



Case report

Neonatal low respiratory tract chlamydia *trachomatis* infection: Diagnostic and treatment managementM. Jouglet^a, I. Guillaume^b, C. Buchs^c, P. Reix^c, C. Schweitzer^a, L. Coutier^{a,c,*}^a Médecine Infantile, Hôpital d'enfants, CHRU de Nancy, 54500, Vandœuvre-lès-Nancy, France^b Service de pédiatrie, Centre hospitalier de Verdun Saint-Mihiel, 55100, Verdun, France^c Service de pneumologie-allergologie-mucoviscidose, Hôpital Femme-Mère-Enfant, 69500, Bron, France

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ABSTRACT

Maternal infection during pregnancy by Chlamydia *trachomatis* (Chlamydia *t.*) can result in neonatal interstitial lung disease. It remains difficult for physicians to establish this diagnosis and to select the best treatment, as there is no recommendation. In these two cases of neonatal low respiratory tract Chlamydia *t.* infection, we proposed successfully a diagnosis method based on Chlamydia *t.* determination by PCR, on any type of sampling, but more specifically on urinary and pharyngeal specimens; and a management based on oral antibiotic therapy, Josamycin 50mg/kg/day during 14 days which is commonly well accepted and not invasive.

1. Introduction

The prevalence of the sexually transmitted Chlamydia *trachomatis* (Chlamydia *t.*) infection is 1.5% in the French population and 7.9% among French pregnant women aged 18 to 24 [1]. Chlamydia *t.* screening by endo-cervical swab is not currently recommended during childbirth except during specific circumstances like with patients presenting clinical signs of cervicitis or urinary tract infection with negative urine test [2]. Contamination of the newborn during delivery is frequent and the main manifestation is neonatal conjunctivitis. Low respiratory tract infections are mentioned, but there are limited data and clinical observations are scarce. Despite the utilization of gene amplification techniques (PCR) to identify bacteria, diagnosis of neonatal Chlamydia *t.* infection remains difficult. There is no recommendation concerning treatment of such infection and their middle and long-term evolution has not been described.

We are reporting two different observations of low respiratory tract Chlamydia *t.* infection collected in two French university pediatric hospitals. Both observations differ by their initial presentation and their evolution.

2. Observations

2.1. First observation

S. was a 22 days-old female new-born hospitalized for acute non-oxygenating dyspnea associated with rhinorrhea. She was born at term, eutrophic, under artificial breastfeeding, with no family history. After 72 hours of observation, signs of respiratory distress, polypnea, moderate oxygen-requary were associated with bilateral diffuse crepitations without any heart murmur. Oral nutrition was going normally. The rest of the clinical examination was normal. A lumbar puncture was justified by the risk of bacteriemia and neuro-meningeal affection. The evolution was marked by a rapid weaning of the oxygen therapy, a decrease of the dyspnea, an improvement of the pulmonary auscultation with a satisfactory height-weight growth (Table 1).

2.2. Second observation

M. was a 2.5 months-old infant admitted for wheezing dyspnea with weight stagnation. This clinical presentation was distinguished from the first case by its subacute evolutionary character (5 weeks) with a bronchial hyper-reactivity during the course of the infection. The evolution was marked by bronchial hyperactivity until 3 months after antibiotic treatment requiring a background treatment with inhaled corticosteroids (Table 1).

Abbreviations: chlamydia *trachomatis*, chlamydia *t.*; Haute autorité de santé, HAS; Sexually transmitted infections, STI

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Table 1
Description of clinical cases.

	1st Observation (S. 22 days)	2nd Observation (M. 2.5 months)
Clinical presentation	Acute dyspnea	Subacute dyspnea, wheezing, weight stagnation
Imaging	Chest X-rays: Bilateral lung interstitial disease UScardiography: no anomaly	Chest CT: predominantly upper and middle-lobe mosaic lungs, diffuse distribution micronodules, subpleural parenchymal condensation
Treatment	Josamycin 50mg/kg/day during 14 days	
Development	Normalization of the auscultation and the chest X-rays Quick oxygen weaning	Bronchial hyperactivity up to 3 months requiring inhaled corticosteroid therapy
Maternal impairment	Asymptomatic	Leucorrhoea in the 1st and 2nd trimesters

Table 2
Biologic results.

1st Observation (S. 22 days)	2nd Observation (M. 2.5 months)
Blood gas measurement: Balanced hypercapnic acidosis	
Procalcitonin and C-Reactive Protein: normal	
Hepatic and renal function: normal	
Hemocultures: sterile	
CMV PCR (blood and urine): negative	
VRS (pharyngeal specimens): negative	
Bordetella <i>Pertussis</i> PCR (pharyngeal specimens): negative	
Chlamydia <i>t.</i> PCR (pharyngeal specimens): positive	
Chlamydia-positive genital specimens made after diagnosis in children	
Chlamydia <i>t.</i> PCR in urine, Chlamydia	Chlamydia <i>pneumoniae</i> ,
<i>t.</i> PCR in cerebrospinal fluid:	Mycoplasma <i>hominis</i>
positive	Ureaplasma <i>urealyticum</i> PCR
	(pharyngeal specimens): negative

The biological results for both cases are presented below (Table 2).

