A Case of TNF-inhibition and disseminated TB

Allison Phillips, DNP, NP

San Francisco Department of Public Health TB Clinic

HPI

67 yoF, born in China

Medical history:

- Rheumatoid arthritis→ Leflunomide, methotrexate and adalimumab (TNF-inhibitor)
- Hx positive QFT x 2
- No past tx for LTBI or active TB
- T2DM (A1C 6.5%)
- HTN
- HLD

Tumor necrosis factor inhibitors (TNF)-alpha inhibitors

- Adalimumab
- Infliximab
- Etanercept

Others

- Certolizumab
- Golimumab

/GHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use HUMIRA safely and effectively. See full prescribing information for HUMIRA.

HUMIRA® (adalimumab) injection, for subcutaneous use
Initial U.S. Approval: 2002

WARNING: SERIOUS INFECTIONS AND MALIGNANCY

See full prescribing information for complete boxed warning.

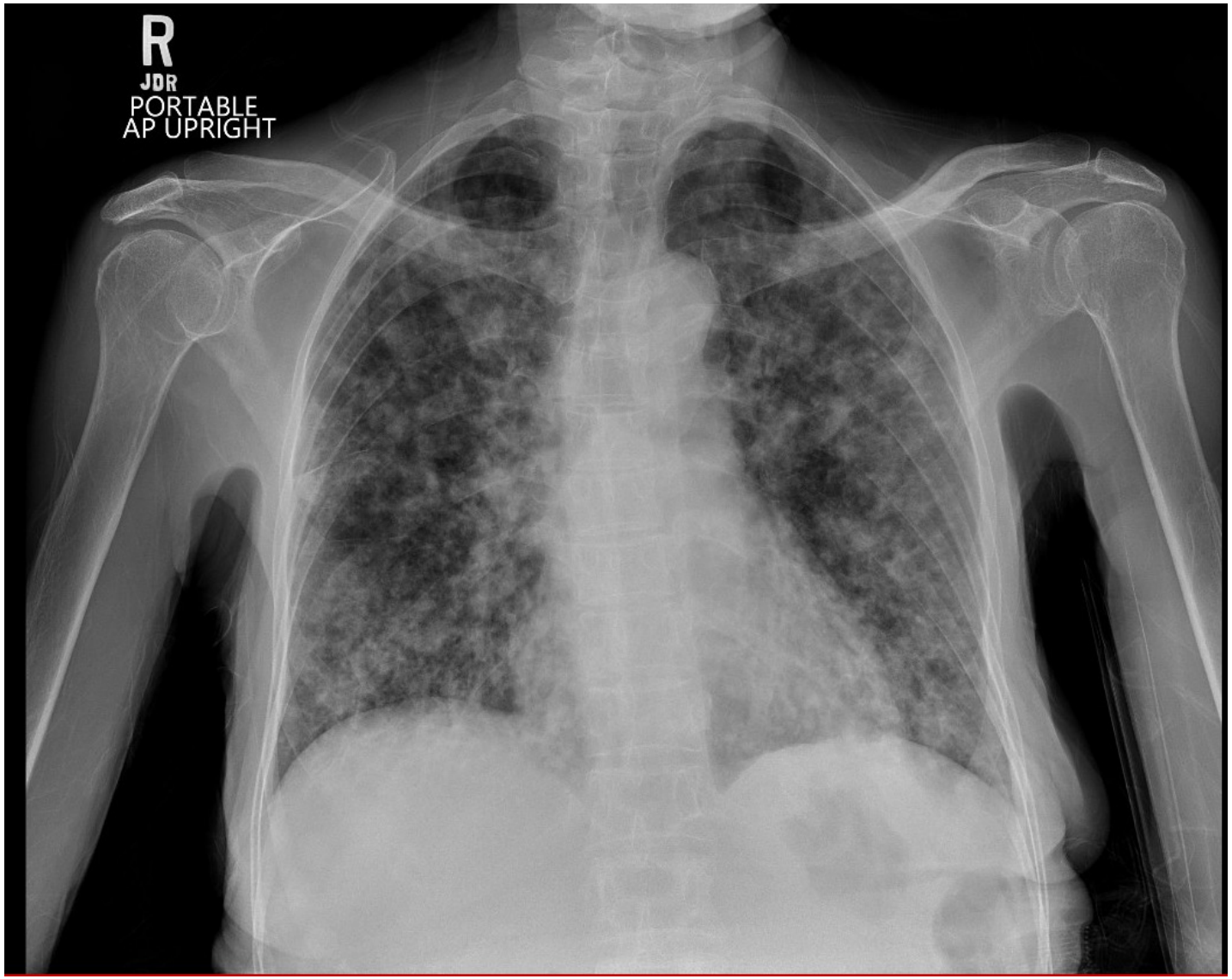
SERIOUS INFECTIONS (5.1, 6.1):

