

West Coast TID Meeting

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Case 1



■ YO ■ s/p OLT ■/■/23

- **Recipient's social history:**

- Originally from: Dairy Farm, ■.
- Now lives in: ■.
- Has also lived in ■, NY and ■, CO.
- Tropical travel: Mexico, Bermuda, Bahamas, Panama, (on cruises). Midwest: Yes. Southwest: Yes. Other: Lithuania, Poland.
- Pets/other animals: 1 dog.
- Sick contacts: No.
- TB - prior testing, exposure: negative. No known exposures.

■ YO ■ s/p OLT ■/■/23

- **Donor's social history:**

- Originally from: Mexico.
- Worked in construction.
- Utox positive for fentanyl. Subjective reports of IVDU history.
- Died of PEA arrest.
- No other social history was able to be obtained.

■ YO ■ s/p OLT ■/■/23

- Tx Summary:

Tx: OLT ■, induction with basiliximab

Complications: anastomotic stricture, ERCP pancreatitis, fluid collection, rejection

IS: Tacrolimus (neurotoxicity) -> Cyclosporine, MMF, Prednisone taper

PPX: Bactrim (leukopenia) -> inh pentamidine ■ -> dapsonе ■.
Acyclovir, Fluconazole

■■ YO ■■ s/p OLT ■■/■■/23

Infectious workup	Donor	Recipient
CMV	+	+
EBV	+	+
Toxoplasmosis	+	-
Syphilis screen	-	IgG + RPR -
Tuberculosis screen	Not tested	TB QuantiFERON negative
Coccidioides	Not tested	-

■■ YO ■■ s/p OLT ■■/■■/23

Represents to the ED ■■: with fever, diarrhea, fatigue

2nd hospitalization: ■■-■■

Second fever ■■ at home. (22 d post tx), then on admission.

Started on Zosyn --> Augmentin x 7 days total.

Blood cultures negative.

EPP negative.

Unclear source of fever.

■■ YO ■■ s/p OLT ■■/■■/23

Represents on ■■: with fever, confusion

Aside from fever, vital signs within normal limits.

3RD hospitalization: ■■-■■

Started on IV Vancomycin + Meropenem.

CT AP : resolved fluid collection porta hepatis.

Unclear source of fever. Given missing donor's social hx, broad infectious workup ordered, including plasma cell-free DNA (Karius[®]).

■ YO ■ s/p OLT ■/■/23

Differential diagnosis

- A. Histoplasma capsulatum
- B. Cryptococcus neoformans
- C. Mycobacterium tuberculosis
- D. Aspergillus fumigatus
- E. Disseminated Adenovirus infection
- F. Coccidioides immitis

Case 2

■ YO ■ s/p deceased donor kidney transplant (DDKT) ■/■/23

PMH

- HTN
- ESRD of unclear etiology

Transplant complications

- None.
- Induction w/ ATG.
- IS: Tacrolimus, prednisone, MMF
- PPx: Valacyclovir, clotrimazole, Bactrim

Post-transplant complications

- C diff infection ■ s/p 10 d of p.o. vancomycin then fidaxomicin.
- Day 1 of fever ■ – 38.6 C

