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Case Report

A mixed infection with macrolide resistant Mycoplasma Pneumoniae and Streptococcus Pneumoniae causing bilateral empyema in an immunocompetent child

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Abstract

Mycoplasma pneumoniae (MP) is the commonest respiratory pathogen and is a frequent cause of community acquired pneumonia (CAP) in children more than five years. Rarely MP may cause a severe and complicated respiratory disease. The drug of choice for MP infection is macrolide antibiotics and recently macrolide resistant strains of MP have been reported in Asian counties. Here we report a case of eight years immunocompetent boy who developed bilateral empyema due to MP and streptococcus pneumoniae as a mixed infection and MP turned out to be macrolide resistant which was successfully identified and treated well with non-macrolide antibiotic with good outcome.

Keywords: Mycoplasma pneumonia, Macrolide resistance, Empyema.

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1. Introduction

Mycoplasma pneumoniae (MP) is the commonest respiratory pathogen causing respiratory and extra respiratory manifestations especially among school going children and is a frequent cause (20-40%) of community acquired pneumonia (CAP).[1] There has been resurgence of cases MP pneumonia post covid in 2024 worldwide including India.[2] The clinical findings are often less severe than chest radiograph picture and hence the term 'walking pneumonia' is often used to describe CAP caused by MP.[3] Rarely MP may cause a severe and complicated respiratory diseases like lobar consolidation, lung abscess, necrotizing pneumonia, and acute respiratory distress syndrome.[4,5]

Historically, the drug of choice for MP infection are macrolide antibiotics and commonly used are either clarithromycin or azithromycin. Recently macrolide resistant strains of MP have been reported in Asia especially countries like Japan and China.[3]

Here, we report a case of eight year immunocompetent boy who developed bilateral empyema due to MP and streptococcus pneumoniae as a mixed infection and turned out to be macrolide resistant Mycoplasma pneumoniae (MRMP) which was successfully recognized earlier and treated well with injection ceftriaxone and non-macrolide antibiotic like levofloxacin with good outcome.

2. Case Report

An eight year old boy was admitted in the pediatric intensive care unit with chief complaints of high-grade fever and cough for 5 days while acute breathlessness for one day. On examination he was tachypneic (RR 50breaths/min with signs of respiratory distress in the form of indrawing), bulging on left side of chest with intercostal fullness, dull note on percussion, decreased air entry and vocal resonance on the left side and bronchial breathing in the left interscapular region. The chest X-ray found to have homogenous opacity on the left side and lung ultrasound

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showed 1250-1300ml of fluid collection in the left pleural cavity [**Figure 1**]. His complete blood counts showed neutrophilic leukocytosis and raised ESR and C reactive protein. The patient was hemodynamically stabilized by intravenous fluids, oxygen support along with injection Ceftriaxone and injection Vancomycin as per hospital antibiotic policy. An urgent intercostal drainage tube was put in left fourth intercostal space in midaxillary line by a pediatric surgeon. The pleural fluid analysis showed exudative (purulent in nature, acidic, proteins 4.2 grams, low sugar, pleural fluid to serum LDH ratio more than 0.7 and total cells 21000cu/mm with 96% neutrophils and proteins 4.1 grams) in nature with CBNAAT negative and culture showed streptococcus pneumoniae which was sensitive to ceftriaxone. Before admission he was started with oral clarithromycin 15mg/kg/day for 4 days by local pediatrician and we continued the same also. The child was better hemodynamically, but had persistence of mild fever and remained less tachypneic and reduced work of breathing after 48 hours.

On day 4 of hospital stay, child became increasingly tachypneic and increased work of breathing with high grade fever and reduced air entry now on right side. He was subjected to urgent bedside Xray chest which showed new homogenous opacity on right side and USG chest revealed bilateral fluid collection of 1000 ml on the right and 150ml on the left side [**Figure 2**]. A second intercostal drain on right side in third intercostal space in mid axillary line was performed by pediatric surgeon. The right-sided pleural fluid analysis showed again exudative (purulent, proteins 4.0 grams, low sugar, pleural fluid to serum LDH ratio more than 0.6 and total cells 15000cu/mm with 92% neutrophils) in nature and repeat CBNAAT was negative. The CT scan chest showed bilateral pleural loculations with effusion.

Considering bilateral empyema in this patient who was previously normal, we had even thought of primary immunodeficiency and we had sent immunological workup which turned out to be normal. Another possibility was atypical organism infection like MP as patient developed empyema on opposite side in-spite of having good anti-streptococcal antibiotic coverage. So, we sent for serum Mycoplasma IgM antibody level and which turned out to be positive. [>27 NTU (More than 11 is considered as positive)] [**Figure 3**]. The patient remained febrile in-spite of clarithromycin therapy, and, also developed new empyema on opposite side we considered it as MRMP and changed the antibiotics from injection Vancomycin to injection Levofloxacin as an anti-mycoplasma drug (10mg/kg/day) and stopped oral clarithromycin.

This child also needed intrapleural fibrinolytic (streptokinase) therapy and intensive chest physiotherapy. The intercostal chest drains on both sides were removed after 7 days. The child responded well to injection Ceftriaxone and Levofloxacin for 21 and 10 days respectively and discharged after total one month of hospital stay with bilateral good air entry.

