OUTBREAK OF ADENOVIRUS TYPE 30 IN A NEONATAL INTENSIVE CARE UNIT

HOWARD FADEN, MD, RALPH J. WYNN, MD, LINDA CAMPAGNA, RN, AND RITA M. RYAN, MD

Objectives To describe an outbreak of adenovirus, type 30, in a neonatal intensive care unit (NICU).

Study design This was a retrospective, observational study.

Results An outbreak of adenovirus infection occurred in an NICU. It lasted 6 months and involved 21 of 333 (6.3%) infants. The introduction of infection control measures controlled the outbreak; however, premature discontinuation of the measures resulted in a second wave of cases. The virus caused pneumonia in 7 infants, conjunctivitis in 7 infants, pneumonia and conjunctivitis in 1 infant, and upper respiratory tract illness in 1 infant. Infection was asymptomatic in 5 infants. Six infants died. Death was associated with the presence of pneumonia ($P = .0001$), administration of steroids ($P = .003$), and mechanical ventilation ($P = .02$). Investigation into the origin of the outbreak suggested that the virus may have been introduced and spread during ophthalmologic procedures.

Conclusions Adenovirus type 30 can cause severe disease among premature infants in an NICU. Infants with severe bronchopulmonary dysplasia requiring mechanical ventilation are more likely to have development of adenovirus pneumonia and die. Standard infection control measures are effective in controlling an outbreak. Ophthalmologic procedures continue to be a potential source of adenovirus outbreaks. *(J Pediatr 2005;146:523-7)*

Adenovirus is a common respiratory virus. It has the capacity to cause upper respiratory tract and lower respiratory tract illnesses, conjunctivitis, gastroenteritis, cystitis, and rash. Adenoviruses are transmitted primarily by direct contact and by the fecal-oral route. Adenoviruses are unusually stable and can persist for prolonged periods in the environment.[1-3] There are 49 serologically distinct types of adenoviruses that can cause human disease.[1] Some types, such as 1, 2, 5, and 6, are endemic in various parts of the world, whereas other types, such as 7, 8, 19, and 37, are associated with outbreaks.

Although the mechanism of protection against adenovirus is not fully understood, severe, often fatal, or chronic infections in individuals with severe combined immunodeficiency, organ transplantation, and AIDS and in neonates suggest that cellular immune mechanisms may play a major role in limiting infection.[4,5] Available data suggest that neonates have diminished cellular immunity. In particular, T-lymphocytes and natural killer cells exhibit reduced cytotoxic activity.[6] Since antibody also may contribute to the defense against adenoviruses, the limited antibody repertoire displayed by the B-lymphocytes of neonates and the markedly reduced concentrations of passively acquired maternal antibodies found in premature infants make the premature infant highly susceptible to adenovirus.[6] The current report describes an outbreak of adenovirus type 30 among 21 infants in a neonatal intensive care unit (NICU).

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METHODS

This is a retrospective, observational study. Data were obtained from medical records and infection control records. The fluorescent antibody tests for the rapid detection of adenoviruses (Imagen Adenovirus by Dako with a sensitivity of 86% and a specificity of 100%) and cultures on human lung carcinoma and monkey kidney cell monolayers were performed in the virus laboratory of the hospital. Infants were screened when symptomatic, and routinely on a weekly basis. Typing of adenovirus isolates were performed by neutralization assays in the New York State Laboratory in Albany, New York. Typing was

BPD	Bronchopulmonary dysplasia	ROP	Retinopathy of prematurity
IVIG	Intravenous immunoglobulin	URI	Upper respiratory infection
NICU	Neonatal Intensive Care Unit		

From the Department of Pediatrics, State University of New York at Buffalo, School of Medicine and Biomedical Sciences, the Divisions of Infectious Diseases and Neonatology, and the Office of Infection Control at the Women and Children's Hospital of Buffalo, Buffalo, New York.

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Reprint requests: Howard Faden, MD, Department of Pediatrics, SUNY School of Medicine at Buffalo, Women and Children's Hospital of Buffalo, 219 Bryant Street, Buffalo, NY, 14222.

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Table. Comparison of characteristics of 15 infants who survived and 6 infants who died with adenovirus infection

Characteristics	Survived	Died	*P* value
Birth weight (g)	1000.9	780.3	NS
Gestational age (wk)	27.1	25.7	NS
Sex (% male)	7 (40.0)	3 (50.0)	NS
Race (% white)	12 (80.0)	4 (66.7)	NS
Age at infection (wk)	9.1	8.8	NS
Pneumonia (%)	2 (13.3)	6 (100.0)	.001
Ventilator (%)	3 (20.0)	5 (83.3)	.02
Eye examinations (No.)	5.8	5.0	NS
Bronchopulmonary dysplasia (%)	11 (73.3)	5 (83.3)	NS
Corticosteroid use (%)	0 (0.0)	4 (66.7)	.003

performed on isolates collected throughout the outbreak. Statistical analysis was performed by the *t* test and Pearson χ^2 test or Fisher exact test, as appropriate, to determine factors associated with death during the adenoviral infection, using STATA (Stata Corporation, College Station, TX).

