

Nontuberculous Mycobacteria (NTM) and other Serious Infections in Patients Receiving Biologic Therapy

INFECTIOUS DISEASES SOCIETY OF AMERICA



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Abstract

Background: Recently, tumor necrosis factor (TNF) antagonists have become widely used to treat selected inflammatory diseases. Numerous cases of tuberculosis (TB) have been reported in patients using these agents (adalimumab, infliximab, etanercept). Less is known regarding NTM infections that might occur in this setting. In addition, little is known regarding the infectious risks of newer biologic agents that target T-cells (abatacept) and B-cells (rituximab).

Methods: In June 2007, we electronically surveyed IDSA members of the Emerging Infections Network (EIN). We asked members to report mycobacterial and other infections occurring in the last 6 months in patients treated with biologic therapies.

Results: 426 (48.9%) EIN members responded and reported a total of 50 mycobacterial infections in patients using these therapies. NTM infections were more common than TB (32 cases vs. 18 respectively). NTM infections included: *M. avium* complex (n=16), *M. chelonae* (n=5), *M. abscessus* (n=3), *M. marinum* (n=3) and others (n=5) consisting of *M. fortuitum*, *M. haemophilum*, *M. kansasii*, and *M. scrofulaceum*. Patients with mycobacterial infections were a median of 57 years old (11-82 years), and taking infliximab (n=18), etanercept (n=12), rituximab (n=8), adalimumab (n=3), or unspecified biologic therapy (n=9). Twenty-one (42%) patients were also receiving prednisone and/or methotrexate concurrently at time of diagnosis. In most cases (86%), the biologic drug was stopped at infection diagnosis; only two (4%) patients subsequently suffered immune reconstitution inflammatory syndrome. Eight (16%) patients died during their treatment for mycobacterial infection. Other commonly reported infections included invasive *S. aureus* (n=73) and histoplasmosis (N=56).

Conclusions: In the US, among patients receiving anti-TNF or other biologic immunosuppressive therapy, NTM infections and those caused by other organisms might be more common than TB disease.

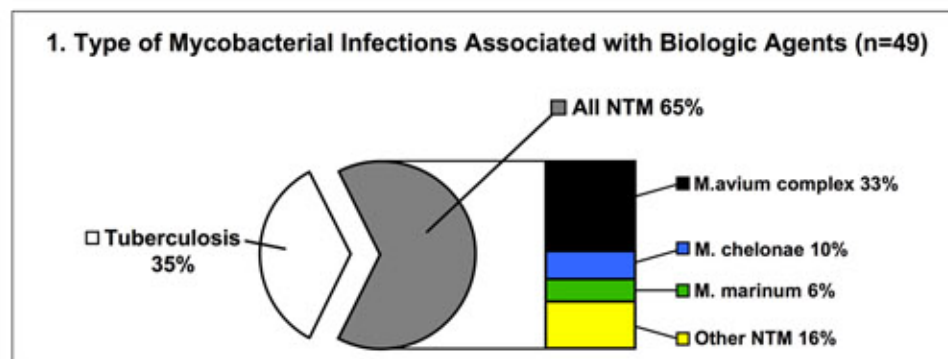
Introduction

- Both *Mycobacterium tuberculosis* (TB) and nontuberculous mycobacteria (NTM) have been reported in patients who receive anti-TNF therapy; to date, the most commonly reported granulomatous infection associated with anti-TNF therapy has been TB.
- Although the epidemiology of TB is well-described, little is known regarding the incidence of NTM infections in the United States.
- Less is known about the frequency, incidence of immune reconstitution, and mortality associated with NTM cases associated with the use of biologic drugs.
- This Emerging Infections Network (EIN) survey was designed to better understand: 1) the type of NTM associated with anti-TNF drugs and the newer biologics abatacept and rituximab, 2) the frequency of mortality and immune reconstitution if biologic therapy is discontinued, and 3) reports of other serious infections seen in patients using biologic drugs.

