Adenovirus type 8 conjunctivitis outbreak in a neonatal intensive care unit

Emanuel Birenbaum, Nehama Linder, Noemi Varsano, Roberto Azar, Jacob Kuint, Abraham Spierer, Brian Reichman

Abstract
An outbreak of adenovirus type 8 conjunctivitis occurred in seven premature infants who had undergone ophthalmological examination four to seven days previously. Three of the affected infants, treated with steroids because of bronchopulmonary dysplasia, showed systemic manifestations and deterioration of their respiratory disease. Second and third waves affected nine staff and 12 family members.

Subjects affected by adenovirus type 8 in three waves of the outbreak. The left hand column represents the seven premature infants who underwent ophthalmological examination before the outbreak.

1st wave
(n = 7)
2nd wave
(n = 13)
3rd wave
(n = 8)

Adenovirus infection is the principal pathogen in epidemics of conjunctivitis or keratoconjunctivitis.1 The most frequently detected strain is type 8 adenovirus, although types 11, 19, and 37 have also been isolated.1 2 A recent review of adenovirus infection in neonates documents systemic invasion of the virus causing severe disease.3 However, cases of adenovirus type 8 conjunctivitis were not reported.

This report describes an epidemic of adenovirus type 8 conjunctivitis in premature infants in hospital and documents the systemic effects of the infection in this population.

Patients and methods
Within a four day period, severe conjunctivitis developed in four of seven premature infants who had undergone ophthalmological examination four to seven days previously. Second and third waves of this outbreak occurred after seven and 14 days and affected a total of nine staff and 12 family members of patients and staff (see figure).

VIROLOGICAL METHODS
For virus identification, specimens were inoculated in three different cell types, Hu-Ki (human kidney carcinoma cells), A-549 (human lung carcinoma cells), and MRC-5 (human lung fibroblasts). Type identification was performed by specific immune serum neutralisation.4

Results
Viral cultures revealed adenovirus type 8 in four symptomatic and three asymptomatic infants who had undergone ophthalmological examination before the onset of the epidemic. The clinical characteristics of the seven infected infants are shown in the table. All four symptomatic infants had previously required mechanical ventilation; three had bronchopulmonary dysplasia and were treated with supplemental oxygen, dexamethasone, and diuretics at the time of the outbreak. The fourth infant was treated with amphotericin B. In the asymptomatic group two infants had previously been mechanically ventilated and neither suffered from chronic lung disease. All four symptomatic infants initially developed acute unilateral conjunctivitis followed by bilateral congestion and oedema of the conjunctiva and eye lids. Ectropion of the eye lids, periorbital cellulitis, and conjunctival haemorrhage, occurred in one patient each.

Systemic manifestations of the infection were noted in the three infants with chronic lung disease. The patients were all febrile and lethargic and showed deterioration of their pre-existing respiratory disease with tachypnoea and a marked increase in oxygen requirement. The white cell count decreased from a mean of 13.3×10⁹/l (range 11.5–15.1) to 7.6×10⁹/l (range 5.4–9.3), and the platelet count decreased simultaneously from a mean of 433×10⁹/l (range 411–450) to 120×10⁹/l (range 97–202). Fever and haematological abnormalities remitted within a week while local manifestations such as conjunctivitis and respiratory distress persisted for three to four weeks. Ophthalmological examination after three months did not show evidence of corneal sequelae.
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Clinical characteristics of infants infected with adenovirus type 8

<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>Birth weight (g)</th>
<th>Diagnosis</th>
<th>Age at outbreak (weeks)</th>
<th>Weight (g)</th>
<th>No of eye examinations before outbreak</th>
<th>Treatment before outbreak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>680</td>
<td>Hyaline membrane disease, bronchopulmonary dysplasia, ROP III</td>
<td>38</td>
<td>4600</td>
<td>24</td>
<td>Oxygen, dexamethasone cryotherapy</td>
</tr>
<tr>
<td>26</td>
<td>905</td>
<td>Hyaline membrane disease, bronchopulmonary dysplasia, ROP III</td>
<td>14</td>
<td>2850</td>
<td>10</td>
<td>Oxygen, dexamethasone cryotherapy</td>
</tr>
<tr>
<td>29</td>
<td>1410</td>
<td>Ureaplasma pneumonia, bronchopulmonary dysplasia, ROP III</td>
<td>6</td>
<td>1520</td>
<td>2</td>
<td>Oxygen, dexamethasone</td>
</tr>
<tr>
<td>28</td>
<td>1195</td>
<td>Hyaline membrane disease, IVH II, Candida albicans sepsis</td>
<td>7</td>
<td>1430</td>
<td>3</td>
<td>Amphotericin B</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>1000</td>
<td>E. coli sepsis, recurrent apnoea, IVH II</td>
<td>5</td>
<td>1300</td>
<td>2</td>
<td>–</td>
</tr>
<tr>
<td>30</td>
<td>1135</td>
<td>PROM</td>
<td>5</td>
<td>1410</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>28</td>
<td>1090</td>
<td>Hyaline membrane disease, IVH II, ROP II</td>
<td>8</td>
<td>1430</td>
<td>2</td>
<td>–</td>
</tr>
</tbody>
</table>

IVH=intraventricular haemorrhage, PROM=premature rupture of membranes, ROP=retinopathy of prematurity.

The second and third waves of the epidemic affected a total of 16 adults and six children. All developed severe bilateral conjunctivitis and most complained of myalgia, weakness, photophobia, severe pain, blurring of vision, and regional lymphadenopathy. Ocular manifestations persisted for three to four weeks.

Conjunctival cultures were positive for adenovirus type 8 in all seven premature infants. In addition, five of six throat cultures, two in symptomatic and three in asymptomatic infants, were positive as were all four rectal cultures taken from one symptomatic and three asymptomatic infants.

Discussion

Hospital outbreaks of adenovirus type 8 keratoconjunctivitis have suggested that direct inoculation of the virus by ophthalmological instruments is a common predisposing factor. A linear relationship between the number of eye examinations and the incidence of infection suggests that repetitive microtrauma to epithelium may facilitate pathogenic invasion of the virus. The seven infected infants had all undergone ophthalmological examination before developing conjunctivitis suggesting that this procedure was associated with the onset of the outbreak either by introducing the virus into the unit or by transmitting the virus from one previously infected infant to others. Systemic illness occurred, however, in only four of the seven infected infants. The severity of the underlying clinical condition in symptomatic infants, combined with prolonged treatment with steroids in three and amphotericin B in one, might have impaired their immunological status facilitating systemic invasion of the virus and subsequent deterioration of the respiratory illness in patients with chronic lung disease.

Premature infants in neonatal intensive care units are subjected routinely to repeated ophthalmological examination for the identification of retinopathy of prematurity. These examinations may introduce or spread conjunctival infections and strict adherence to appropriate aseptic procedures may prevent this potentially hazardous complication.

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