Influenza A (H1N1) and Respiratory Syncytial Virus (RSV) Coinfection in a Newborn Child: A Case Report

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Abstract

This paper presents a case of coinfection of influenza A virus (H1N1) and respiratory syncytial virus (RSV) in a male newborn. On the first day of life, the newborn required passive oxygen therapy, followed by respiratory support with nasal continuous positive airway pressure (nCPAP) due to respiratory insufficiency. As the newborn’s respiratory effort was intensifying, he was intubated. In the second day of life, a nasopharyngeal swab was taken yielding the presence of H1N1 and RSV in the RT-PCR test. The child was isolated and given oseltamivir and empirical antibiotic therapy, which improved his condition. Other newborns who initially stayed with the sick child in the post-delivery room did not obtain oseltamivir prophylactically as their nasopharyngeal swabs were negative. The child’s parents denied the occurrence of influenza-like symptoms within 14 days of delivery, which suggests a transplacental transmission of the child’s infection or asymptomatic course of infection in the parents. In conclusion, this report confirms the possibility of viral coinfections in newborns, which points attention to considering a panel of respiratory viruses in the diagnostics. Symptoms of influenza in newborns may be atypical, including a fever-free course. Oseltamivir treatment in newborns with influenza seems an effective therapeutic measure.

Keywords

Coinfection · Influenza · Newborn · Nasopharyngeal swab · Respiratory syncytial virus

1 Introduction

Influenza is an acute infectious disease caused by a virus from the Orthomyxoviridae family. It is mainly spread by droplet and contact transmission. The World Health Organization (WHO) estimates that 5–15% of the global population suffers from influenza every season, which corresponds to 3–5 million cases with about 500,000 deaths related to influenza and its complications (WHO 2018). Children, in particular those under the age of 5, present a reservoir of influenza viruses and the incidence is in this age group is highest (Wang et al. 2020). The global mortality associated with influenza in children under 5 years of age was estimated at 28,000 to 111,500 cases in 2008, with deaths reported nearly exclusively in poor and developing
countries (Nair et al. 2011). Data on the influenza epidemiology in young children, infants up to 6 months of age, and newborns are scarce and they come mainly from the United States, where the estimated number of influenza-associated hospitalizations of children up to 5 years of age is about 900,000 a year, including 228,000 hospitalizations of infants under 6 months (Nair et al. 2011). In the United States, the cumulative influenza incidence was 44 hospitalization per 100,000 children aged under 5 years in the 2016/2017 season. Wang et al. (2020) have concluded that 23% of children’s hospitalizations can be associated with influenza and 36% of deaths among infants under 6 months of age with influenza and its complications.

It has been believed for many years that newborns are unaffected by an influenza virus infection because they are protected by transplacentally acquired antibodies and are exposed to a rather small number of social contacts associated with infection transmission (Puck et al. 1980). Reports on influenza in newborns are scarce. Wilkinson et al. (2006) and Sert et al. (2010) have reviewed influenza cases in prematurely born infants and show that the infection course is either asymptomatic or severe; in the latter case, it may involve respiratory failure and death. These authors have also described influenza outbreaks in neonatal units. Due to the rarity of influenza in newborns and rather ill-defined disease course, this report presents a case study of coinfection of influenza A (H1N1) virus and respiratory syncytial virus (RSV) in a newborn child. To the best of our knowledge, this is the first description of such coinfection in a newborn child.

2 Case Report

A male newborn from second pregnancy but the first childbirth. The first pregnancy ended in miscarriage. The newborn was delivered in the 38th week of pregnancy by C-section due to premature drainage of amniotic fluid and uterine fibroids. The birth weight of 3.245 g and an average general condition, Apgar score of 7-7-9-10. At birth, he required suctioning and assisted breathing with a Neopuff resuscitator to provide positive pressure ventilation (Fisher & Paykel Healthcare GmbH, Schorndorf, Germany). A Streptococcus agalactiae test gave a negative result and the umbilical artery blood gas content was normal. The baby was moved to the observation unit and placed in an incubator. A physical examination revealed skin pallor, slight tenderness, lung crackles on auscultation, respiratory effort in the form of expiratory grunting, systolic murmur (1–2/6 on the Levine scale). The parenchymal organs in the abdominal cavity were of normal size. Peripheral capillary O₂ saturation decreased 75%, which necessitated the implementation of supplemental oxygen therapy of inspiratory fraction of oxygen (FiO₂) of 0.4. Capillary blood gasometry was the following: pH 7.29, PCO₂ 55.4, HCO₃⁻ 22.1 mM, and BE 2.4 mM.

