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Original Article

Characteristics of *Chlamydia trachomatis* infection in hospitalized infants with lower respiratory tract infection

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Background and Purpose: To study the epidemiology, presentation and laboratory findings of *Chlamydia trachomatis* pneumonia in hospitalized infants younger than 6 months.

Methods: Between January 2001 and December 2005, infants younger than 6 months admitted to the children's medical center of Taipei Veterans General Hospital with the diagnosis of acute bronchiolitis, bronchopneumonia or pneumonia were prospectively studied. Chest radiograph findings were reviewed in all patients. Basic laboratory examinations performed included white blood cell count and eosinophil count. *C. trachomatis* was detected via enzyme-linked immunosorbent assay antigen test and the titers of immunoglobulin G and immunoglobulin M by indirect immunoperoxidase assay.

Results: A total of 60 infants, 32 males and 28 females, were included. *C. trachomatis* infection was detected in 30% of patients (18/60). The median age was 2.5 months (range, birth to 6 months). Fever was not detected in 72% of patients (13/18). Only 22% (4/18) of these patients had the characteristic staccato cough. The mean duration of symptoms before admission was 8 days (range, 1 day to 2 months). Rhinorrhea was a prodromal symptom in 67% (12/18) of patients, with a mean pre-onset duration of 7 days (range, 1 to 14 days). Eighty three percent (15/18) of the patients had tachypnea, with a mean duration of 3.2 days (range, 1 to 7 days). Conjunctivitis was noted before admission in 6 patients (33%). Only peripheral eosinophils showed statistically significant difference between *Chlamydia*-positive and -negative disease (p=0.046), and may be clinically useful in cases of suspected *C. trachomatis* infection. Mixed infection with other pathogens including adenovirus, respiratory syncytial virus, *Mycoplasma pneumoniae*, cytomegalovirus and *Streptococcus pneumoniae* was found in 27% (5/18) of patients.

Conclusions: *C. trachomatis* is not infrequent and plays an important role in infants younger than 6 months old hospitalized due to lower respiratory tract infection.

Key words: *Chlamydia trachomatis*; Disease transmission, vertical; Hospitalization; Respiratory tract infections

Introduction

Chlamydia trachomatis infection is the most prevalent sexually transmitted infection in the United States today [1,2]. Among sexually active adolescents, the prevalence commonly exceeds 10% and may exceed 20% [3]. Approximately 50 to 75% of infants born to infected women become infected at one or more anatomic sites, including the conjunctiva, nasopharynx, rectum and vagina.

Conjunctivitis develops in approximately 30 to 50% of infants born to *Chlamydia*-positive mothers [4-7]. The nasopharynx is the most frequent site of perinatally acquired *Chlamydia*, with rates of approximately 70% in infected infants [6,8]. Only about 30% of infants who have nasopharyngeal infection develop pneumonia.

C. trachomatis pneumonia in infants usually presents between 4 and 12 weeks of age. A few cases presenting as early as 2 weeks of age have been

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reported, but none beyond 4 months of age. Infected infants frequently have a history of cough and congestion without presence of fever. Tachypnea and rales on auscultation may be noted during physical examination.

Without adequate treatment, cough may persist for as long as 2 months. Follow-up studies suggested that patients may present with abnormal pulmonary function and respiratory tract symptoms 7 to 8 years after recovery from acute *C. trachomatis* infection [3].

Although 70% or more of endocervical infections in women are asymptomatic, some patients may develop bartholinitis, endometritis, salpingitis and infertility. The definite diagnosis of *C. trachomatis* infection in infants may be the only clue that the mother has the same infection. There have been few studies of *C. trachomatis* in Taiwan. The aim of this study was to investigate the characteristics of *C. trachomatis* infection in hospitalized infants with lower respiratory tract infection.

Methods

Between January 2001 and December 2005, infants younger than 6 months admitted to the children's medical center of Taipei Veterans General Hospital with the diagnosis of acute bronchiolitis, bronchopneumonia or pneumonia, were prospectively studied. The patients were selected on the basis of: 1) history and physical examination confirming lower respiratory tract illness; 2) pulmonary infiltrates on chest roentgenogram; and 3) no known cardiac or chronic respiratory disease that might explain their illnesses. Patients who had other organ infections or had antibiotic treatment within two weeks before admission were excluded.

