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Maternal and infant *Bordetella pertussis* infection

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Background. Pertussis continues to be a public health concern around the world because of increasing morbidity among vaccinated children and adults, severe disease forms in infants and late diagnosis. It is frequently believed that pertussis is exclusively a "childhood disease", but there have been increasing reports of *B. pertussis* infection among adolescents and adults, although the peak incidence and the highest mortality occur among infants.

Case presentation. 7-week-old infant illness started with a dry cough, on the 8th day of her illness it became paroxysmal. The infant's recurrent apnea episodes started on the day 12 of the illness, she started vomiting and developed severe respiratory failure. The patient required intubation and ventilation and stayed in PICU for 9 days. Blood showed lymphocytic leukocytosis. Pertussis diagnosis was confirmed by specific IgM antibody seroconversion. Disease to her 30-year-old mother began with catarrhal symptoms, later her paroxysmal coughing became accompanied by vomiting. Atypical bacterial bronchitis was suspected. Rigorous epidemiological history and detection of pertussis antibodies have helped to the confirmation of the pertussis diagnosis. The clinical course of *B. pertussis* infection in the infant was severe, and the mother's course was mild.

Conclusions. Our presented clinical case of the infant and her mother's *B. pertussis* infection illustrates the complex diagnostic difficulties in diagnosing pertussis, requiring laboratory confirmation, analysis of epidemiological data and appropriate evaluation. Pertussis to the infant and the mother occurred with the typical three stages: catarrhal, paroxysmal and convalescente. The infant underwent a severe form of the disease, but the outcome was good. Understanding the source of pertussis may provide new approaches to preventing pertussis in the most vulnerable infants.

Key words: pertussis, cough, diagnosis, children, adults

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BACKGROUND

Pertussis (whooping cough) continues to be a public health concern around the world because of increasing morbidity among vaccinated children and adults, severe disease forms in infants and late diagnosis. The actual prevalence of pertussis among children, adolescents and adults is not known, because pertussis is often not only undiagnosed but also is not suspected (1). Until recently, many considered whooping cough to be an infectious disease only affecting children and not affecting vaccinated children, adolescents or adults (2). However, pertussis – an acute highly contagious air-borne disease – can affect at any age. Classical pertussis disease is characterized by three stages: catarrhal, paroxysmal and convalescent. Paroxysms of coughing are often accompanied by vomiting (throwing up), a "whoop" sound, apnea and cyanosis (3, 4).

The clinical presentation of pertussis depends not only on the patient's age but also on the pertussis vaccination status. The use of pertussis whole-cell vaccines in infants and toddlers has led to decreased circulation of the bacterium in the child population and a marked decrease in the incidence of the disease. However, vaccine does not result in life-long immunity; indeed, the circulation of the bacterium has not been controlled in the adult population (5). Adults and adolescents are the main reservoir for *B. pertussis* today and pertussis remains an endemic disease worldwide despite the availability of comprehensive immunization programmes that primarily target the pediatric population. There are many reasons for this, including incomplete immunity following natural infection, as well as immunization and waning immunity over time.

CASE PRESENTATION

A baby girl was born prematurely at 36 weeks' gestation by spontaneous vaginal delivery. She was her parents' second child. She received two vaccines, BCG and hepatitis B, at birth. She was completely breastfed and was doing well. Her illness started at 7 weeks of age with a dry cough and mild coryzal symptoms. She had no fever. On day three her cough worsened, mostly at night. On day eight of her illness a paroxysmal cough started and she was admitted to the Children's Hospital with a suspected lower respiratory tract infection. On clinical examination T was 37.4 °C with a respiratory rate of 54–60 breaths per minute. She had mild coryzal symptoms and a non-productive cough. On auscultation the chest was clear with good air entry bilaterally. Heart sounds were normal; heart rate was 132 beats per minute. On day eleven of her illness a whooping cough followed by vomiting started. Apnea started on day twelve of her illness. The girl was transferred to the Pediatric Intensive Care Unit (PICU) on day thirteen because of 9 episodes of post-tussive vomiting and 10 episodes of apnea. She required intubation and ventilation. On day fifteen of her illness, she was extubated. On the same day she developed bradycardia (50–60 beats/min). She had a lumbar puncture, which appeared normal. On day sixteen she was intubated again because of episodes of apnea, cyanosis and vomiting occurring every 30 minutes. Her O_2 saturation decreased to 40%. On day seventeen of her illness she was extubated. She was treated in PICU for a total of 9 days. On days 18–27 of the illness the cough improved and the apnea episodes became less frequent. Chest x-ray showed peribronchial cuffing on day eight and segmental infiltration of the right upper lobe on day fourteen. During her stay in PICU an electrocardiogram, electroencephalogram and head computed tomography were performed, with no significant findings. The full blood count showed lymphocytic leukocytosis (Table 1).