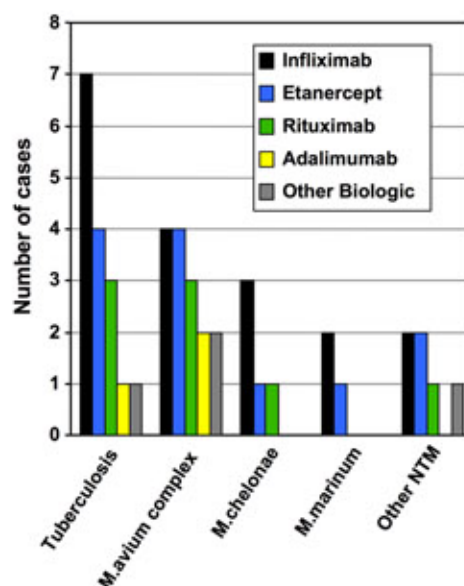
Copy of Survey

Results

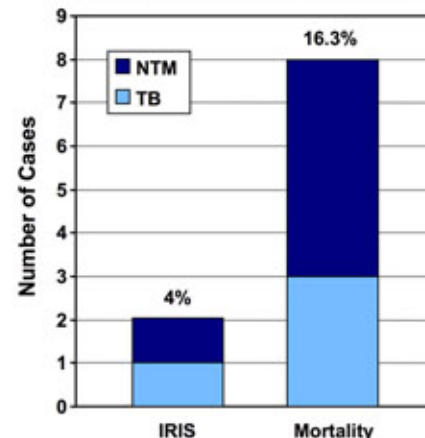
- 48.9% response rate to survey (426 of 871 members)
- 1867 mycobacterial infections reported
- 2.6% (n=49) of TB/NTM cases were associated with the use of biologic agents
 - 35% (n=17) were due to TB
 - 65% (n=32) were due to NTM, half of which were *M. avium* complex
- 43% of TB/NTM cases were associated with prednisone and/or methotrexate
- Immune reconstitution was seen in 2 cases; in 1 case the biologic was known to have been stopped (in the other it was unknown)
- 16.3% mortality rate in TB/NTM cases associated with biologics



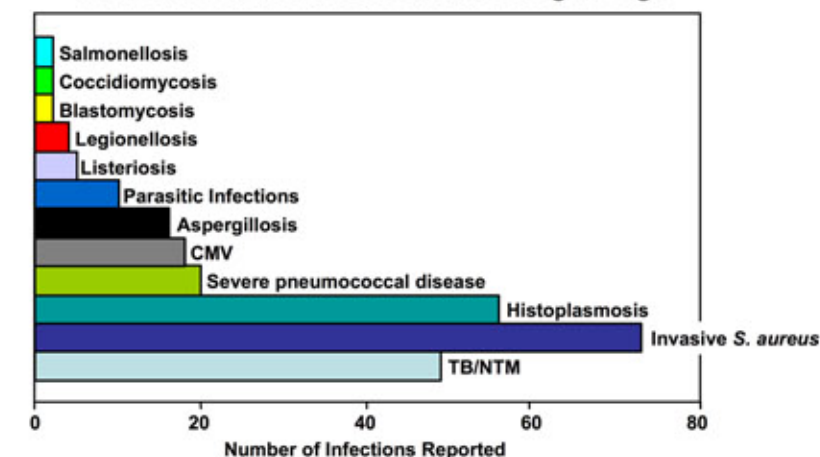
2. Tuberculosis and NTM Cases Associated with Specific Biologic Agents (n=45)



3. Immune Reconstitution Inflammatory Syndrome (IRIS) and Mortality with Biologic-Associated TB or NTM Infection (n=49)



4. Other Infections Associated with Biologic Drugs



Summary

- Amongst patients receiving biologic immunosuppressive therapy, nontuberculous mycobacterial infections (NTM) were seen twice as frequently as tuberculosis (TB).
- The most common NTM reported was *M. avium* complex followed by *M. chelonae* and *M. marinum*
- This is the first known report of an association between TB and NTM infections with rituximab.
- In most cases of biologic-associated TB or NTM infection, the biologic drug was stopped (86%) and immune reconstitution was rare (4.2%). Mortality was reported in 16.3% of cases.
- Invasive *S. aureus* and histoplasmosis were reported more often than tuberculosis and NTM infections combined. In addition, numerous other bacterial, viral, fungal, mold and parasitic infections were described in patients receiving biologic drugs.

HANDOUTS
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