- **Increased risk of serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens.**
- **Discontinue HUMIRA if a patient develops a serious infection or sepsis during treatment.**
- **Perform test for latent TB; if positive, start treatment for TB prior to starting HUMIRA.**
- **Monitor all patients for active TB during treatment, even if initial latent TB test is negative.**

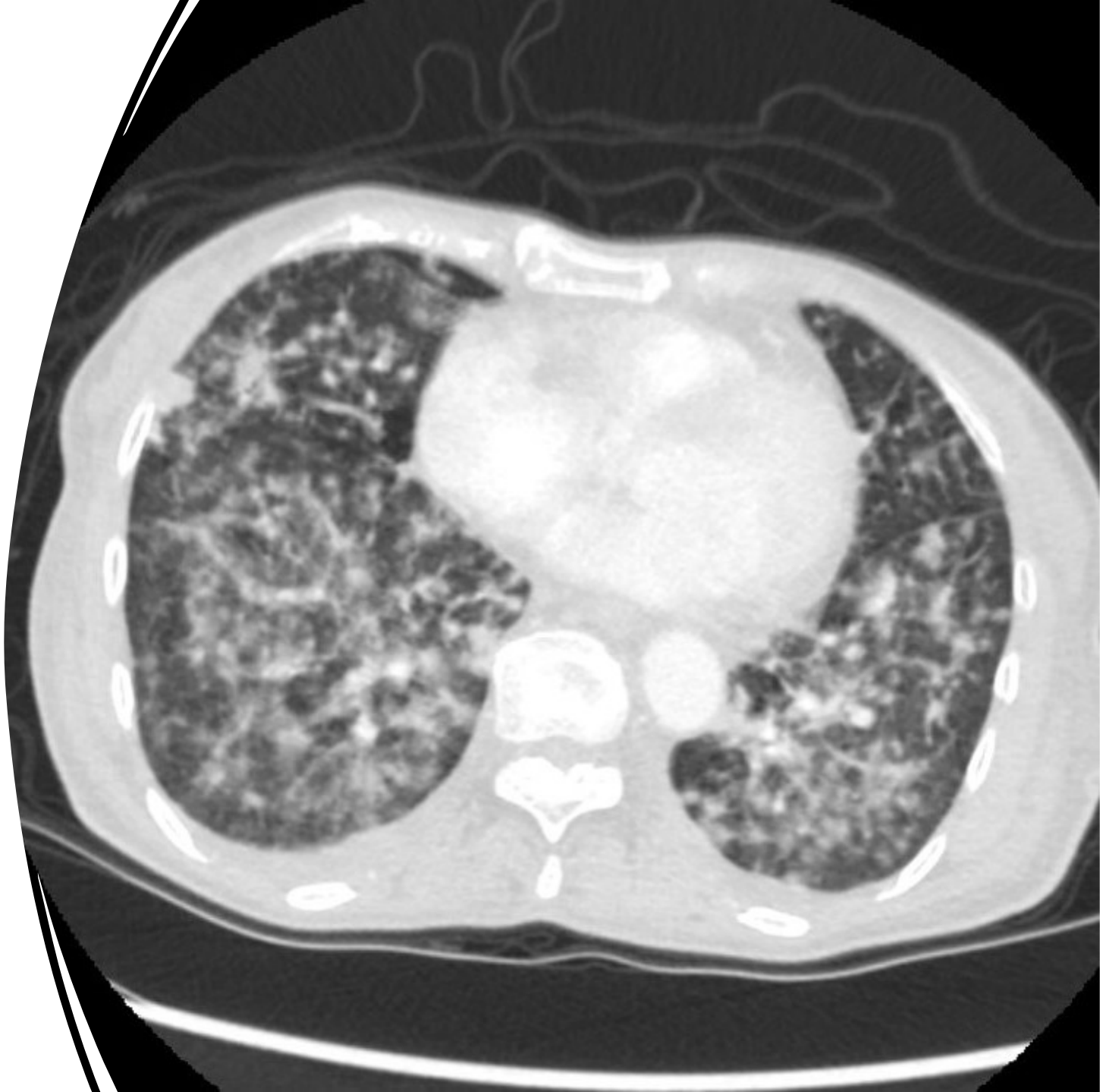
MALIGNANCY (5.2):