RESULTS

Cases

Twenty-one infants became infected with adenovirus. There were 11 girls and 10 boys. Sixteen infants were white and 5 infants were black. Almost all (20 of 21) of the infants were premature. Birth weights ranged from 444 to 2568 g, with a mean of 937.9 g; gestational age of the infants ranged from 24 to 37 weeks, with a mean of 26.7 weeks. Postnatal age at the time of adenovirus infection ranged from 3 to 22 weeks, with a mean of 9.1 weeks. Adenovirus infection was manifest primarily as pneumonia (a significant increase in respiratory support, a new infiltrate, and a change in the quantity and quality of secretions) in 7, conjunctivitis in 7, pneumonia with conjunctivitis in 1, asymptomatic in 5 (diagnosed during surveillance studies), and upper respiratory tract infection in 1.

Six infants received therapy directed specifically at the infection. Intravenous immunoglobulin (IVIG) was given as a one-time dose of 400 mg/kg. Ribavirin was administered intravenously according to the manufacturer's suggestions for 3 to 7 days under a compassionate use protocol. Five of these infants died. The lone survivor was a relatively healthy infant who would not have been selected for treatment except for the death of her twin, who was infected with adenovirus. In addition to specific antiviral therapy, all infants were supported with conventional or high-frequency ventilation or pressor agents or both, as needed.

Characteristics of the infants who died and who survived are compared in the Table. The two groups were similar with respect to sex, race, birth weight, gestational age, age at time of infection, presence of bronchopulmonary dysplasia (BPD), and number of eye examinations. However, corticosteroid use, the diagnosis of adenovirus pneumonia, and being on a mechanical ventilator at the onset of the adenovirus infection were each significantly more common in the infants who died. Three of the four infants who received corticosteroids and died received hydrocortisone (1.5 to 10 mg/kg per day IV) after they had become acutely severely ill with adenovirus pneumonia but before the diagnosis of adenovirus had been made. Two of three had had prior exposure to hydrocortisone, but it was at least 1 month before their adenovirus infection. Overall, these infants had respiratory failure, and, in addition to corticosteroids, other treatments such as albuterol, ipratropium, terbutaline, DNAse, acetylcysteine, surfactant, and nitric oxide were used in life-saving attempts. The fourth patient was considered to be receiving chronic steroids. He had been receiving long-standing systemic dexamethasone 1 month before his adenovirus infection. He was given inhaled budesonide in an attempt to decrease systemic corticosteroids 2 weeks before his adenovirus infection. He continued to receive inhaled budesonide at the time of adenovirus illness. Five infants who died were being mechanically ventilated for severe BPD before the adenovirus infection.

Epidemiology of the Outbreak

The NICU consisted of 3 rooms designated A, B, and C. Typically, room A housed up to 18 infants who were moderately to severely ill; room B, 22 infants who were mildly to moderately ill; and room C, 14 infants who were mildly ill or were recovering premature infants. The average daily census in the NICU during the outbreak varied between 32 and 43, with a median of 42. A total of 333 infants were cared for in the NICU during the outbreak and were at risk of being infected. Thus, the overall attack rate was 6.3%.

Case 1 was identified on day 1 of the outbreak during an evaluation for pneumonia in a ventilated infant (Figure). A rapid fluorescent antibody screen for respiratory viruses was positive for adenovirus. The baby was moved from the open area in room B to one of the two isolation rooms and placed in contact precautions with gowns and gloves. Three days later, on day 4 of the outbreak, case 2 was identified during an evaluation for pneumonia in a ventilated infant located in the open area of room B. A rapid screen for respiratory viruses was positive for adenovirus. The baby was moved to the second isolation room, on contact precautions. Two days later, on day 6, of the outbreak, case 3 was identified in room A during an evaluation for pneumonia. A rapid screen for respiratory viruses was positive for adenovirus. Case 3 was moved to room B to begin the process of cohorting adenovirus-positive infants. Room B was closed to new admissions, and none of the infants in room B were moved to other rooms in the NICU. However, infants in room B were moved to other units in the hospital or discharged to home whenever possible. Cases 4 to 6 occurred from day 9 through day 13. They exhibited conjunctivitis, upper respiratory tract symptoms, or pneumonia.

Mandatory use of gowns and gloves for handling all infants in room B was introduced on day 18; only gloves were mandatory in rooms A and C. Cases 7 and 8 presented on days 19 and 25 with conjunctivitis or pneumonia. All