



# A Rare Cause of Newborn Apnea That Has Not Been Seen for A Very Long Time with the Effect of the Vaccine: Pertussis

Aşı Etkisiyle Çok Uzun Süredir Görülmeyen Nadir Bir Yenidoğan Apne Nedeni: Boğmaca

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<sup>1</sup>Gazi University Faculty of Medicine, Department of General Pediatrics, Ankara, Turkey

<sup>2</sup>Gazi University Faculty of Medicine, Department of Pediatric Intensive Care, Ankara, Turkey

<sup>3</sup>Gazi University Faculty of Medicine, Department of Pediatric Infectious Disease, Ankara, Turkey

## Abstract

Pertussis, caused by *Bordetella pertussis*, is an important cause of morbidity and mortality in newborn and infancy. Pertussis is diagnosed clinically. It is confirmed by microbiological-serological tests. In recent years, polymerase chain reaction method has also been used in diagnosis. Macrolide group antibiotics are used in the treatment. Pertussis can occur at any age. However, it can cause mortality in infants who have not been vaccinated. A case report is presented in a 30-day-old newborn patient who was admitted to the pediatric intensive care unit due to apnea and respiratory superficial, and *Bordetella pertussis* was found to be the causative agent.

**Keywords:** Neonatal, apnea, pertussis

## Öz

Boğmaca, *Bordetella pertussis*'in etken olduğu, yenidoğan ve süt çocukluğu döneminde önemli bir morbidite ve mortalite nedenidir. Boğmaca tanısı klinik olarak konular, mikrobiyolojik ve serolojik testlerle kesinleştirilir. Son yıllarda tanıda polimeraz zincir reaksiyonu yöntemi de kullanılmaktadır. Tedavide makrolid grubu antibiyotikler verilir. Boğmaca, her yaşta görülebilir. Ancak aşılama başlanmamış bebeklerde mortaliteye neden olabilmektedir. Bu olgu sunumumuzda 30 günlük yenidoğan hastada apne ve solunum yüzeyelleşmesi nedeniyle çocuk yoğun bakım servisine yatırılan ve etken olarak boğmaca tespit edilen bir *Bordetella pertussis* olgusu sunulmuştur.

**Anahtar Kelimeler:** Yenidoğan, apne, boğmaca

## Introduction

Babies with pertussis often require hospitalization; apnea and pneumonia are commonly seen and it may lead to seizures, encephalopathy, and rarely death.<sup>1</sup> In infants younger than three months of age, the catarrhal phase usually lasts for several days or is absent. The disease begins abruptly with apnea, cyanosis, and gasping attacks. Coughing is not prominent.<sup>2</sup> Cyanosis may follow seizures or apnea may occur without coughing. Apnea may also be the only finding.<sup>2</sup> In infants under one year of age, spasmodic cough attacks last longer in the paroxysmal and convalescent period.<sup>2</sup> In babies under two months of age, hospitalization is seen at the rate of 82%, pneumonia at the rate of 25%, convulsions at the rate of 4%, encephalopathy at the rate of 1%, and mortality

at the rate of 1%.<sup>2-4</sup> The age group with the highest mortality include unvaccinated infants. The case of pertussis infection, which has been rare in Turkey since 2008 with effective vaccination, in this study highlights the importance of the vaccine. In a retrospective study conducted in France, it was reported that 13% of 100 deaths due to bacterial infection were due to pertussis infection and most of them were under 2 months of age.<sup>5</sup>

In our country, there are studies in the literature showing that pertussis in infants has a very serious course, causing hospitalization in intensive care units and causing mortality.<sup>6,7</sup>

In this article, we aimed to present the clinical course and response to macrolide treatment of a patient who presented with cough and bruising in the newborn period, was diagnosed with pertussis by polymerase chain reaction (PCR)

**Address for Correspondence/Yazışma Adresi:** Kürşad Kemal Kara, Gazi University Faculty of Medicine, Department of General Pediatrics, Ankara, Turkey

**E-mail:** kursadkemalkara@gmail.com **ORCID ID:** orcid.org/0000-0001-5961-3918

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rapid diagnostic test, and had apnea, in the light of current literature.