█ YO █ s/p DDKT █/█/23



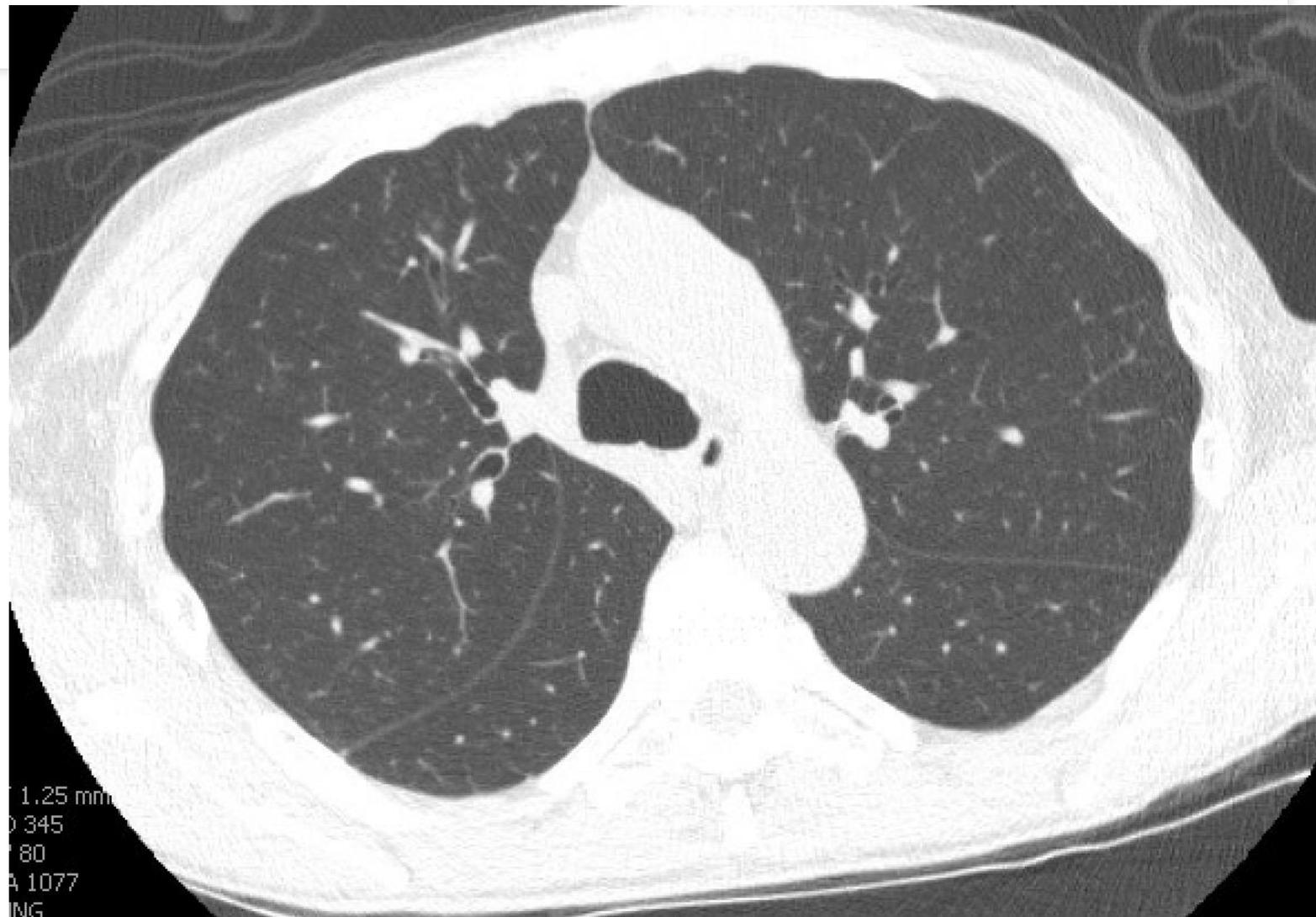
CXR 12/7/23

■■ YO ■■ s/p DDKT ■■/■■/23

CT Chest WO Contrast

Right lung solid nodules
measuring up to 7 mm, new
compared to prior.

Para-aortic lymphadenopathy
measuring up to 1 cm short axis,
likely reactive.



■■ YO ■■ s/p DDKT ■■/■■/23

CT AP W Contrast

Peritoneum: Rim-enhancing perinephric fluid collection about the posterior and medial aspect of the transplant kidney measures up to 4.1 x 2.4 x 9.5 cm, c/f abscess. This lesion abuts the R psoas m.



■ YO ■ s/p DDKT ■/■/23

• **Recipient's social history:**

- Originally from the Midwest and now lives in WA state.
- Occasional gardening and lives rurally near farms.
- Pet cat
- No Southwest or international exposures.
- No known TB exposures.

