Adenovirus Type 3 Viremia in an Adult with Toxic Shock–Like Syndrome

Nathaniel O. Price,1 Jill K. Hacker,1,2 Jeffrey H. Silvers,2 Leta Crawford-Miksza,3 R. Michael Hendry,4 Jennifer Flood,1,a Rana A. Hajjeh,3 Arthur L. Reingold,5 and Douglas J. Passaro1,3,b

1California Emerging Infections Program, Oakland, 2San Leandro Hospital, San Leandro, 3Division of Infectious Diseases and Geographic Medicine, Stanford University Medical School, Stanford, 4Viral and Rickettsial Disease Laboratory, California Department of Health Services, Richmond, and 5Division of Public Health Biology and Epidemiology, University of California at Berkeley, Berkeley, California; and 6Meningitis and Special Pathogens Branch, Division of Bacterial and Mycotic Diseases, Centers for Disease Control and Prevention, Atlanta

Surveillance by the Unexplained Deaths and Critical Illnesses Project (UNEX) uncovered a novel presentation of adenovirus type 3 infection that satisfied the criteria for toxic shock–like syndrome in a 28-year-old immunocompetent man. Adenovirus may be a cause of toxic shock syndrome; surveillance systems such as UNEX may uncover additional causes of this and other clinically defined infectious syndromes.

Since the original description of toxic shock syndrome (TSS) in 1978, reports have emphasized its association with staphylococcal infection due to tampon use by young women [1]. The list of pathogens that cause TSS has grown to include group A streptococci [2] and, rarely, Pseudomonas species [3] and group C streptococci [4]. We report an illness that fulfilled diagnostic criteria [5] for TSS in which adenovirus type 3 was detected by PCR. This is the first report of adenovirus associated with TSS in an adult.

Case report. In October 1996, a 28-year-old man was hospitalized after he developed rapidly progressive myalgia, profuse diarrhea, nausea, vomiting, and fever. He had neither dyspnea, nor an altered mental status. His temperature was 39.2°C, his pulse was 130 beats/min, and his respiratory rate was 24 breaths/min. The patient had borderline hypotension (systolic blood pressure during resuscitation with fluids, 90 mm Hg). His conjunctivae, tympanic membranes, and oropharynx were hyperemic. He had mild erythema on his face and anterior chest, and a grade 1/6 systolic murmur was noted. Other than mild, diffuse abdominal tenderness, the remaining findings of the examination were normal. The patient had camped on the central California coast immediately before the onset of illness and had swum repeatedly in a freshwater lake.

The patient was admitted to the intensive care unit with a leukocyte count of 20,000 cells/mm³ (20% band forms), a blood urea nitrogen level of 39 mg/dL, and a creatinine level of 2.1 mg/dL. Serum levels of creatine kinase and aspartate aminotransferase were normal. Urinalysis demonstrated a protein level of 3.0 mg/dL and the presence of 40–50 leukocytes per high-powered field. Findings on chest radiography were considered normal. Intravenous fluids, ciprofloxacin, and cefotaxime were administered. The patient developed severe swelling of the hands and fingers 36 h after admission, followed by dissipation of the rash and diarrhea. Blood, urine, and stool cultures were negative for bacterial pathogens (including Escherichia coli O157:H7). The patient fully recovered, although desquamation of the hands occurred 10–14 days after the onset of illness. Because of the severe nature of the illness and because of the absence of a known etiology, the case was reported to the Unexplained Deaths and Critical Illnesses Project (UNEX).

In 1995, UNEX was established by the Emerging Infections Program of the Centers for Disease Control and Prevention (CDC; Atlanta) as a population-based surveillance system to identify and evaluate unexplained critical illnesses and deaths due to presumed infectious etiologies in previously healthy persons. The project is a collaboration between the CDC and the health departments in Minnesota; Oregon; New Haven County, Connecticut; and 3 counties in the San Francisco Bay area. Previously healthy individuals who either die of or present with a critical illness that has infectious hallmarks, but for whom the etiology of disease is unknown at the time of initial laboratory testing, are reported to UNEX by health care providers. Clinical and epidemiologic data are collected, and clinical specimens are tested at the CDC and other collaborating laboratories.

A battery of conventional microbiologic tests did not reveal a definite cause of the patient’s illness (table 1). However, PCR analysis identified adenovirus in a sample of whole blood col-


a Present affiliation: Tuberculosis Branch, California Department of Health Services, Berkeley.

b Present affiliation: Division of Epidemiology and Biostatistics, University of Illinois School of Public Health, Chicago.

Reprints or correspondence: Dr. Douglas Passaro, Div. of Epidemiology and Biostatistics, University of Illinois School of Public Health, 2121 W. Taylor St., Chicago, IL 60612 (doug@uic.edu).