## Case Report

A 30-day-old girl baby, who was born to a 42-year-old mother as G4P4Y3 at 37 weeks +5 days via C/S, started coughing one week ago. Due to the complaints of increased secretions and bruising, she was discharged from the outpatient center with antibiotic (clarithromycin) treatment. Afterwards, she was admitted to the Pediatric Infectious Diseases Department of the Gazi University Medical Faculty Hospital on 13/04/2022, because she had bruising and wheezing at home. The patient was hospitalized in the Pediatric Infection Clinic by starting intravenous ceftriaxone for a preliminary diagnosis of pneumonia. She was transferred to the pediatric intensive care unit due to the development of apnea, prolonged capillary filling time and respiratory distress during monitorization. The laboratory findings of the patient were as follows; hemoglobin: 11.8 g/dL, platelet count:  $454,000 \times 10^3/\mu\text{L}$ , white blood cell:  $18.600 \times 10^3/\mu\text{L}$ , neutrophil count:  $4.100 \times 10^3/\mu\text{L}$ , Coronavirus PCR: negative, procalcitonin: 0.074 ng/mL. No abnormality was detected in her biochemical parameters.

It was learned from her history that her 8.5-year-old sibling died due to cardiomyopathy 2 months ago, so cardiac markers and echocardiography were evaluated. Pro-brain-type natriuretic peptide value was 3656 pg/mL and hs-troponin T-value was 90 ng/L. Echocardiography revealed left heart chambers to be dilated, but it was not clinically significant, and follow-up was recommended.

Because the patient's apnea continued in the pediatric intensive care unit, transfontanel ultrasonography was performed for etiology and found to be normal. Electrolyte abnormality was not observed. Moreover, thyroid function tests and metabolic diseases were investigated and detected to be negative.

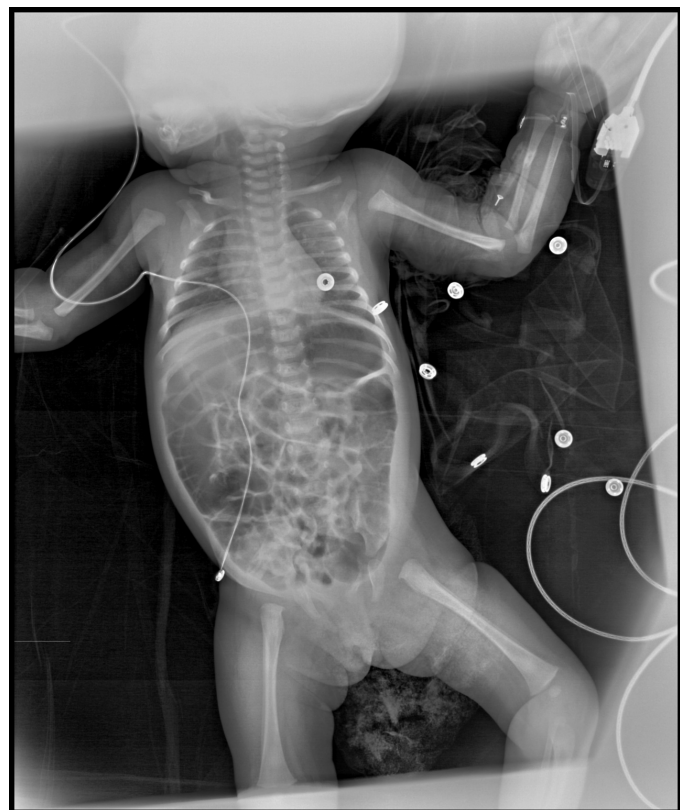
The chest X-ray findings of the patient are shown in Figure 1. Rapid PCR panel test for the respiratory tract was run because the patient had coughing attacks, which suggested pertussis as a clinical picture. As a result of the rapid PCR panel test, *Bordetella pertussis* was detected. Azithromycin was orally started at a single dose of 10 mg/kg/day, and the patient, whose apnea and respiratory distress improved, was transferred to the pediatric infection service. After 5-day treatment with azithromycin, the patient was discharged in good health and azithromycin prophylaxis was given by the pediatric intensive care team following the patient.