YO s/p DDKT / /23

Infectious workup	Donor	Recipient
CMV	+	-
EBV	+	+
Toxoplasmosis	+	+
Syphilis	-	-
Tuberculosis	Not tested	TB QuantiFERON negative
Coccidioides	Not tested	-

■ YO ■ s/p DDKT ■/■/23

- **Notable Labs:**

- Cryptococcal antigen 1:2
- Repeat Cryptococcal ag was negative.
- Adenovirus VL 79,000 in the blood and 240,000 in the urine

■ YO ■ s/p DDKT ■/■/23

Differential diagnosis

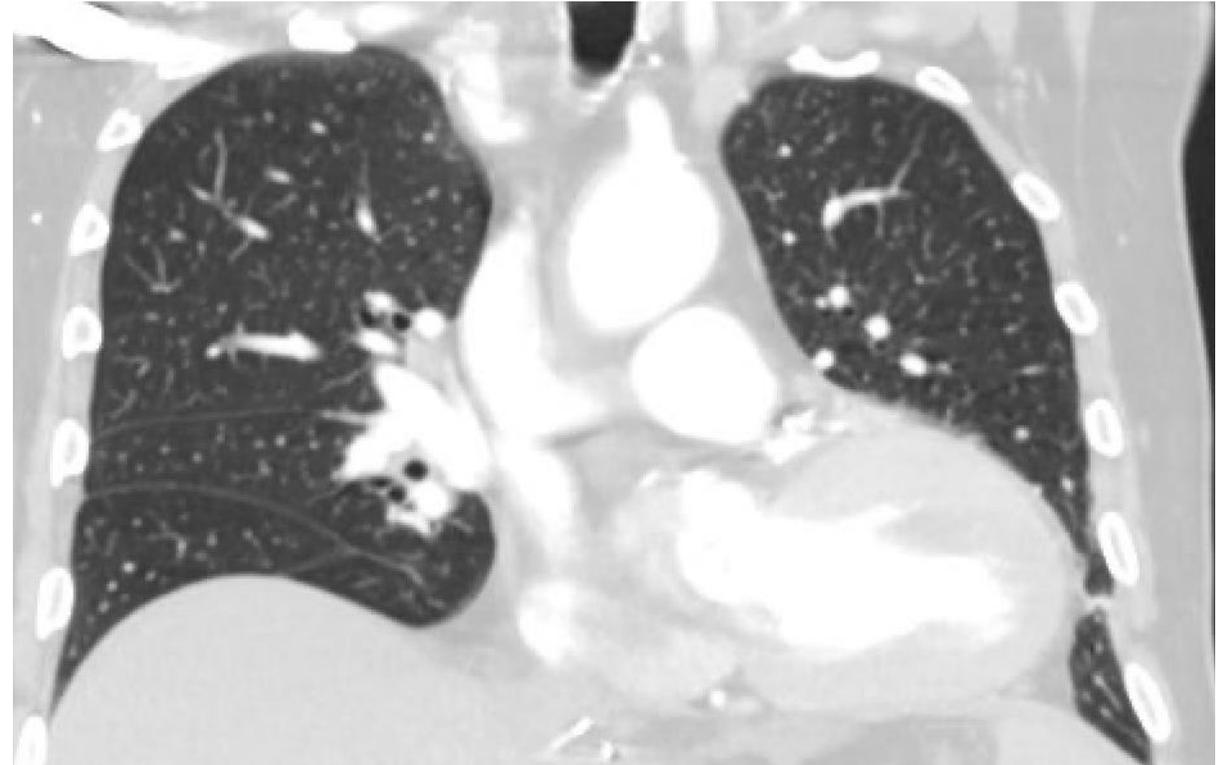
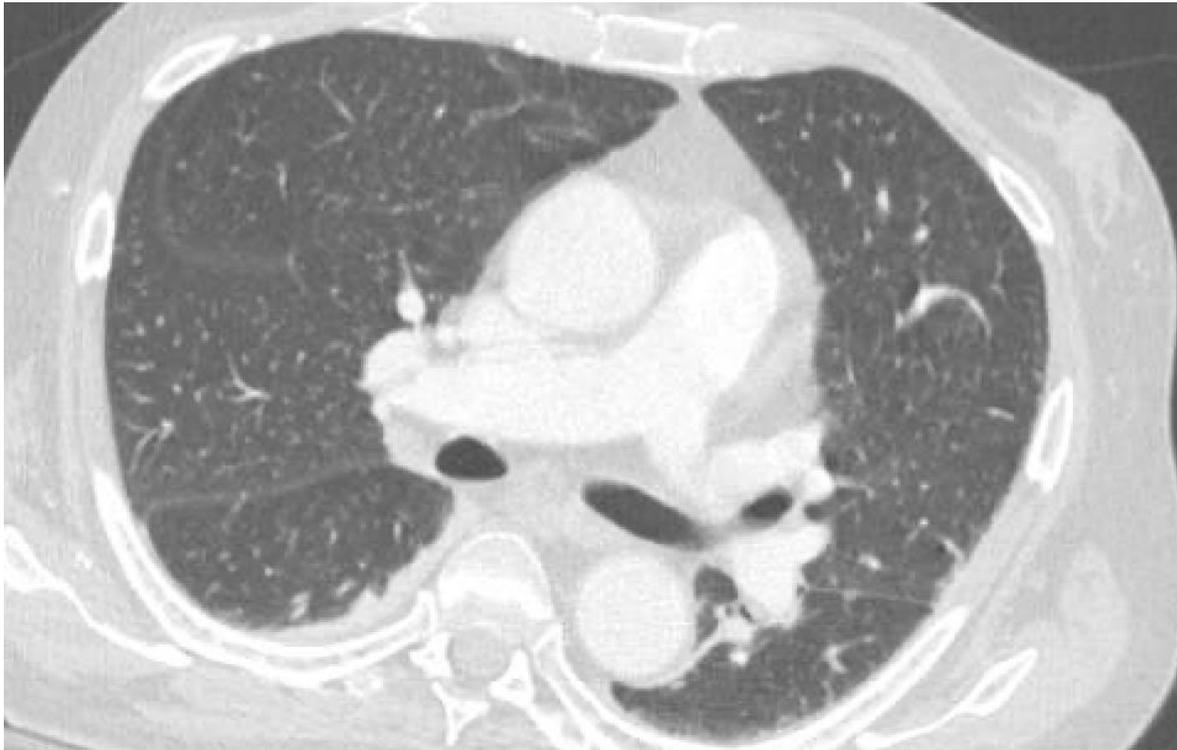
- A. *Histoplasma capsulatum*
- B. *Cryptococcus neoformans*
- C. *Mycobacterium tuberculosis*
- D. *Aspergillus fumigatus*
- E. Disseminated Adenovirus infection
- F. *Coccidioides immitis*