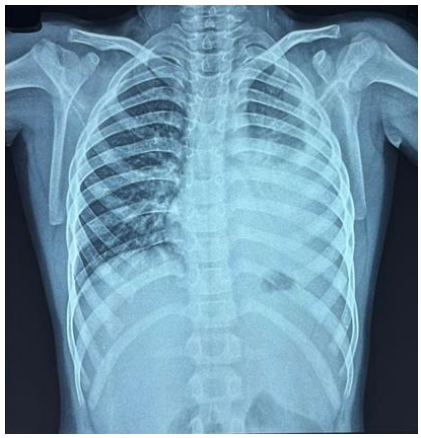


Figure 1: Showing empyema on left side.

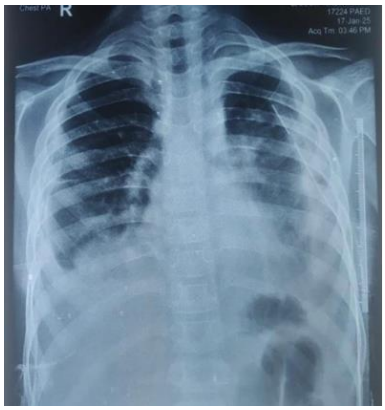
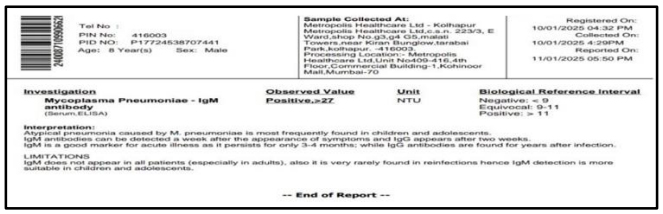


Figure 2: Showing new development of empyema on right side with intercostal drainage tube on left side.



Investigation	Observed Value	Unit	Biological Reference Interval
Mycoplasma Pneumoniae - IgM antibody (Serum,ELISA)	Positive,>27	NTU	Negative: < 9 Equivocal: 9-11 Positive: > 11

Interpretation:
Atypical pneumonia caused by M. pneumoniae is most frequently found in children and adolescents.
IgM antibodies can be detected a week after the appearance of symptoms and IgG appears after two weeks.
IgM is a good marker for acute illness as it persists for only 3-4 months; while IgG antibodies are found for years after infection.
LIMITATIONS
IgM does not appear in all patients (especially in adults), also it is very rarely found in reinfections hence IgM detection is more suitable in children and adolescents.

-- End of Report --

Figure 3: Showing mycoplasma pneumoniae IgM report

3. Discussion

Mycoplasmas are ubiquitous and the smallest bacteria that can survive alone in nature and was first isolated in cattle with pleuropneumonia in 1898. In 1938, Reimann described the first case of mycoplasma pneumoniae in human and coined the term primary atypical pneumonia.[1]

Despite having pneumonia, the chest examination may not have significant findings in early phase and might develop scattered rales, wheeze or both later and with proper treatment the pneumonia resolves without any serious complications.[3] However, most of the MP infections have mild presentations but still can cause severe complicated pneumonia in children and has recently been associated with

acute chest syndrome in sickle cell anemia.[5] The clinical and radiological manifestations of complicated pneumonia like empyema are mainly modulated by the immunological, physiological, and cardiopulmonary status of the host. The pathogenesis of empyema is still not clear in MP infection but probably its an immunologic reaction causing lung damage.[7]

The laboratory diagnosis of MP infection depends on isolation of the organism by culture or by polymerase chain reaction or serologic diagnosis by enzyme immunoassay.[8] In our patient Mycoplasma IgM came strongly positive. The limitation of this test incudes its rise after 7-10 days and may remain elevated for months hence there is a concern for its sensitivity and specificity. Even we could not able to do repeat test for confirmation of twofold rise in titers which is more diagnostic due to financial constraints.

A mixed infections with both typical and atypical organisms may occur in about 10-20%. The multiple simultaneous infections might interfere significantly with pulmonary defense function and might cause pneumonia. MP also exerts a toxic-effects on ciliated human epithelium and invites other agents to invade and infect. Whether, one of the pathogens serves as a co-pathogen that facilitates the penetration of the second pathogen which acts as pathogen or will both pathogens cause CAP, by an additive, synergistic or perhaps even antagonistic clinical expression of both remains unclear.[5] Similarly, our patient had mixed infection due to streptococcus pneumoniae and MP organisms which was macrolide resistant.

The guidelines suggest MRMP infections should be suspected in patients with severe infections not responding to macrolide therapy within the first 48 to 72 hours of treatment especially if they have history of exposure to macrolide.[3,9] Similarly, in our patient who was on oral clarithromycin and still developed bilateral complicated empyema. MRMP present therapeutic challenge while the clinical significance of MRMP infections has not been completely elucidated. However, if MRMP is suspected, a switching to non-macrolide antimicrobial regimen such as doxycycline or levofloxacin might be prudent. Considering the age of the child in our patient we decided to start injection Levofloxacin instead of Doxycycline The exact mechanism of macrolide resistance in MP infections is unclear however it usually occurs due to point mutation in domain V of the 23S subunit of ribosomal RNA and is associated with widespread use of macrolides. The commonest mutations are A2063G and A2064G.[7]

4. Conclusion

Complicated respiratory tract infection like empyema may be caused by MP infection alone or as a mixed infection with typical organisms like streptococcus pneumoniae. Also, one need to consider MRMP infection if patient is not responding to macrolides and should be treated with non-macrolide antibiotic earlier like either levofloxacin or doxycycline.

5. Source of Funding

None.

6. Conflict of Interest

None.

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