Maternal pertussis is hazardous for a newborn: a case report

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Pertussis, or whooping cough, a highly contagious disease caused by *Bordetella pertussis*, is making a comeback globally and nationally in spite of reasonable vaccination coverage. Worldwide, there have been increasing reports of *Bordetella pertussis* infection among adolescents and adults, but the peak incidence and highest mortality occur among infants. We report a 19-day-old female infant presenting with progressive respiratory failure. The mother was the only familial contact who complained of mild cough. However, occasional apneic episodes with cyanosis and peripheral lymphocytosis prompted us to examine the presence of *Bordetella pertussis*, which remains a significant cause of morbidity and mortality in unimmunized infants. Understanding the source of pertussis transmission to infants may provide new approaches to prevent pertussis in the most vulnerable infants. Various potential strategies have been reviewed or recommended in countries with the aim of better protecting infants against pertussis. Public health measures to prevent the disease could be strengthened and booster vaccinations against pertussis considered.

Key words: Bordetella pertussis, neonatal, maternal, booster pertussis vaccine.

Pertussis, or whooping cough, is a vaccine-preventable disease of respiratory tract infection caused by *Bordetella pertussis*, a gram-negative bacillus[1]. Pertussis is a highly contagious disease that may occur at any age[2]. Globally, pertussis is ranked among the 10 leading causes of childhood mortality in the world and causes an estimated 294,000 pediatric deaths each year, predominantly among young nonvaccinated children[3]. Pertussis is a particular concern in infants under six months of age because this age group has the highest reporting rates and severity (hospitalization or death) of disease, but are too young to be protected by current vaccination schedules[4]. The most common cause of death from pertussis in young infants is pneumonia, which may be complicated by apnea, seizures and encephalopathy[5,6].

In Turkey, pertussis vaccine coverage (three doses) reached a level of about 80% among children younger than six years of age following the National Vaccination Campaign of 1985, and it was maintained over the following years with improvement in vaccination procedures by the Ministry of Health[7,8]. However, pertussis still affects all age groups, especially adolescents, adults, and young infants in Turkey, and occurs endemically with 2-to-5-year cycles of increased disease incidence[9]. Among adults who received a booster dose of an acellular pertussis (aP) vaccine without tetanus or diphtheria toxoids, concentrations of IgG anti-pertussis toxin (anti-PT) declined 58% and 39%, respectively, after six months. By 18 months after vaccination, concentrations declined 73% and 56%, respectively[10]. Pertussis is most severe in young infants, yet vaccination against this disease begins no earlier than six weeks of age and frequently as late as three months of age, depending on the local vaccination schedule[11]. The mechanisms of protection against pertussis are incompletely understood. The protection that results from *B. pertussis* infection or pertussis vaccines persists for an estimated 5-10 years or more. Protection wanes over time, leaving infants susceptible to infection or reinfection[12,13].

In the present article, we describe a case of maternal transmission of *B. pertussis* to a neonate in whom treatment was successful.

