Case Report

CHLAMYDIAL PNEUMONIA: DIAGNOSTIC PROBLEMS IN PAEDIATRIC PRACTICE

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Summary

Atypical causing agents are common pathogens leading to respiratory tract infections. The majority of the cases diagnosed with *Chlamydia pneumoniae* are asymptomatic, or mild. However, in about 30% of the cases bronchitis and pneumonia develop. The patients with complication are usually subfebrile, with deterioration in general health status, headache, and unproductive cough. Assessment of the clinical presentation is not sufficient to make the diagnosis, and laboratory, image and immunological investigations are necessary. We present three cases of chlamydial infection with a variety of clinical manifestations, treated at the Paediatric Clinic of University Hospital – Pleven. Serological diagnosis and the treatment for Chamydial pneumonia are discussed.

Key words: pneumonia, chlamydiae pneumonia, children, diagnostics

Introduction

Pneumonia is one of the commonest diseases in childhood. Worldwide, 1.9 million children under 5 years of age die of pneumonia every year. There are over a hundred bacteria that may cause an infection of the lung parenchyma. The frequency of these infections depends on age, accompanying diseases and risk factors. The term "atypical pneumonia" refers to pneumonias mainly caused by *Chlamydia pneumoniae*, *Mycolasma pneumoniae, Legionela spp*.

Chlamydia pneumoniae was discovered in 1989. Like *Chlamydia psitacii* and *Chlamydia trachomatis,* it belongs to the genus of *Chlamydiae*. This is an obligate intracellular agent with a unique biphasic life cycle in the respiratory tract epithelial linings and the alveolar macrophages. There are two distinct morphologically and functionally different forms, and an adequate humoral and cellular response is necessary for it to be eliminated [1].

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It is through contact with or inhalation of droplets carrying the infection, and most commonly causes upper respiratory tract infections such as otitis, sunuitis, laryngitis, as well as bronchitis and pneumonia. *Chlamydia pneumoniae* may also cause non-respiratory damages, including meningoencephalitis, Guillain-Barré syndrome, arthritis, myocarditis, and pyelonephritis. This is possible because of the dissemination of infected mononuclears from the respiratory tract to other parts of the body via the circulation. In such cases, the pathogen may not remain at the initial entry region of the infection. A trigger factor, commonly a virus or a bacterium, is necessary to facilitate the spread of the infection to other systems of the body [2, 3].

We present three cases of chamydial pneumoniae infection in children treated at the Paediatric Clinic in Pleven. The cases illustrate the variety of clinical presentation of the infection.

Case 1

A 19-month-old girl with a history of frequent respiratory infections was admitted to the clinic. The right wrist of the child was red, swollen and painful, with limited range of motion for two weeks prior to admission. On admission, the child had a high temperature, dry cough and vomiting. The child had been treated for pneumonia with amoxicillin/clavulanate three months before, with a history of stiffness and pain in both lower extremities and the left hand since then. The child was diagnosed with juvenile chronic arthritis. Treatment with NSAIDs provided a short-time relief.

Examination revealed deteriorated general health, febrility, and intoxication, and hyperaemia of upper palatal vaults and tonsils. Breathing was acute and vesicular, with isolated small wet rales. The right wrist joint was swollen, slightly hyperaemic, painful and limited in movement. Left wrist and knee joints were also slightly painful.

Blood tests revealed high ESR (40mm/h) and mild leukocytosis ($13.7x10^9$/l). ASAT, ALAT, ALP, GGT, Creatinine, Urea, Uric acid, Total protein, Albumin, Fibrinogen, AST, W. Rous were within normal range. Metabolite acidosis was found (pH – 7.29; pO_2 – 83.5 mm Hg; pCO_2 – 31.5 mmHg; SB – 16.4 mmol/l; AB – 14.9 mmol/l; BE – 9.9/-10.2 mmol/l; $SatO_2$ – 94.3 %). Sweat test and Mantoux test were negative. No growth was observed at microbiology investigations of sputum, faeces and hemoculture. Immunodiagnostic tests revealed decreased levels of IgG-antibodies, (66 mg/dl), increased levels of IgG antibodies specific to *Chlamydia pneumoniae* (2.22 U/ml), low level of T-helper cells (21.7/µl), low T-helper/T-cytotoxic cell ratio (0.74). Anti-nuclear antibodies and C-reactive protein were within normal range. Chest X-ray (Figure 1) revealed bilateral peribronchial and perivascular interstitial infiltrates. Right wrist did not reveal pathological bone changes.