- **Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers including HUMIRA.**
- **Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have occurred in adolescent and young adults with inflammatory bowel disease treated with TNF blockers including HUMIRA.**

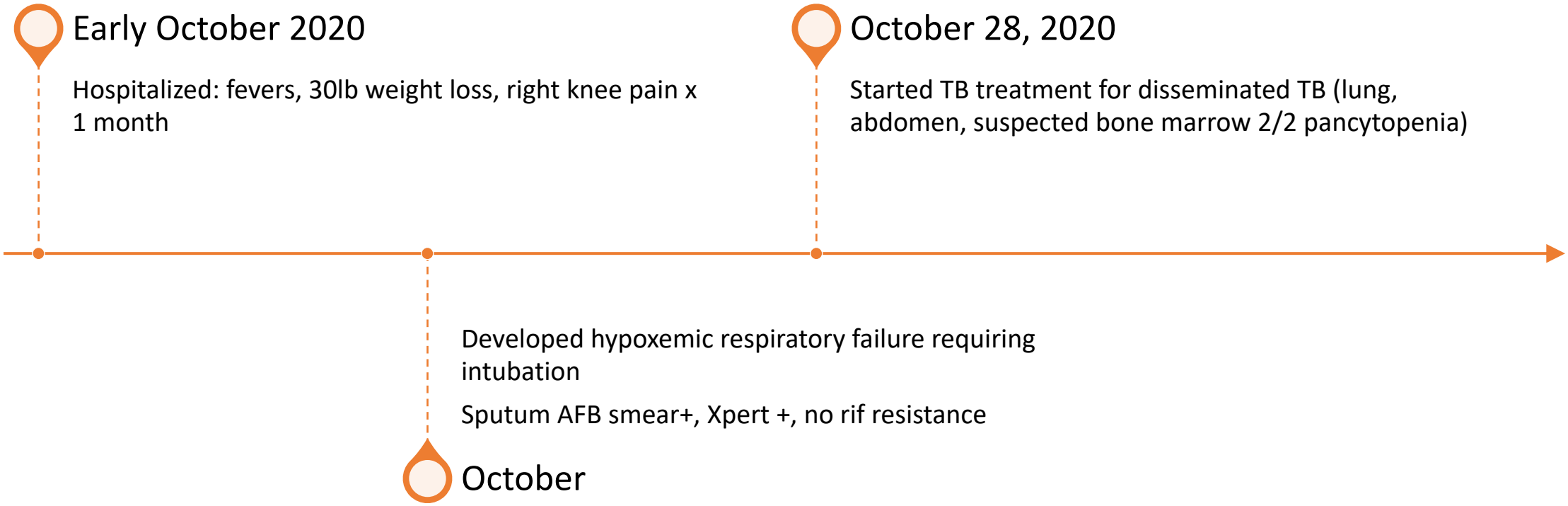
CXR
October
2020



CT chest, abdomen, pelvis October 2020



Timeline


Early October 2020
Hospitalized: fevers, 30lb weight loss, right knee pain x 1 month
October 28, 2020
Started TB treatment for disseminated TB (lung, abdomen, suspected bone marrow 2/2 pancytopenia)
Developed hypoxemic respiratory failure requiring intubation
Sputum AFB smear+, Xpert +, no rif resistance
October

November

Extubated. Then, fell out of bed resulting in brain MRI: multiple ring-enhancing lesions/tuberculomas