Due to threatening respiratory failure, the baby was transferred to the intensive care unit. He was connected to the respiratory support with nasal continuous positive airway pressure (nCPAP). The resulting clinical improvement enabled a reduction of supplemental oxygen concentration to FiO₂ of 0.25. The levels of interleukin 6 (IL-6) and C-reactive protein (CRP) were increased; 525.2 pg/mL (normal range: 0.0–9.7) and 0.9 mg/L (normal range: 0.0–5.0), respectively. The leukocyte count was with the normal range – 15.1 × 10⁹/L (normal range: 9.0–30.0 × 10⁹/L). Bilateral interstitial inflammatory infiltrates were found in a chest X-ray. Empirical antibiotic therapy consisting of ampicillin and gentamicin and enteral feeding with mother’s milk was initiated. In the following hours, respiratory support with nCPAP continued. Nonetheless, increasing respiratory effort and demand for oxygen (FiO₂ of 0.4), anxiety, possetting, and periodic saturation dips were present. The access to the umbilical vein was made to begin trophic nutrition. At this stage, blood leukocyte count increased to 24.1 × 10⁹/L, with a stable gasometry profile.

At the end of the first day of newborn’s life, there was no clinical improvement and respiratory acidosis was observed, necessitating the intubation, mechanical synchronized intermittent mandatory ventilation (SIMV) with peak inspiratory pressure
(PIP) +23 cmH₂O, positive end-expiratory pressure (PEEP) +4 cmH₂O, FiO₂ of 0.6–0.5, and sedation with fentanyl in a dose of 1–5 μg/kg/h in a continuous drip, depending on the pain scale result. The measure undertaken led only to a temporary improvement of the condition. Therefore, the ventilatory parameters used were upwardly modified, with the maximum FiO₂ of 0.7 and a breathing rate of 60–75 per min. Blood pressure was at a normal level throughout, no signs of circulatory failure were observed, and blood gas content remained stable. Repeated chest X-ray showed bilaterally decreased lower lung aeration and a small right pneumothorax that did not require pleural drainage. Blood cultures remained negative. The echocardiographic screening showed a patent foramen ovale and normal structures of the heart and large vessels according to the baby’s age. The leukocyte index, i.e., the mean ratio of immature to total neutrophils (I/T), was in the normal range of <16 as were the levels of serum transaminases. The serum gamma-glutamyltranspeptidase (GGTP) (154.0 U/L) and procalcitonin (PCT) (8.8 ng/mL) were moderately increased. The following PCT apportioning was considered: < 0.5 ng/mL – low risk of early bacterial infection or possible local infection; 0.5–2.0 ng/mL – possible systemic bacterial infection, recommended control test within 6–24 h; and > 2.0 ng/mL – probable systemic infection or sepsis. The general condition of the baby was rather severe but stable on the second day of life, with no tendency to improve. An ultrasound transdermal examination and the abdominal cavity examination were performed, both showing no abnormalities. Any cardiological causes of the health condition, particularly a congenital heart disease or pulmonary hypertension, were excluded as well. Suspicion of infection of viral etiology arose due to the current presence of the epidemic influenza season. The suspicion was strengthened by the ambiguous clinical picture, no symptoms of a defined perinatal infection, and an unclear medical history of the mother. However, a rapid diagnostic test for the respiratory syncytial virus (RSV) was negative.

