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Case Report of Acute Myocarditis due to Mycoplasma Pneumoniae in a Healthy Adolescent in Saudi Arabia

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Abstract: ***Mycoplasma pneumoniae (M. pneumoniae) causes respiratory tract infections in adult and children. Bronchopneumonia and Tracheobronchitis are the commonest clinical symptoms with M. pneumoniae infection. Complications due to this infection are unusual. Cardiac involvements are very rare and most of the reported cases were in adults. Non-respiratory illness can be explained by the frequency of cross reactions between human antigens and M. pneumoniae. Here we are presenting a case of Mycoplasma pneumoniae in a healthy adolescent associated with acute sever myocarditis according to 2013European Society of Cardiology (ESC) position statement criteria.***

Keywords: Mycoplasma pneumonia, acute Myocarditis, Mycoplasma diagnoses IGA

1. Introduction

Mycoplasma pneumoniae is a frequent cause of upper and lower respiratory tract infections affecting all age groups [1-2]. It is still the most common atypical cause of community acquired pneumonia [3]. Although it is highly transmissible, most infections caused by this organism are relatively minor [4]. Mycoplasma pneumoniae has been associated with a variety of extra-pulmonary diseases, as many as25 % of patients infected by Mycoplasma pneumoniae may develop extra pulmonary manifestations [3]

Among these extra-pulmonary complications skin or mucosal involvement are the most common, while cardiac and central nervous involvement are still very rare to happen [5.6.7]. Cardiac involvement, including pericarditis, cardiac tamponade, myocarditis, and endocarditis, is rare but well documented, and the reported cases in the literatures were mainly in adults [8]. A review by Paz and Potasman of 21 cases of Mycoplasma associated carditis identified the mean age of patients was 33 years [9]. The effects ranged from mild or asymptomatic conditions to fatal illness [10]. Many patients with cardiovascular manifestations do not have concurrent pneumonia [6].Extra pulmonary involvement in Mycoplasma infection was explained by different theories [1, 2, 3]. Culturing the organism is very difficult because it is a wall-less organism, so investigators rely on clinical manifestations along with serology for a definitive diagnosis.

2. Case History

A 15 year old boy with past medical history of familial hypoparathyroidism presented to the Emergency Department with history of documented fever 39^{o}C, vomiting, abnormal jerky movement, skin rash and lethargy for 4 days. The patient was admitted and treated with Ceftriaxone, Vancomycin and Acyclovir as a case of suspected meningitis. On the second day of admission, the patient developed shortness of breath at rest (NYHA 4), cough, fever 39.4^{o}C and lethargy became more obvious. On examination *hemodynamically*stable.S3 presented upon cardiovascular examination, bilateral basilar crepitations. Petechial rash was observed over extremities and upper back with no meningeal signs. Blood test results showed hemoglobin of 11.5gm/dl, white blood cell count was 10.4/micro L with neutrophilic count of 8.7/micro L, platelets 121/ micro L, alanine aminotransferase was 42 U/L, aspartate aminotransferase was 29 U/L, total bilirubin was 22.8 micromole/L, creatinine kinase (CK) was 1380 IU/L, lactate dehydrogenase was 528 U/L, B type natriuretic peptide 2623pg/ml, erythrocyte sedimentation rate 84, C-reactive protein was 424.8 mg/L, procalcitonin 11.9Mycoplasma pneumonia IgG ++20 AU/ml, IgA+11.3 AU and IgM <10 Au/ml Serology for viral infections was negative (i.e., Human immunodeficiency virus, Epstein-Barrvirus, dengue, measles, influenza A and B, and cytomegalovirus).Malaria antigen test and serology as well as Brucella antibodies were negative. Cerebrospinal fluid analysis showed white blood cells 40 per cm (polymorphonuclear leukocytes 52%, mononuclear cells 48%), red blood cells 10 per cm, and CSF PCR multiplex was negative. Chest X ray identified prominent

