Table of *M. kansasii* cases

Parameter	Case 1	Case 2
Age, Gender	31, Female	59, Male
Underlying comorbidities	SLE, kidney transplant, non-ischemic cardiomyopathy	Insulin dependent diabetes, hypertension, kidney transplant
Immunosuppressive medications	mycophenolate , tacrolimus , prednisone 10 mg daily	mycophenolate, belatecept , prednisone 10 mg daily
Presenting symptoms of infection and duration	Anterior neck swelling/pain, 1st MCP pain/swelling, left 3rd finger swelling, subjective fevers for 8 days	Generalized weakness, fever, generalized arthralgia for 2 months. Found to have significant pericardial effusion
T max/fever at presentation	Afebrile	101 F
WBC with %N	16800/µL (88% neutrophils)	4600 /µL (79% neutrophils)
ESR mm per hr	53 mm/hr	83 mm/hr
AFB blood culture	Not done	Positive
AFB culture result (other than blood)	Thyroglossal cyst aspiration (post admission day 2) AFB stain 4+ AFB culture positive on post admission day 8 Identified as *M. kansasii* on post admission day 29	Site: AV graft and stent resection (post admission day 14): AFB stain 1+ AFB culture positive on post admission day 27 Identified as *M. kansasii* on post admission day 36
Imaging modality and other diagnostics *	CT soft tissue neck: 4.5x 4.6cm multilocular cystic lesion of thyroglossal duct cyst Right hand X-ray: 8 mm lucent lesion in the 1st proximal phalanx Left hand ultrasound: fluid in the 3rd flexor tendon sheath	Left upper extremity ultrasound: subcm fluid along the inferior margin of the AV graft, no deep fluid. PET/CT: hypermetabolic activity in the soft tissue involving the vascular graft
Karius Test result molecule/microliter (MPM)	M kansasii: (284) Teno torque virus 15: (56) Peptoniphilus harei: (109)	M kansasii: (1314) Cytomegalovirus: (225)
Time to result from Karius Test collection	4 days	3 days
Time to result from Karius Test sample receipt	3 days	1 day
Location of infection	Infected thyroglossal duct cyst Possible right MCP septic arthritis and left 3rd finger tenosynovitis	Infected AV graft and stent Mycobacteremia Possible pericarditis and synovitis (knees/wrists)
Empiric antibiotics	Vancomycin x 3 days ; Cefepime x 4 days; Azithromycin x 5 days; Pyrazinamide x 7 days (continued until MTB probe was negative) INH, Rifampin and ethambutol started on post admission day 5	Vancomycin x 8 days Ceftriaxone/cefepime x 11 days (continued for 3 more days after KT) Doxycycline x 4 days
Duration of empiric antibiotics before Karius test result	9 days	8 days
Antimicrobials after Karius Test (and clinical impact)	Azithromycin and pyrazinamide stopped Ethambutol, Isoniazid and Rifampin continued	Ethambutol; Rifabutin; Isoniazid
Karius Test impact on decision to biopsy	Right hand effusion drained	None (AV graft explantation done before diagnosis)
Duration of anti-tubercular drugs	Ongoing	Ongoing
Duration of hospitalization	17 days	42 days (excluding rehab)
Outcome	Improving	Improving

*Other diagnostics:
Case 1: HIV Ag/Ab, CT chest, CXR, right knee and foot Xray, Bacterial blood culture- negative
Case 2: CT chest and abdomen, CXR, X ray hand, MRI of lower extremities, HIV Ag/Ab, serum cryptococcal antigen, urine histoplasma antigen, serum Blastomyces antigen, serum coccidioides antibody, RPP, malaria smear, serum1,3 BDG, serum Parvovirus PCR, bacterila blood culture, pericardial fluid AFB , fungal and bacterial culture: all negative

Rapid diagnosis of disseminated *M. kansasii* infection

Conclusion. Open-ended NGS plasma testing for mcfDNA identified disseminated *M kansasii* infection much earlier than standard microbiology and thus helped in initiation and modification of pathogen directed treatment.

Disclosures. **All Authors**: No reported disclosures

646. Increasing Use of Interferon-Gamma Release Assay to Test for Pediatric Tuberculosis in a Low-Burden Setting

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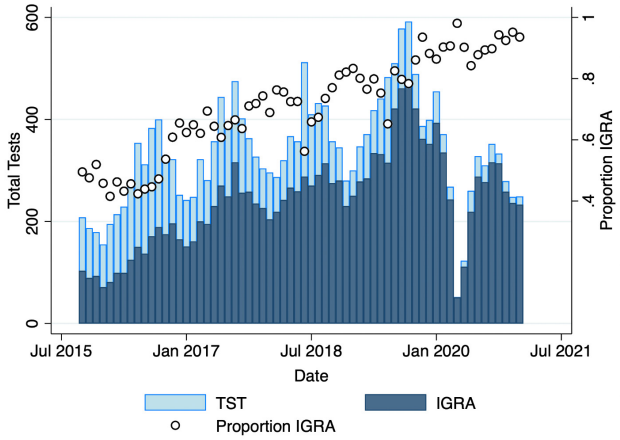
Session: P-29. Diagnostics: Bacteriology/mycobacteriology