CASE 1: ■■■ y/o ■■■■ s/p OLT ■■■/■■■/23

- ■■■/12: Kidney recipient in ■■■ from same donor, prelim histopathology showing multiple abscesses with large burden of AFB.
- ■■■/12: Started on HRZE (with rifabutin)
- ■■■/13: Plasma cell-free DNA (Karius[®]) test from liver recipient positive for MTB.

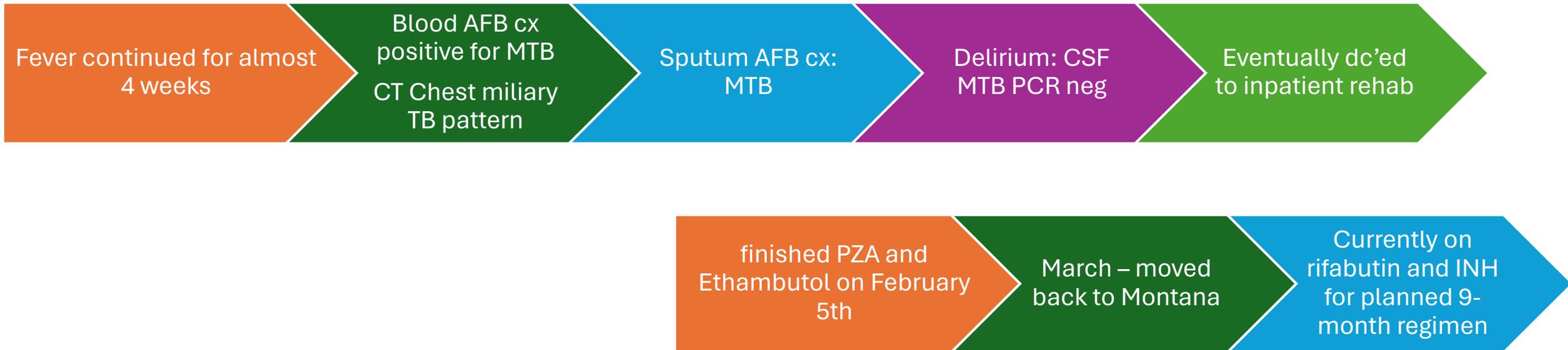
Case 1: [REDACTED] YO [REDACTED] s/p OLT [REDACTED]/[REDACTED]/23

CT chest [REDACTED]/[REDACTED]/23



CASE 1: [REDACTED] YO [REDACTED] s/p OLT [REDACTED]/[REDACTED]/23

Course post-TB diagnosis



Final culture: drug-susceptible MTB.

