An Update on Atypical Mycobacteria

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DISCLOSURES?

NONE

JOKES?

PLENTY
1999
• Don’t get into strangers’ cars
• Don’t meet people from the internet

2019
• Literally summon strangers from the internet to get into their car
DIAGNOSIS (skin biopsy, left index finger):

MYCOBACTERIAL INFECTION (ACID FAST ROD-SHAPED ORGANISM) with associated suppurative and granulomatous inflammation, granulation tissue, foreign body reaction and fibrosis

ACID FAST STAIN confirms the presence of ACID FAST ROD-SHAPED ORGANISM keeping with a diagnosis of a MYCOBACTERIAL INFECTION
ACID FAST STAINS: Ziehl-Neelsen, Fite, Kinyuon’s

1. Mycobacterium tuberculosis
2. Mycobacterium leprae
3. Atypical mycobacterioses
4. +/- Nocardia
<table>
<thead>
<tr>
<th>Agent</th>
<th>Local</th>
<th>Systemic medications: alone or combined</th>
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</thead>
<tbody>
<tr>
<td><em>M. ulcers</em></td>
<td>For ulcers, surgical excision; local heat</td>
<td>Rifampin plus streptomycin, clarithromycin, and/or a quinolone (e.g. moxifloxacin, ciprofloxacin) for at least 4–8 weeks†</td>
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<td></td>
<td>(40°C); hyperbaric oxygen</td>
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<tr>
<td><em>M. marinum</em></td>
<td></td>
<td>Clarithromycin, minocycline &gt; doxycycline†, rifampin, ethambutol, trimethoprim–sulfamethoxazole; two agents for serious infections (e.g. clarithromycin + rifampin or ethambutol)</td>
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<tr>
<td><em>M. kansasii</em></td>
<td></td>
<td>Isoniazid (or clarithromycin) + rifampin + ethambutol ± pyridoxine; other options (depending on susceptibilities) include azithromycin, moxifloxacin, streptomycin and sulfamethoxazole</td>
</tr>
<tr>
<td><em>M. fortuitum</em></td>
<td>Surgical excision</td>
<td>Ciprofloxacin, ofloxacin, clarithromycin‡, trimethoprim–sulfamethoxazole, minocycline, doxycycline, at least two agents for serious infections</td>
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<tr>
<td><em>M. chelone</em></td>
<td>Surgical excision</td>
<td>Clarithromycin; for severe infections, combine clarithromycin with linezolid, imipenem, tobramycin, amikacin, doxycycline and/or ciprofloxacin (often resistant to latter two agents)</td>
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<tr>
<td><em>M. abscessus</em></td>
<td>Surgical excision</td>
<td>Clarithromycin or azithromycin + (for serious infections) amikacin, cefoxitin or imipenem</td>
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<tr>
<td><em>M. avium</em></td>
<td></td>
<td>Clarithromycin or azithromycin + ethambutol ± rifampin or rifabutin</td>
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<tr>
<td>complex</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>M. haemophilum</em></td>
<td>Surgical excision</td>
<td>Clarithromycin + rifampin ± ciprofloxacin or amikacin</td>
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<tr>
<td><em>M. scrofulaceum</em></td>
<td>Surgical excision</td>
<td>Isoniazid + rifampin, clarithromycin</td>
</tr>
</tbody>
</table>
Mycobacterium marinum

- Primary contact
- Aquatic environments
- Single lesion or sporotrichoid lymphocutaneous nodules
Mycobacterium avium complex

- AIDS patients
- Pulmonary infection m/c
- Disseminates to skin
M. abscessus, M. cheloneae, M. fortuitum = RGM

- Infection after trauma, surgery, or procedure
  - Liposuction
  - Implants
  - Tattoo, Acupuncture
  - Pedicures
  - Botox, Filler
  - CO2 Laser
Work-up for a suspected Atypical Mycobacteria infection

**TISSUE STUDIES**
- Fresh tissue culture
- AFB PCR identification

**LAB STUDIES**
- CBC
- CMP
- HIV
- PPD
- QuantiFERON-TB Gold
Fresh tissue culture

1. Fluorochrome smear
2. AFB culture

- Grow at 30 °C, 37 °C, and 42 °C
- 6-8 weeks

MYCOBACTERIA, CULTURE, WITH FLUOROCHROME SMEAR

MICRO NUMBER: 91046696
TEST STATUS: FINAL
SPECIMEN SOURCE: RT. LOWER LEG
SPECIMEN QUALITY: ADEQUATE
SMEAR: No acid fast bacilli seen.
RESULT: No Mycobacterium species isolated after 6 weeks incubation.
Acid-Fast Bacillus (AFB) Identification, Sequencing and Stain, Paraffin Block

Test code(s) 90870

Question 1. Why perform AFB PCR-pyrosequencing on paraffin-embedded tissue samples?