Clinical Infectious Diseases 2001;33:260–2
© 2001 by the Infectious Diseases Society of America. All rights reserved.
1058-4838/2001/3302-0018$03.00

260 • CID 2001:33 (15 July) • BRIEF REPORTS
Table 1. Selected microbiologic test results for an adult patient with toxic shock–like syndrome.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Specimen</th>
<th>Date of specimen collection</th>
<th>Test(s)</th>
<th>Type</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antistreptolysin O</td>
<td>Serum</td>
<td>6 October 1996</td>
<td>ASO titer&lt;sup&gt;a&lt;/sup&gt;</td>
<td>EIA&lt;sup&gt;b&lt;/sup&gt;</td>
<td>37 Todd units (normal)</td>
</tr>
<tr>
<td>TSST-1 Ab</td>
<td>Serum</td>
<td>9 October 1996</td>
<td>EIA&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Light microscopy&lt;sup&gt;c&lt;/sup&gt;</td>
<td>&lt;1:4</td>
</tr>
<tr>
<td>Parasites</td>
<td>Stool</td>
<td>10 October 1996</td>
<td>EIA IgM, IFA, EM&lt;sup&gt;d&lt;/sup&gt;</td>
<td>EM, IEM&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Negative</td>
</tr>
<tr>
<td>Cryptosporidium species</td>
<td>Stool</td>
<td>8 October 1996</td>
<td>Culture&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Viral pathogens</td>
<td>Stool</td>
<td>8 October 1996</td>
<td>Culture&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Small round viruses</td>
<td>Stool</td>
<td>8 October 1996</td>
<td>Culture&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Leptospira interrogans</td>
<td>Blood, urine</td>
<td>7 October 1996</td>
<td>EIA IgM, IFA&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Toxoplasma gondii</td>
<td>Bloods</td>
<td>8 October 1996</td>
<td>Consensus 16S PCR&lt;sup&gt;f&lt;/sup&gt;</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Bacterial pathogens</td>
<td>Blood</td>
<td>8 October 1996</td>
<td>PCR&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Legionella pneumophila</td>
<td>Blood</td>
<td>8 October 1996</td>
<td>PCR&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>Blood</td>
<td>8 October 1996</td>
<td>PCR&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>Blood</td>
<td>8 October 1996</td>
<td>PCR&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Enterovirus</td>
<td>Blood</td>
<td>8 October 1996</td>
<td>PCR&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Adenovirus</td>
<td>Blood</td>
<td>8 October 1996</td>
<td>PCR&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Positive (type 3)</td>
<td></td>
</tr>
</tbody>
</table>

**NOTE.** EM, electron microscopy; IEM, immune electron microscopy; IFA, immunofluorescence assay; TSST-1 Ab, toxic shock syndrome toxin–type 1 antibody.

<sup>a</sup> Hospital reference laboratory.

<sup>b</sup> Unexplained Deaths and Critical Illnesses Project (UNEX) collaborating laboratory of Dr. Jeffrey Parsonnet (Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire).

<sup>c</sup> Hospital laboratory (San Leandro Hospital, San Leandro, California).

<sup>d</sup> Centers for Disease Control and Prevention laboratories (Atlanta).

<sup>e</sup> Viral and Rickettsial Diseases Laboratory of the California Department of Health Services (Richmond, California).

<sup>f</sup> UNEX collaborating laboratory of Dr. D. Relman (Palo Alto Veterans Administration Hospital, Palo Alto, California).

lected on day 3 of the illness [6]. This result was confirmed using an additional, nested PCR [7]; the amplified sequence showed homology to currently circulating strains of adenovirus type 3 [6].

**Discussion.** Criteria for the diagnosis of toxic shock syndrome include fever, hypotension, myalgia, a “sunburnlike” rash, and desquamation of the hands and feet that occurs 1–2 weeks after the onset of illness. In addition, 3 or more of the following organ systems must be involved: gastrointestinal, hepatic, renal, mucous membrane, muscular, CNS, or hematologic.

Our patient’s illness was similar to “classic” staphylococcal TSS. However, PCR detection of adenovirus type 3 in whole-blood samples suggests that adenovirus, not *Staphylococcus aureus*, was the etiologic agent. In contrast to adenovirus subgenus C, which has been isolated from the lymphocytes of immunocompetent subjects [8], the detection of DNA in adenovirus subgenus B (which includes adenovirus type 3) has not been described in healthy hosts. Furthermore, although reactivation of latent adenovirus may occur in immunocompromised patients [9], it has not been described in immunocompetent adults. We do not suspect contamination because 2 independent laboratories obtained an adenoviral PCR product from different regions of the hexon gene while running appropriate negative controls [6].

The epidemiological findings for this case are consistent with those associated with adenovirus infection, since adenovirus type 3 has been associated with the occurrence of pharyngoconjunctival fever among persons who have gone swimming in contaminated water [10]. Although studies have not been done to confirm that the freshwater lake was the source of adenovirus type 3, our patient swam there frequently during the week before the onset of illness.

A previous case report described an immunocompetent 5-year-old child with TSS-like disease that was caused by an untyped adenovirus [11], but this is the first report of such disease in an immunocompetent adult. Clinicians should be aware that adenovirus may be a cause of TSS. Surveillance systems such as UNEX may uncover additional etiologies for TSS and other clinically defined infectious syndromes.

**References**