18 Month Experience of Latent TB Management in the STH Infectious Diseases Department

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Background:

Anti-tumour necrosis factor (TNF) therapy is associated with an increased risk of reactivation of latent tuberculosis infection (LTBI)[1]. National guidelines recommend screening for LTBI in patients before the use of anti-TNF and other immunosuppressing biological agents[2]. Sheffield Teaching Hospitals' (STH) infectious diseases (ID) department receives many referrals for LTBI assessment, and a significant proportion are referred after a QuantiFERON gold plus positive result during pre-biological therapy screening. Optimising the preventing of LTBI reactivation in these individuals requires a robust screening strategy and careful risk assessment and use of anti-tuberculous chemoprophylaxis.

Aims:

To review the management of LTBI screened patients referred to the STH ID department with a focus on those screened as part of a biological therapy assessment.

Objectives:

- Identify all the TB and LTBI cases managed in the STH ID clinic between September 2015 and June 2017.
- Describe the characteristics of those with LTBI and use of adjunctive CXR in screening.
- Describe the assessment and use of chemoprophylaxis in those with LTBI.

Methods:

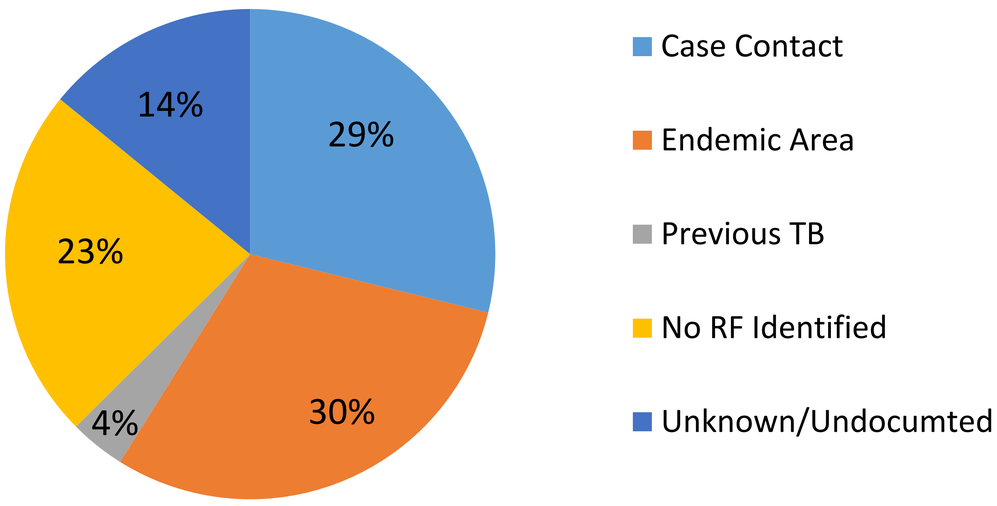
- TB cases were identified through visual inspection of all infectious disease clinic letters stored on the hospital system from September 2015 through to June 2017. Cases were included if TB management decisions were undertaken at the STH ID clinics.
- Data extracted: patient age, referral reason, TB exposure risk, CXR use and result, past medical history, planned biological therapy (if applicable), treatment risk factors adverse events, management outcome.

Results:

Of over 4000 clinic letters screened, 398 related to TB. 353 of these were included as TB management decisions were made at the STH ID clinic.

46% (163) were referred via LTBI screening, including 5% (17) who were referred as possible contacts of TB.
50% (176) were referred as suspected active TB. 13 cases were non-tuberculous mycobacteria and 1 case was disseminated BCG infection.
The median age at referral was 38 years.

