Non-tuberculous mycobacterial infection:
Non-tuberculous mycobacteria (NTM) are commonly found in the sputum of patients with CF (USA prevalence 7 - 24%; increased in southern states). Prevalence increases with age. NTM are widespread in water and soil samples. There is no evidence of person-person spread. There are >125 species of NTM which may be separated into rapid growing mycobacteria (M. abscessus, M. chelonae, M. fortuitum) and the slow growers (most others including M. avium-intracellulare and M. kansasii). A few patients will grow >1 species. M. abscessus is emerging as a significant pathogen in CF.

Diagnosing NTM disease:
All patients with CF should be screened for NTM at Annual Review, at times of clinical deterioration and before Azithromycin is commenced. NTM may be isolated due to environmental contamination. Earlier theories of airways “colonisation” without infection, are unproven and should be viewed with suspicion. If NTM are identified in sputum samples, recent American Thoracic Society guidelines (AJRCCM 2007; 175:367; not specific to CF) recommend assessment of clinical, microbiological and radiological criteria.

Clinical symptoms:
Symptoms of NTM infection include cough, breathlessness, chest discomfort, haemoptysis, fatigue, weight loss and fever. These lack specificity in patients with CF, particularly when P. aeruginosa and S. aureus are also present. Treat for conventional CF respiratory pathogens first.

Microbiological:
At least 2 positive culture results from at separate expectorated sputum samples, or 1 Positive bronchial lavage culture or granulomata on transbronchial lung biopsy with positive BAL or sputum culture.

Radiological:
High Resolution CT scan often show multiple small, potentially cavitating nodules in addition to multi-focal bronchiectasis, which may allow discrimination from changes due to CF alone. If patients do not meet criteria for treatment (eg single isolated NTM culture or clinically stable), they should be kept under close microbiological surveillance. Treatment of M. abscessus should be considered even when patients with CF are apparently clinically stable in view of the increasing evidence of damage caused by this NTM.

Suggested Treatment:
- M. abscessus
  - Initial treatment - 2-8/52 until clinical response:
    - IV Amikacin 30mg/kg od - 2000mg max - or 10mg/kg tds. Levels sent to Bristol.
    - IV Imipenem 500mg qds.
    - PO Clarithromycin 500mg bd.
  - Maintenance therapy:
    - Nebulised Amikacin - upto 500mg bd.
    - PO Clarithromycin 500mg bd.
    - PO Ethambutol 15mg/kg.
Second line agents to consider:
- IV Cefoxitin 3g qd
- IV Tigecycline 100mg bd loading, then 50mg bd.
- PO Linezolid 600mg bd - 1/12 course as SEs.
- PO Moxifloxacin 400 - 800mg.
- PO Minocycline 100mg bd.
- ??? Nebulised G-Interferon ??? surgery

M. avium-intracellulare complex:
- Maintenance therapy:
  - PO Alarithromycin 500mg bd or PO Azithromycin 250mg od - 500mg 3x/week when stable.
  - PO Ethambutol 15mg/kg od
  - PO Rifampicin 450-600mg od or PO Rifabutin 150-300mg od

- Second line agents to consider:
  - Nebulised Amikacin - up to 500mg bd.

- Third line agents to consider:
  - PO Moxifloxacin 400mg.
  - PO Linezolid 600mg bd - 1/12 course.

Other NTM species see ATS guidelines:
- Laboratory testing of NTM for sensitivity to Clarithromycin is recommended as this influences choice of antibiotics. Resistance to macrolides is associated with worse clinical outcome. In vitro resistance to other antibiotics do not reflect response of M. abscessus and MAC in vivo.
- Eradication is difficult & requires multiple antibiotics. The addition of a third antibiotic such as Ethambutol may not increase mycobacterial killing, but does reduce development of antibiotic resistance.
- Continue antibiotic treatment until consistently culture negative for 12/12.
- Persistence of M. abscessus may prevent lung transplantation. Data suggests that other NTM should not be considered exclusion criteria for transplantation.
- Discussions with local microbiologists about indentifying and treatment of organisms is helpful.

References:
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