Declined LP

Dexamethasone + RIF increase

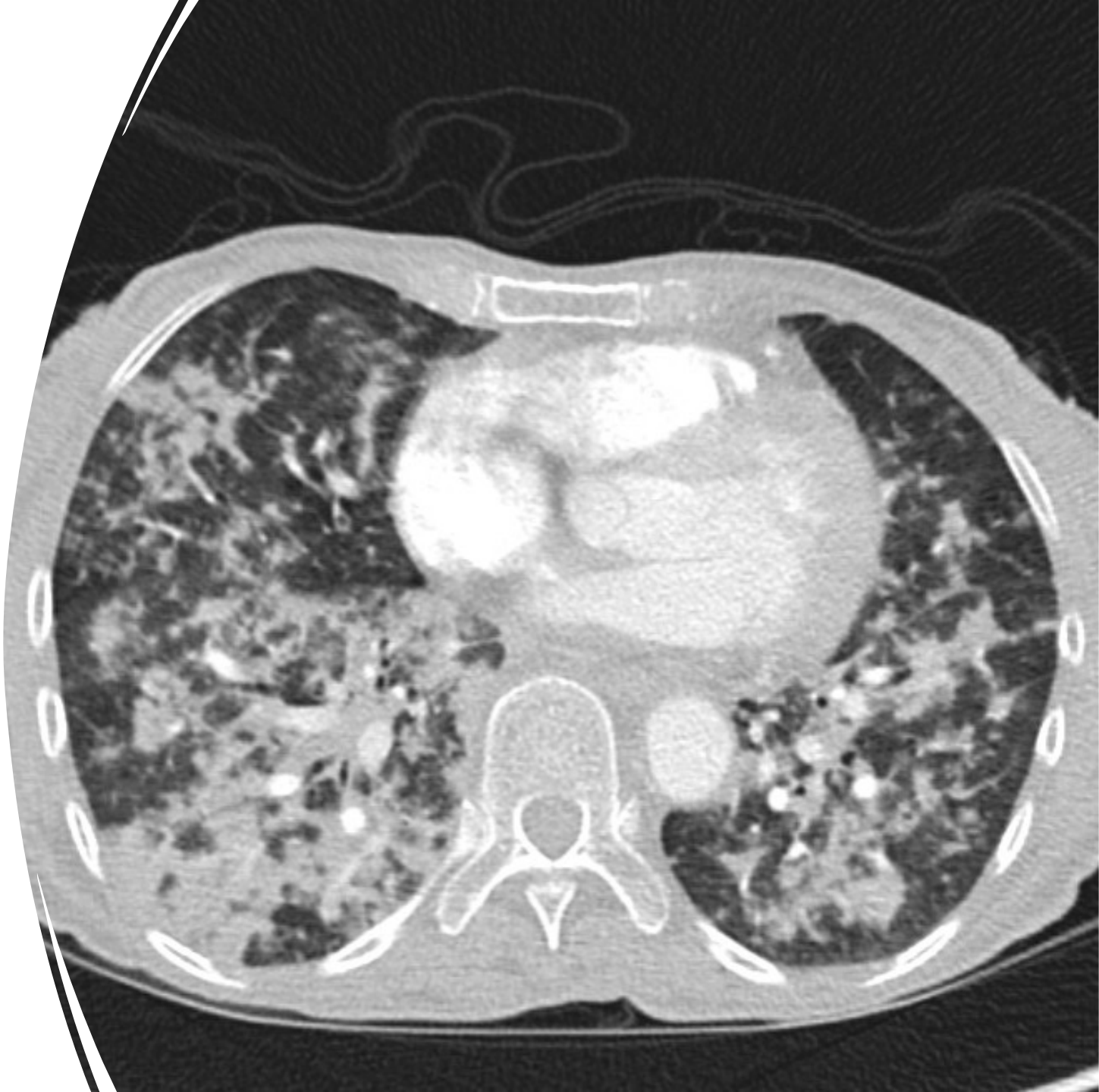
December 2020

D/c to home on orals: INH 300 mg, RIF 750mg (~20 mg/kg), EMB, Levo 750 mg, Prednisone 60 mg daily (no PZA due to elevated LFTs)

