

(88%) had pulmonary TB disease only; two (12%) had both pulmonary and extrapulmonary disease. Of all patients, 16 had *Mycobacterium tuberculosis* isolated from sputum and 7 (44%) had cavitary disease. The preliminary drug susceptibilities were 8 MDR patterns, 8 pre-XDR, and 1 unreported. Three patients received BPaL as their only treatment; six first received treatment for drug-susceptible TB, and eight received other regimens for MDR TB before BPaL. Eleven (65%) patients had ≥ 1 side effect reported during any TB treatment, including peripheral neuropathy (n=5), depression (n=4), vestibular dysfunction (n=3), and vision changes (n=3). Timing related to specific TB drug use was not reported. Sixteen (94%) patients received less than the approved initial dose of 1200 mg linezolid daily, and 15 (88%) patients underwent monitoring of linezolid exposure. All 16 patients with *M. tuberculosis* in initial sputa converted to negative culture results within 6 months of starting treatment. At 12 months after BPaL initiation, all patients had completed treatment, without TB recurrences or deaths reported.

Conclusion. In the early period after FDA approval, most U.S. patients received BPaL off-label with an initial linezolid dose lower than the approved 1200mg yet still achieved good outcomes. Most reported patients underwent some monitoring of linezolid exposure. Monitoring of BPaL use is important and should continue.

Disclosures. All Authors: No reported disclosures

1401. Infliximab for Immune Reconstitution Inflammatory Syndrome (IRIS) in Tuberculous Meningitis: A Treatment Paradox

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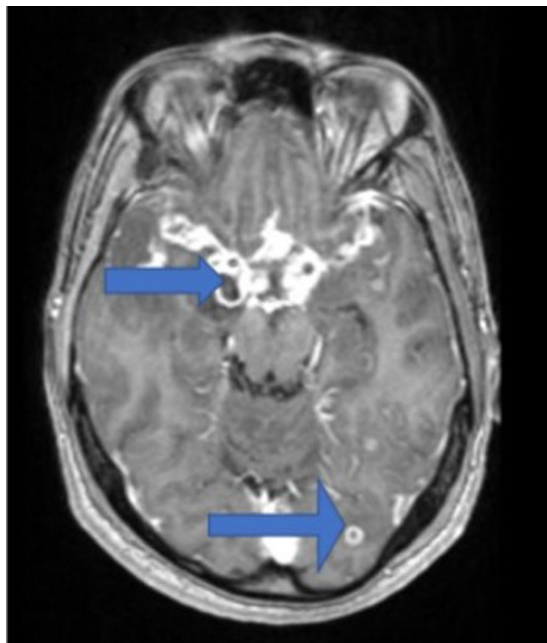
Session: P-80. Tuberculosis and other Mycobacterial Infections

Background. Tumor necrosis factor (TNF)- α inhibitors are known for the reactivation of latent tuberculosis (TB). As a paradox, it has been reported to have a role in the treatment of immune reconstitution inflammatory syndrome (IRIS) from anti-TB therapy.

Methods. We report a case of paradoxical worsening of central nervous system TB after initiation of anti-TB medications, which was treated successfully with infliximab (TNF- α inhibitor).

Results. A 34-year-old man from Nepal with a history of untreated latent TB presented with complaints of occipital headache, slurred speech, and witnessed seizure. His physical exam was consistent with hyperreflexia. MRI of the brain revealed multiple small contrast-enhancing lesions in cerebral hemispheres. CT Chest showed bilateral centrilobular nodules suggestive of miliary TB. Cerebrospinal fluid (CSF) analysis showed pleocytosis, high protein, and low glucose. He was started on isoniazid, rifampin, ethambutol, and pyrazinamide along with high-dose dexamethasone for TB meningitis. Later, MTB DNA probe from bronchioalveolar lavage and CSF detected *Mycobacterium tuberculosis* which was pan-susceptible. Repeat MRI of the brain 6 months into therapy revealed worsening of brain lesions. Moxifloxacin and linezolid were added to the regimen given clinical progression on first-line therapy. 6-months into this enhanced regimen he started experiencing blurring of vision. Visual field mapping showed left homonymous hemianopia. Repeat MRI of the brain confirmed extensive changes of basilar meningitis completely enveloping the optic chiasm. IRIS from TB was suspected. His prednisone dose was increased, and 3-doses of infliximab infusion were, 2-weeks apart were administered which showed clinical and radiological improvement.