On the second day of the admission (10th day of illness) she was suspected of having pertussis. Blood was taken for investigation of specific *B. pertussis* IgM and IgA antibodies on the 10th, 18th and 47th days of the illness (Table 2).

At that time we had no opportunities to perform the pertussis polymerase chain reaction (PCR). Only a third serological blood test detected pertussis IgM antibodies. On the 10th day of the illness she was investigated for *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* – specific IgM, IgA, and IgG antibodies. This was because her mother was coughing and was suspected having bronchitis caused by atypical infection. Antibodies were not found. Serological tests were performed by an enzyme-linked immunosorbent assay (ELISA) and estimated according to the manufacturer's instructions (Labsystems, Finland). Secretions

Table 1. Full blood count result of the infant

Parameter	Day of illness				
	9	13	16	20	28
WBC, 10^9/l	20.7	27.4	32.5	21.4	14.4
Granulocytes, %	12	20	35	34	16
Middle, %	6	4	5	9	12
Lymphocytes, %; 10^9/l	82; 16.9	76; 20.7	60; 19.4	57; 12.2	72; 10.4
ESR, mm/h	3	3	3	3	5

WBC – white blood cells, ESR – erythrocyte sedimentation rate.

Table 2. Immunoserological test results of the infant and his mother

Antibodies of *B. pertussis*, IU/ml	Infant's day of illness			Mother's day of illness
	10	18	47	19
IgM	0.4	2.5	33.0	82.0
IgA	0.6	1.1	0.7	18.0

IgM – immunoglobulin class M; IgA – immunoglobulin class A.
To un-vaccinated (<3 months of age infants), anti-*B. pertussis* IgM and IgA 4 IU/ml is positive.
To adults: anti-*B. pertussis* IgM 55–100 IU/ml – borderline, >100 IU/ml – positive;
anti-*B. pertussis* IgA 15–30 IU/ml – borderline, >30 IU/ml – positive.

from the trachea were taken on the 16th day of the illness and when tested by the Ligase chain reaction were negative for *C. trachomatis* DNA. The patient received amoxicillin for 5 days at home and the first 3 days in the hospital and was later commenced on clarithromycin for 7 days. On the 28th day of her illness the baby was discharged home. The community pediatrician saw her 19 days after discharge. She was well and settled with less frequent cough, no apnea episodes, and normal physical and neurodevelopmental examinations.

Her 30-year-old mother felt ill one day before her daughter's illness started. She developed a dry cough and several days later she vomited twice while coughing due to thick mucus in her airways. The general practitioner suspected bronchitis caused by atypical infection. A throat swab was taken and tested for *C. pneumoniae* and *M. pneumoniae* antigens by direct immunofluorescence. *C. pneumoniae* antigen was found and she was started on amoxicillin on day four and was subsequently switched to azithromycin. She continued to cough, though on day 20 the cough became less significant, occurring mostly at night. She had not been ill with pertussis previously. We did not have any data about her pertussis vaccination. On day 11 she was tested for *C. pneumoniae* IgM, IgA and IgG antibodies. *C. pneumoniae* IgG antibodies were positive. On day 19 she was found to be positive for *B. pertussis* IgM and IgA antibodies.

Epidemiology history. The infant's family at home consisted of her parents and a 9-year-old sister. Her 52-year-old maternal grandmother, who lived alone, was the first family member who started to cough. She had been visiting her granddaughters episodically. The grandmother started to cough 22 days before the infant's illness began. The grandmother's cough lasted for five weeks altogether. Pertussis was not suspected and no investigations were performed to determine the aetiology of her cough. The infant's 9-year-old sister started to cough 14 days after her grandmother. It was a non-productive medium-intensity cough lasting for three weeks. She had received 4 doses of whole-cell vaccine by 2 years of age. As pertussis was not suspected, no tests were performed to explain the cause of her cough. The mother has started to cough after 7 days, and the younger daughter after 8 days since the older daughter has started to cough. The father did not have any cough over the whole 3-month-period.