January 2021

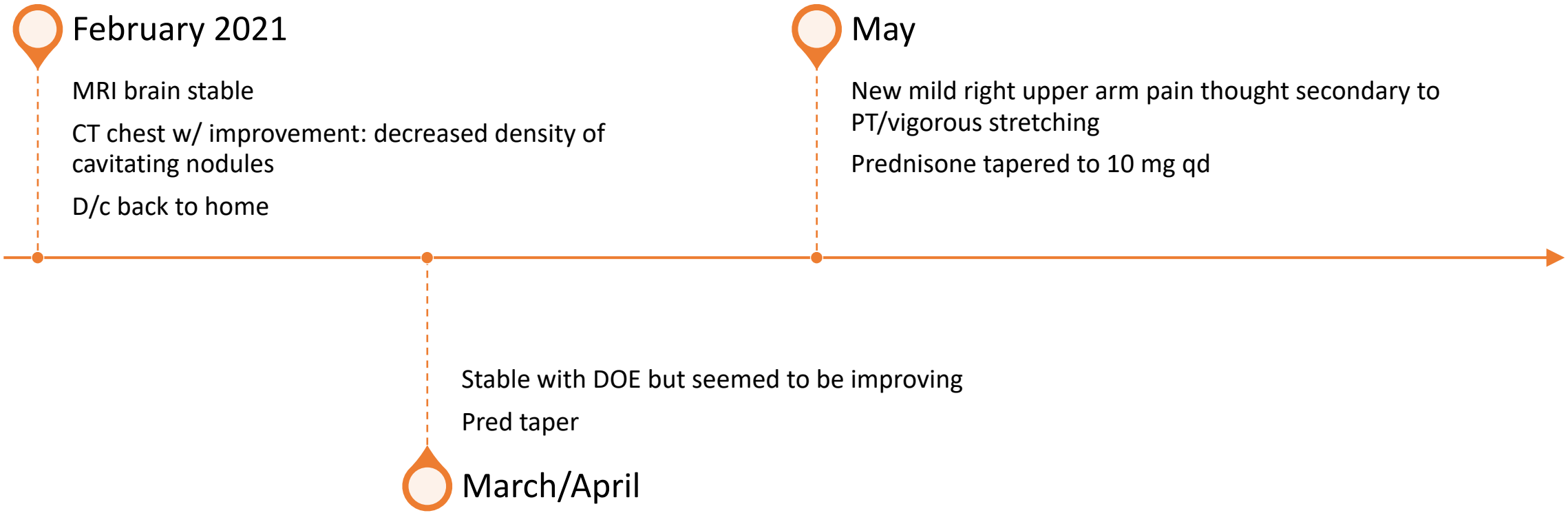
Patient with persistent subjective fever and dyspnea on exertion. Hospitalized .

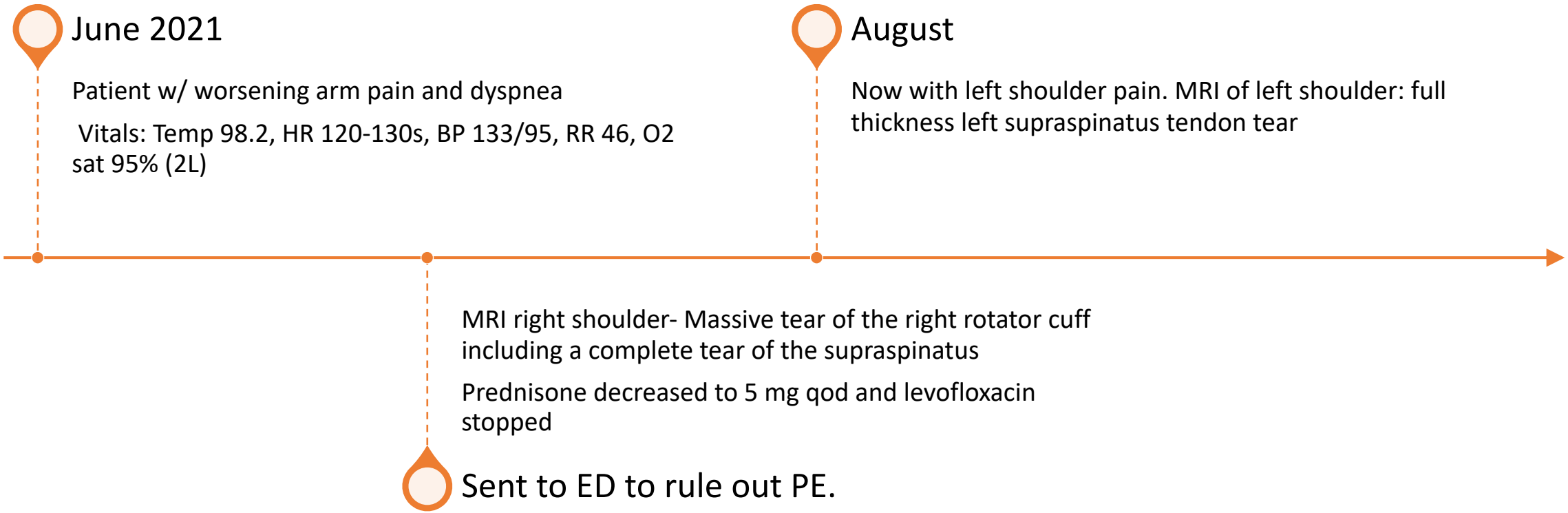
Vitals: RR 28-30, HR 131, SpO2 87% on RA