MRI Brain



MRI Brain (axial T2/flair sequence) shows hyperintensities in multiple locations including the involvement of the left optic nerve and the left occipital region.

Conclusion. Exacerbation of pre-existing clinical symptoms, formation of new lesions, or cavitation of prior pulmonary infiltrates is known as tuberculosis IRIS or paradoxical reaction. Despite the clinical and radiological exacerbation, mycobacterial cultures usually stay negative. Continuation of anti-TB medications and high-dose corticosteroids are the backbone of treatment but in refractory cases, immune modulation is needed with anti-TNF- α agents.

Disclosures. All Authors: No reported disclosures

1402. NTM Infections; A Rising Global Health Problem/Clinical Characteristics and Outcomes of Patients with Non-Tuberculous Mycobacterial Infections at Two Tertiary Academic Medical Centers

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Session: P-80. Tuberculosis and other Mycobacterial Infections

Background. Non-Tuberculous Mycobacteria (NTM) cause infections in immunocompetent as well as immunocompromised individuals affecting pulmonary and extra pulmonary sites. These pathogens are widely distributed globally and recent reports have shown their rise in many developed countries. Our study aimed to assess the disease magnitude, describe patient characteristics and risk factors, assess diagnostic and therapeutic measures and review outcomes furthering our understanding of the overall disease process.

Methods. We conducted a retrospective, multicenter review of patients with positive NTM cultures treated at University Hospital System and South Texas Veterans Health Care System (STVHCS) from 2011 to 2018. Infections were classified as pulmonary or extrapulmonary, and we recorded demographics, microbiological data, treatment regimens, duration, complications, follow-up and mortality. All categorical variables were described using percentages and compared between groups using the chi-square test.

Results. A total of 176 patients were included for analysis, of which 111 (63.1%) met criteria for NTM disease (2020 ATS/IDSA). The most common cultured mycobacterium was *M. Avium* Complex (MAC). *M. abscessus-chelonae* was more commonly associated with clinical disease and isolated from an extra pulmonary site whereas *M. simiae* complex had similar distribution between the infected and un-infected groups. Over 50% of patients received treatment (80% in the infected group). Cure was seen in 47.2%, all-cause mortality was 27% at last follow-up. Median duration of therapy was 10 months. 47% of patients experienced adverse effects which led to treatment discontinuation in one third of patients. Patients who were able to achieve a cure received a longer duration of therapy (12 vs 7 months; not statistically significant) and treatment was halted more commonly in the group that did not achieve eventual cure (42.6% vs. 16.7%, p=0.007).

Table 1. Characteristics of patients overall (all culture positive patients) and by clinical infection