The symptoms and signs of patients, including cough, rhinorrhea, conjunctivitis, fever, etc., were recorded at admission. We also performed laboratory examinations including white blood cell count and eosinophil count. All patients received chest radiograph at admission and follow-up studies if abnormalities had been noted before. Throat swabs were collected for bacterial and viral culture. Nasopharyngeal aspirates were used for *C. trachomatis* culture with iododeoxyuridine-treated McCoy cells and antigen test of adenovirus (Adenovirus Antigen test; Cambridge Biotech, Cambridge, UK), respiratory syncytial virus (Abbott TESTPACK RSV; Abbott Laboratories, Chicago, IL, USA) and *C. trachomatis* enzyme-linked immunosorbent assay (ELISA) [Dako, UK]. Serum was analyzed for the immunoglobulin G (IgG) and immunoglobulin M (IgM) of *C. trachomatis* by indirect immunoperoxidase assay (IPAzyme™ Chlamydia Diagnostic Kit; Savyon Diagnostics, Ashdod, Israel). Acute infection was defined as culture-positive status or the presence of IgM antibody titers equal to or greater than 1:16 or IgG antibodies titers with quadruple elevation.

Statistical analysis

Chi-squared test was used to test the significance of the relationship between *Chlamydia*-positive and *Chlamydia*-negative groups. A p value <0.05 was considered as significant.

Results

Between January 2001 and December 2005, 336 infants younger than 6 months admitted to our hospital with the diagnosis of acute bronchiolitis, bronchopneumonia or pneumonia, were prospectively studied. A total of 60 infants, 32 males and 28 females, were included in this study. The median age of the patients was 2 months 3 weeks (range, birth to 6 months). *C. trachomatis* infection was detected in 30% (18/60) of infants younger than 6 months with the diagnosis of acute bronchiolitis, bronchopneumonia or pneumonia via nasopharyngeal culture.

Clinical manifestations

The clinical manifestations of these eligible populations are summarized in Table 1. Fever was not detected in 72% (13/18) of infants. Only 22% (4/18) of infants had the characteristic staccato cough. All of the remaining patients (78%) had cough with sputum production. The mean duration of symptoms before admission was 8 days (range, 1 day to 2 months). Rhinorrhea was a prodromal

Table 1. Clinical manifestations in infants with *Chlamydia trachomatis* infection

Clinical manifestation	No. of cases (n = 18) No. (%)
Afebrile	13 (72)
Fever	5 (28)
≥38°C and <38.5°C	2 (11)
≥38.5°C and <39°C	1 (6)
≥39°C	2 (11)
Cough	18 (100)
Staccato cough	4 (22)
Cough with sputum	14 (78)
Rhinorrhea	12 (67)
Tachypnea	15 (83)
History of conjunctivitis	6 (33)

symptom in 67% (12/18) of patients. The mean duration of rhinorrhea was 7 days (range, 1 to 14 days).

Symptoms of tachypnea were noted in 83% (15/18) of patients, with a mean duration of 3.2 days (range, 1 to 7 days). Conjunctivitis was noted in 6 patients before admission and these symptoms later resolved spontaneously. Table 2 lists these characteristics and shows the percentage of *Chlamydia*-positive and *Chlamydia*-negative infants with each.

Five patients (5/18) had mixed infection with other pathogens including adenovirus, respiratory syncytial virus, *Mycoplasma pneumoniae*, cytomegalovirus and *Streptococcus pneumoniae*.

Chest radiograph findings

Diffuse interstitial infiltration of bilateral lung fields consistent with pneumonia was found in 78% (14/18) of patients. Hyperinflation characteristic of bronchiolitis was seen on chest radiograph in 22% (4/18) of patients.

Peripheral blood examination

The median white cell count was 14,533 ± 5283/mm^3 (range, 5800 to 27,000) and was >15,000/mm^3 in 44% (8/18) of patients. Only 5 patients (28%) had greater than 5% eosinophils. One of these patients had 25% eosinophils. The total eosinophil count was >300/mm^3 in 7 cases (39%). The median total eosinophil count was 243 ± 201/mm^3 (range, 32 to 640).

C. trachomatis detection

Eighteen patients showed culture-positive findings (Table 3); *Chlamydia* antigen was detected by ELISA test in 14/18 (78%). Anti-*C. trachomatis* IgM was noted in 16/18 patients (89%) and serum IgG with 4-fold elevation was present in only 2/18 (11%).

Table 3. Laboratory examination for the detection of *Chlamydia trachomatis* infection

	Positive (%)	Negative (%)	Total
Immunoglobulin G 1/128	2 (11)	16 (89)	18 (100)
Immunoglobulin M	16 (89)	2 (11)	18 (100)
Chlamydia antigen	14 (78)	4 (22)	18 (100)

Treatment

All patients with a definite diagnosis of *C. trachomatis* infection received a 14-day course of erythromycin or 5 days' azithromycin treatment, and symptoms subsided within 3 to 4 days.

