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Carditis as unrecognized extra-pulmonary complication of *Mycoplasma pneumoniae* infection in adults: a case report

Abstract

A 44 years old man admitted to the hospital with fever and sudden onset of severe oppressive chest pain localized in the left breast area, radiating to the left arm. Examination revealed blood pressure 120/80 mm Hg, respiratory rate 18/min, heart pulse rate 100 beats/min, oxygen saturation (SpO_2) of 96—98 % on room air, flatness to percussion and presence of inspiratory crackles in the left basal area. EKG showed sinus tachycardia and non-specific alteration of repolarization in the anterolateral area of left ventricle. Troponin I and CK-MB, CRP and erythrosedimentation rate were considerably elevated. Chest radiograph performed at the admission revealed left basal consolidation with an effusion, suggesting pneumonia. On the basis of this data atypical pneumonia with cardiac complication was suspected and serum titers for respiratory viruses and atypical microorganism was performed. Antibodies (IgM) to *M. pneumoniae* were positive with high titer. Cardiac MRI was performed and showed tissue edema areas and multiple «late enhancement» myocardial areas on the anterolateral wall of left ventricle. Pneumonia and carditis due to *Mycoplasma pneumoniae* were successfully treated with clarithromycin 500 mg twice daily and ceftriaxone 2 g one daily for fifteen days.

Key words: *Mycoplasma pneumoniae*, infections, carditis, complications.

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CASE REPORT

A 44 years old Caucasic male was admitted to the Emergency Department for the sudden onset of chest pain. The pain started three hours before admission, was described as oppressive, localized in the left breast area, radiating to the left arm, not exacerbated with cough or inspiration, constant with pressure over the left chest. The intensity rating was initially 10 out of 10, but it gradually decreased within a few hours spontaneously. Furthermore the patient referred weakness, not productive cough and fever of 38.7 °C in the previous week. No significant risk factors for cardiovascular disease were identified, but family history of early coronary artery disease was reported. He denied any substance use. His medical history was negative, except for a previous facial paralysis due to Herpes Zoster infection when he was twenty years old. Patient did not take any drugs. At the admission, blood pressure was 120/80 mm Hg, respiratory rate 18/min, heart pulse rate 100 beats/min and oxygen saturation of 96—98 percent on room air. Cardiac examination revealed normal S1S2, no murmur, no rub, gallop or distended jugular venous pulse. No lower limb edema was evident. Chest examination revealed areduction of tactile fremitus, flatness to percussion and presence of inspiratory crackles in the left basal area. Abdomen examination was normal. Electrocardiogram (EKG) (Figure 1) showed sinus tachycardia and non-specific alteration of

repolarization in the anterolateral area of left ventricle. Troponin I and CK-MB were elevated: troponin I 0.433 μg/L (normal < 0.014 μg/L); total CK 283 UI/L (normal range 39—308); CK-MB 11.2 ng/ml (normal range 0—6.73); myoglobin 39 ng/ml (normal range 28—72). Inflammatory markers were elevated: C-reactive protein (CRP) was 7.46 mg/dl (normal range 0—0.5) and erythrosedimentation rate (ESR) was 78 (normal range 0—25). Chest radiograph performed at the admission revealed left basal consolidation with an effusion, suggesting pneumonia (Figure 2, Panel A).

The echocardiogram showed structurally normal heart with normal origin of coronary arteries, a left ventricular ejection fraction of 58.7 % without regional wall motion abnormalities. Right ventricular ejection fraction was reduced (TAPSE 17 mm). Minimal pericardial effusion was evident. Serum titers (*Coxsackie, Adenovirus, Echovirus, Mycoplasma* and *Influenza* A and B) was sent. Serologies for Adenovirus, Influenza virus types A and B, Respiratory Syncytial virus and Coxsackie virus were negative. Antibodies to *M. pneumoniae* (IgM) were positive by ELISA with a titer of 6.4 index (> 1.1 positive; < 0.9 negative; 0.9—1.1 grey zone). Cardiac magnetic resonance imaging (MRI) was performed and showed tissue edema areas with «patchy» distribution (T2 sequences) and multiple «late enhancement» myocardial areas (postcontrast-enhanced T1 sequences) on the anterolateral wall of left ventricle, suggestive of necrosis phenomenon. Minimal pericardial effusion was observed. Left basal pulmonary consolidation and pleural effusion were also evident. Thus, pneumonia associated to myocarditis was diagnosed. Patient was treated with clarithromycin 500 mg twice daily and ceftriaxone 2 g one daily for fifteen days. Therapy with low dosage beta blocker was also begun. Patient became asymptomatic, afebrile. At discharge blood pressure was 120/80 mm Hg and heart rate 70 beats/min. Chest examination became normal. Troponin I and CK-MB values normalized (0.003 μg/L and 0.84 ng/ml respectively). A chest radiograph showed complete resolution of pulmonary consolidation and pleural effusion (Figure 2, Panel B).