During hospitalization wide work-up initiated:

- Switched to IV TB medications (RIF 750 mg, INH 300, Levo 750 mg, LZD 600 mg, PZA 1000 mg started) and continued on prednisone 60 mg qd
- Bronchoscopy- endobronchial anthracosis (history of exposure to wood burning stoves). Pathology negative, PJP neg
- CT guided FNA-> necrotizing granulomatous inflammation and rare AFB, cytology negative
- Working diagnosis: presumed paradoxical reaction
- Prednisone increased to 120 mg po qd
- Discharged with PICC line on IV TB regimen, steroids and home O2(2L)


February 2021
MRI brain stable
CT chest w/ improvement: decreased density of cavitating nodules
D/c back to home
May
New mild right upper arm pain thought secondary to PT/vigorous stretching
Prednisone tapered to 10 mg qd
March/April
Stable with DOE but seemed to be improving
Pred taper


June 2021
Patient w/ worsening arm pain and dyspnea
Vitals: Temp 98.2, HR 120-130s, BP 133/95, RR 46, O2 sat 95% (2L)
August
Now with left shoulder pain. MRI of left shoulder: full thickness left supraspinatus tendon tear
MRI right shoulder- Massive tear of the right rotator cuff including a complete tear of the supraspinatus
Prednisone decreased to 5 mg qod and levofloxacin stopped
Sent to ED to rule out PE.

October 2021

persistent tachycardia, tachypnea, weight loss of ~8 lbs since start of treatment