cardiomegaly with progressive opacity over both lower lungs. Electrocardiogram (ECG) showed Sinus tachycardia, Prolonged QT and incomplete RBBB. ilated left ventricle with moderate systolic dysfunction with ejection fraction of 35-40% along with moderate mitral regurgitation were identified through Echocardiography. On the basis of the reported findings, acute myocarditis was the diagnosis. Upon admission, the patient received ceftriaxone 2gm every 12 hour, vancomycin 1g every 12 hour and acyclovir 10mg/kg every 8 hour as a case of meningitis. However, the respiratory symptoms did not improve. Therefore, we was started on doxycycline 100mg every 12 hour and decreased the dose of ceftriaxone to 1gm q24hour on the second day of admission, the patient was started on intravenous diuretic (furosemide 40mg intravenously every 12 hour). On the fourth day of admission, the respiratory symptoms improved significantly with improvement in laboratory markers. On the eighth day, cardiomegaly and opacities improved on chest x ray. Furthermore, ejection fraction based on echocardiography improved to 52.6% along with mild eccentric mitral regurgitation. On the fifteenth day, the patient was discharged without sequelae with procalcitonin of 0.2 and white blood cells of 4.2 (Tables 1, 2, 3).

Table 1: Laboratory parameters

Variable	Day 1	Day 3	Day10
Hgb (gm/dl)	11.5	10	11.7
WBC (micro L)	10.4	13.7	6.6
Platelets (micro/L)	121	209	663
Procalctonin (micro/L)	11.9 (Day 2)	7.90	0.20 (Day11)
CRP (mg/L)	424.8	288	13.3 (Day 11)
Creatine Kinase (IU/L)	246	1380	
Lactate Dehydrogenase (U/L)	528	409	
Troponin I (pg/ml)		98.3	
BNP (pg/ml)		2623	1559 (Day4)
ALT (U/L)	42	24	24
AST (IU/L)	18	39	20
Albumin (g/L)	34	27	34
GGT (IU/L)	88	54	46