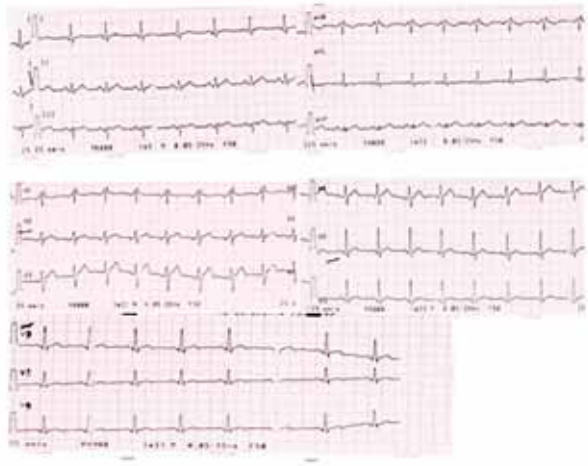
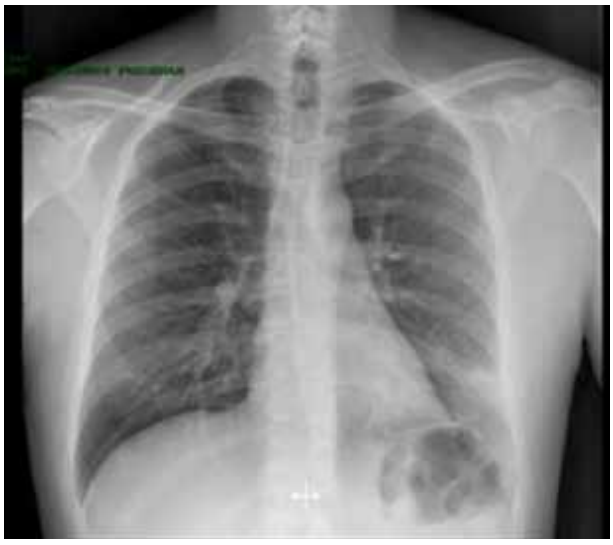


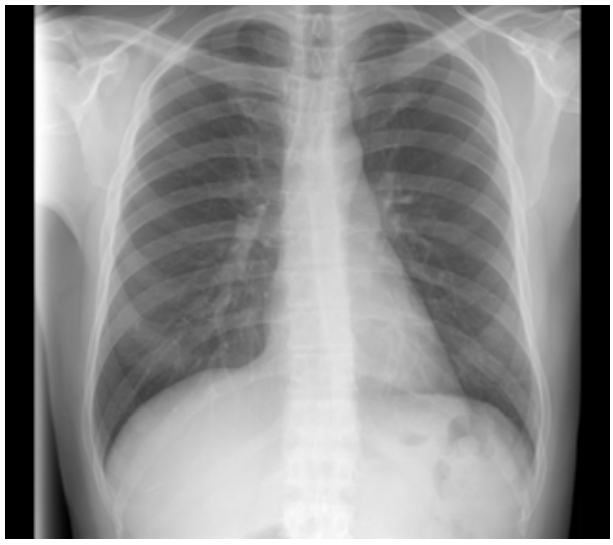
Figure 1. **EKG at the admission showing sinus tachycardia and no specific alterations of the cardiac repolarization (aVF, aVL, V6, V7, V8, V9)**

DISCUSSION

M. pneumoniae is a common pathogen causing primary atypical pneumonia, tracheobronchitis,



A



B

Figure 2. **Chest radiograph at the admission showing the left basal consolidation at admission (panel A) and normal chest radiograph at discharge (panel B)**