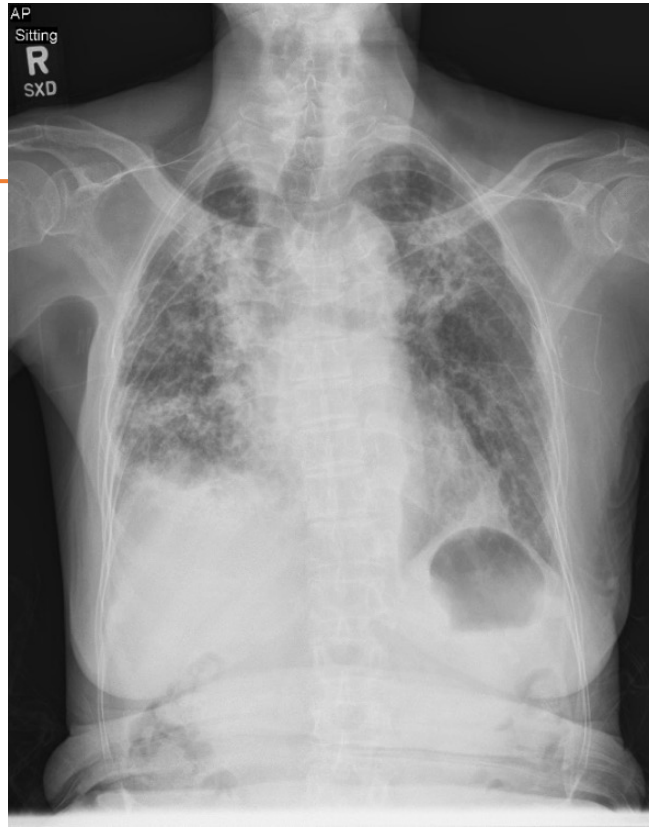
Adrenal suppression workup – negative

Cardiac echo- unremarkable

PFTs- patient unable to perform due to tachypnea

November 2021

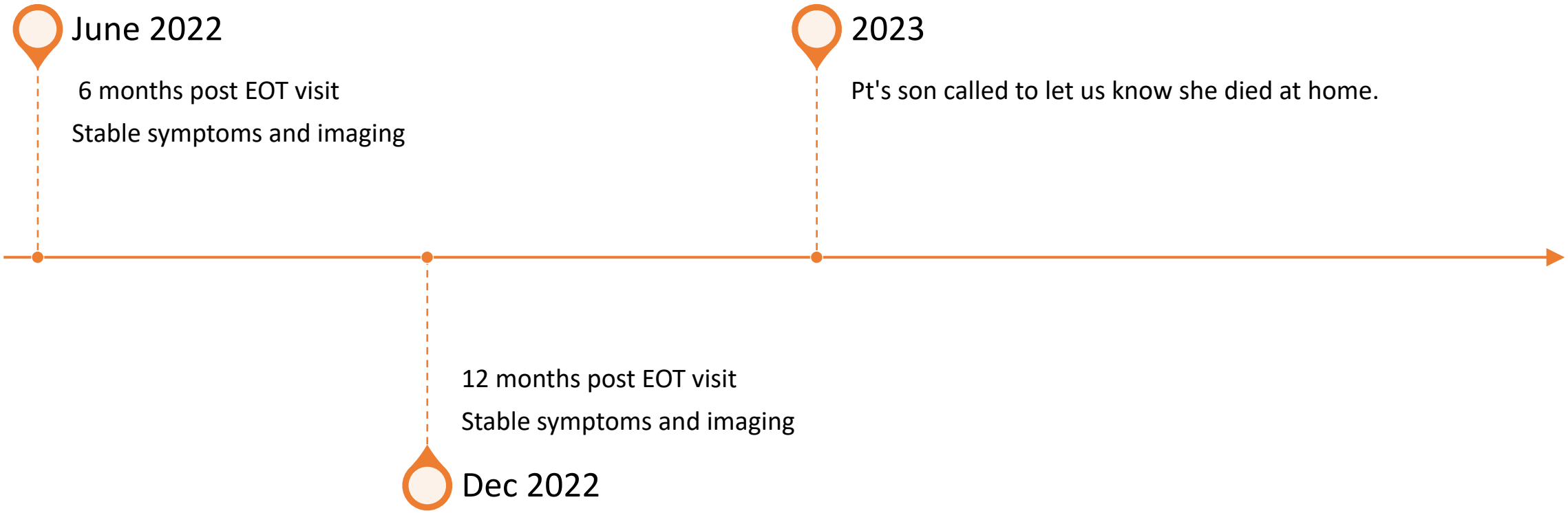
Given overall stability and clinical markers, ended treatment at 365 doses



EOT CXR

Pt w/ extensive bilateral lung parenchymal scarring with fibrosis as sequelae of TB. Rx for pulmonary PT. Offered referral for lung transplant: patient declined

Pulm evaluation


June 2022
6 months post EOT visit
Stable symptoms and imaging
2023
Pt's son called to let us know she died at home.
12 months post EOT visit
Stable symptoms and imaging
Dec 2022

Take Homes

Importance of TB testing in patients receiving TNF inhibitors, certain biologics, newer monoclonal agents (CDPH, USPSTF, CDC, and American College of Rheumatology recommend)

