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Review

PROTRACTED ATYPICAL PNEUMONIA IN CHILDREN

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ABSTRACT

Pneumonia in children is very common and of great social relevance. Despite the big advance in prophylaxis, diagnostic methods and the development of new antibiotics, there is no significant decrease in morbidity and mortality, and the incidence of recurrent and protracted pulmonary infections is rising. Mycoplasma pneumoniae and Chlamydia pneumoniae are the likely etiological causing agents in persisting pneumonia in children. Non-specific clinical, laboratory and x-ray findings in cases related to these agents are discussed, laying particular stress on the serological diagnosis and its interpretation.

Key words: protracted pneumonia, children, diagnostics

There is no precise definition of protracted pneumonia in literature. According to Fein, protracted pneumonia is a pathological process of accumulation of inflammatory cells and exudate in the alveoli in response to microorganisms invading in the normally sterile lung (1).

Lakser defines protracted pneumonia as characterized by persisting symptoms and abnormal x-ray findings for a period longer than expected. The period expected and its duration are defined subjectively, and vary according to criteria such as causing agent, the presence of additional complications, and the severity of the disease course (2). Fein и Feinsilver define protracted pneumonia as presenting with focal infiltrates, associated with acute pulmonary infection that would not subside during the period expected despite a ten-day antibiotic treatment (3, 4).

Epidemiology

Recent studies report that 10% of hospitalized patients with community-acquired pneumonia have slowly resolving disease. There is not such information in pediatric literature. Marston reported reasons for slowly resolution of pneumonia: 1. there is not exact definition of normal resolution of acute pneumonia; 2. etiological agent is identified in only half of patients; 3. there is mixed infection in part of children (5).

Etiology

The microorganisms that cause acute lower respiratory tract infections are the same that can be associated with protracted pneumonias. Special attention is paid to highly virulent microorganisms, with expressed tropism to pulmonary tissue -Streptococcus pneumonia, Haemophilus influenza, and Staphylococcus aureus. Prolonged resolution is common for Legionella pneumonia. This microorganism is associated with the highest frequency of residual radiographic abnormalities, but it is meeting rarely in childhood (6). Haemofilus influence type b is implicated in more than 50% of persistent pneumonia in elderly, Streptococcus pneumonia-9-10% of cases (7).Unusual pathogen can be considered such as Pneumocystis carinii, Coxiella burnetii, and Listeria monocytogenes. These microorganisms are not sensitive to usual empiric therapy at pneumonia. (8). Savenkova (2005) has reported that atypical pneumonias in children may often become chronic (74%), and have a dramatic and

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protracted course (12.9%) (9). According to Ylish (2002), 12.2% of the children under five suffer from chronic chlamydial pneumonia (10). Hahn has also confirmed the role of Chlamydia pneumonia in protracting lung infections (11). This fact is attributed to the unique biphasic life cycle of the bacterium, which facilitates its transition into a non-infectious inactive form, which can persist for a long time in the infected cells and not susceptible to treatment with β-lactams.

Other authors express opinions contrary to those above. According to Lauren (2001), recovery takes the shortest time to recover (8). Cheryl (2005) associates the protracted course with the invasion of a second pathogen, most often Streptococcus pneumoniae (12).

Baer(2003), Somer(2006), Korppi(2004) have reported that atypical pneumonias were most common in school-age children(13,14,15). However, Principi (2001), Waites (2004), Kichinski (2011) have reported that these are most common in children under 5 years (16, 17, 18).

Clinical Manifestations

Clinical presentation is non-specific. The onset is gradual, following an upper respiratory tract infection, with persistent subfebrility and general ill health that precede pulmonary symptoms. In mycoplasma pneumonia, subfebrility is quite common, the cough is dry, distressing, and bringing up sputum is difficult (19).

Chlamydial pneumonia is also likely to take a biphasic course: a subacute onset accompanied by pharyngitis and hoarseness, followed by clinical improvement before an episode of worsening and development of symptoms of pneumonia (Kuo1995) (20, 21). The temperature could be normal, slightly elevated or high, accompanied by general health deterioration. The cough could be either dry and paroxysmal or wet. Other non-pulmonary symptoms are common, such as myalgia, arthralgia and headache, as well as neurological and gastrointestinal symptoms (22).

Pneumonia due to Chlamydia trachomatis develops in infants born woman with active, untreated chlamydial infection. Onset is usually between 1and 3 months of age and is often insidious with persistent cough, tachypnea, and absence of fever.

Onset of Chlamydia psitacii pneumonia is usually abrupt with fever, cough, headache, and malaise. The fever is high and often is associated with rigors and sweats. Psittacosis is uncommon in children, because they may be less likely to have close contact with infect birds.

Diagnosis

Blood tests do not reveal specific changes. Usually, slight leukocytosis and moderately elevated erythrocyte sedimentation rate are often found, and images from chest X-rays do not reveal specific abnormalities (23). Usually, peribronchial and perivascular infiltrates are seen, but focal consolidations and lobar infiltrates are also likely (24, 25, 26). According to Waites, lobar consolidations and bilateral changes are signs often seen in severe mycoplasma pneumonia (17).

Microbiological tests are not used in making the diagnosis in view of the slow growth and specific media conditions required.

Serological and molecular methods are successfully applied to identify Chlamydia pneumoniae и Mycoplasma pneumoniae. Serological methods help to determine the serum levels of specific antibodies, or specific antigens in samples collected. (18). Widely spread carrier ship, persisting chlamydial infection, the existence of three types of chlamydiae with a common genetic specific antigen all make the interpretation of the results difficult (27). This is why serological methods such as ELISA, MIF, RIA, complement fixation reaction are the methods of choice in determining specific antibodies in the serum. CBR allows finding antibodies to chlamydial polysaccharide antigens, but it lacks specificity (21). When using the MIF test, differences have been reported in the assessment of results and diagnostic criteria. Results in the diagnostic interpretation of MIF tests vary greatly from one laboratory to another. In serological diagnosis in cases of primary infection, IgM antibodies are first identified, followed by IgG and then by IgA. When the immune response weakens, their concentration lowers. In the case of recurrent infection the titres of IgG and IgA rise quickly, while IgM titre is absent. If therapy is adequate,

the decrease in titres is two or three fold. If the level of IgA is still high after treatment is completed, this is a sign that the infection is persisting or has become chronic.

PCR has been introduced lately to prove the presence of specific nucleotide chains. Though highly specific, the method is of low sensitivity, which makes it inapplicable in everyday practice.

In literature, there is insufficient data showing that atypical pathogens develop against the background of compromised immunity with predominant cellular immune deficiency (Savenkova, 2005) and combined cellular and humoral deficiency (Ylish, 2002) (9, 10). This makes it necessary to include determination of the immune status in protracted pneumonias and, in cases of immune deficiency states, to undertake an appropriate treatment.

Therapy

Drug resistance, inadequate dose, short course of treatment also may be associated with lower resolution pneumonia. Atypical pathogens are resistant to beta-lactams. Macrolides are a medicament for children. They have intracellular penetration, high concentration in lung tissue and immunomodulating effect. The treatment must be longer than 10-`14 days (19).If there was found immunological deficiency, must be added the immunomodulator to treatment.

A conclusion can be drawn that in protracted pneumonia in childhood the presence of atypical causing agents such as Chlamydia pneumonia and Mycoplasma pneumonia should be considered. Using modern immunological diagnostic methods can help to make a timely diagnosis and administer an appropriate treatment.

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