Mycoplasma pneumoniae in community acquired pneumonias

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***Mycoplasma pneumoniae* is best thought of as a bacterium without a cell wall, a property that has important therapeutic considerations. It is an exclusively human pathogen. As most cases of human infection are either sub clinical or result in a relatively mild infection of the respiratory tract, infections with this organism are much more common in the community than people generally realize.[1]**

Epidemiology

An organism of worldwide prevalence, *M. pneumoniae* tends to cause sporadic illness throughout the year. In addition, in most countries, it has been noted that the infection rates tend to peak every 3 to 5 years as an epidemic.[2]

As these epidemics tended to involve schoolchildren and military recruits, the trend has been to associate this organism with these younger age groups. However, endemic illness (occasionally even epidemics) does occur at ALL ages. In particular, the incidence of mycoplasma pneumonia in the under fives seems to be increasing in most developed countries, possibly because of the increasing use of day care centers for the very young. In the elderly, it is second only to *S. pneumoniae* as a cause of community acquired pneumonia.[3,4]

The disease is transmitted person to person, by droplet infection. While patients with active disease are the ones most likely to transmit the illness, the organism may persist in the respiratory tract of asymptomatic carriers for long periods of time, even when these would have been active cases treated with antibiotics.[1] It is thought that such persons serve as a reservoir or carrier from which the disease is maintained within the human population. Re infection readily occurs.

The clinical illness

Apart from pneumonia, the organism is capable of causing upper respiratory tract infections, such as pharyngitis. Once again, as an etiological agent of sore throats, it is probably a much more common cause than it is usually given credit for. While mycoplasma infections may trigger off bronchospasm in chronic asthmatics, more recent evidence is suggesting that the organism can be a primary cause in the development of this chronic lung disease. In the future, it shall be interesting to see if the incidence of asthma goes up as children are exposed to the organism at ever-younger ages, for reasons explained above.

The pneumonic illness is typically a mild one, and sometimes referred to as the "walking pneumonia". Certainly, compared to the classical pneumococcal pneumonia, the onset is more gradual. Many adult patients will have little or no symptoms, yet physical and X-ray examination will show very definite signs of a chest infection. The disease tends to be more marked in children, possibly since, on their first encounter with the organism they would have no form of acquired immunity to give them at least partial protection against the disease.[5]

When symptoms are severe, these would usually be ascribed to an aggressive immune response to the infection, rather than the organism itself, which, with rare exceptions, does not spread beyond the mucosal epithelial surface.

Laboratory diagnosis

As the illness, both clinically and radiologically, is very non-specific, microbiological tests are essential to confirm the diagnosis. Over the years, various such tests have been developed:

1. Mycoplasma culture - apart from being laborious and expensive, and relatively insensitive[6] compared to DNA amplification techniques, there is also the problem of the organism persisting in the patient's respiratory tract for (in some cases) weeks or months after the acute episode. With all these drawbacks, it is not surprising to learn that most microbiological labs would never attempt to culture mycoplasma.
2. Antigen detection techniques - this has been tried using many different laboratory methodologies. Two examples would be direct immunofluorescence[7] and antigen capture enzyme immunoassay. In these cases, the already discussed problem of detecting a presence of the organism in a human carrier is compounded by the tendency of such tests to cross react with other non pathogenic mycoplasma which are normally present in the human respiratory tract. This low specificity, together with a low sensitivity means that they cannot really be recommended for use, especially now that superior molecular diagnostic techniques are available.

3. Molecular identification techniques - Labeled probes that target the non-amplified mycoplasma DNA, have been supplanted by the superior amplified technologies, and specifically PCR (polymerase chain reaction).[6] Its advantages include a high specificity (but beware the mycoplasma human carrier!), the ability to detect the organism's DNA or RNA (depending on the kit used) in preserved tissue, as well as the short turnaround time for completing the test and the fact that, at least theoretically, it should give a quicker result than an antibody test in a positive case.

On the other hand, the PCR test may turn negative very soon after the start of antibiotic treatment (in some cases, within 24 hours) while the antibody test will remain positive for a considerably longer period of time. Thus, the result of a PCR specimen taken after the start of antibiotic therapy has to be interpreted with caution. There have also been problems with false negative results, probably from the presence of reaction inhibitors present in the patient's upper respiratory tract.

At this stage, the mycoplasma PCR tests available are still in use as a research tool, rather than as a routine diagnostic method. Together with cost, this renders this technique not quite ready for widespread use.

In the light of all of the limitations mentioned above, it is not surprising that antibody testing is still the most commonly performed microbiological test to confirm suspected mycoplasma pneumonia.

4. Serology - Antibodies to *M. pneumoniae* would be expected to reach their maximum serum concentration 3 to 6 weeks after exposure. Bearing in mind that most cases of the illness would be associated with a relatively long incubation period (1 - 3 weeks), it can be expected that by the time most patients present to their doctor, an antibody response can usually be demonstrated.

In a primary infection (most likely in peadiatric age group), the specific IgM antibodies would start to appear within one week of the infection. IgG antibodies would typically show up two weeks later. Where reinfection occurs (most adult cases) the patient may show up only IgG immunoglobulins, without ever exhibiting an IgM response.[8] On the other hand an IgM response has occasionally been shown to persist for months or even years following the primary infection! This sometimes makes the proper interpretation of the patient's IgM + IgG response to a mycoplasma infection, and specifically when it comes to distinguishing a past from a recent infection difficult.

In the future, one other possible diagnostic tool is the detection of a specific IgA response, which preliminary studies suggest might be the most reliable indicator of a recent mycoplasma infection than both IgG and IgM antibodies.

In view of the above, it would appear prudent to test suspected cases both of IgG and IgM antibodies simultaneously, and then repeat the tests 2 to 3 weeks later to detect any changes in titre.

Treatment

The organism is exquisitely sensitive to the macrolides and related compounds (azalides and ketolides), as well as the newer respiratory quinolones. As such, it is no surprise to find these antibiotics forming the mainstay of treatment.

Treatment duration varies according to the agent selected: in most cases it would hover around the 10-day mark. However, there are those who would insist that cases of mycoplasma pneumonia should be treated for at least 2 to 3 weeks.

Over the years, various antibiotics have been successfully used to treat mycoplasma pneumonia in the published literature. However, one should point out that in some of these studies, the number of patients involved where quite small.

These have included:

- Clarithromycin and Erythromycin for 10 or 14 days[9]
- Telithromycin for 7 to 10 days[10]
- Azithromycin for 3 or 5 days[11]
- Moxifloxacin for 7 to 14 days[12]
- Levofloxacin for 7 to 14 days[13]

This is not a comprehensive list of all studies done on the subject. In fact, one would expect all macrolides and fluoroquinolones to be effective against *M. pneumoniae.* Furthermore, tetracyclines should also work against this organism.[14]

Curiously, in one small comparator study, co-amoxiclav, together with various other beta lactam antibiotics[12,13] appeared to achieve a very good clinical cure rate after 7 to 14 days of treatment, despite the fact that this antibiotic is definitely inactive against *M. pneumoniae.* As described above, most of these "walking pneumonias" are usually mild and self-limited, and the majority of patients can be expected to make a full recovery even in the absence of antibiotic treatment.

Vaccine research

Attempts to develop a *M. pneumoniae* vaccine have been going on for many years, unfortunately without success. In a way this is not surprising, considering that some individuals who succumb to the infection, and develop an immune response to the organism may still get reinfected later on in their lives. After a number of failures with different experimental vaccines, interest in the subject appears to be low at the moment.

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