CASE 2: ■■■ y/o ■■■ s/p DDKT ■■■/■■■/23

- ■■■/12: Kidney recipient in ■■■ from same donor required explant, prelim histopathology showing multiple abscesses with large burden of AFB.
- ■■■/12: IR aspirate of perinephric/psoas fluid collection MTB ID by MALDI-TOF-MS.
- ■■■/12: Started on HRZE (with rifabutin)
- ■■■/13: plasma cell-free DNA (Karius[®]) test from liver recipient positive for MTB.

CASE 2: [REDACTED] YO [REDACTED] s/p DDKT [REDACTED]/[REDACTED]/23

Course post-TB diagnosis

Fever nearly immediately subsided [REDACTED]/12/23

Perinephric fluid, blood, urine, and sputum MTB positive

Developed elevated liver enzymes and pyrazinamide was stopped [REDACTED]/18

Liver enzymes normalized and he d/c'd on [REDACTED]/31/23

Completed 2 months of Ethambutol on [REDACTED]

Currently on rifabutin and INH for planned 9-month regimen

Final culture: drug-susceptible MTB.

Case 2: ■ YO ■ s/p DDKT ■/■/23

Current status

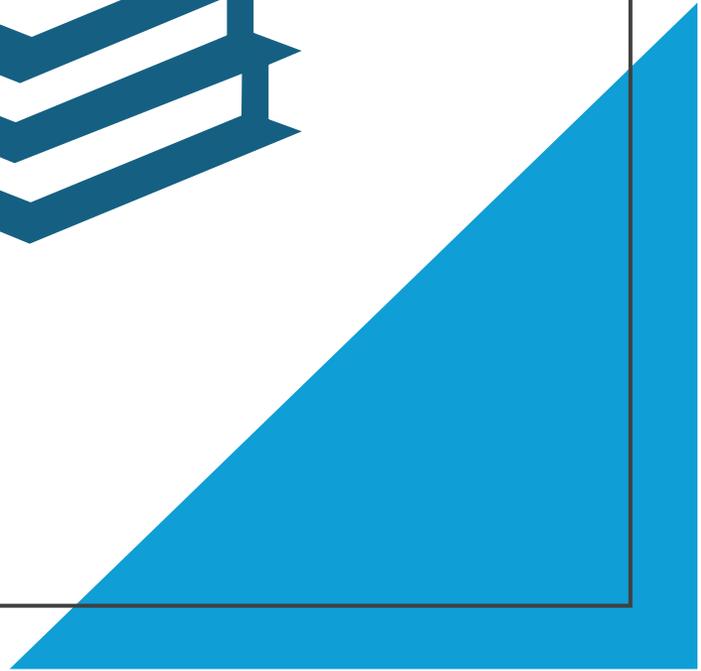
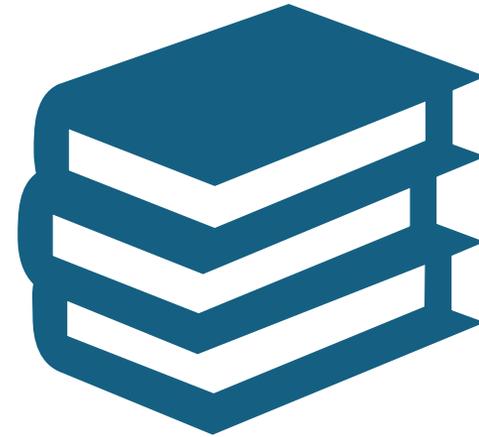
- **Most recent CT AP 2/26:**

- Previously reported perinephric fluid collection in the transplant kidney is now much smaller.
- The hypoenhancing component in the right psoas, measures approximately 1.2 on axial plane.
- In the coronal images, the right psoas fluid collection now measures approximately 6.2 x 1 cm compared to 8.4 x 1.8 cm previously.