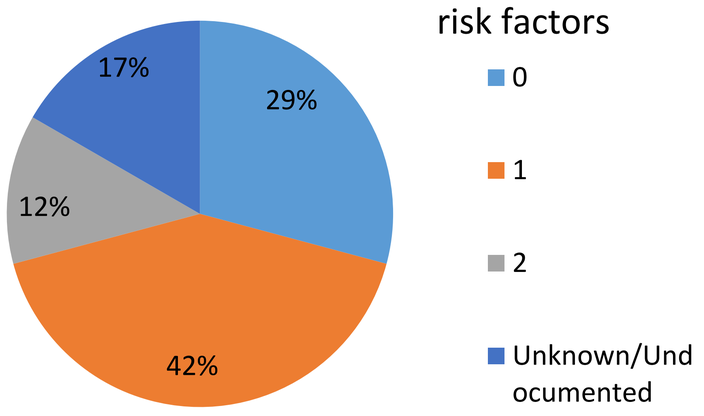
TB exposure risk for all LTBI referrals



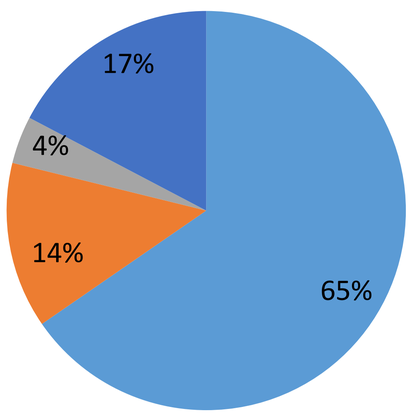
Chemoprophylaxis all LTBI referrals

75 of 163 patients referred for suspected LTBI received chemoprophylaxis, 26 with isoniazid (H) and 49 with rifampicin + isoniazid (RH).
Chemoprophylaxis was not used where LTBI was excluded or where the treatment risks were judged to outweigh the benefits.
Patients prescribed H monotherapy had more risk factors than those prescribed RH.

Isoniazid alone



Rifampicin and Isoniazid



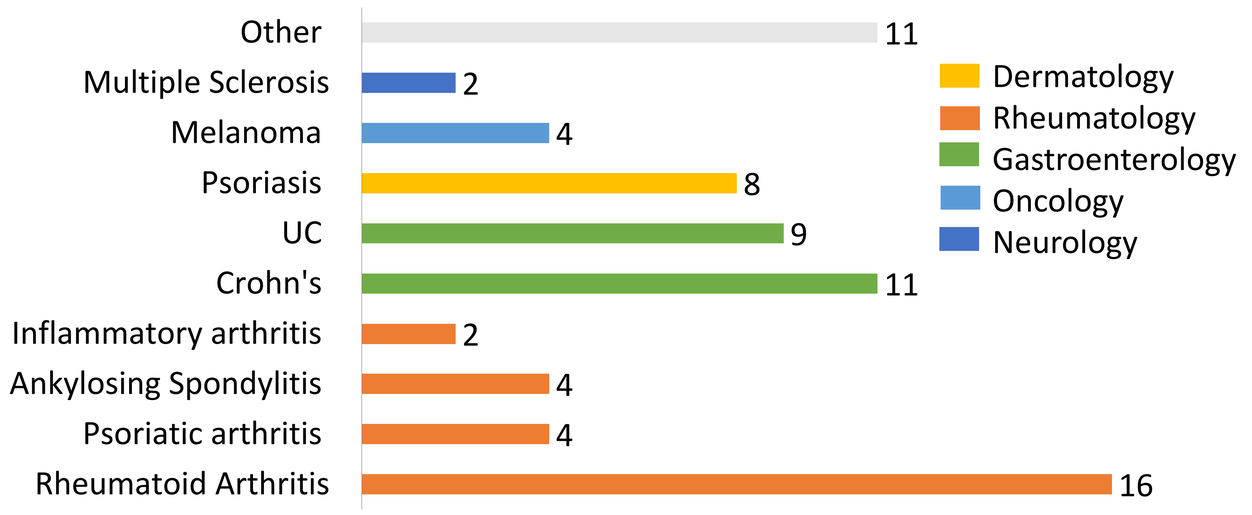
Pre-biological therapy LTBI cases

71 of 163 possible LTBI cases were identified through screening pre-biological Rx.