## Discussion

*Bordetella pertussis*, the causative agent of whooping cough, is a highly contagious, hard-to-produce, gram-negative polymorphic rod. The disease is transmitted from person to person through respiratory secretions. Both vaccination and having the disease do not provide lifelong immunity. For this reason, vaccination is very important and a booster dose is administered. The disease characterized by spasmodic cough can last about 6-10 weeks. Macrolides are used in the treatment.<sup>8</sup>

Pertussis is seen in all age groups today, but the highest morbidity and mortality rates are observed in infants, especially in those younger than 6 months.<sup>9</sup> Although low antibody titers transplacentally pass from mother to baby, all babies are susceptible to pertussis from the newborn period since the level of antibodies passed is not at a level to protect the disease. Newborn babies usually get whooping cough from their parents and siblings. Armangil et al.<sup>10</sup> identified the source of pertussis infection as the baby's mother in a 9-day-old baby.

Protective pertussis toxin (PT) and filamentous hemagglutinin (FHA) antibodies are passed from the maternal blood to the baby through the placenta. Studies have shown that anti-PT



**Figure 1.** Chest X-ray findings of the patient: There is parallelization and flattening of the ribs, no active infiltration is observed

immunoglobulin-G levels in maternal blood and cord blood samples are close to each other, they decrease by half in the 6<sup>th</sup> week in infants, and undetectable low antibody levels are seen in the 4<sup>th</sup> month. Since there are not enough antibodies to provide effective protection until the beginning of primary immunity in babies, the probability of getting an infection is high.<sup>11</sup>

Apnea can be seen frequently in the neonatal period, especially in preterm infants, due to central nervous system immaturity. However, apnea in term babies mostly indicates an underlying pathology, such as sepsis, intraventricular bleeding, and seizure. Although it is rarely seen after these common pathologies, pertussis should be kept in mind in the differential diagnosis.

Culture method is the "gold standard" in the laboratory diagnosis of pertussis. However, patient-related factors (vaccination status, duration of symptoms, antibiotic use and age), sample collection and transportation conditions, and type and quality of media used affect sensitivity. In the catarrhal stage, very successful results can be obtained with direct culture. The microorganism can be isolated most frequently in the catarrhal and early paroxysmal stages, and it is rarely detected after the 3<sup>rd</sup> week of the disease. Although it turns negative and gives false results with the use of antibiotics, a positive culture provides definitive diagnosis and allows antibiotic susceptibility testing.

Different PCR methods targeting different gene regions of *Bordetella pertussis* have been developed and are used in laboratories for both diagnostic and research purposes. Among them, real-time PCR methods are preferred because they give results in a short time after DNA extraction, are closed systems that minimize contamination, and have high specificity and sensitivity captured with specific probes.

Specific antibodies against pertussis antigens can be detected by the "enzyme-linked immunosorbent assay" method. Serology is specific and sensitive, but not clinically practical. It is particularly sensitive in individuals who have been vaccinated and have a cough lasting more than two weeks. A single high level of antibodies against one or more pertussis antigens or a significant increase in the level of repetitive antibodies are diagnostic criteria. Antibodies are usually formed about two weeks after the onset of symptoms in natural infection. More than 90% of antibodies against *B. pertussis* are developed against PT and FHA. The immune response to other antigens such as pertactin (PRN) and fimbrial antigens is more variable and is seen in 30-60% of them. Past infection can be determined by measuring the increase in the titer of immunoglobulin-A against PT, FHA, PRN antigens of *B. pertussis* in individuals who have administered whole-cell vaccine. Anti-PT antibodies are specific for *B. pertussis*. Antibodies against FHA, PRN,

and fimbrial antigen (FIM) can cross-react with antigens of *B. pertussis* with other microorganisms such as *B. parapertussis*, *H. influenzae*, and *M. pneumoniae*.<sup>12</sup>