Case Report

A 19-day-old female infant was admitted to the neonatal intensive care unit (NICU) of Hacettepe University İhsan Doğramacı Children's Hospital, Ankara, Turkey. She was delivered by spontaneous vaginal delivery at 39 weeks' gestation with a birth weight of 3500 g. The infant had begun to have manifestations of mild viral upper respiratory tract infection at the age of 15 days. Her condition worsened abruptly at 18 days of age, with cough, cyanosis, apnea, and progressive respiratory failure requiring admission in the NICU. The infant's mother, who had received diphtheria-pertussis-tetanus (DPT) vaccination in childhood, had complained of mild cough four weeks before the onset of the infant's illness, but had not been treated with any antibiotics. On admission in our hospital, the infant had apneic episodes with cyanosis, and oxygen saturation decreased to 36% during a fit of coughing. Routine hematological tests showed a white blood cell count of 27,200/uL with a lymphocyte count of 16,320/uL, and C-reactive protein was 0.01 mg/dl. Chest X-ray showed mild pulmonary emphysema. Initially, the infant was treated with ampicillin and gentamycin. However, her condition deteriorated and she developed severe apnea and bradycardia during the night after admission and intubation was required. Intubation and ventilation was discontinued on the second day. Nasopharyngeal washing fluid was negative by polymerase chain reaction (PCR) for respiratory syncytial virus, influenza A and B viruses, adenovirus, parainfluenza viruses 1, 2, and 3, and coronavirus. These were PCR-negative and there was no co-infection with pertussis. In addition, the apneic episodes with cyanosis, whooping cough and lymphocytosis suggested neonatal pertussis, and erythromycin was started on day four after admission. Nasopharyngeal aspirates obtained before erythromycin treatment, on day four, were positive for *B. pertussis* using a culture with Bordet-Gengou-agar (BGA) and by a real time PCR assay based on the insertion sequence IS481 target[14]. Anti-PT was detected by the enzyme linked immunosorbent assay (ELISA) method in infant's serum and it was negative. After a few days of erythromycin treatment, her condition improved with one or two bouts of paroxystic coughing every 12 hours. The mother was the only familial contact who complained of mild cough and was also the only contact positive for *B. pertussis* by ELISA, with a titer of >100 Eu/ml and negative by culture. She was also treated with erythromycin, and contact of the parents with their infant was protected by having them wear a procedure mask. Ampicillin, gentamycin and erythromycin were continued for 10 days for the infant's treatment. When the infant had no clinical manifestations of pertussis, she was discharged from the hospital, and her mother continued her treatment for 10 days. Telephone follow-up three weeks later revealed no further cases of suspected pertussis in this family.

Discussion

Worldwide, there have been increasing reports of *B. pertussis* infection among adolescents and adults, but the peak incidence and highest mortality occur among infants[15,16]. Infants are especially vulnerable because maternal placental antibodies decline to negligible levels by the age of two months, before active immunization is initiated[17]. Infants under one year of age are not fully immunized for pertussis and several studies have pointed out that pertussis is underestimated in this age group[2,18].

Pertussis is an unusual cause of apnea in the NICU. The diagnosis of pertussis is based on clinical and laboratory factors. The clinical diagnosis criteria for pertussis are: prolonged cough lasting from 14 to 21 days, paroxysmal coughing, whooping cough, or post-tussive vomiting[17,19]. The laboratory criteria for diagnosis of pertussis are: isolation of *B. pertussis* from a clinical specimen or detection of Bordetella-specific antibodies in serum in the presence of a clinically compatible illness[17-20]. *B. pertussis* is fastidious and quite difficult to grow in the laboratory. It can be recovered from patients only in the first three to four weeks of illness, and is particularly difficult to isolate from previously immunized persons[21]. The use of PCR has made the rapid diagnosis of pertussis possible and is more sensitive than culture[2]. The PCR assay is also less affected by antimicrobial therapy[22]. Additionally, because infected infants do not usually present with

symptoms of classic pertussis, clinicans need to adopt a high index of suspicion and use modern laboratory testing to assist in diagnosis.

Despite good vaccination coverage, recent studies indicate that young infants continue to suffer from pertussis. Infants <12 months constitute the highest proportion of hospitalizations, complications and even death because they have not completed their primary pertussis immunization[23]. In the present study, it was found that a female infant who was hospitalized in the NICU because of lower respiratory tract infection with apnea and nasopharyngeal aspirate was positive for *B. pertussis*. The source of the infection was probably the mother since she had begun to cough one month before her baby. When there are typical manifestations of the disease in the mother, serology tests should be performed for the diagnosis. Among immunized patients, especially adolescents and adults, a prolonged cough may be the only manifestation of pertussis. However, because of low antibody titers, the newborn faces severe disease[16]. Our case was culture-negative and the diagnosis was optimized by the use of ELISA. We found lymphocytosis to be an accurate criterion for the diagnosis of pertussis or for the severity of the cough, although such correlation had been demonstrated before[18]. We did not find a correlation between pertussis infection and other viral pathogens (co-infection), although co-infection of *B. pertussis* with respiratory syncytial virus (RSV) was also described in other studies[24,25].