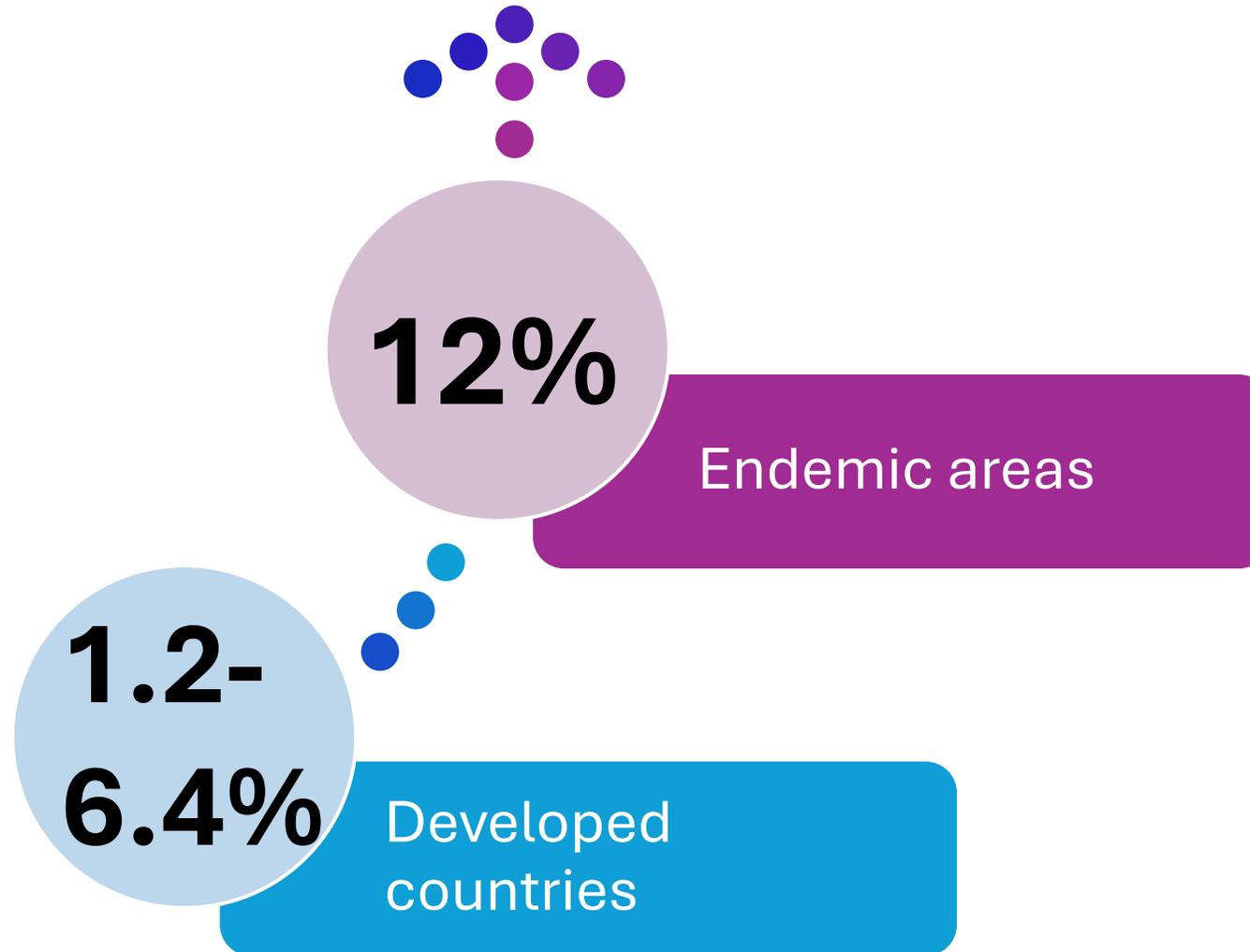


Discussion

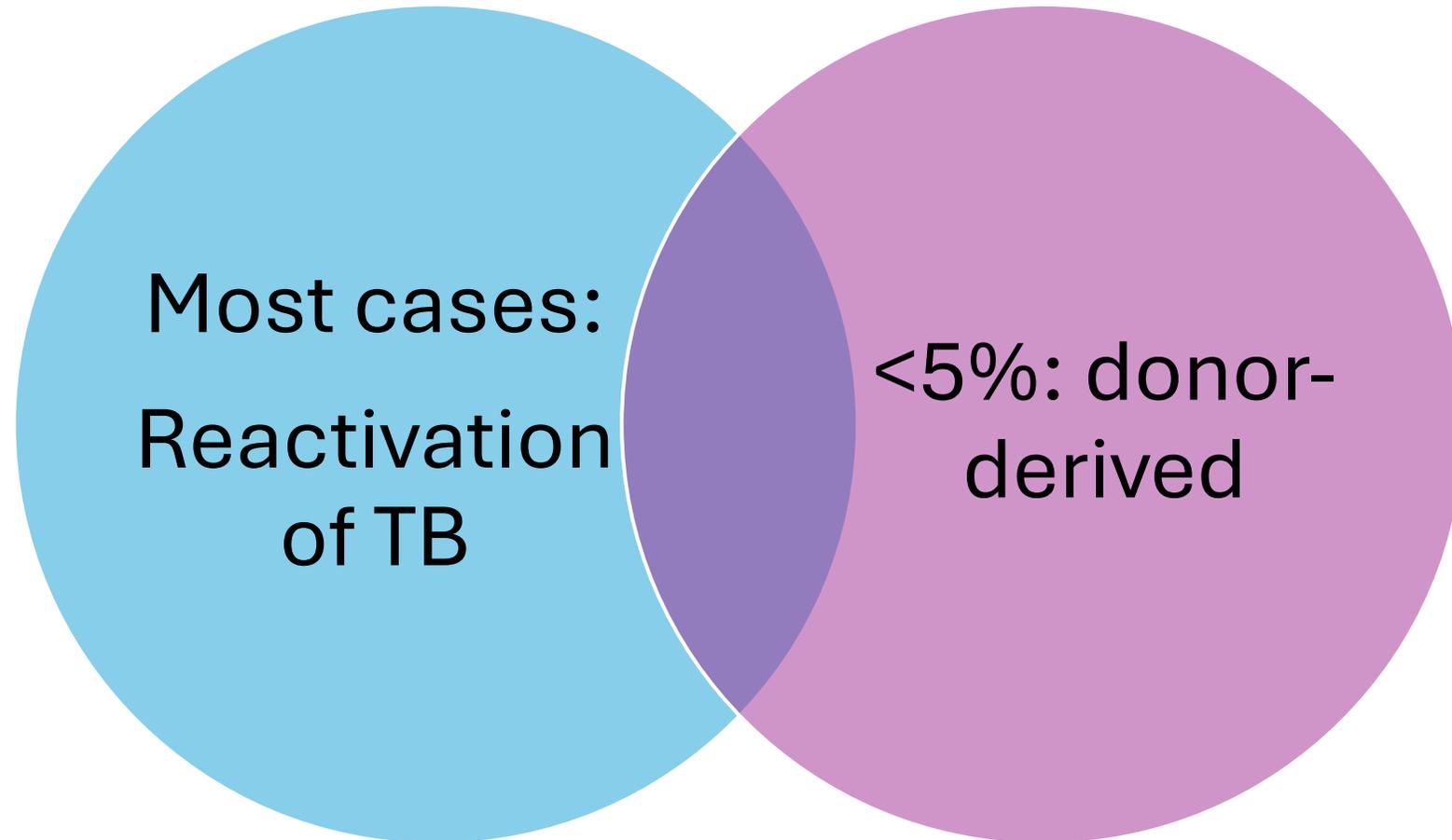
TB in solid organ
transplant



TB Prevalence in SOT recipients



TB in SOT recipients



TB in SOT patients – Risk Factors

- Born in endemic countries
- Poor environment
- Smoking
- Malnutrition
- DM
- CKD
- TB exposure
- Older age
- Hep C positive

TB in SOT patients

- Patients with posttransplant TB were more likely to have extrapulmonary disease and more than twice as likely to die as TB patients without SOT (RR = 2.2 [1.6-2.9]).
- The median time from transplantation to TB diagnosis was 1.2 years, with the shortest time among lung transplant recipients.

