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Mycoplasma pneumonia infection in Cancer Patients at a Regional Cancer Center, South India

(Original Article)

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Abstract

Purpose: *Mycoplasma pneumoniae (M.pneumoniae) forms one of the major causes of the community acquired respiratory infections in paediatric and adult populations. A prospective study was done to evaluate the frequency of M.pneumoniae infections in cancer patients at a regional cancer hospital in South India.*

Materials and Methods: *Blood was sampled from 65 adult patients with confirmed solid and haematological malignancies during febrile episodes. Serological estimation for IgM antibodies to M. pneumoniae was done using IgM enzyme – linked immunosorbent assay (ELISA) kit (EuroImmun, Germany). Thirty age and sex matched normal healthy adult subjects served as control.*

Results: *The breakup of the patients was as follows: Of the 65 patients 51(78.46%) were males and 14 were females (21.53%). Of the total number studied 51(78.46%) had solid tumor while 14 (21.53%) patients had haematological malignancy. Patient who received chemotherapy alone were 18 (27.69%) radiotherapy 14 (21.53%);surgery 10(15.38%); chemotherapy and radiotherapy16(24.61%); chemotherapy and surgery 3(4.61%); radiotherapy and surgery 3 (4.61%); chemotherapy and radiotherapy and surgery1(1.53%). Only one female patient of squamous cell carcinoma post cricoid had IgM antibodies to M. pneumoniae. Two of the 30 control sera were also positive for IgM antibodies to M. Pneumonia*

Conclusion: *From our study we inferred that the frequency of M.pneumoniae infections amongst cancer patients at our centre is infrequent and low. However, detection of IgM antibodies by serological assay is not the only ideal test to know the true frequency of M.pneumoniae infection.The actual frequency could be assessed by simultaneous detection of M.pneumoniae DNA in the sputa along with detection of IgM during febrile episodes .*

Keywords: *M.pneumoniae, Immunocompromised, IgM ELISA, Cancer, Solid tumors, haematological malignancy.*

INTRODUCTION

Mycoplasmas are primarily extracellular mucosal pathogens coexisting in the epithelial cells of respiratory tract of the host. *Mycoplasmal* infection is transmitted through aerosols from person to person in close contacts as in schools, military barracks and institutions. Previously thought to cause acute, self-limited disease primarily in persons between 6 and 21 years of age [1] is now the cause of atypical pneumonia in 20% to 25% of all age groups and to persist in certain persons for weeks to months resulting in prolonged reduced pulmonary clearance and airway hyperresponsiveness[2,3] to severe occasionally fatal pneumonia[4]. Atypical pneumonia is caused by only three bacteria *Chlamydophila pneumophilia (C. pneumophilia), Legionella pneumophila (L.pneumophilia),*and *M.pneumoniae* while gram negative bacteria *E.coli, Pseudomonas, Klebsiella* are frequent eitiological factors of pneumonia besides the gram positive bacteria *Staphylococci* , *Streptococcus pneumonia* and *Pneumocyctis jeroveci* and fungi.[5] The differential diagnosis for atypical pneumonia besides bacteria, viruses, and other unusual infectious agents are non-infectious etiologies such as haemorrhage, metastatic disease and pulmonary embolism.[6]

We undertook a prospective study to know the frequency of *M. pneumoniae* infection by detecting IgM antibodies in adult cancer patients at our hospital, a Regional Cancer Institute, South India.

INSTITUTE ETHICAL CLEARANCE APPROVAL

The study was approved by Medical Ethics committee of Kidwai Memorial Institute of Oncology (KMIO), Bangalore. Informed consent was taken from each patient recruited into the study group. Clinical data, including gender, age, first day of illness, antibiotic usage, and the presence of underlying malignancy whether on chemotherapy or receiving radiotherapy was recorded for every patient.

MATERIALS AND METHODS

Sixty five patients registered at KMIO, a regional cancer centre for the diagnosis and treatment of cancers in South India between the period with haematological malignancies and /or solid tumors presenting with fever and with clinical suspicion of pneumonia formed the study group. Thirty age and sex matched healthy subjects were included as controls. Sera were collected from the study group, prior to antibiotic treatment and during the febrile episode. All patients were HIV, HBsAg and HCV were nonreactive and negative.

Sera of study and control group were analysed for IgM antibodies to *M.pneumoniae* using commercial Enzyme Linked Immunosorbent Assay (ELISA) kits (EuroImmun, Germany). Culture of *M.pneumoniae* from sputum or bronchoalveolar washings was not attempted.

RESULTS

Out of the 65 patients only one female patient had IgM antibodies to *M.pneumoniae* in her blood as analyzed by ELISA. The patient was a 45 year old female diagnosed with squamous cell carcinoma post cricoid–grade II, Stage IV and while on the 9th day of first cycle of chemotherapy developed high grade fever with mild productive cough where a clinical diagnosis of aspirated pneumonitis was made. Sputum culture yielded heavy growth of *E.coli* sensitive to Amikacin, cefaperazone and sulbactum, Gentamicin, Imipenem, Meropenam, blood culture did not yield any bacterial pathogen isolated. Chest x-ray had signs of pneumonitis. The patient was subsequently treated empirically with injectable antibiotics viz. amikacin and cefaperazone and sulbactum combination. She responded to the antibiotics and recovered from pneumonitis. Blood of two control subjects were also positive for M.*pneumoniae* IgM antibodies. Other relevant details were not obtained from the control study group.