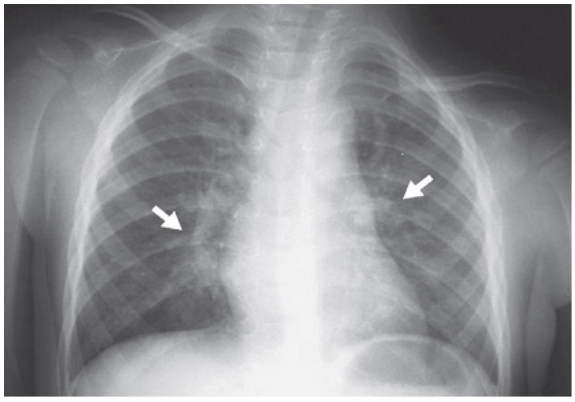

Figure 1. Chest x-ray – bilateral peribronchial and perivascular interstitial infiltrates

Treatment was started with ceftriaxone. After confirming *Chlamydia pneumoniae* infection, clarithromycin was applied for 7 days, together with NSAIDs. The child was discharged without lung pathology. Further therapy with immunostimulants and antioxidants was recommended.

Case 2

A twelve-year-old boy, born after an uneventful first pregnancy, with a family history of diabetes, obesity and allergic diseases was admitted. On admission, the child had rhinitis, fluctuating temperature and dry cough, all persisting for a month despite treatment with cefuroxime or symptomatic medications.

The child was in good general health, with high-pitched vesicular breathing, and isolated dry rales.

Results from blood and biochemistry tests were within normal range, except for increased ESR – 25mm/h. Pulmonary reography (Figure 2) visualized a limited non-homogenous shadow in the lower right lung. There was a history of tuberculosis on the father's side, so a Mantoux test and a QuantiFERON test were performed to rule out the possibility of tuberculosis infection. Results from the immunological investigations were as follows: low levels of IgA (84mg/dl), IgG (550mg/dl), lower total T-lymphocyte count (42.7 /µl), T-helper cells (22.98 µl), T-helper cells/T-cytotoxic lymphocytes - (0.91) and increased specific IgA to *Chlamydia pneumoniae* (1.80 U/ml). After 5-day treatment with clarithromycin and immunostimulating drugs the child was discharged in good health. Further treatment on an outpatient basis was recommended.

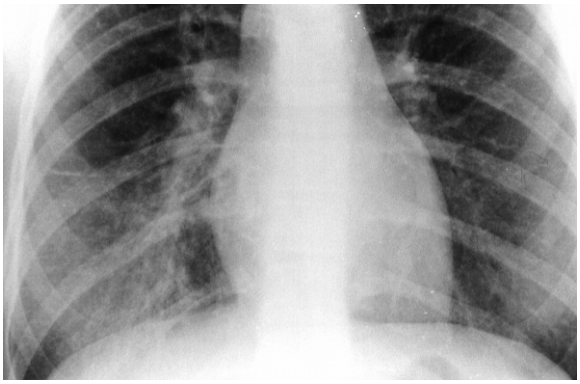

Figure 2. Pulmonary reography – limited non-homogenous shadow in the lower right lung

Case 3

A two-year old boy was admitted, born after a second uneventful pregnancy, without a family history of serious conditions. On admission, the child had been subfebrile, with dry cough and earache for more than a month that had not responded to treatment with amoxicillin and a two-day treatment with azithromycin.

The examination on admission revealed deteriorated general health with tachydyspnea, acute vesicular breathing, small wet rales bilaterally, worse on the right. Heart sounds were clear and regular.

Laboratory investigations revealed leukocytosis ($19.7x10^9$/l), increased CRP (24mg/l), increased CPK – 501 IU/L CPK – MB-48 ng/ml. Results from other blood and biochemistry tests were normal. Echocardiography revealed enlarged left heart chambers and pump dysfunction. Chest reography (Fig.3) showed non-homogeneous shadow in the right lower lung and no cardiac abnormality. Lung CAT established interstitial inflammation in the right lung. Immunology tests revealed IgA deficit (123 мг/dl), decreased total lymphocyte count (33.1/µl), T-lymphocytes (51.37 /µl), B-lymphocytes (19/µl), T-helper cells(16,86/µl), T-helper cells/T-cytotoxic lymphocytes (0.91), mild increase of T-cytotoxic lymphocytes (34.51/µl), increased specific IgG to Chlamydia pneumoniae (3.20 U/ml), and increased IgG to Mycoplasma pneumoniae (1.56 U/ml).