Background. The American Academy of Pediatrics recommends tuberculin skin tests (TSTs) or interferon gamma release assays (IGRAs) to test for tuberculosis (TB) infection in children ≥2 years old, and prioritizes IGRA testing in Bacille Calmette-Guérin vaccine recipients due to cross-reactivity. TSTs require a return visit, which frequently results in loss to follow up. Growing evidence supports accuracy of IGRA testing in pediatric patients, including young children, leading to calls for preferential use of IGRA over TST. We sought to evaluate trends in IGRA use in children over time.

Methods. We identified all TB infection tests conducted in children 5-17 years old at 2 academic medical systems in Boston from October 2015–January 2021. TSTs were identified using medication administration records, and IGRAs were identified using laboratory records. We computed the proportion of tests per month that were IGRA and TST. We used Pearson correlation to determine the association between month of testing and proportion of tests that were IGRAs.

Results. 21,471 TB infection tests were obtained from 16,778 patients during our timeframe. Median age of testing was 13.4 years (IQR 9.2 – 16.2 years). During the study period, there was a significant increase in the monthly proportion of TB infection tests that were IGRAs (Pearson correlation coefficient 0.92, $P < 0.001$). The total number of tests performed per month also increased, with seasonal increases in testing in late summer and early fall and a substantial decline in testing early in the COVID-19 pandemic.

Tuberculosis infection tests and proportion IGRA.



Total number of tuberculosis infection tests per month and proportion of tests that were interferon gamma release assays, from October 2015 - January 2021.

Conclusion. Use of IGRAs among patients age 5-17 years of age increased significantly overall and compared to TST in two large Boston healthcare systems over a 5-year period. These results suggest a shift towards blood-based TB infection testing in a low-burden setting, which may improve completion of the pediatric TB infection care cascade. Future research is needed to determine reasons for changing testing modalities, and similar patterns in other settings.

Disclosures. **Gabriella S. Lamb, MD, MPH**, Nothing to disclose

647. Investigation of Heteroresistance Among *Klebsiella pneumoniae* (KP) Inner Colonies (IC) Observed During Fosfomycin Disk Diffusion (DD) Testing

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Session: P-29. Diagnostics: Bacteriology/mycobacteriology

Background. During fosfomycin DD testing, the frequent occurrence of non-susceptible IC within the zone of inhibition of susceptible isolates has been noted. The Clinical & Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) have contradicting recommendations on how IC should be interpreted; CLSI recommends considering IC when interpreting DD results whereas EUCAST recommends ignoring them. This study sought to identify the susceptibility of these IC and to understand whether heteroresistance contributes to the appearance of IC during fosfomycin DD.

Methods. This study included a convenience sample of 71 KP clinical isolates from 3 United States locations. During DD testing, 58 (81.7%) of these isolates displayed at least one IC. Broth microdilution (BMD) minimal inhibitory concentration (MIC) testing, using extrapolated CLSI *Escherichia coli* breakpoints, was performed on a subset (n=32) of the IC in duplicate for comparison to the corresponding parent MIC values. This was followed by a modified disk elution screening test for heteroresistance to compare the frequency of low level resistance (LLR) and high level resistance (HLR) between the susceptible isolates that produced resistant IC (n=6) and those that did not produce any IC (n=3).

Results. The MIC range for the IC isolates (128 to > 1024 µg/mL) increased as compared to the parent isolates (< 2 to > 256 µg/mL) and $MIC_{50/90}$ increased from the parent (128/ > 256 µg/mL) to IC (1024/ > 1024 µg/mL) isolates. All IC isolates had a resistant MIC value vs. 46.5% of parent isolates, and over 90% of IC isolates had an MIC at least 2 dilutions higher than their corresponding parent isolate. Heteroresistance screening found all tested isolates to be positive for LLR, and 8 of 9 positive for HLR, while the one HLR-negative isolate was IC-producing.

Conclusion. IC were frequent during fosfomycin DD testing and were commonly more resistant than their corresponding KP parent isolates. A small subset of these isolates tested via a modified disk elution test displayed either LLR or HLR regardless of the absence of IC. These results call for further investigation among a larger isolate set to understand what mechanisms are responsible for the frequency of IC and their increased fosfomycin resistance.

Disclosures. **All Authors**: No reported disclosures