3. Discussion

In these two observations, we proposed successfully a diagnosis method based on Chlamydia *t.* determination by PCR, on any type of sampling, but more specifically on pharyngeal specimens; and a management based on oral antibiotic therapy, Josamycin 50mg/kg/day during 14 days which is commonly well accepted and not invasive.

The report of Chlamydia *t.* interstitial pulmonary diseases in neonate raises one principal issue: the true prevalence of this infection is not known, and its diagnosis by physicians remains difficult because the presentation can differ between newborns and infants. This infection should systematically be considered when a newborn presents a neonatal interstitial pneumonitis. Better diagnosis of these infections would improve our knowledge on this pathology and particularly on the occurrence of long-term consequences following that infection.

3.1. Epidemiology and screening

Chlamydia *t.* infection is one of the most common sexually transmitted infections (STI) in the world. It is currently recommended to take endo-cervical swabs of pregnant women showing clinical signs of cervicitis, urinary tract infection or leucocyturia, any kind of sexually transmitted infection, or in case of multiple partners. The French Public Health Agency, Haute Autorité de Santé (HAS), is currently conducting an assessment of practices and it seems that an extension of screening to all pregnant women need to be considered [3] in France, in line with the recommendations in England, Scotland, the USA and Canada [4].

3.2. Diagnosis and initial assessment

Chlamydia *t.* infection in the newborn and the child is neither consistently suspected nor searched when facing an interstitial lung disease when Mycoplasma *genitalium*, Ureaplasma *spp.*, and Mycoplasma *hominis* are more usually described. Non-specific signs are usually observed: tachypnea, wheeze, coughing fits appearing within the first

4–11 weeks of life, with usually no fever but with conjunctivitis for nearly half of the observations [5]. In France, the HAS currently recommends molecular biology with PCR as first examination for any collection site, all kinds of samples and for any clinical form, but the validity of this test is recognized only for vaginal, urinary, rectal and pharyngeal specimens. Serologic testing is not recommended except for infants.

3.3. Therapeutic management

There is no consensus for the therapeutic management of interstitial Chlamydia *t.* lung diseases. The usefulness of the treatment is still unanswered. These data should make us wonder whether or not it is necessary to treat an infant with Chlamydia *t.* infection in early neonatal period. Since no additional studies are available, it remains difficult not to initiate curative antibiotic therapy when faced with newborn infants with acute respiratory distress. Antibiotics with a good intracellular penetration are the only ones that are active against Chlamydia *t.* (Tetracyclines, Macrolides, Fluoroquinolones, and Rifampicin). The traditional treatment used is the Erythromycin 50mg/kg/day in 4 doses, 14 days. The Public Health Agency of Canada recommends for children under 1 month: Erythromycin for 14 days (first week of life: 20mg/kg/day if < 2000g, 30mg/kg/day if > 2000g, from 1 week to 1 month: 40mg/kg/day) and for Children older than 1 month: Azithromycin, 12–15mg/kg/day, maximum 1g single dose or Erythromycin 40 mg/kg/day, in 4 divided doses for 14 days or Sulfamethoxazole 75mg/kg/day, maximum 1g, in 2 doses/day for 10 days. Josamycin (50 mg/kg/day, 14 days) has been favored in these two cases observed for its action on intracellular pathogens, and its good tolerance compared with the other molecules of this class (less risk of cardiac rhythm disorder). In front of a more severe respiratory infection and/or bacteremia, a longer treatment time would probably have to be considered with a change in administration route.

3.4. Evolution

Despite the efficacy of antibiotic therapy during the acute phase, it is suspected that long-term complications such as broncho-pulmonary dysplasia might occur. Since 1998, about twenty clinical studies in newborn children suffering from atypical pulmonary infection have reported a significant association between the colonization of the respiratory tract by Ureaplasma *Urealitycum* within 24–72 hours of birth and the appearance of broncho-pulmonary dysplasia [6]. An experimental study in young mice has brought out the fact that Chlamydia *Pneumoniae* pulmonary infection may result up until adulthood with respiratory sequelae in the form of bronchial hyperactivity, fibrosis and reduced lung volumes [7]. Because of the potential respiratory sequelae, systematic long-term monitoring seems appropriate. As for antibiotic therapy, the studies showed no conclusive evidence of its benefit in the prevention of asthma but early-life exposure to antibiotics seems to improve asthma with a dose-response relationship [8].

4. Conclusion

These two observations help to enrich the rare descriptions of Chlamydia *t.* lung disease in the infancy, whose management remains unclear. A diagnosis method based on systematic Chlamydia *t.* determination by PCR, specifically on urinary and pharyngeal specimens, when facing an interstitial lung disease in newborns or infants seems to be indicated. The treatment of Chlamydia *t.* infection with Josamycin 50mg/kg/day during 14 days seems to be an effective treatment. The middle-term follow-up of these infants is justified.

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Conflicts of interest

None.

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