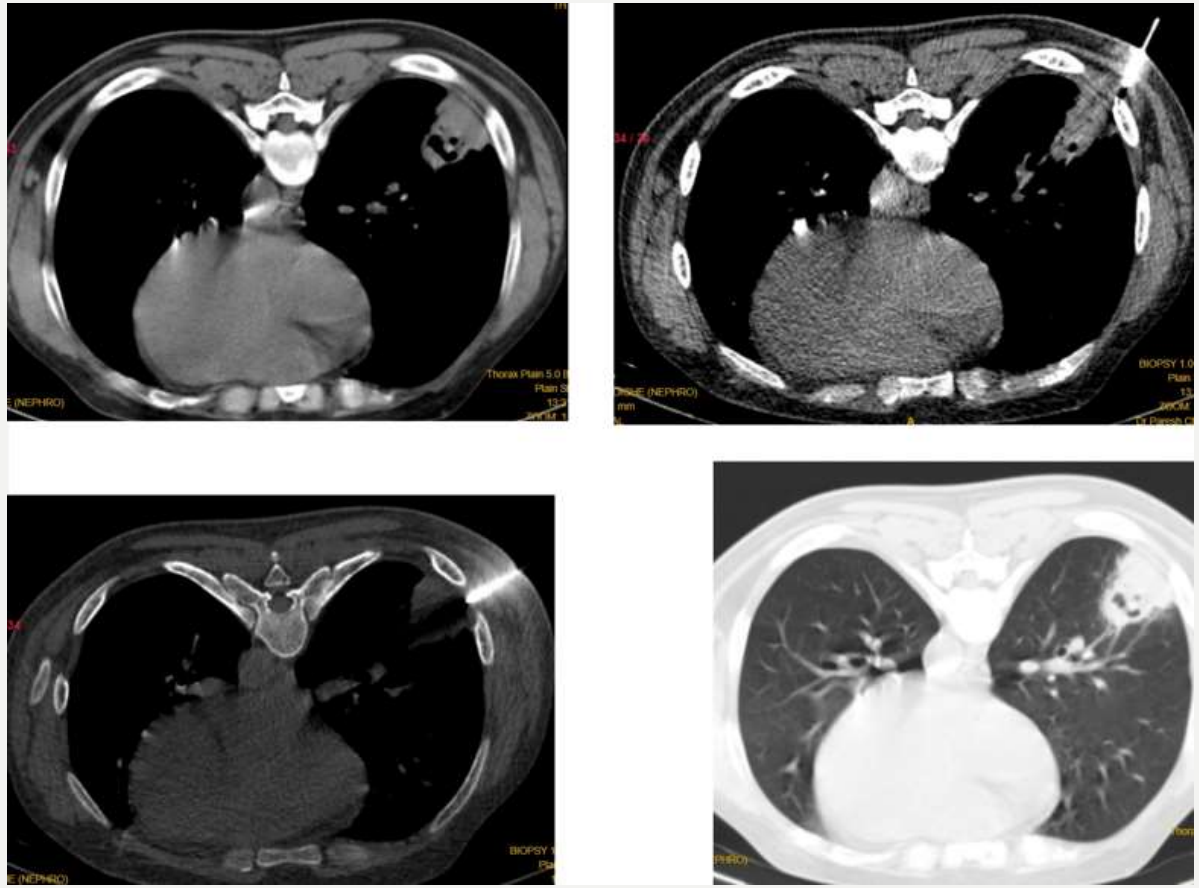


Day 3



Day 8

CT guided biopsy – Day 3



Only liquid aspirate

No solid core

Gram stain– no organism

ZN stain – No organism

Modified ZN – No organism

No bacterial growth in culture

- Patient was discharged
- Afebrile, no breathlessness
- Creatinine: 2.2 mg/ dL
- End of story??

