Three Nonfatal Cases of Neonatal Adenovirus Infection

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Neonatal adenovirus infection is considered a rare and fatal disease. Three nonfatal neonatal adenovirus infections manifesting as conjunctivitis or conjunctivitis with other nonspecific symptoms are described. Adenovirus DNA was detected by PCR in eye swabs from two patients and in both cerebrospinal fluid and eye swabs in the third patient.

CASE REPORTS

Case 1. A female neonate (18 days old) presented with a 2-day history of vomiting after feeds, high fever, and irritability. A screen for bacterial sepsis, which included examination of the cerebrospinal fluid (CSF), was initiated. Intravenous antibiotics were administered but discontinued once negative bacterial culture results for CSF and blood were obtained. At 20 days of age, the patient’s symptoms resolved, but residual conjunctivitis was noted. Eye swabs (left and right eye) were taken for Chlamydia trachomatis investigation, and chloramphenicol treatment was commenced. The patient’s symptoms settled, and she was discharged from the hospital 3 days after admission.

Case 2. A 1.9-kg male was born via vaginal delivery at 35 weeks of gestation. His 17-year-old mother was well during delivery and showed no signs or symptoms of infection prenatally. Examination of the neonate at delivery was entirely normal, but jaundice that was mild and did not require phototherapy developed on day 4. On day 8, the patient developed conjunctivitis and received chloramphenicol. Eye swabs showed only very scanty growth of coliforms.

Case 3. A 3-kg female neonate was born at 38 weeks of gestation by Caesarean section. Conjunctivitis was noted on day 5 of life, and a conjunctival swab was investigated for C. trachomatis. At 35 days of age, the baby presented with symptoms of an upper respiratory tract infection and was discharged without specific treatment. Subsequently, she had recurrent cough and chest infections with a probable diagnosis of virus-induced wheezing. All tests for immunofunction were normal. X-ray of her chest showed perihilar bronchial wall thickening. She was noted at one point to have a squint and was referred to the ophthalmologists, but no ocular pathology was noted.

Eye swabs collected for C. trachomatis investigation were placed in sucrose phosphate transport medium and extracted using a simple lysis buffer procedure as described previously (6). Guanidinium thiocyanate was used for extraction of DNA from the CSF sample (5). Extracted samples were tested by PCRs for detection of adenovirus, herpes simplex virus, and C. trachomatis (6, 8). In addition, an antigen detection method (immune dot blot test) was used for detection of C. trachomatis (15). For virus isolation, the untreated swabs were inoculated into three cell lines (Vero, HEL 229, and Hep-2) and maintained for 4 weeks. Typing of adenovirus was performed using a PCR-based identification method (7).

Although chlamydial conjunctivitis was suspected clinically, all three neonates were C. trachomatis negative by both PCR and immune dot blot. PCR for herpes simplex virus was also negative. Adenovirus DNA was detected by PCR in all conjunctival swabs tested and in the CSF specimen taken from patient 1. Subgrouping of adenovirus PCR products using a PCR-based identification method indicated the presence of adenovirus subgroup D (possibly adenovirus type 8) in patients 1 and 2 and subgroup E (adenovirus type 4a) in patient 3. The one eye swab taken for virus culture (patient 1) was isolation negative even after 4 weeks of incubation. The adenovirus PCR utilized in this study is sensitive and has been shown to be significantly superior to adenovirus isolation (6, 8). Failure to isolate the virus from specimens that are PCR positive may be due to the fastidious cell culture requirements of certain adenoviruses which preclude their isolation in routine cell culture, the very slow growth rate of some strains of adenoviruses, or loss of virus infectivity during transport to the laboratory (22).

Adenoviruses are common pediatric pathogens that result in respiratory illnesses which are usually benign but which can sometimes be severe (4, 11). Neonatal adenovirus infection has rarely been reported, but in most cases the outcome of the infection was fatal (1–3, 12, 14, 16, 21), although cases with and without complications have been reported (19). A fatal disseminated adenovirus infection was described for a neonate born after spontaneous vaginal delivery who suffered from severe keratoconjunctivitis, pneumonitis, pharyngitis, skin lesions, hepatosplenomegaly, and hemorrhagic diathesis (14).

Another study (2) described adenovirus infection of four neonates and reviewed nine further neonatal adenovirus cases.
reported in the literature. In all cases, adenovirus infection followed vaginal delivery, and symptoms began within 10 days of birth. One half of the mothers were ill with upper respiratory symptoms, fever, and/or constitutional symptoms in the perinatal period. All infants had pneumonia, lethargy, fever, and hepatomegaly, but none developed any form of ocular abnormality. In 11 of the 13 neonates (85%), infection was fatal, with death occurring 4 to 19 days after onset of symptoms.

Three further cases of neonatal adenovirus infections where adenovirus pneumonia was diagnosed postmortem have been described (12). In two cases, the patients were born by Cesarean section at 35 or 36 weeks of gestation, and the other patient was born by vaginal delivery at 43 weeks of gestation. Respiratory insufficiency was detected just after birth or in the immediate postnatal period and was associated with lethargy and chest X-ray findings of pneumonic infiltration. Postmortem findings of these neonates were consistent with predominant lung involvement.

More recently, nonfatal adenovirus infection has been described for seven neonates (19). All manifested with nonspecific symptoms, such as excessive crying, apnea, cyanotic episodes, maculopapular rash, and fever, but none developed conjunctivitis. The serotypes of adenovirus involved were not described.

Potential sources of adenovirus infection in neonates include horizontal transmission (from mother or other family members) and vertical transmission. Vertical transmission may be suggested by the presence of symptoms in mothers preceding or shortly after delivery and the occurrence of symptoms in the neonate evident within the first 3 days of life. Acquisition of the virus from the genital tract is possible. Several reports have documented adenovirus infection of the genital tract (9, 10, 13, 18, 20). The most predominant serotypes were adenovirus type 37 followed by adenovirus types 8 and 19; adenovirus types 1, 2, 9, 10, 18, 22, 26, and 32 have also been reported but were not associated with conjunctivitis.

The factors that control the severity of adenovirus infection in neonates remain to be elucidated, although the presence of marked abnormalities in blood lymphocytes and cytokine profile has been noted in cases of fatal adenovirus infection in children aged between 30 and 730 days (17). The variation in severity may be serotype dependent, as fatal infection appears to have been mainly associated with serotypes of subgroup B, possibly due to their predilection for respiratory tissues. It is possible that infection with subgroup D strains results in only transient conjunctivitis. Conjunctivitis in neonates is usually investigated for possible C. trachomatis infection, but our results indicate that adenovirus infection should also be considered.

REFERENCES