Characteristic	Culture Positive (n=176)	Clinical Infection (n=111)	No Clinical Infection (n=65)	P-value*
Age (years), median (IQR)	66 (56-74)	62 (53-71)	70 (61-80)	0.0003
Male sex, n (%)	122 (69.7)	71 (64.0)	51 (80.0)	0.0263
Charlson Score, median (IQR)	4 (2-6)	4 (2-6)	5 (4-7)	0.0009
Pulmonary source, n (%)	137 (77.8)	75 (67.6)	62 (95.4)	<0.0001
Organism, n (%)				<0.0001
<i>M. avium</i> complex	54 (30.7)	30 (27.0)	24 (36.9)	
<i>M. abscessus-chelonae</i> complex	44 (25.0)	40 (36.0)	4 (6.2)	
<i>M. simiae</i> complex	29 (16.5)	16 (14.4)	13 (20.0)	
<i>M. goodii</i>	21 (11.9)	5 (4.5)	16 (24.6)	
<i>M. fortuitum</i>	14 (8.0)	10 (9.0)	4 (6.2)	
<i>M. kansasii</i>	8 (4.5)	7 (6.3)	1 (1.5)	
<i>M. mucogenicum</i>	2 (1.1)	2 (1.8)	0 (0.0)	
<i>M. szulgai</i>	2 (1.1)	0 (0.0)	2 (3.1)	
<i>M. scrofulaceum</i>	1 (0.6)	0 (0.0)	1 (1.5)	
<i>M. marinum</i>	1 (0.6)	1 (0.9)	0 (0.0)	
Any treatment, n (%)	93 (52.8)	89 (80.2)	4 (6.2)	<0.0001
Initial treatment, n (%)				
Macrolide/ethambutol/rifampin	88 (50.0)	84 (75.7)	4 (6.2)	<0.0001
Amikacin	30 (17.0)	30 (27.0)	0 (0.0)	<0.0001
Fluoroquinolone	19 (10.8)	19 (17.1)	0 (0.0)	<0.0001
Cefoxitin	10 (5.7)	10 (9.0)	0 (0.0)	0.0020
Imipenem	3 (1.7)	3 (2.7)	0 (0.0)	0.0945
Tigecycline	5 (2.8)	5 (4.5)	0 (0.0)	0.0303
Linezolid	20 (11.4)	20 (18.0)	0 (0.0)	<0.0001
Salvage treatment, n (%)	15 (8.5)	15 (13.5)	0 (0.0)	0.0001
Treatment duration, median (IQR)	10 (2-17)	10 (2-17)	5 (3-11)	0.4762

*P-value indicates comparison between clinical infection versus no clinical infection Treatment by bug

Table 2. Health outcomes of treated patients with clinical infection

Characteristic	Overall (n=89)
Cure, n (%)	42 (47.2)
Treatment failure, n (%)	15 (16.9)
Relapse/recurrence, n (%)	8 (9.0)
All-cause mortality, n (%)	24 (27.0)
NTM-related mortality, n (%)	13 (14.6)
Adverse effects, n (%)	42 (47.2)
Treatment halted, n (%)	27 (30.3)
Treatment duration, median (IQR)	10 (2-17)

Table 5. Cure among patients treated with clinical infection

Characteristic	Cure (n=42)	No Cure (n=47)	P-value
Age (years), median (IQR)	62 (49-68)	65 (56-72)	0.2963
Male sex, n (%)	30 (71.4)	27 (57.4)	0.1683
Charlson Score, median (IQR)	4 (2-6)	4 (2-5)	0.4949
Pulmonary source, n (%)	29 (69.0)	33 (70.2)	0.9050
MAC, n (%)	14 (33.3)	13 (27.7)	0.5612
Initial treatment, n (%)			
Macrolide/ethambutol/rifampin	39 (92.9)	45 (95.7)	0.5545
Amikacin	12 (28.6)	18 (38.3)	0.3312
Fluoroquinolone	8 (19.0)	11 (23.4)	0.6158
Cefoxitin	5 (11.9)	5 (10.6)	0.8503
Imipenem	1 (2.4)	2 (4.3)	0.6207
Tigecycline	3 (7.1)	2 (4.3)	0.5545
Linezolid	9 (21.4)	11 (23.4)	0.8235
Salvage treatment, n (%)	8 (19.0)	7 (14.9)	0.6015
Treatment duration, median (IQR)	12 (3-19)	7 (2-16)	0.3309
Adverse effects, n (%)	22 (52.4)	20 (42.6)	0.3536
Treatment halted, n (%)	7 (16.7)	20 (42.6)	0.0070

Conclusion. NTM infections represent a therapeutic challenge with low cure rates and high mortality. An understanding of the risk factors, treatment options and outcomes is essential to guide appropriate management. Our study highlights high rates of adverse effects and discontinuation which precludes prolonged courses of therapy required to achieve cure.

Disclosures. All Authors: No reported disclosures

1403. Tuberculous sacroiliitis: Clinical and Imaging Characteristics

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Session: P-80. Tuberculosis and other Mycobacterial Infections

Background. Osteoarticular tuberculosis remains a common disease among which the spine is the most affected site. Less frequently, sacroiliac joint is involved. Its diagnosis is often delayed due to misleading and varied symptoms. The aim of this work was to study the clinical features and the contribution of imaging results in the diagnosis of tuberculous sacroiliitis.