Backache and Neck pain: 1 week later

Duration: 1 week

Afebrile, good urine output

No other complaints

O/E: Swelling on back, lower neck region

X ray chest: Resolving pneumonitic patch

Laboratory investigations:

Hb: 9 gm/dL
TLC: 3510
Platelet: 2.96 lakh/ cumm

Urea: 46
Creatinine: 2.96
Na: 140
K: 4.14
Urine R: Unremarkable
Urine C: Sterile

Cotrimoxazole stopped inview of hyperkalemia

USG of Local Swelling: Intramuscular lipoma

MRI Posterior Chest wall: Intramuscular abscess in left trapezius and adjoining muscle edema.

- Presumptive diagnosis: ?Cold abscess ?tubercular ?nontubercular mycobacteria
- Pulmonology: BAL
- Sputum, BAL Culture: Negative

- Pus Routine Microscopy:
- ADA: 537
- Proteins: 2.7
- WBC: Plenty
- CBNAAT: Negative

- Pus Culture: Nocardia farcinicia

- Sensitivity: Amikacin (S), Cotrimoxazole (S), Linezolid (S), Moxifloxacin (IS),

- GTCS, 30 seconds

MRI Brain: Multi focal areas in Right parietal and left FPO subcortical region, left centrum semiovale, right cerebellar region.