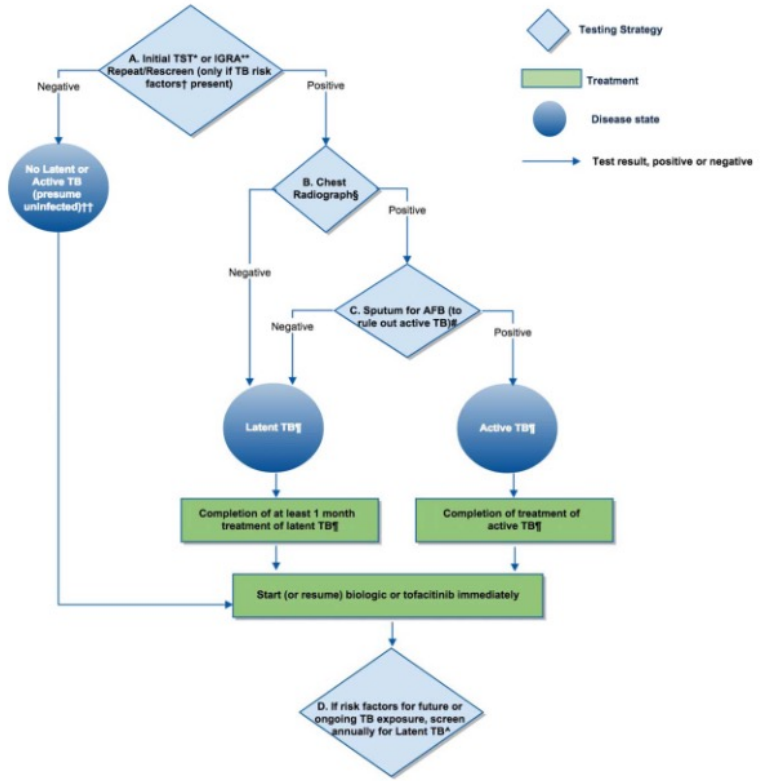


Figure 6. Tuberculosis (TB) screening algorithm for biologics or tofacitinib (endorsed and modified from the 2012 American College of Rheumatology RA treatment recommendations). The Voting Panel reviewed and endorsed the 2012 TB screening algorithm with 1 change, that tofacitinib should be included alongside biologics. * = anergy panel testing is not recommended. ** = interferon-gamma release assay (IGRA) is preferred if patient has a history of BCG vaccination. † = risk factors for TB exposure are defined based on a publication from the US Centers for Disease Control and Prevention as: close contacts of persons known or suspected to have active TB, foreign-born persons from areas that have a high incidence of active TB (e.g., Africa, Asia, Eastern Europe, Latin America, and Russia), persons who visit areas with a high prevalence of active TB, especially if visits are frequent or prolonged, residents and employees of congregate settings whose clients are at increased risk for active TB (e.g., correctional facilities, long-term care facilities, and homeless shelters), health care workers who serve clients who are at increased risk for active TB, populations defined locally as having an increased incidence of latent *Mycobacterium tuberculosis* infection or active TB, possibly including medically underserved, low-income populations, or persons who abuse drugs or alcohol, and infants, children, and adolescents exposed to adults who are at increased risk for latent *M tuberculosis* infection or active tuberculosis (159,160). †† = if patient is immunosuppressed and false-negative results more likely, consider repeating screening test(s) with tuberculin skin test (TST) or IGRA. § = chest radiography may also be considered when clinically indicated in patients with risk factors, even with a negative result on repeat TST or IGRA. # = obtain respiratory (e.g., sputum, bronchoalveolar lavage) or other samples as clinically appropriate for acid-fast bacilli (AFB) smear and culture. Consider referral to TB specialist for further evaluation and treatment. ¶ = in a patient diagnosed as having latent or active TB, consider referral to a specialist for the recommended treatment. ^ = patients who test positive for TST or IGRA at baseline (pretreatment) often remain positive for these tests even after successful treatment of TB. These patients need monitoring for clinical signs and symptoms of recurrent

2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis

Take Homes

- Patients on a TNF inhibitor with TB can present with severe, extrapulmonary/disseminated disease
- There appears to be some risk for TB even after discontinuation of TNFs
- Paradoxical reaction can be more likely to occur in previously immunosuppressed patients, including those on a TNF inhibitor
- The consequences of both TB and paradoxical reaction can be devastating

References

- Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2022. Available at URL: https://www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/
- Dixon WG, Hyrich KL, Watson KD, Lunt M, et al. Drug-specific risk of tuberculosis in patients with rheumatoid arthritis treated with anti-TNF therapy: results from the British Society for Rheumatology Biologics Register (BSRBR). Ann Rheum Dis. 2010;69(3):522.
- Carmona L, Gómez-Reino JJ, Rodríguez-Valverde V, et al. Effectiveness of recommendations to prevent reactivation of latent tuberculosis infection in patients treated with tumor necrosis factor antagonists. Arthritis Rheum. 2005;52(6):1766.
- Singh, JA, Saah, KG, Bridges Jr, SL, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis & Rheumatology. 2016; Jan;68(1):1-26. doi: 10.1002/art.39480
- List of targeted immunotherapies: Murrill MT, Velásquez GE, Louie J, Tahir P, Kim A, D. Szumowski JD, Salazar J, Minter D, Casalegno ML, Phillips A, Ernst J. Latent tuberculosis screening recommendations for targeted immunotherapies. Presented at the 2023 National Tuberculosis Conference. June 12, 2023, Atlanta, United States

Big thank you to Dr. Janice Louie, TB clinic nursing team, and clinic for all they do for our patients.