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis*, an acid-fast bacillus (AFB). TB is one of the most common diseases worldwide. This organism infects both compromised (eg, those with HIV infection) and noncompromised hosts. Rapid and accurate detection is important to prevent spread of the disease and for initiation of appropriate chemotherapy. Typically, TB infections produce a wide range of tissue changes including granulomatous inflammation. This inflammation may present as caseous necrosis, aggregates of epithelioid cells, and frequently multinucleated Langhans’ giant cells.

Normally, culture is essential for definitive diagnosis of AFB infections, including those caused by *M tuberculosis*, *M avium* complex, or *M marinum*. Sometimes, clinical lesions are biopsied and all the tissue is embedded in paraffin. When subsequent histological review reveals the presence of an AFB infection (AFB smear-positive tissue and/or presence of granulomatous changes), culture is no longer possible. But, identification of the AFB to the genus/species level can be performed directly from the fixed, paraffin-embedded tissue using pyrosequencing.

Question 2. What is pyrosequencing?

In contrast to traditional Sanger sequencing, pyrosequencing is a rapid method that is actually sequencing by synthesis. After amplification of specific 16S rRNA sequences using AFB PCR primers, short sequences of approximately 30-50 bases are identified and then compared to public or private databases to determine the AFB genus and species. Pyrosequencing is highly accurate for the identification of AFB.
Question 3. How sensitive is the PCR-sequencing technique for detecting AFB?

In vitro studies indicate that the PCR-sequencing assay requires as little as 100 AFB to be present in order to produce a positive AFB sequencing result.

Question 4. How rapid is the PCR-sequencing technique for detection AFB?

Normally, AFB culture can require up to 8 weeks for incubation. Results by PCR-sequencing may be available within the same week after submission of the paraffin block.

Question 5. Will antibiotic susceptibilities be available when PCR-sequencing detects an AFB on the paraffin block?

Currently, PCR-sequencing cannot assess antibiotic susceptibility. In most cases, antibiotic susceptibilities are performed on viable AFB recovered by culture.
TREATMENT WHILE YOU WAIT?

- Clarithromycin 500mg PO QD
- +/- a tetracycline

| Table III. Antimicrobial susceptibility profile of nontuberculous mycobacteria isolates in our case series |
|--------------------------------------------------|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                                                  | M. abscessus group n = 32       | M. fortuitum complex n = 18 | M. marinum n = 14 | M. moriokaense n = 1 | M. neoaurum n = 2 | M. avium complex n = 2 |
| Amikacin                                         | 75.0% S (21) 25.0% I (7)        | 100% S (14)        | 100% S (3)       | 100% S (1)       | 100% S (2)       | No data          |
| Cefoxitin                                        | 82.8% I (24) 17.2% R (5)        | 6.7% S (1)         | 73.3% I (11)     | No data          | 100% S (1)       | No data          |
| Ciprofloxacin                                    | 3.4% I (1) 96.6% R (28)        | 93.3% S (14)       | 6.7% R (1)       | 100% S (1)       | 100% S (2)       | No data          |
| Clarithromycin                                   | 50.0% S (14)* 10.7% I (3) 39.3% R (11) | 20.0% S (3) | 13.3% I (2) | 100% S (1) | 100% S (1) | 100% S (2) |
| Doxycycline                                      | 100.0% R (11)                  | 33.3% S (1)       | 66.7% R (2) | 33.3% R (1) | No data | No data |
| Ethambutol                                       | No data                        | No data           | 100% S (3)      | No data         | No data         | No data         |
| Imipenem                                         | 69.2% I (18) 30.8% R (8)       | 33.3% S (5)       | 60.0% I (9)     | No data         | 100% S (1)       | No data         |
| Linezolid                                        | 3.6% S (1) 53.6% I (15) 42.9% R (12) | 61.5% S (8) | 15.4% I (2) | 23.1% R (3) | No data | 100% S (1) |
| Minocycline                                      | 100% R (27)                    | 7.7% S (1)        | 23.1% I (3)     | 69.2% R (9)     | 100% S (1)       | No data         |
| Moxifloxacin                                     | 100% R (11)                    | 100% S (5)        | No data         | No data         | No data         | No data         |
| Rifampin                                         | No data                        | No data           | 100% S (4)      | No data         | No data         | No data         |
| TMP/SMX                                          | 100% R (29)                    | 92.9% S (13)      | 100% S (4)      | 100% S (1)      | No data         | No data         |
| Tobramycin                                       | 50% S (1) 50% R (1)           | 100% S (1)        | No data         | No data         | No data         | No data         |

S, Sensitive; I, Intermediate; R, Resistant
PEARLS...

- Atypical mycobacteria are ubiquitous
- They are usually acquired through environmental exposure
- The microorganism is resistant to the standard levels of chlorination, therefore it can be found in tap water
- There have been no reports of spread via person-to-person contact
- You’re in for the long haul
- Get ID and your local TB clinic involved
- Sometimes it’s best to cut these out
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