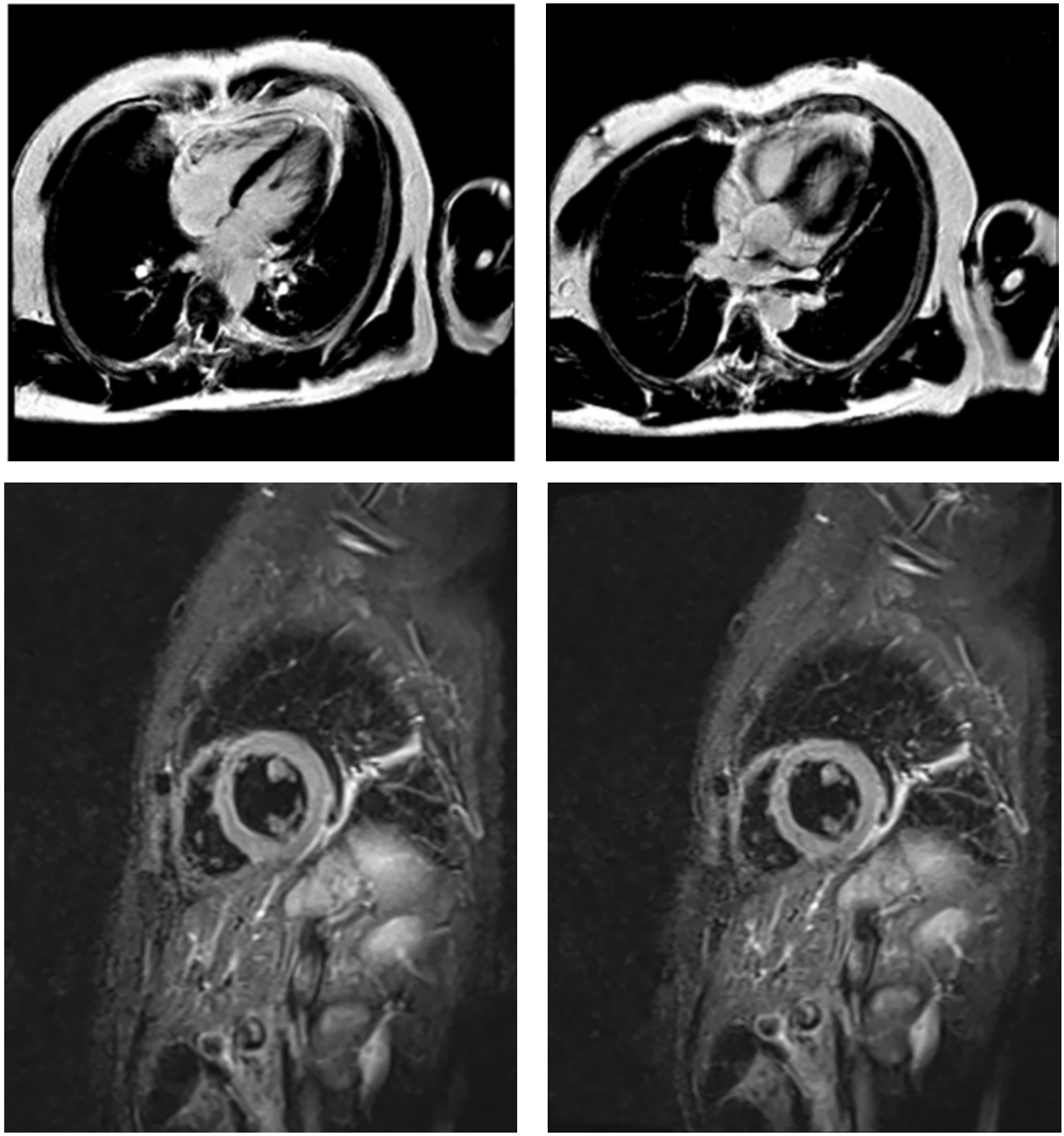


Figure 3. **MRI showing patchy distribution and late enhancement myocardial areas of the anterolateral wall of left ventricle, suggesting myocarditis**