Discussion

C. trachomatis has been recognized as a common cause of ophthalmia neonatorum since 1911, but was not associated with infantile pneumonia until 1975 when Schachter et al described an infant with previous inclusion conjunctivitis who developed afebrile interstitial pneumonia associated with isolation of *C. trachomatis* from a throat culture [9]. Tipple et al showed that infants with *C. trachomatis* alone or *C. trachomatis* plus a virus isolate were similar clinically and differed significantly from other infants without *C. trachomatis* infection in the following seven characteristics: 1) onset of symptoms before 8 weeks of age; 2) gradually worsening symptoms; 3) presentation for care at 4 to 11 weeks of age; 4) presence of conjunctivitis and ear abnormalities; 5) chest roentgenograms showing bilateral, symmetrical, interstitial infiltrates and hyperexpansion; 6) peripheral blood eosinophil count ≥300/mm^3; and 7) elevated values of serum total IgM, IgG, and immunoglobulin A [10]. Epidemiologic evidence strongly suggests that the infant acquires chlamydia infection from the mother during vaginal delivery [5-7,11]. Infection after cesarean

Table 2. *Chlamydia*-positive vs *Chlamydia*-negative pneumonia: selected clinical findings

Clinical attribute	*Chlamydia*-positive (n = 18) No. (%)	*Chlamydia*-negative (n = 42) No. (%)	*p*
Clinical finding			
Afebrile	13 (72)	24 (57)	0.387
Staccato cough	4 (22)	5 (12)	0.431
Rhinorrhea	12 (67)	26 (62)	0.778
Tachypnea	15 (83)	30 (71)	0.517
Conjunctivitis	6 (33)	8 (19)	0.319
Chest X-ray			
Bilateral, symmetrical, interstitial infiltrates	14 (78)	28 (67)	0.542
Hyperinflation	4 (22)	8 (19)	0.740
Laboratory values			
Eosinophils >300/mm^3	7 (39)	6 (14)	0.046

section occurs rarely, and usually after early rupture of the amnionic membrane [12]. In this study, 2 of 18 patients with chlamydia infection were delivered via cesarean section.

The gold standard of diagnosis for *C. trachomatis* pneumonia remains isolation by culture of a specimen from the nasopharynx. However, this method is time-consuming due to the requirement for tissue culture. Several non-culture methods for the diagnosis of *C. trachomatis* infection have been approved by the Food and Drug Administration. In this study, antigen test performed by ELISA and direct detection of *C. trachomatis* IgM and IgG were used for diagnosis. Anti-*C. trachomatis* IgM had the highest sensitivity rate in 89% of patients and the lowest false-negative rate in 11% of patients. The methods of four-fold elevation of serum IgG had the lowest sensitivity rate (11%) and the highest false-negative rate [16/18 patients (89%)]. In conclusion, due to its time-consuming nature and technique requirement, nasopharyngeal aspirate culture is less clinically useful for diagnosis. Anti-*C. trachomatis* IgM and nasopharyngeal aspirate antigen test may be the most useful diagnostic tool.

Mixed infection with other pathogens including adenovirus, respiratory syncytial virus, *M. pneumoniae*, cytomegalovirus and *S. pneumoniae* and presentation with fever were found in 5 (28%) of these infants. The others (13/18) had afebrile pneumonia. Adenovirus and respiratory syncytial virus pneumonia was detected via antigen test from nasopharyngeal aspirate. *M. pneumoniae* was diagnosed via IgG antibodies titers with quadruple elevation. Cytomegalovirus was cultured from urine in one patient and *S. pneumoniae* was cultured from sputum of one patient, who received 7-day treatment with penicillin G.

Although staccato cough is considered a characteristic clinical symptom of *C. trachomatis* infection, only 4/18 patients (22%) had this symptom. Previous data from Harrison et al [13] showed significant peripheral eosinophilia (>300 cells/cm^3). In this study, 7 (39%) patients had eosinophil count greater than 300/mm^3. A previous study of 30 cases of *C. trachomatis* infection from Taiwan reported peripheral eosinophilia in 47% of cases [14], which is similar to the findings of this study.

The chi-squared test was used to test the significance of the relationship between *Chlamydia*-positive and *Chlamydia*-negative status. Among several symptoms and signs, including fever, rhinorrhea, staccaco cough, and conjunctivitis, only peripheral eosinophils had statistical significance (p=0.046) and may have clinical usefulness for the suspicion of *C. trachomatis* infection (Table 2). Atypical presentations of *C. trachomatis* pneumonia and mixed infection may increase the difficulty of diagnosing *C. trachomatis.*

In conclusion, this study found *C. trachomatis* infection in 30% of infants younger than 6 months admitted to the children's medical center with the diagnosis of acute bronchiolitis, bronchopneumonia or pneumonia. Lack of suspicion and atypical presentation of pneumonia may lead to failure to perform the necessary diagnostic tests, resulting in delay of diagnosis and treatment. Routine testing for *C. trachomatis* may be needed in infants who are hospitalized due to pneumonia, due to the high incidence of this condition.

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