Swabs were taken from both nostrils for the polymerase chain reaction (PCR) examination of 12 respiratory viruses, including influenza, parainfluenza 1,2,3,4, human metapneumovirus, adenovirus, rhinovirus, coronaviruses 229E/ NL63 and OC43/HKU1, enterovirus, and RSV. The examination confirmed the presence of the genetic material of influenza A virus and RSV. The decision was made to continue the antibiotic therapy for another 7 days despite a negative blood culture, which could have to do with too short a microbiological incubation period. In the meantime, the causal treatment with oseltamivir, a neuraminidase inhibitor, was implemented in a dose of 2 mg/kg daily, bid, for 5 days. The baby was isolated but the mother’s visits were allowed observing strict sanitary regimes. The baby’s condition started improving gradually and he was extubated on the fifth day of his life. Respiratory support was altered to a noninvasive nCPAP with the FiO₂ of 0.35–0.23. Only was slight physiological jaundice noticed. The enteral nutrition was gradually increased, first with a tube and then with a feeding teat. On the sixth day of life, respiratory support and parenteral nutrition were terminated and the umbilical vein catheter was removed. From the eighth day, the baby was breastfed, with a modified milk supplement. Complete blood count, white cell smear, CRP, and acid-base balance all showed no irregularities. The biochemical markers of potential heart muscle damage such as troponin, phosphocreatine kinase, and CK-MB were within the normal limits.

On the first day of life, the baby was vaccinated against hepatitis B and was subjected to metabolic and hearing screenings. BCG vaccination was postponed for 2 weeks after discharge from the hospital due to a severe course of the infection. The baby was discharged after 12 days in a good general condition and a weight gain of up to 3302 g. A control visit in a neonatal outpatient clinic was recommended 1 week after discharge and a temporary ultrasound examination 2 months later. Additionally, control audiological, ophthalmological, and cardiological examinations were scheduled for the near future.

Two other prematurely born neonates who stayed in the same post-delivery room were closely monitored for disease symptoms and had nasal and throat swabs taken for the PCR tests for...
the presence of influenza virus and RSV. The genetic material of RSV and enterovirus was identified in one, whereas the other tested negative. Neither child showed any disease symptoms related to influenza or coinfection. These newborns were discharged from the hospital when they reached the minimum weight of 2000 g, had no sign of infection, did not have desaturations or apneic episodes, and were mature enough to draw breast milk or be bottle-fed.

3 Discussion

The case of symptomatic influenza A (H1N1) in a male baby born at term, presented in this paper, is one of a few ever reported. The notable features of this case were the early onset of symptoms on the day of birth, a mismatch between a fever-free course and increasing respiratory insufficiency that necessitated the intubation and respiratory support, and no influenza-like symptoms in the mother and her immediate environment during the perinatal period. The baby’s nasopharyngeal sample was positive for the genetic material of influenza A (H1N1) virus. The diagnosis of influenza was confirmed by a significant improvement after the implementation of oseltamivir treatment. However, the nasopharyngeal sample also tested positive for the respiratory syncytial virus (RSV), which points to a coinfection. Coinfections with respiratory viruses have previously been reported but the severity of symptoms appears to be independent of the number of etiological factors (Pichler et al. 2018). In the literature, there are single descriptions of influenza cases in the first hours of life, whereas symptomatic cases of RSV concern newborns aged 5–282 days (58 days on average) and mostly are nosocomial infections related to epidemic outbreaks in intensive care units for premature babies (Pichler et al. 2018). The RSV alone infections, notably, have a favorable course with low mortality, which makes the disease similar to the influenza of the neonatal age (Marcone et al. 2018; Reese et al. 2016; Reid et al. 2011).

The first description of pneumonia caused by influenza A (H1N1) in a baby born from a full-term uncomplicated pregnancy newborn was reported by Sert et al. (2010). In that case, the parents had reported influenza-like symptoms 2 weeks before delivery. There were also other differences in the infection course when compared with the case reported in the present report. The infection appeared on the 6th day after birth, and it was highly symptomatic with fever, bilateral crackles on auscultation, interstitial bilateral inflammatory lung changes in X-ray, and increased serum CRP. Sepsis was excluded based on negative blood and urine cultures. Empirical antibiotic therapy consisting of cefazoline and gentamycin was implemented, which was ineffective. Since viral etiology was then confirmed, oseltamivir was added on to the antibiotic treatment, which improved the baby’s condition.