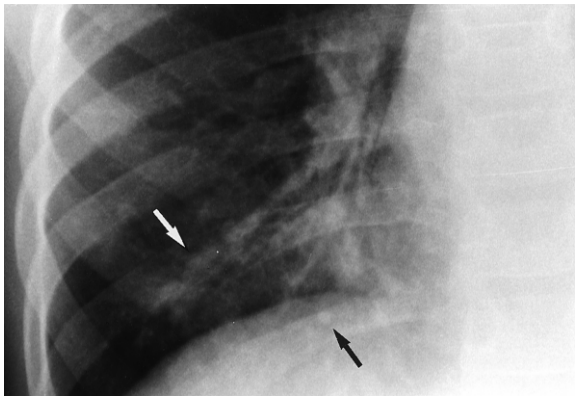

Figure 3. Chest reography – non-homogeneous shadow in the right lower lung

Treatment was administered with ceftriaxone, meropenem. After establishing the etiology, clarithromycin was added for 7 days. Corticosteroids, ACE inhibitors, diuretics and immunostimulating drugs were administered. The child was discharged in good general health. Further treatment with macrolides was recommended.

Discussion

There is little data on protracted childhood *Chlamydia pneumonia* in the literature. Baer (2003), Somer (2006), Korppi (2004) have reported that atypical pneumonias are most common in school age children. Principi (2001), Waites (2004) and Kichinski (2011) state that these microorganisms are more common in children under 5, while Block has found that it is evenly distributed among children between 3 and

12 years of age.[4-7]. Risk groups comprise children susceptible to health problems, ones raised in isolated communities, children born parents positive for *Chlamydia pneumonia*, who are often treated with antibiotics of the penicillin group, the latter causing the so-called respiratory dysbacteriosis and facilitate the chlamydial invasion. [8].

The clinical manifestations of *Chlamydia pneumoniae* infection are often difficult to differentiate. The onset is gradual, after an upper respiratory tract infection. There are persisting subfebrility and intoxication, followed by lung symptoms. A bi-phasic course is also possible in chlamydial pneumonia. A subacute onset is accompanied by pharyngitis and hoarseness, followed by a clinical improvement. The second phase is a new episode of decline and development of pneumonia [9, 10]. The temperature may be normal, mildly elevated or high, and the cough can be dry and paroxysmal, or wet and productive cough with copious purulent secretions. Non-pulmonary symptoms are often seen, such as affecting the skin, the cardio-vascular, nervous, and the digestive system [12].

In the cases we present the leading symptoms were febrility, paroxysmal cough and non-pulmonary symptoms: one child with arthritis and the other had heart complaints – enlarged left cardiac chambers and pumping dysfunction.

As can be seen, laboratory and x-ray findings were not specific, and making the diagnoses was based on the immunology tests. The microscopic method is not the method of choice today. The microbiology method is not convenient either on account of the slow growth of the bacterium and specific culture medium required. The main immunological methods to identify antigens or antibodies against them are PCK, ELISA, MIF [8, 12, 13]. Wide-spread carriership and a persisting chlamydial infection, the existence of three types of chlamydia with a common specific antigen all render the interpretation of results obtained through methods based on antigen identification.

In immunological methods for determination of specific antibodies in primary infection, IgM-specific antibodies are the first detected, followed by IgG-specific antibodies and finally – IgA-specific antibodies. Immune response in a secondary invasion of the pathogen is characterized by rapid increase of IgG antibodies and IgA antibodies, and absence of IgM antibodies. Adequate therapy brings about three-fold decrease in the levels of IgG, IgM and IgA antibodies. If IgA levels do not lower after treatment, chronic or persisting infection is the most likely cause [1]. During the last years, high-sensitivity molecular biology methods have been introduced, providing rapid diagnosis. However, they necessitate special preparation and this reduces their specificity. Therefore, none of the methods mentioned above is completely reliable, it is recommendable to use a combination of two methods that complement each other.

Since *Chlamydia pneumoniae* infections are mostly seen in patients with lower immunity. In the cases presented, lower levels of IgG, IgA and T-helper lymphocytes were found, while cytotoxic lymphocyte counts were higher. The latter probably contributes to prolong the course of the infection and recurrent acute episodes. This determines the necessity of combining antibiotic treatment (macrolides) with immuno-corrective therapy. Chronicity of chlamydial infection causes damages to the tissues involved, as well as to many other organs. It may trigger off autoimmune processes. Therefore, timely diagnosis and treatment are of crucial importance.

Conclusions

In children with recurrent respiratory infections and protracted pneumonias, an investigation for chlamydial infection should be considered.

In case *Chlamydia pneumoniae* is detected in children, macrolide treatment is the treatment of choice.

If a chlamydial infection is proved, the immune status should be evaluated, and in cases of lowered immunity, immunomodulators should be added to antibiotic treatment.

The detection of chlamydial infection in a child suggests that parents are carriers too, and they should eventually undergo treatment.

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