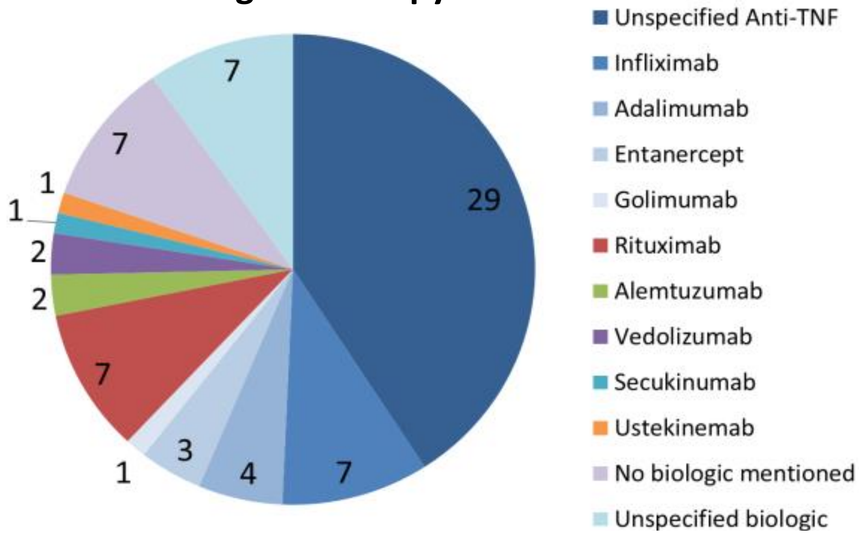
LTBI screening tools used pre-biological

- QuantiFERON-TB Gold Plus 71 (100%), Tuberculin skin test 0 (0%),
- Chest imaging: CXR = 60 (85%). CT thorax = 4 (5.6%).
- 54 (76%) had imaging within 30 days of QFN. 7 with no imaging had this performed in the TB clinic.
- 9/54 patients (17%) had imaging suggestive of active or latent TB infection (3 calcified opacities, 4 lymph nodes, 2 consolidation). None had active TB diagnosed and 4/9 (44%) then received LTBI chemoprophylaxis.
- No common theme emerged among those with no CXR.

Underlying inflammatory diagnosis requiring biological



Planned Biological Therapy



- 57/71 had biological therapy specified
- 44 (77%) were anti-TNF
- For 13 (23%) alternative biological therapy was planned

LTBI treatment pre-biological

- 36 (51%) were prescribed LTBI chemoprophylaxis; 17 H and 19 RH.
- RH was more likely to be used in:
  - Younger patients; median age 49 vs 58.5, p=0.26 (Mann Whitney).
  - Women (13/21) than men (4/15), OR 3.97 (95% CI 0.95 to 13.72, p=0.05, χ^2)
- 5 (14%) patients could not complete treatment, all were prescribed RH,
  - Drug intolerance = 3, Allergy = 1, deranged LFT =1.
- 1 patient intolerant to RH was subsequently intolerant of H monotherapy.

Summary and Conclusions:

- This clinic sees an even split of active & latent TB patients.
- Many cases referred through LTBI screening do not receive chemoprophylaxis when it is deemed unnecessary.
- TB exposure risk is often not documented. This may represent a clinician's lack of documentation of risk or a patient's genuine lack of awareness of an exposure risk.
- Risk factors for adverse effects of chemoprophylaxis were often not documented.
- 1 in 4 patients screened pre-biological therapy did not receive contemporaneous chest imaging before referral for LTBI.
- Documentation of planned biologic therapies was incomplete.
- A significant proportion of LTBI screened cases were for non-anti-TNF biologics.
- H and RH were used equally for chemoprophylaxis pre-biologic therapy.
- A large minority were intolerant of RH chemoprophylaxis
- Specialists using biological therapy underuse chest imaging and may be over-reliant on negative QFN to rule out LTBI.
- Standardised recording of exposure risk and treatment risk in LTBI case management could improve LTBI treatment decision making, H monotherapy appears to be better tolerated.

References:

1. Zhang Z, Fan W, Yang G, Xu Z, Wang J, Cheng Q, Yu M. Risk of tuberculosis in patients treated with TNF-α antagonists: a systematic review and meta-analysis of randomised controlled trials. *BMJ open.* 2017 Mar 1;7(3):e012567.
2. Ormerod LP, Milburn HJ, Gillespie S, Ledingham J, Rampton D, British Thoracic Society Standards of Care Committee. BTS recommendations for assessing risk and for managing Mycobacterium tuberculosis infection and disease in patients due to start anti-TNF-alpha treatment. *Thorax.* 2005 Oct 1;60(10):800-5.

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