Laboratory methods can be used to confirm the diagnosis in cases in which pertussis infection is clinically suspected. In the complete blood count, the leukocyte count is between 15,000 and 100,000/mm<sup>3</sup> at the end of the catarrhal phase and in the paroxysmal phase, and lymphocytosis is typical. Lymphocytes are T and B lymphocytes and are normal cells unlike those seen in viral infections. Excessive elevation of leukocytes with the presence of thrombocytosis is the sign of poor prognosis. Perihilar infiltration, atelectasis, and sometimes butterfly-like infiltration can be seen on chest X-ray, the presence of parenchymal consolidation should be considered as the finding of secondary bacterial infiltration. Rarely, pneumothorax, pneumomediastinum or subcutaneous emphysema may develop.

At the "Global Pertussis Initiative" meeting held in 2005, various strategies were developed for vaccination against pertussis disease. These were determined as the continuation of current infant vaccination, fifth dose vaccination of all preschool children, general vaccination of adolescents, cocooning strategy (vaccination of mothers who have given birth, their families and those in close contact with newborns), selective vaccination of health workers, selective vaccination of workers in childcare centers, and general vaccination of adults.<sup>12</sup>

Vaccination is the best way to reduce pertussis infection and deaths caused by pertussis in early infancy. Vaccination is also of great importance in the scope of preventive medicine. In the light of current information, all babies should be vaccinated starting from the newborn period. In their study on newborns, Knuf et al.<sup>13</sup> showed that acellular pertussis vaccine (Tdap) was quite safe to be administered to babies on postnatal second and fifth days, and antibody titers increased significantly in the early period.<sup>14</sup>

In recent years, a vaccination program called the cocooning strategy has been implemented to prevent pertussis infection in newborns and early infancy. In the cocooning strategy, it is aimed to vaccinate all family members, even uncles, aunts, and babysitters, if any, together with the mother, in order to protect the newborn baby from whooping cough. With this method, the baby is surrounded by an imaginary cocoon against whooping cough. Although it is a somewhat expensive method, when evaluated in terms of cost-effectiveness, it is seen as a positive application and this strategy is applied in developed countries. In studies conducted, the source of pertussis infection in unvaccinated infants was found to be the relatives of the baby, especially the mother at a rate of 30-57%. In another study, it was determined that there was

a 65-70% decrease in the incidence of pertussis in under-risk infants of families in which the cocooning strategy was applied. For this reason, it is recommended that adults who have close contact with infants under 12 months of age should be administered a single dose of acellular pertussis (Tdap) vaccine to protect both themselves and their babies against pertussis.<sup>15,16</sup>

## Conclusion

As in our case, pertussis should be kept in mind in the presence of recurrent apnea and bruising attacks and respiratory distress in a 30-day-old baby, and rapid PCR tests should be used for diagnosis. Cocooning strategy and vaccination should be performed in infants younger than 6 months in primary care preventive medicine. Pregnant women should be informed about acellular pertussis vaccine and they should be followed closely in this respect at regular check-ups.

## Ethics

**Informed Consent:** Informed consent was obtained from the family.

**Peer-review:** Internally and externally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: Concept: K.K.K., M.U.Y., N.K.U., Design: K.K.K., M.U.Y., H.T., Data Collection or Processing: K.K.K., M.U.Y., Analysis or Interpretation: K.K.K., M.U.Y., N.K.U., N.A.Ü., H.T., Literature Search: K.K.K., M.U.Y., Writing: K.K.K., M.U.Y., N.K.U., N.A.Ü., H.T.

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