pharyngitis and asthma in humans. The incidence of *M. pneumoniae* infection is greatest among school-aged children of 5—15 years old, with a decline after adolescence [1]. *M. pneumoniae-causes* not only respiratory tract infections but it is involved in frequent but often not recognized extra-pulmonary complications, including neurological, cardiac, dermatological, musculoskeletal, renal, hematological and gastrointestinal diseases [2]. As many as 25 % of subjects infected by *M. pneumoniae* may experience extra-pulmonary complications at variable time periods after onset or even in the absence of respiratory illness [3]. Central nervous system (CNS) complications are recognized as among the most common of extra-pulmonary manifestations of *M. pneumoniae* infection and may consist in pyramidal and extrapyramidal tract dysfunction, seizures, cognitive abnormalities, optic neuritis, diplopia, meningitis and cerebellar dysfunction [4]. It has been estimated that 6 to 7 % of hospitalized patients with serologically confirmed cases of *M. pneumoniae* pneumonia may experience neurological complications of varying severity [3]. Whereas neurological

disorders may be the most severe extra-pulmonary manifestations of *M. pneumoniae* infections, dermatological disorders, including erythematous maculopapular and vesicular rashes, are others common and clinically significant complications, occurring in up to 25 % of patients. Although these disorders are usually self-limited, severe cases of Stevens — Johnson syndrome, conjunctivitis, ulcerative stomatitis, and bullous exanthems have been reported and the organism has been detected directly in the cutaneous lesions [3—5]. Conversely, other extra-respiratory disease manifestations such as arthritis and carditis occurred somewhat less frequently. Nonspecific myalgias, arthralgias, and polyarthropathies occur in approximately 14 % of patients with acute *M. pneumoniae* infection and may sometimes persist for long periods [6]. Cardiac complications associated with *M. pneumoniae* are relatively uncommon. Cardiac involvement has been reported in 1 to 8.5 % of subjects with serological evidence of infection, being more common in adults and adolescents than in children [3, 7]. In a children population, the median serum CK-MB concentration was significantly higher in children who were *M. pneumoniae* IgM^+ compared with those who were *M. pneumoniae* IgM^- [8]. However, carditis due to *Mycoplasma pneumoniaeis* more frequent in adult population. Some cases of *M. pneumoniae* carditis are described in the literature: they concern adolescent and adult subjects [9—12] and more rarely children [13, 14]. As a matter of fact, in a review of Paz and Potasman of 21 cases of *Mycoplasma associated* carditis, the mean age was 33 years [15]. Similarly, our case of pneumonia complicated by a myocarditis due to *M. pneumoniae* in a 44 years old man well reflects this age distribution.

The mechanisms involved in the generation of cardiac damage is not well known. Different pathogenetic mechanisms linking *M. pneumoniae* infection and extra-pulmonary (particularly neurological) involvement have been proposed [16]. The direct invasion of the organism in the target tissue and the generation of soluble toxins responsible of distant damage are two possible, but not demonstrated, damage mechanisms. Moreover, a immunological mechanism has been proposed [16]. It is known that infectious agents may modify host tissues and induce autoantibodies. The normal T-lymphocyte suppression of self-immunity can be bypassed by cross-reacting antigens, alteration of host cell antigen by the infecting organism and non-specific activation of lymphocytes with consequent manifestations of systemic immune response. All of these activities could be elicited in *M. pneumoniae* infections. In fact, it is known that *Mycoplasma* activates the immune system by inducing B- and T-lymphocyte proliferation, secretion of major histocompatibility complex class I and II proteins and final release of multiple cytokines (e.g., interleukins, interferons, tumour necrosis factor and colony-stimulating factors). These effects may result in local or systemic manifestations in the infected host [2]. Thus, the cross reaction between organisms and human antigens could be a possible mechanism underlying the extra-pulmonary complications of *M. pneumoniae* infection. Thomas et al. observedin patients with primary atypical pneumoniacross-reacting antibodies directed against pulmonary tissue and, occasionally, to other tissues, including the heart [17]. The reason of a major incidence of carditis in adults compared to young people is not known. Probably, it could depend on different age-specific immune responses to *M. pneumoniae* [8]. No clinical features of the host or microbiological characteristics of organism predisposing to higher risk of extra-pulmonary complications are known. A recent study demonstrated that the incidence of extra-pulmonary complications in the macrolide-resistant (MR) *M. pneumoniae* group was significantly higher than that in the macrolide-sensitive (MS) *M. pneumoniae* infections [18]. So a MR *M. pneumoniae* infection could be a risk factor not only for severe clinical features, but also for extra-pulmonary complications.

