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A case of undiagnosed *Bordetella pertussis* infection in a neonate

Przypadek nierozpoznanego zakażenia *Bordetella pertussis* u noworodka

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ABSTRACT

Case report: We encountered a 28-day-old infant with progressive respiratory failure diagnosed with pertussis after discharge from the hospital. Here, we describe the disease course, diagnostic difficulties and treatment procedure. After 20 days of treatment based on the doctors' experience (without an established diagnosis), the child was deemed healthy and discharged. At the 6-month follow-up, the child was healthy and showed normal development. No other *Bordetella pertussis* infections among newborns or hospital staff who were in contact with the patient and his family were reported.

Conclusion: Pertussis morbidity is high in infants younger than 6 months, and the disease should be suspected in any case of respiratory failure. The serological diagnosis of pertussis depends mostly on the organization and effectiveness of the healthcare system; therefore, medical history and physical examination are vital factors in the diagnostic process. The treatment of pertussis in infants should take place in centres with an intensive care unit.

Keywords: *Bordetella pertussis*; neonatal pertussis.

ABSTRAKT

Opis przypadku: W pracy przedstawiono przypadek 28-dniowego noworodka przyjętego do kliniki z objawami narastającej niewydolności oddechowej, u którego rozpoznanie krztuśca zostało ustalone dopiero po wypisaniu ze szpitala. Omówiono przebieg choroby, trudności diagnostyczne i terapeutyczne. Po 20 dniach leczenia empirycznego, opartego na doświadczeniu lekarzy, pacjent został wypisany do domu jako zdrowy. Dziecko rozwija się prawidłowo. Nie odnotowano innych przypadków zachorowania na krztusiec wśród noworodków i personelu, który miał kontakt z pacjentem.

Wniosek: Ponieważ śmiertelność z powodu krztuśca wśród dzieci do 6. miesiąca życia jest duża, podejrzenie zakażenia *Bordetella pertussis* powinno mieć miejsce w każdym przypadku zaburzeń oddechowych u małych dzieci. Z uwagi na trudności diagnostyczne nadal kluczowy dla rozpoznania krztuśca u niemowląt jest wywiad chorobowy i badanie kliniczne. Leczenie małych pacjentów powinno odbywać się na oddziałach ze stanowiskami do prowadzenia intensywnej terapii oddechowej.

Słowa kluczowe: *Bordetella pertussis*; noworodek.

INTRODUCTION

The incidence of *Bordetella pertussis* infection among adolescent and adults is increasing worldwide; however, the peak incidence and highest mortality rates occur among infants [1]. In 2012, 4684 cases of *B. pertussis* infection were registered in Poland (12.2/100,000), 2183 in 2013, and 2102 in 2014 [2]. The morbidity was 6.3 per 100,000 persons, but this value is highest in children below 3 years of age at 38.1 per 100,000. Infants are especially vulnerable to this infection because maternal placental antibodies decline to negligible levels by 2 months of age. In Poland, the first pertussis vaccination is administered after 6 weeks of age, and 98.3–99.7% of children are vaccinated [3]. Despite this good coverage, recent studies have reported that young infants continue to suffer from pertussis due to low antibody titres [4]. The disease course is most severe in infants, with 95% of patients requiring mechanical ventilation. Mortality is directly related to age, and is approximately 24% among infants [5].

CASE REPORT

An infant was delivered at the Pomeranian Medical University in Szczecin, by spontaneous vaginal delivery after 37 weeks of gestation. The birth weight was 3000 g and the infant was in good clinical condition (9/10 Apgar score). At 28 days after birth the infant was admitted to the Department of Neonatal

Diseases, Pomeranian Medical University, a few days after exhibiting symptoms of mild viral upper respiratory tract infection. His mother experienced weakness and coughing since the day of childbirth, and was administered antibiotics (7-day amoxicillin and clavulanate therapy) but did not show clinical improvement. The patient's father and grandfather complained of similar symptoms but were not treated.

The patient was admitted to our department after the coughing and cyanosis worsened abruptly. Clinical observation revealed dyspnoea, peripheral cyanosis, and pronounced jaundice; body temperature was normal. The heart and respiratory rates were within the normal range, but during a fit of coughing the heart rate dropped to 72 bpm with a concomitant decline in blood oxygen saturation to 80%. Lung auscultation revealed prolonged expiration and bilateral crackles. During heart auscultation a systolic murmur was recorded along the left side of the sternum. The liver was palpable 3 cm below the costal margin. Routine haematological tests showed 18,600 white blood cells/μL and 48% lymphocytes. C-reactive protein (<0.2 ng/L) and procalcitonin (0.06 ng/L) were within the normal range. Bacterial infection was excluded on the basis of biochemical test results. Chest X-ray showed small patches, shadows around the hilum, suggesting lung inflammation and cardiac enlargement. A cardiologist was consulted, who excluded myocarditis and heart failure. Bacteriological investigations of blood culture and throat and rectal smears were negative. Serological tests for *B. pertussis*, Epstein–Barr virus, herpes simplex virus (HSV), *Chlamydia pneumoniae*, *Mycoplasma hominis,* and *Mycoplasma pneumoniae* were negative. Polymerase Chain Reaction (PCR) assay for enterovirus, HSV, adenovirus, *Pneumocystis jiroveci*, and human cytomegalovirus were negative. Due to technical problems, PCR for *B. pertussis* DNA was not performed.