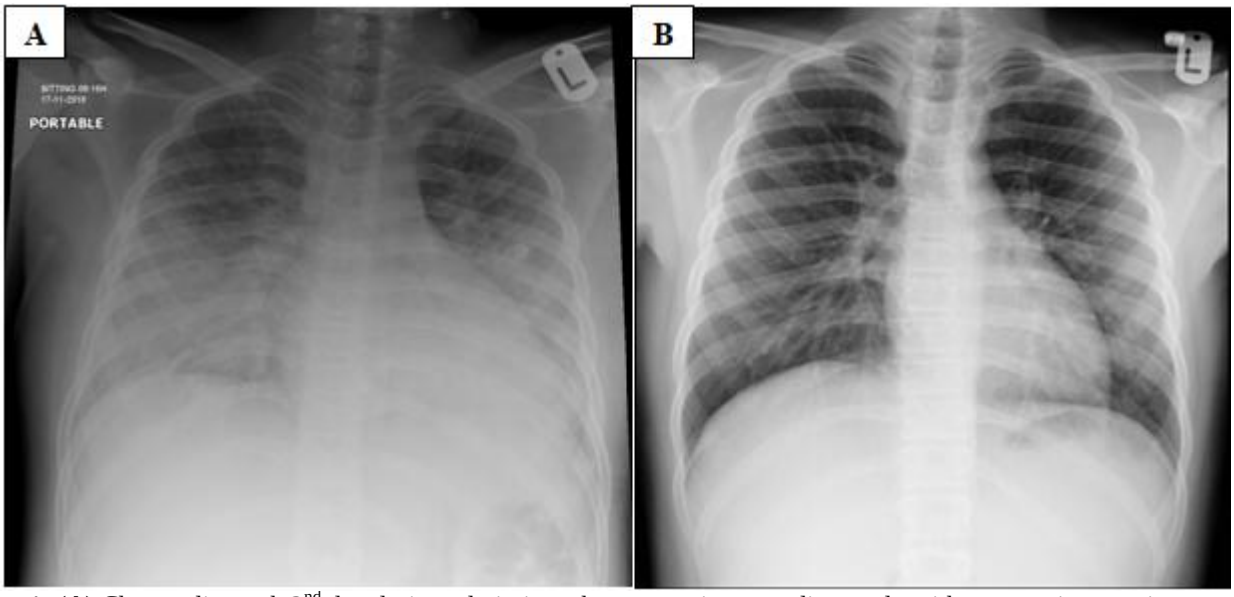
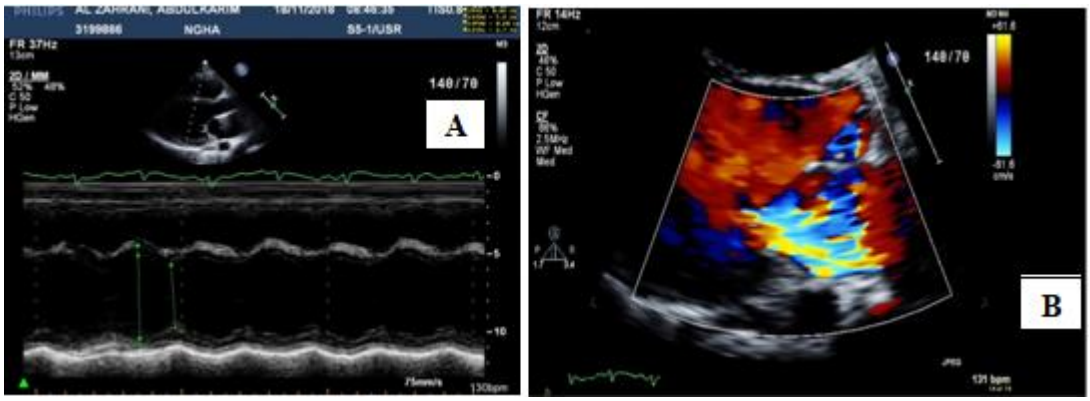


Figure 1: (A) Chest radiograph 2nd day during admission, shows prominent cardiomegaly with progressive opacity over both lower lungs. **(B)**: No abnormal valvular disease



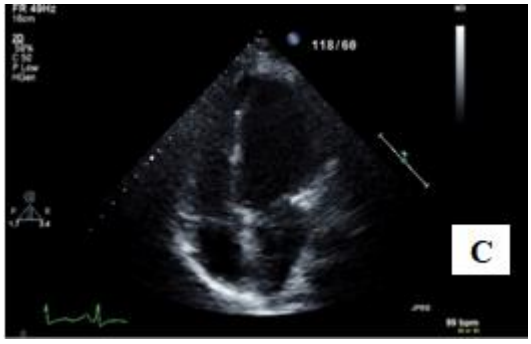


Figure 2: (**A**) and (**B**) Echocardiography with Moderate MR and EF of 35-40%. (**C**) Post treatment by 3 days with EF improvement up to 52.6 %

3. Discussion

Mycoplasma pneumoniae is one of the most common organism causing upper respiratory tract infection and pneumonia, but other clinical manifestations still difficult to be diagnosed, as often the disease is underestimated due to mild disease or to atypical presentation [11]. While Cutaneous, mucocutaneous manifestations and hepatitis are the most common non respiratory symptoms in mycoplasma pneumoniae infection, Central nervous symptoms are very rare in non-hospitalized patients and approximately occur in7 percent of the patients who require hospitalization [12]. Cardiac involvement with Mycoplasma pneumonia is relatively uncommon. There are reported cases of myocarditis, cardiac thrombi and pericarditis, which have been described in adults more than in children [13]. Most cardiac involvement were thought to be due to direct transmission from respiratory system, but recent studies suggest other explanations for extra pulmonary diseases associated with Mycoplasma infection [14].