Methods. We conducted a retrospective study including all patients hospitalized in the infectious disease department for tuberculous sacroiliitis. The diagnosis was based on clinical, laboratory and radiological features.

Results. In total, we encountered 12 women with a median age of 51 [39-63] years. Three patients had a family history of tuberculosis (25%). The median diagnostic delay was 155 [48-331] days. The revealing symptoms were lower back pain (75%) and hip pain (25%) associated with fever (83.3%) and weight loss (75%). Reduced mobility was noted in 3 cases (25%). Pulmonary tuberculosis and tuberculous spondylodiscitis were associated with tuberculous sacroiliitis in 5 cases (41.7%) and 4 cases (33.3%), respectively. Tuberculin skin test was positive in 6 cases (50%). Laboratory investigations revealed elevated C-reactive protein levels in 11 cases (91.6%) and accelerated erythrocyte sedimentation rates in 9 cases (75%). Needle biopsy of the sacroiliac joint (41.7%) and soft tissues abscess puncture (16.6%) were performed. Computed tomography scan revealed joint space widening (83.3%), peripheral joint erosions (83.3%) and osteolysis (58.3%). Soft tissue abscesses were noted in 66.7% of the cases. Magnetic resonance imaging was performed in 4 cases (33.3%). Sacroiliac joint was hypointense in T1-weighted images (75%), hyperintense in T2 weighted images (50%) and in STIR images (50%). Bone scintigraphy, performed in 5 cases, revealed hyperfixation of the sacroiliac area (100%). All patients received antitubercular therapy. Percutaneous abscess drainage was indicated in 4 cases (33.3%).

Conclusion. Because of its deep localization, the diagnosis of tuberculous sacroiliitis is mainly based on imaging results associated with epidemiological, clinical and laboratory features. Antitubercular therapy initiated promptly leads to recovery.

Disclosures. All Authors: No reported disclosures

1404. Tuberculosis and HIV Coinfection: A Review of 135 Cases Experience of the Infectious Diseases Department- CHU Mohamed VI- Marrakech

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Session: P-80. Tuberculosis and other Mycobacterial Infections

Background. Tuberculosis is a health problem in Morocco, which is increasingly indicative of human immunodeficiency virus (HIV) infection.

Objective. To determine the epidemiological, clinical and paraclinical, therapeutic and evolutionary aspects of tuberculosis and HIV co-infection.

Methods. we report 135 cases co-infected with HIV and tuberculosis, collected by the infectious diseases department at the Mohammed VI University Hospital in Marrakech. This is a 12-year retrospective study (2007 to 2020) that involved all HIV-infected patients hospitalized for tuberculosis regardless of its location.

Results. The mean age of the patients was 40 years (17-73 years). A male predominance was noted in 69% of cases. In 74.6% of cases, tuberculosis was indicative of HIV infection. Nine patients were receiving antiretroviral (ARV) treatment at the time of the discovery of tuberculosis. There were 24% pulmonary tuberculosis, 25.3% extrapulmonary tuberculosis and 49% disseminated tuberculosis. Tuberculosis was

confirmed in 31.7% of cases. At the time of tuberculosis diagnosis, the average CD4 count was 86 cells / mm. Quadruple therapy with isoniazid, rifampicin, pyrazinamide and ethambutol was started in 83% of patients. The average time to start ARVs was 7 weeks. All patients who received ARVs received a combination therapy comprising the combination of 2 nucleoside analogs and one non-nucleoside analog. At the end of our work, the evolution was favorable in 53% of cases, death occurred in 25% of cases, 18.6% of patients were lost to follow-up, two cases of failure and another of relapse. Immune restoration syndrome was noted in 8 cases. Drug toxicity was observed in 24.5% of patients, 73% of which was related to hepato-toxicity of antibiacy drugs.