Other reports concerned outbreaks of influenza infection in prematurely born babies in intensive neonatal care units during the pandemic of 2009/2010. Milupi et al. (2012) have reported an outbreak of influenza A in the UK where three newborns aged 13–28 days became ill. The predominant symptoms were bradycardia, desaturation, tachypnea, and apnea. Tsagris et al. (2012) have reported a similar outbreak in Greece where three newborns aged 47–84 days became ill, with the symptoms of runny nose, fever, and apnea. Rocha et al. (2010) have reported influenza in 12 newborns aged 3–38 days in Portugal, in whom deterioration of respiratory function necessitated the initiation of mechanical ventilation. Another two influenza A outbreaks took place in the United States. In one, influenza A was diagnosed in three prematurely born babies aged 16 to 51 days, with the symptoms of lung crackles, apnea, desaturation, and convulsions, which necessitated the artificial ventilation (Vij et al. 2011). In the other, Pannaraj et al. (2011) have reported influenza was reported in 11 newborns aged 5–192 days, with fever, desaturations, and other typical respiratory symptoms as outlined above. In all those reports, oseltamivir treatment was implemented in each newborn, regardless of the time that had elapsed since the occurrence of symptoms, and the treatment was effective. There were other single cases of influenza in newborns reported. One such case was in Israel where a baby born at 32 weeks
developed the symptoms of respiratory failure on the 50th day of life. After a course of oseltamivir treatment, the child was discharged from the hospital in a good condition 10 days later (Barak et al. 2010). The other was in India where a baby also born at 32 weeks developed the symptoms of respiratory failure on the 6th day of life. Influenza A (H1N1) was diagnosed 4 days later and oseltamivir treatment was implemented. In this case, the treatment was ineffective and the baby died after a week (Jajoo and Gupta 2010). Noticeably, however, the influenza mortality rate in newborns is very low, which distinguishes this age-group from infants and the elderly. The reasons behind this phenomenon are unknown, but it is usually ascribed to better care and closer supervision in intensive care units, where newborns with influenza are treated (Pichler et al. 2018). The anti-epidemic measures, akin to those used in the present report, such as patient isolation, withholding of family visits, and close observation of other babies who could have been in contact with the sick, were implemented. In the present case, no pharmacological post-exposure prevention in babies who were in contact with the sick one was used, whereas in some of the previous reports such prevention was used (Pannaraj et al. 2011; Rocha et al. 2010). The sources of infection, whenever identifiable, were unvaccinated medical staff and sick members of the children’s immediate family. In the present case, the source of the influenza infection could not be identified. There was no influenza infection or any respiratory symptoms in the baby’s parents in the 2 weeks preceding the delivery. Therefore, there were two possible origins of the infection: asymptomatic infection in the parents with transmission to the baby or vertical transmission from mother to baby during the time just before and after birth across the placenta, the breast milk, or through direct contact about the delivery.

Viral etiology should be considered in the differential diagnosis of respiratory infections in newborns. Viral coinfections in newborns also are possible. Therefore, the diagnostics should include a panel of respiratory viruses. Symptoms of influenza in newborns may be atypical, including a fever-free course but the presence of respiratory insufficiency necessitating the initiation of mechanical ventilation. Transplacental
transmission of the influenza virus cannot be excluded in newborns. Oseltamivir treatment of influenza seems to be effective in newborns.

Conflicts of Interest The authors declare no conflicts of interest concerning this article.

Ethical Approval All procedures performed in studies involving human participants were compliant with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The paper was accepted by a Review Board of Warsaw Medical University in Poland.

Informed Consent Written informed consent was obtained from the parents of the newborn baby presented in this case report.

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