DISCUSSION

Despite successful infant vaccination programmes, pertussis remains endemic in many countries. Waning immunity leaves adolescents and adults

susceptible to disease and creates potential reservoirs of infection, allowing transmission to vulnerable infants (6). A reported study from Poland revealed protective immunity against pertussis in 70% of six-year-olds, 68% of seven-year-olds, and only 45% of eight-year-olds (7). Many studies have reported the importance of household and school contacts for pertussis infection. According to the literature (8) in up to 83% of paediatric pertussis cases, the source of pertussis was a close contact at home. As described in our case, it can be assumed that for the baby and mother the source of pertussis was the maternal grandmother and / or the older fully vaccinated sibling in the household. Specific antibodies obtained from the mother through the placenta during pregnancy protect a newborn for only a month (9). Shakib et al. (10) investigated pertussis antibodies in postpartum women and their newborns, and their study showed that approximately 75% of infants were born with pertussis antibody levels lower than the modest levels associated with potential protection. Despite effective antibody transfer, nearly 90% of infants were predicted to have little antibody by 6 weeks. As our clinical case showed, the infant's mother did not have protective immunity, and she also became ill with pertussis. The clinical course of *B. pertussis* infection in our infant was severe, although the mother's was mild. The infant's apnea episodes started on day 12 of the illness and were recurrent. She required intubation and ventilation and stayed in PICU for 9 days. The study from New Zealand comparing 1992 with 2003 shows us that infants are now being treated in PICU more often (11). Out of 72 children treated in PICU with pertussis, 97% were younger than 12 months old and 81% were less than 3 months old. 35 (49%) received assisted ventilation. Four of them died. 19% were readmitted to PICU. Crowcroft et al. (12) investigated 126 infants <5 months old admitted to London PICU's with respiratory failure, apnea and / or bradycardia, or acute life threatening episodes. Pertussis was diagnosed in 25 (19.8%). Pertussis was clinically suspected on admission in 28% of patients. Two infants died. Only 6 (4%) out of 126 infants had a positive *B. pertussis* culture. Compared to infants without pertussis, the infants with pertussis had been coughing for longer, had apneas and whooping more often, and had a higher lymphocyte count. In conclusion, it is stated that severe pertussis is under-diagnosed. In a large multicentre surveillance study in Germany, apnea or cyanosis occurred in 16% and complications in 24% of infants younger than six months of age (13). Most deaths from pertussis occur in infants younger than six months of age (14). In a case-control study designed to identify predictors of deaths in cases of fatal pertussis, 15 of 16 fatalities occurred in infants <2 months of age (15). Infants intubated for pneumonia were more likely to die than those intubated for apnea. Leukocytosis and pneumonia on initial presentation were predictors of poor outcome. A clinical case of pertussis for endemic or sporadic cases is defined as an acute cough illness lasting at least 14 days, accompanied by at least one of the following: paroxysms of coughing, inspiratory whoop or post-tussive vomiting (16).

Pertussis should be suspected in any infant death associated with marked leukocytosis, bronchopneumonia or refractory pulmonary hypertension, particularly in children aged <4 months (17). Pertussis should be differentiated from respiratory tract infections caused by *M. pneumoniae*, *Chlamydiae* spp., respiratory viral infections and tuberculosis. The mainstays are epidemiological data, laboratory investigations. Laboratory diagnosis of pertussis can be confirmed in 3 ways: isolation from nasopharyngeal secretion (bacteriological method) is a highly specific but little sensitive method as the use of antibiotics reduces sensitivity and the specimen collection is too late in the illness. *B. pertussis* DNA detection test using PCR is more sensitive than the bacteriological method. Serologic tests detecting *B. pertussis*-specific antibodies by ELISA, using highly purified antigens, may be useful. Therefore, if for the confirmation of the diagnosis is not possible to perform PCR, it is appropriate to determine specific antibodies in dynamics.