Conclusion. Tuberculosis is the most common opportunistic infection in people with HIV. Despite the advent of highly active triple therapy, tuberculosis is still a major cause of death in HIV positive people.

Disclosures. All Authors: No reported disclosures

1405. The Accuracy of Mycobacterium tuberculosis Specific IFN-γ/IL-2/TNF-α-FluoroSpot in Differential Diagnosis of Active Tuberculosis and Latent Tuberculosis Infection: A Case-Control Study

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Session: P-80. Tuberculosis and other Mycobacterial Infections

Background. To establish the Mycobacterium tuberculosis (MTB) specific IFN-γ/IL-2/TNF-α-FluoroSpot assay, and preliminarily evaluate its accuracy of differential diagnosis of active tuberculosis (ATB) and latent tuberculosis infection (LTBI).

Methods. Patients with pathologically confirmed and clinically diagnosed ATB in Peking Union Medical College Hospital and Beijing Chest Hospital from April 2020 to May 2021 were enrolled as case group, while patients with LTBI in the same period were enrolled as control group. The FluoroSpot assay was used to simultaneously detect the secretion of IFN-γ, IL-2 and TNF-α in T cells stimulated by the MTB specific antigens ESAT-6 and CFP-10 at the single-cell level. A binary logistic regression model was used to fit the combined diagnostic parameters, and the sensitivity, specificity, predictive value and likelihood ratio of the differential diagnosis of ATB and LTBI were calculated.

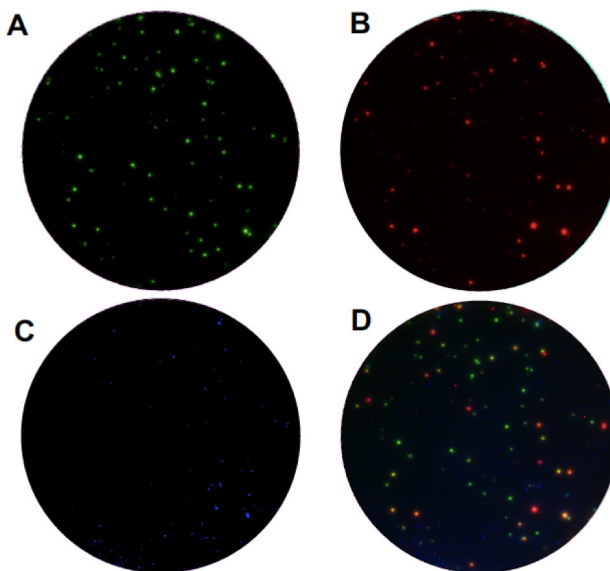


Figure 1. Schematic diagram of FluoroSpot (IFN-γ/IL-2/TNF-α) detecting cytokine-secreting specific T cells after stimulation with MTB specific antigen. A. The green spots are the total IFN-γ-secreting T cells; B. The red spots are the total IL-2-secreting T cells; C. The blue spots are the total TNF-α-secreting T cells; D. The green spots are the single IFN-γ-secreting T cells; the red spots are the single IL-2-secreting T cells; the blue spots are the single TNF-α-secreting T cells; the yellow spots are the dual IFN-γ/IL-2-secreting T cells; the cyan spots are the dual IFN-γ/TNF-α-secreting T cells; the purple spots are the dual IL-2/TNF-α-secreting T cells; the white spots are the triple IFN-γ/IL-2/TNF-α-secreting T cells.

Results. 62 patients with ATB (37 pathogen-confirmed ATB, 25 clinical diagnosed ATB), 87 patients with LTBI were included. There was significant correlation of the frequencies of total IFN-γ-secreting T cells detected by IFN-γ/IL-2/TNF-α-FluoroSpot assay compared with T-SPOT.TB after stimulation of MTB-specific antigen (r=0.829 for ESAT-6, P<0.001, r=0.804 for CFP-10, P<0.001). ROC curve was drawn for both T-SPOT.TB and FluoroSpot. For T-SPOT.TB, the AUROC was 0.669 (95%CI 0.574-0.765), the sensitivity and specificity of differentiating ATB from LTBI