TB in SOT

Table 3

Incidence of posttransplant tuberculosis disease in California, 2010-2020, by organ type.

Transplant type	Number of California transplants	Number of TB cases ^{a,b}	Person-years of transplant follow-up ^c	Incidence rate (cases per 100 000 person-years)
All solid organs	37 064	96	171 455.2	56.0
Heart ^d	3680	6	15 866.6	37.8
Intestine	64	0	356.7	0.0
Kidney	23 148	54	111 702.5	48.3
Liver	9289	26	41 186.7	63.1
Lung	2412	12	8735.2	137.4
Pancreas	866	0	4770.2	0.0

TB, tuberculosis.

^a TB cases whose transplants occurred during or after 2010.

^b Individual organ types sum to 98. Two TB cases had 2 separate organ transplants (both liver and kidney), thus occurring in incidence calculations for each of those organs.

^c Person-years started at the date of organ transplant and were censored at (1) TB case report dates, (2) death date, or (3) December 31, 2020.

^d Because of the small counts, estimates may be unreliable.

Donor-derived TB

Usually occurs within the first 3 months after transplantation.

36 cases were identified in published literature in 2018, of which 17 were proven.

Fever is the most common presenting symptom.

The most common risk factor: residence in a TB-endemic area.

From 2019 review: equal proportions of pulmonary, extra-pulmonary and disseminated TB.

- Median duration of treatment: 10.5 months.
- All cases of pulmonary TB were identified in lung Tx recipients.

LTBI/Active TB pre-transplant assessment

- In endemic countries, a thorough history should be taken from all transplant candidates, their donors, and other family members.

CXR

TST >5mm

IGRA

T-SPOT TB if TST
negative?

AFB sputum
cultures from
High-risk donors?

LTBI in SOT recipients

- LTBI treatment has proven to be effective in preventing active TB in kidney and liver Tx recipients.
- Among 41 cohort studies active TB developed in only 1.8% of all recipients given prophylaxis compared to 2.5% who were not on ppx. [RR =0.69, $p<0.04$]
- 20/641 developed active TB while on ppx, compared to 62/544 who did not receive ppx. [RR=0.25, $p<0.00001$]

TB screening in transplant candidates

- A retrospective nested case-control study of liver transplant recipients showed that CT scans with evidence of prior healed TB were predictive of post-transplant TB even in those with normal CXR.

TB screening in transplant candidates

A systematic review and meta-analysis of 43 studies with 36,403 patients.

-Both TST and IGRA had low PPV (2.13% and 1.2% respectively) and high NPV (95.5% and 99.6% respectively) in predicting post-transplant TB.

-Positive predictive value is higher when TB burden is higher.

TB screening in transplant donor candidates

Test type/criteria	Type of patients	Sensitivity	Specificity	Reference
TST at 5 mm	Sensitivity: active TB patients	75–90%	NA	Huebner (42)
TST	Sensitivity: active TB patients	70%	NA	Diel (43)
T-SPOT.TB	Specificity: low risk controls	88%	86%	
QFT-G or QFT G in tube		81%	99%	
TST	Sensitivity: active TB patients	77%	97% (59% BCG)	Pai (16)
T-SPOT.TB	Specificity: low risk controls	90%	93%	
QFT-G or QFT G in tube		70%	96%	
TST	Sensitivity: active TB patients	65%	75%	Sester (15)
T-SPOT.TB	Specificity: TB suspects with diagnosis other than TB	81%	59%	
QFT G in tube		80%	79%	

TST = tuberculin skin test; TB = tuberculosis; QFT-G = Quantiferon Gold; BCG = Bacillus Calmette Guerin vaccine recipients; NA = not applicable.

Would you have accepted organs from donor with active untreated TB?

A. Yes

B. No

C. I do not know

TAKE HOME MESSAGES

1. TB should be part of the differential in solid organ transplant recipients with unexplained fevers within 3 months of transplantation.
2. For donors from TB-endemic areas, perform a TB rule out with AFB sputum cultures and MTB PCR, if possible, especially if any signs of active or prior Tb infections.



Bibliography

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