The possible pathogenicity of distant organ diseases in mycoplasma are explained by three main mechanisms:(1) direct effect where the cytokines are locally induced by lipoproteins which are contained in the bacterial cell membrane; (2) indirect by autoimmune alternation through cross-reaction between the cell antigens of bacteria and human cells; and (3) via a vascular occlusion type by causing vasculitis and/or thrombosis due to transient antiphospholipid antibodies [5, 6, 7, 15]. The reason behind these hypotheses that antiphospholipid antibodies were found in the blood through active neumonia infection and these antibodies does not last long after recovery [15]. Narita et al, reported that Kawasaki disease associated with M. pneumoniae infection is not unusual in Japan and it has been seldom reported from western countries [16]. Animal studies have shown that M.*pneumonia* infection behavior influenced by factors may lead to a broad range of clinical manifestations, like age, gender, genetic background and environmental stress [17].

Paz and Potasman et al, concluded that 43% of patients with carditis developed pneumonia, while only 19%had pleural effusions. Same study showed that some patients with mycoplasma myocarditis who were treated with macrolide had long term sequelae[18]. But still no studies showed whether severe respiratory disease or depressed immune system increases the risk of myocarditis or extra pulmonary manifestations in mycoplasma pneumoniae.

The best method to diagnose the pathogenesis causing myocarditis is the direct tissue biopsy but it is non-practical high-risk procedure. Using culture and gram stain for diagnosis of M. pneumoniae are rarely used and generally not helpful due to difficulties in isolating such fastidious atypical bacteria. Cold agglutinins were considered a valuable test in diagnosing Mycoplasma pneumonia as it is the first humoral *response to* this organism, however it is not reliable cause its sensitivity reaches only 50-60% and it has low specificity due to false positive result with some other bacterial and viral infection in addition to lymphoma [19, 20]. Serology might help in diagnosing acute infection. Specific IgG antibodies indicate either early stage of Mycoplasma pneumoniae disease or resolved infection, as it starts to rise after first week of the infection, reach the peak within 5 weeks, then it might disappear after 4 years more or less, but at least a four-fold increase of the titer is required to establish a diagnosis. IgM antibody is a method for detecting acute Mycoplasma pneumonia infection. It elevates during the first week and disappears within months Disadvantage of IgM that is the antibodies are not constantly generated in adults, most likely as a result of recurrent previous infections, which for a negative test will not rule out a new infection [21, 22]. Latest studies have suggested that the detection of specific IgA provides better diagnostic accuracy [23]. Zhang et al, published a systematic review in 2011 about PCR versus serology in diagnosing mycoplasma pneumonia, concluded that PCR has high specificity but still has low sensitivity due to different causes. Potential explanations for these variations may include the different types of PCR and reference standard, the time point for sampling and the qualities of samples, *etc*. So, the combination of serology and PCR will give higher yield of diagnoses [24].

Macrolides are the drug of choice in Mycoplasma pneumonia. Choices differ according to age, side effects and the likelihood of drug resistant [25]. As some forms of Mycoplasma infection that happen outside the respiratory system are explained by immune related causes, immunomodulatory drugs like steroids along with antibiotics might be warranted for favorable response and better prognosis [26, 27].

4. Conclusion

We reported a case of an adolescent with Mycoplasma pneumonia presented with seizure and acute myocarditis responded well to Doxycycline. Mycoplasma myocarditis

should be suspected in all patients with pneumonia who develop acute respiratory distress syndrome or pulmonary disease with extra pulmonary manifestations. It should also be a part of differential diagnoses of pathogenesis causing myocarditis. Giving the difficulties in diagnosing acute mycoplasma It is important to do further studies in diagnosing mycoplasma pneumonia based on IgA in adults.

Conflicts of Interest: authors declare no conflict of interest.

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