In conclusion our case is an example of healthy adult man with pneumonia caused by *M. pneumoniae* complicated by a myocarditis. In consideration of the increasing prevalence of MR *M. pneumoniae*, it is important to suspect this complication of *M. pneumoniae* infection also in subjects without risk factors to avoid severe cardiac outcomes.

Conflicts of interest

Authors declare no conflicts of interest.

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КАРДИТ ЯК РІДКІСНЕ ПОЗАЛЕГЕНЕВЕ УСКЛАДНЕННЯ ІНФЕКЦІЇ *MYCOPLASMA PNEUMONIAE* У ДОРОСЛИХ: ОПИС КЛІНІЧНОГО ВИПАДКУ

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Резюме

Чоловіка віком 44 роки було госпіталізовано з лихоманкою і раптовим початком інтенсивного болю в грудях зліва, який віддавав у ліву руку. Об'єктивно: артеріальний тиск — 120/80 мм рт. ст., частота дихальних рухів — 18 за 1 хв, частота серцевих скорочень — 100 за 1 хв, насичення крові киснем (SpO_2) 96—98 % при диханні повітрям, притуплення перкуторного звуку і наявність хрипів у лівих нижніх відділах легень. На електрокардіограмі — синусова тахікардія і неспецифічні зміни реполяризації в передньолатеральній ділянці лівого шлуночка. Рівні тропоніну I, MB-фракції креатинфосфокінази та С-реактивного протеїну, а також швидкість осідання еритроцитів були значно збільшені. На рентгенограмі грудної клітки виявлено ліву базальну консолідацію з випотом, що вказує на пневмонію. На підставі цих даних було запідозрено атипову пневмонію із серцевими ускладненнями і проведено панель аналізів на сироваткові титри респіраторних вірусів і атипових мікроорганізмів. Виявлено високий титр антитіл (IgM) до *Mycoplasma pneumoniae*. Проведено магнітно-резонансну томографію серця. Виявлено ділянки набряку тканин і множинні ділянки пізнього посилення міокарда на передній частині бічної стінки лівого шлуночка. Пневмонію і кардит, спричинені *M. pneumoniae*, успішно проліковано за допомогою кларитроміцину в дозі 500 мг двічі на добу і цефтріаксону в дозі 2 г один раз на добу протягом 15 днів.

Ключові слова: *Mycoplasma pneumoniae*, інфекції, кардит, ускладнення.

КАРДИТ КАК РЕДКОЕ ВНЕЛЕГОЧНОЕ ОСЛОЖНЕНИЕ ИНФЕКЦИИ *MYCOPLASMA PNEUMONIAE* У ВЗРОСЛЫХ: ОПИСАНИЕ КЛИНИЧЕСКОГО СЛУЧАЯ

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Резюме

Мужчина в возрасте 44 лет был госпитализирован с лихорадкой и внезапным началом интенсивной боли в груди слева, отдающей в левую руку. Объективное обследование: артериальное давление — 120/80 мм рт. ст., частота дыхательных движений — 18 в 1 мин, частота сердечных сокращений — 100 в 1 мин, насыщение крови кислородом (SpO_2) 96—98 % при дыхании воздухом, притупление перкуторного звука и наличие хрипов в левых нижних отделах легких. На электрокардиограмме — синусовая тахикардия и неспецифические изменения реполяризации в переднелатеральной области левого желудочка. Уровни тропонина I, МВ-фракции креатинфосфокиназы и С-реактивного протеина, а также скорость оседания эритроцитов были значительно увеличены. На рентгенограмме грудной клетки выявлена левая базальная консолидация с выпотом, что указывает на пневмонию. На основании этих данных была заподозрена атипичная пневмония с сердечными осложнениями и проведена панель анализов на сывороточные титры респираторных вирусов и атипичных микроорганизмов. Выявлен высокий титр антител (IgM) к *Mycoplasma pneumoniae*. Проведена магнитно-резонансная томография сердца. Выявлены области отека тканей и множественные области «позднего усиления миокарда» на передней части боковой стенки левого желудочка. Пневмонию и кардит вызванные, *M. pneumoniae*, успешно пролечили с помощью кларитромицина в дозе 500 мг два раза в сутки и цефтриаксона в дозе 2 г один раз в сутки в течение 15 дней.

Ключевые слова: *Mycoplasma pneumoniae*, инфекции, кардиты, осложнения.

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