?embolic abscess ?Opportunistic infection

Linezolid 600mg q12h

Moxiflox 600mg q24h

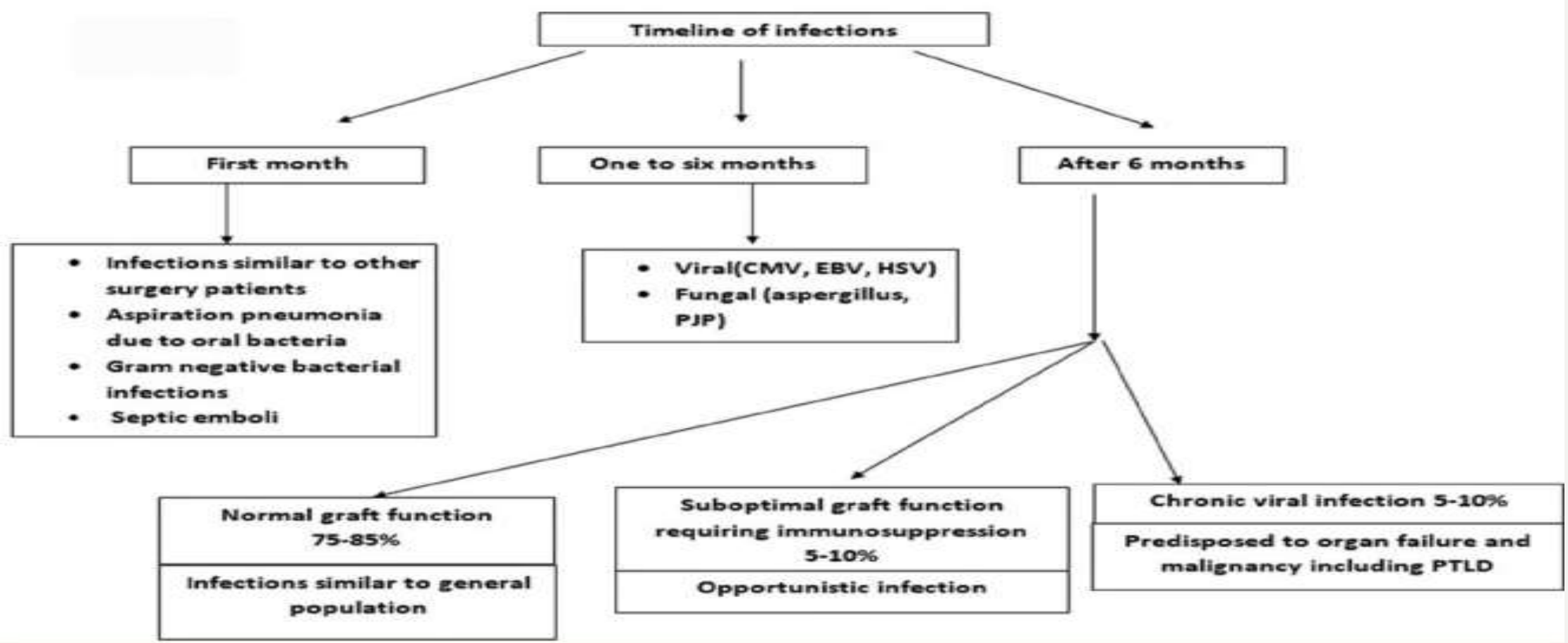
Patient discharged

Afebrile, no seizures

Urea 74 mg/dL

Creatinine 3.3 mg/dL

Discussion - Clues from timing of infection



Ahmad Z, Bagchi S, Naranje P, Agarwal SK, Das CJ. Imaging spectrum of pulmonary infections in in renal transplant patients. Indian J Radiol Imaging. 2020 Jul-Sep;30(3):273-279.

Clues from travel , occupation and specific risk factors

- Travel– Endemic fungi (eg, H. capsulatum, Coccidioides spp),
- Soil (Aspergillus spp, Nocardia spp in landscapers and gardeners)
- Occupation - Cryptococcus neoformans (eg, pigeon breeders)
- Frequent antimicrobial exposure
- Potential or witnessed aspiration (risk for anaerobic infection)
- Cardiac abnormalities (endocarditis), indwelling catheters, or intravascular clot (bacteremic seeding of the lungs)

- Nocardiosis: Rare, opportunistic, filamentous gram-positive Nocardia bacteria [1].

- Most common route: Inhalation, ingestion and direct inoculation through the skin [2].

- SOTR: Reported incidence is 0.7% to 3.5%.
- N nova, N farcinica, and N cyriacigeorgica
- Kidney transplants have the lowest Nocardia infection rate compared to patients with other solid organ transplants [3].

1. Brown-Elliott B.A., Brown J.M., Conville P.S., Wallace R.J., Jr. Clinical and laboratory features of the Nocardia spp. based on current molecular taxonomy. Clin Microbiol Rev. 2006;19(2):259–282. doi: 10.1128/cmr.19.2.259-282.2006.
2. Beaman B.L., Beaman L. Nocardia species: host-parasite relationships. Clin Microbiol Rev. 1994;7(2):213–264. doi: 10.1128/cmr.7.2.213.
3. Shrestha S., Kanellis J., Korman T., et al. Different faces of Nocardia infection in renal transplant recipients. Nephrology (Carlton) 2016;21(3):254–260. doi: 10.1111/nep.12585.

- Disseminated nocardiosis: infection involving 2 or more organ systems.
- Most frequently involved: lung, brain, skin, subcutaneous tissue [4].

- Studies suggest 88% of KTR: pulmonary involvement, high rate of disseminated disease [5].

- Early and accurate diagnosis is important
- Symptoms: overlap with other disease entities, such as malignancy or other atypical infections.
- Better prognosis is associated with earlier diagnosis and proper duration of antibiotic therapy.

4. Lederman E.R., Crum N.F. A case series and focused review of nocardiosis: clinical and microbiologic aspects. Medicine (Baltimore) 2004;83(5):300–313. doi: 10.1097/01.md.0000141100.30871.39.
5. Wilson J.P., Turner H.R., Kirchner K.A., Chapman S.W. Nocardial infections in renal transplant recipients. Medicine (Baltimore) 1989;68(1):38–57. doi: 10.1097/00005792-198901000-00003

- Mean onset of infection post transplant: 34.41 months [6].

- Associated risk factors [7]:
- 1) high calcineurin inhibitor trough levels in the month before diagnosis,
- 2) use of tacrolimus and corticosteroids at the time of diagnosis,
- 3) length of stay in the intensive care unit after solid organ transplant

- Premature discontinuation of TMP-SMX of leukopenia, may increase the risk of Nocardia colonization [8].