Among case-infants with an identifiable source, family members (at any age) were the main source of pertussis. Understanding the source of pertussis transmission to infants may provide new approaches to prevent pertussis in the most vulnerable infants. Various potential strategies have been reviewed or recommended in countries with the aim of better protecting infants against pertussis. These include selective vaccination of close contacts of neonates, universal adult immunization, adolescent or preschool pertussis boosters, and maternal immunization[26]. Waning of immunity in adults induced by vaccination and/or reduced levels of immunity from natural infection are important factors. Because vaccination has been reported to provide immunity against infection for a maximum of 12 years, widespread immunization has reduced the potential for individuals to acquire long-lasting exposure-induced immunity[27]. Esen et al.[28] showed that estimated titers of protective antibody for newborns are absent in 43% of the women of childbearing age.

Potential strategies for decreasing pertussis infection and deaths from pertussis in early infancy include vaccination of neonates at birth and of mothers during pregnancy. The few reported studies that have compared infants receiving current routine vaccination schedules with infants receiving vaccination at birth found that, although antibody levels rise earlier, responses to later vaccine doses may be diminished[4]. Knuf et al.[11] showed that vaccination of newborn infants at age 2 to 5 days with an aP vaccine was safe, well tolerated, and resulted in earlier antibody responses, seen after the first dose of a DTaP combination vaccine.

As the routine vaccination for pertussis increases, the incidence of disease has markedly diminished, and parallel to this, incidence of exposure to pertussis in the public has decreased. This causes antibody titers in the population to be low and leaves adolescents and women of childbearing age at risk of pertussis[29]. Immunity gained by pertussis vaccine lasts for a short time. When whole-cell and acellular vaccines are compared, the immunity seems longer (10-14 years) with whole-cell vaccine. Whole-cell vaccines are known to be highly effective but have been associated with frequent local and systemic reactions[30].

In Turkey, routine childhood pertussis immunization with whole cell pertussis vaccine (DTP) has been given since 1968. Pertussis vaccine has been administered in the 2nd, 3rd, and 4th months of life, in combination with a booster dose administered between the 16th and 24th months[31]. Consequently, the four doses of infant pertussis vaccination administered in Turkey are not sufficient for long-lasting protection against the infection. A large number of schoolchildren, adolescents, and adults are susceptible to pertussis infection, and thus improvement in vaccination procedures in our country is necessary. In 2005, two Tdap (tetanus toxoid, reduced diphtheria toxoid, aP) vaccines were licensed in the United

States: ADACEL® (Sanofi Pasteur, Swiftwater, PA) for use in persons aged 11-64 years and BOOSTRIX® (GlaxoSmithKline Biologicals, Rixensart, Belgium) for persons aged 10-18 years[32]. Both vaccines are licensed for single-dose administration. aP vaccines formulated with tetanus and diphtheria toxoids also are available for adults and adolescents in other countries, including an increasing number of European countries[33,34]. Canada, France, Germany, Italy, Spain, New Zealand and the United States use pertussis vaccine as a routine adolescent vaccination, and in the United States, not only the pregnants but also adults are recommended to have routine vaccination with aP vaccine boosters[30]. DTap-inactivated poliovirus vaccine (IPV) was licensed in Turkey (ADACEL-POLIO) for adolescents[35]. Vaccinating adults and adolescents using Tdap reduces the burden of pertussis among vaccine recipients and might prevent transmission of *B. pertussis* to infants[36].

The Advisory Committee for Immunization Practices (ACIP) recommendations encourage adult and adolescent women of childbearing age to receive Tdap at a routine health assessment before conception to prevent the morbidity of pertussis that could occur during pregnancy and encourage use of Tdap among adults and adolescents who anticipate contact with an infant aged <12 months both for personal protection and to reduce the risk for transmitting *B. pertussis* to the infants[37]. The adult formulation five component aP vaccine given as TdaP-IPV is safe and immunogenic in adolescents and adults and is a candidate vaccine for adolescent and adult immunization programs. Booster doses of pertussis vaccine for pre-school children, adolescents, and for the households of pregnant women might be considered[35].

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