In the case we described above, pertussis was suspected because of clinical symptoms and signs (a dry cough of increasing severity which later became paroxysmal, associated with vomiting, whooping, apnea episodes and cyanosis), epidemiological data (household contacts – prolonged cough in her grandmother and sister), and the full blood count (FBC) result (lymphocytic leukocytosis). *B. pertussis* infection was confirmed by laboratory tests when *B. pertussis* IgM antibodies were detected in

the serum (seroconversion). Bronchitis caused by atypical bacteria was suspected in the mother of our patient. The diagnosis of *B. pertussis* infection in the mother was confirmed on day 19 of her illness by the detection of *B. pertussis* IgM and IgA antibodies in serum. The diagnosis was also confirmed epidemiologically. The investigations performed on the mother and the infant enabled us to exclude atypical infection and confirmed *B. pertussis* infection.

Vaccination is a major preventive measure against *B. pertussis* infection. Paediatric immunization programmes vary from country to country, but many of them start with a pertussis component contained in vaccine doses received during the first year of life, followed by booster doses during the second year of life and before starting school. In order to establish better pertussis control worldwide, the Global Pertussis Initiative Team suggested an extensive advanced vaccine strategy. They proposed the establishment of a global vaccination strategy for adolescents and adults, pregnant women and families (a "cocoon" strategy), and also health workers and childcare workers, using Tdap vaccine (18). The "cocoon" strategy is intended to protect newborns and infants from whooping cough.

CONCLUSIONS

Whooping cough can affect people of all ages. Our presented clinical case of *B. pertussis* infection to the infant and her mother illustrates the complex diagnostic difficulties in diagnosing pertussis, requiring laboratory confirmation, analysis of epidemiological data and appropriate evaluation. Pertussis to the infant and the mother occurred with the typical three stages: catarrhal, paroxysmal and convalescent. The infant underwent a severe form of the disease, but the outcome was good.

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MOTINOS IR KŪDIKIO KOKLIUŠO INFEKCIJA

Santrauka

Įvadas. Dėl didėjančio vakcinuotų nuo kokliušo vaikų bei suaugusių žmonių sergamumo, sunkių kūdikių ligos formų, vėlyvos diagnostikos kokliušas išlieka viena svarbiausių visuomenės sveikatos apsaugos problemų visame pasaulyje. Nors neretai manoma, kad kokliušas yra išimtinai vaikų liga, tačiau pranešimai rodo, kad didėja paauglių ir suaugusiųjų sergamumas kokliušu.

Klinikinis atvejis. Septynių savaičių kūdikio liga prasidėjo sausu kosuliu, kuris vėliau tapo priepuoliniu. Dvyliktą ligos dieną prasidėjo apnėja, vėmimas, triko kvėpavimas. Pacientė buvo intubuota, taikyta dirbtinė plaučių ventiliacija. Ji buvo gydyta intensyviosios terapijos skyriuje 9 dienas. Atlikus bendrąjį kraujo tyrimą buvo nustatyta limfocitinė leukocitozė. Kokliušo diagnozė buvo patvirtinta specifinių IgM antikūnų serokonversija.Trisdešimties metų motinos liga prasidėjo nedideliais katariniais simptomais, vėliau atsirado priepuolinis kosulys, kuris pasibaigdavo vėmimu. Buvo įtartas netipinių bakterijų sukeltas bronchitas. Detali epidemiologinė anamnezė ir kokliušo antikūnų aptikimas patvirtino kokliušo diagnozę. Kūdikis kokliušu sirgo labai sunkiai, o motina – lengvai.

Išvados. Mūsų pateiktas kūdikio ir motinos kokliušo klinikinis atvejis atskleidė diagnostikos sunkumus, epidemiologinių duomenų bei laboratorinių tyrimų svarbą. Kūdikio ir motinos kokliušas buvo tipinės formos su trimis ligos stadijomis (katarine, kosulio priepuolių ir sveikimo). Kūdikis kokliušu sirgo labai sunkiai, o motina – lengvai. Gilesnės žinios apie kokliušą gali suteikti naują požiūrį į kūdikių, kaip labiausiai pažeidžiamų asmenų, apsaugą.

Raktažodžiai: kokliušas, kosulys, diagnostika, vaikai, suaugusieji