Due to the initial symptoms of poor sucking and paroxysmal cough, nasogastric feeding and eventually total parenteral nutrition were administered. The patient was treated with passive oxygen therapy, inhalation with physiological salt and a mixture of fenoterol hydrobromide and ipratropium bromide (Berodual; 0.1 and 0.05 mg, respectively, 3× daily) and ambroxol hydrochloride (Mucosolvan, 7.5 mg 2× daily). Subsequently, we observed attacks of dry coughing and wet coughing, followed by apnoea (blood oxygen saturation: 56%, heart rate: 60 bpm). On the 5^{th} day of hospitalisation the clinical condition worsened, increasing the white blood cells and lymphocyte counts (30.2 G/L and 72%, respectively). Clarithromycin (7.5 mg/kg 2× daily) and trimethoprim-sulphamethoxazole (Biseptol 480; 8 mg/kg 2× daily) were administered intravenously. The baby was intubated, and a yellow secretion was removed from the trachea and main bronchi via an endotracheal tube. Artificial mechanical ventilation (synchronised intermittent mandatory ventilation) was applied for the next 5 days due to the persistent yellow secretion from the respiratory tract.

From the 7^{th} day after admission encephalopathy was observed with altered consciousness, body stiffness with hands in fists, and sensitivity to being touched. There were no changes in the cerebrospinal fluid (leukocytes/mm^3: 2 lymphocytes, 12 neutrophils; 52.7 mg/dL protein, 55 mg/dL glucose). Ultrasonography of the brain did not reveal any abnormalities. The patient suffered a cardiac arrest the next day, and the blood oxygen saturation declined to 20%. Reanimation with adrenaline and hydrocortisone was successful. Urine output decreased to <2 mL/(kg·h), but returned to normal after furosemide treatment. Since there was no clinical improvement and increasing lymphocytosis, viral infection was suspected and antimicrobial treatment was replaced with acyclovir (10 mg/kg 3× daily for 10 days) and systemic steroid therapy (5 mg/kg hydrocortisone daily for 5 days). From day 10 after admission the infant's clinical condition (including neurological symptoms) improved, and an electroencephalogram revealed no abnormalities. Oxygen therapy and parenteral treatment were discontinued after 13 and 15 days of hospitalisation, respectively, and he was discharged on day 20 in good clinical condition, receiving breast milk, and with occasional coughing. He is currently being followed up at the outpatient clinic of the neonatology and pulmonology department. At the 6-month follow-up, the child was healthy and showed normal development.

Thereafter, *B. pertussis* serological tests of the patient's mother, father, and grandfather revealed increased IgG titre. The IgA titre of the grandfather was ambiguous. A serological control test performed after 1 month revealed increased IgG titre (31,924–33,103 NTU; normal, <11 NTU) and IgA titre (14,581 NTU) in the mother; high IgG titre (33,492–28,074 NTU) and ambiguous IgM titre in the father. The serological tests of the child remained negative.

DISCUSSION

Bordetella pertussis-infected young infants present with atypical symptoms, including apnoea, cyanosis and wheezing, and laboratory findings like leukocytosis and lymphocytosis, and are often treated for acute bronchitis and bronchiolitis [6]. The same manifestations were found in our patient, who required symptomatic treatment.

We performed different serological tests as well as a PCR assay, which were negative. Unfortunately, due to technical problems, PCR for *B. pertussis* DNA was not performed. A study in neonates and young infants suggests that PCR and/or culture should be done using nasopharyngeal swabs or aspirates as soon as possible after the onset of symptoms. The IgG-anti-PT titres are only meaningful in older children/adults, including parents and other household members. In vaccinated children the culture of sputum samples from adolescents and adults with coughing for >2 weeks and PCR of nasopharyngeal samples should be carried out. PCR and IgG-anti-PT titres should be used for adolescents and adults with symptoms of coughing for >3 weeks. The IgG-anti-PT titres are detectable only if the cough persists for at least 2–3 weeks. In outbreaks, PCR and culture should be performed from nasopharyngeal samples, and IgG-anti-PT titres of serum should be obtained [7]. Ragucckas et al. reported that the serum IGA, IgG, and IgM antibodies to specific antigens increase after *B. pertussis* infection [5]. We could not culture *B. pertussis*; moreover, antibodies against

whole cells were used for serological testing. Serology is frequently negative in young infants with pertussis, such as in our case [8]. However, *B. pertussis* infection was confirmed in the family, and characteristic symptoms were observed in the infant with concomitant lymphocytosis. Family members are the main source of pertussis among infants with an identifiable source [1, 6]. The symptoms first appeared in the grandfather, followed by the mother shortly after delivery. The father and child suffered 3 weeks thereafter. All the adults in the family had been vaccinated during childhood. It is known that vaccination confers resistance for only 5–10 years [9].

Azithromycin (5-day course) or clarithromycin (7-day course) are used to treat neonatal pertussis. Systemic corticosteroids may reduce the severity and duration of cough paroxysmus but are only recommended in infants with life-threatening illness [5]. In our case, despite clarithromycin administration, there was no clinical improvement and the patient developed encephalopathy. Due to the lack of confirmation of pertussis, clarithromycin was discontinued after 3 days of treatment, and acyclovir and systemic corticosteroids were administered. While this treatment elicited clinical improvement, the reason this treatment was successful remains unclear. Further, we are unable to clarify whether pharmacological treatment was necessary at all.

Pertussis morbidity is high in infants younger than 6 months. Fast dissemination of the pertussis infection among children in hospitals has been reported [10]. During the first 3 days of hospitalisation our patient was in a room with other 3 infants and was visited by parents. Since pertussis was diagnosed only after the newborn was discharged, no special prophylactic measures could be taken. No pertussis infection was reported over the next 6 months in children or hospital staff who had contact with the patient.

CONCLUSION

Pertussis morbidity is high in infants younger than 6 months, and the disease should be suspected in any case of respiratory failure. The serological diagnosis of pertussis depends mostly on the organization and effectiveness of the healthcare system, and therefore medical history and physical examination play key roles in the diagnostic process. The treatment of pertussis in infants should take place in centres with an intensive care unit.

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