Illustration of Solid tumors and Haematological malignancies treatment

Treatment wise distribution of the Seventy Solid tumors and Haematological malignancies who received CT,RT, CT/RT, SURGERY, SURGERY /CT, SURGERY/RT,CT/RT,SURGERY									
Males Female	RT only	CT only	CT/RT	Surgery	CT/Surgery	RT/Surgery	CT/RT/Surgery		
Solid tumors	38	16	11	8	17	11	3	____	1
Haematological malignancies	15	1	1	11	2	1	_____	3	1

DISCUSION

Pulmonary infections are the most common cause of mortality and morbidity in the immunocompromised host[6,7]. Data and literature on *C. pneumoniae, L. pneumophila and M. pneumoniae* infections in patients with cancer is limited. Pneumonias due to *M. pneumoniae* can be a significant cause of hospitalisation especially in elderly population and immunocompromised patients[13.] Frequency of nonspecific respiratory infections due to *M. pneumoniae* is varied and usually missed therefore studies on atypical pneumonias due to *M.pneumoniae* in cancer population is needed to establish the prevalence to avoid morbidity. Diagnosis of *M.pneumoniae* in cancer patients are compliment fixation tests, serological assays with concomitant simultaneous detection of *M.pneumoniae* DNA in the sputa of febrile patients, molecular techniques and fibreoptic bronchoscopy and its associated procedures as the open lung biopsy,or transtracheal aspiration and analyses of brushings, washings,and biopsy specimens[5].

Literature on the usefulness of serological diagnosis of *M. pneumonia* in immunocompetant patients are done extensively. The appearance of *M.pneumoniae* IgM antibodies is inconsistent among adolescents, adults and the elderly with respiratory infections partly because the majority of these infections are re-infections[8]while serological tests are the only means by which *M.pneumoniae* infections are diagnosed on a wide scale and this method has a number of limitations[9]. In another study Matti E.W et al observed that detection of specific IgM antibodies was an accurate and cost-efficient tool for the diagnosis of *M. pneumoniae* pneumonia in children[10] while Anna et al proved the use of polymerase chain reaction was superior to serology for diagnosing acute M.*pneumoniae* infections during the first two weeks after onset of illnes in paediatric and adult population[11].

Many studies mention PCR is a highly sensitive diagnostic tool versus the serological assays for the detection of *M. pneumoniae* but with a small percentage of false positivity.

Lei Zhang[9] et al in their systemic review and meta-analysis suggest commercial PCR tests having superiorities in diagnosing *M. pneumoniae* infections but yet cannot replace serology.

In a prospective cohort study by[12] Ligia S. C. F. et al on non-atypical pathogens,state that severe pneumonia is associated with high mortality rates in cancer patients. A relatively low rate of multi resistant pathogens is observed and severity of illness and organ dysfunction seems to be the best predictors of outcome in this population[12]

Two studies so far have reported on *M. pneumonia* infection in cancer patients by serological diagnoses.

One study by Srinivasan A[14] et al in on respiratory pathogens in paediatric cancer population showed that out of 253 cancer children 3 were positive for *M. pneumonia* and diagnosis was made by using multiplexed-polymerase chain reaction. Another report by Carlos R.P. 1991[15] et al. established the diagnosis for the persistent pneumonia in a patient of Ewing's sarcoma as *M. pneumonia* by culturing BAL fluid. This is the only report where in *M.pneumonia* has been documented by culture in an adult immunocompromised patient. And mention that despite the frequent occurrence of *M pneumonia* in the school-age and young adult

population, M. pneumoniae is rarely considered in the immunocompromised host Carlos R.P. 1991[15]

An important mention by Riitta Ra¨ty[9] specify that sample type is crucial for diagnoses of *M.pneumoniae* in comparing sputum, nasopharyngeal aspirate and throat swabs by PCR.

In our study the finding of *E.coli* in sputum culture could be a coinfection and the primary source from the throat presenting as mild lower respiratory tract infection as pneumonia due to *E.coli* was absent. Our study subject had significant pneumonitis clinically and no history of chronic obstructive pulmonary disorder or chronic bronchial asthma.

Atypical *M. pneumoniae* infection if present in the cancer patient maybe over seen in the context of underlying disease or to prior vigorous antibiotic regimens, protocol or due to lack of specific laboratory tests or to wrong sample type. However underlying cancer disease may alter or mask the respiratory clinical signs. Atypical pneumonia is fairly common in patients with immunosuppression due to chemotherapy or after organ transplantation[16]

Positivity percentage for *M. pneumoniae* antibodies results are low when serological diagnosis of convalescent sera are considered in cancer patients during chemotherapy. The very low seropositivity to IgM antibodies to *M. pneumoniae* in our study may actually be truly representing the frequency of *M. pneumoniae* infection in the patient population at our center or alternatively, there could have been cases of M. pneumonia which were reinfections. Hence, the true frequency of *M.pneumoniae* infection would be known only after assessing either the presence of *M.pneumonia* antigen or the DNA of the infectious agent.

Despite its drawbacks for use with immunosuppressed persons who are unable to mount an antibody reponse serological diagnosis of *M.pneumoniae* respiratory infections has long been the cornerstone of *M.pneumoniae* for epidemiological studies because of the relative lack of sensitivity and time-consuming nature of culture[17].

Early detection of *M.pneumoniae* in cancer patients with fever and pulmonary infiltrate will help in cost effectiveness of emperic therapy and shorten the duration of hospital stay though immunosuppressed persons with established *M.pneumoniae* infection may lack pulmonary infiltrates[17]. *M.pneumonia* must be considered as a differential diagnosis in pulmonary infiltrates in a large scale setting as in our regional cancer centre where the near maximum patient load of diagnosed cancer patients undergo treatment. Combined polymerase chain reaction tests and serological assays for detection of both low avid IgG and IgM *M.pneumoniae* antibodies would be helpful to know the actual prevalence of the infection in cancer patients.

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