6. Santos M., Gil-Brusola A., Morales P. Infection by Nocardia in solid organ transplantation: thirty years of experience. Transplant Proc. 2011;43(6):2141–2144. doi: 10.1016/j.transproceed.2011.06.065
7. Coussement J., Lebeaux D., van Delden C., et al. Nocardia infection in solid organ transplant recipients: a multicenter European case-control study. Clin Infect Dis. 2016;63(3):338–345. doi: 10.1093/cid/ciw241
8. El Chediak A, Triozzi JL, Schaefer H, Shawar S. Disseminated Nocardiosis in Kidney Transplant Recipients: A Report of 2 Cases. Kidney Med. 2022 Sep 30;4(12):100551. doi: 10.1016/j.xkme.2022.100551. PMID: 36471817; PMCID: PMC9719090.

- Antibiotics effective in most cases.
- Initiated for 2 to 6 weeks, targeted maintenance therapy for 6 to 12 months.
- Sulfamethoxazole-trimethoprim: activity against nocardial infections
- Achieves high tissue concentrations in the lung, brain, skin, and bone [9].

- Linezolid has potential as a second-line agent for antibiotic-resistant Nocardia species. In infections that involve the central nervous system, imipenem or amikacin are sometimes added as adjunctive antibiotic therapies[10].

- Central nervous system involvement: antibiotic therapy for a year or longer based on clinical and imaging response [11].

9. Restrepo A., Clark N.M. Infectious Diseases Community of Practice of the American Society of Transplantation. Nocardia infections in solid organ transplantation: guidelines from the Infectious Diseases Community of Practice of the American Society of Transplantation. Clin Transplant. 2019;33(9) doi: 10.1111/ctr.13509.
10. Clark N.M., Reid G.E., AST Infectious Diseases Community of Practice Nocardia infections in solid organ transplantation. Am J Transplant. 2013;13(suppl 4):83–92. doi: 10.1111/ajt.12102.
11. Ambrosioni J., Lew D., Garbino J. Nocardiosis: updated clinical review and experience at a tertiary center. Infection. 2010;38(2):89–97. doi: 10.1007/s15010-009-9193-9.

Conclusion

- TMP-SMX was not started for our patient due to creatinine never touching the normal baseline levels.
- After initiation patient could not tolerate TMP-SMX well and had to be maintained on second line drugs.
- Patient did not have breakthrough seizures.

Clues from hypoxia

- Hypoxemia with an elevation in lactic dehydrogenase or beta-1,3-glucan and minimal radiographic findings are common in Pneumocystis pneumonia (PCP)

- The absence of hypoxemia with pulmonary consolidation is more common in nocardiosis, tuberculosis, and fungal infections until later in the course.

Clues from radiology

- Multifocal lesions with a subacute to chronic progression - fungal, tuberculous, or nocardial infections.
- Large nodules particularly if they are subacute to chronic in onset - fungal or nocardial
- Cavitation - Nocardia spp, mycobacteria, certain gram-negative bacilli (most commonly Klebsiella pneumoniae and Pseudomonas aeruginosa).
- Nodules with surrounding hypoattenuation (the "halo sign") followed by cavitation (the "air-crescent sign") – Angioinvasive aspergillus

Clues from radiology

- Rapidly expanding pulmonary lesions with cavitation and/or hemorrhage - Mucorales, diabetics,
- Small Pulmonary Nodules in the lung periphery - septic or hemorrhagic Aspergillus infarcts (especially if cavitary).
- Opacities in a peribronchial (or interstitial) distribution - fluid overload, viral infection such as CMV or P. jirovecii infection .
- Dense regional or lobar consolidation - bacterial pneumonia or invasive fungal infection
- Lymphadenopathy - lymphoma or posttransplant lymphoproliferative disorder associated with Epstein-Barr virus. Lymphadenopathy may be observed with some acute viral infections (CMV), sarcoidosis, and infections due to mycobacteria and Cryptococcus spp