Kazunobu Ouchi · Keiko Hasegawa · Yukiko Nonaka
Hiroshi Matsushima · Hayashi Komura · Takashi Maki
Teruko Nakazawa

Rapid diagnosis of adenovirus respiratory tract infections
by immunochromatography

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Abstract
A one-step diagnostic test based on an immunochromatographic (IC) assay for adenovirus was evaluated with purified adenovirus and clinical specimens. According to five clinically common serotypes of purified adenovirus tested, the IC test was more sensitive than two commercially available enzyme immunoassay (EIA) test kits. For tonsilopharyngeal specimens from 63 febrile pediatric patients with suspected adenoviral upper respiratory tract infection, the sensitivity and specificity of the IC test against viral isolation by cell culture was 88.5% (23/26) and 100% (37/37), respectively. The IC test, which is quicker and easier to perform than EIA test kits, is very useful in the rapid diagnosis of adenoviral upper respiratory tract infection of pediatric patients.

Key words  Adenovirus · Respiratory tract infection · Rapid diagnosis · Immunochromatography

Introduction
Adenoviruses have been implicated in a wide variety of clinical syndromes ranging from acute respiratory tract infections to ocular diseases and gastrointestinal disorders.1 Serology, virus isolation by cell culture, and antigen detection assays, such as latex agglutination, immunofluorescence assay, enzyme immunoassay (EIA), radio immunoassay (RIA), or polymerase chain reaction (PCR)-based protocols, have been used for the diagnosis of adenovirus infection.2–5 However, these methods require at least 70 min to obtain the results and do not help the clinician with the acute problems of this infection in a pediatric outpatient practice.

Pediatric patients with adenoviral upper respiratory tract infections frequently have high fever, with laboratory data indicating bacterial infections, such as leukocytosis with left shift and high C-reactive protein (CRP) value. Therefore pediatricians often prescribe unnecessary antibiotics for patients with adenoviral upper respiratory tract infections. This inappropriate oral antibiotic use has influenced the increasing resistance of many bacteria, which is increasing concern in the medical community all over the world.6 Moreover, as adenovirus type 7, which causes more severe infections, has been emerging in Japan,7 we need a simple quick diagnostic test for detecting adenovirus from nasopharyngeal specimens at outpatient clinics. We therefore evaluated a new one-step diagnostic test based on an immunochromatographic (IC) assay using an adenovirus-specific monoclonal antibody; the procedure is very easy to perform and results are obtained within 10 min.

Methods
Sensitivity assay in commercial test kits
We compared the sensitivity for detecting five different serotypes of purified adenovirus in three test kits; a new simple one-step immunochromatographic test (IC test; SA Scientific, San Antonio, TX, USA), Adenoclone (Cambridge BioScience, Worcester, MA, USA), and IDEIA Adenovirus (Dako Diagnostics, Cambridgeshire, UK). Briefly, adenovirus of serotypes 3, 4, 7, 19, and 37, grown in HEp-2 cells and harvested at about 80% cytopathic effect (CPE), was sonicated and purified from a band of specific gravity 1.34 with a cesium chloride density gradient. The virus suspension was dialyzed against 10 mM Tris-HCl (pH 8.0) buffer containing 1 mM MgCl2 and 10% glycerol at 4°C overnight. The protein concentration of each virus suspension after dialysis was measured by the bicinchoninic acid
Table 1. Comparison of sensitivity for detection of purified adenovirus among three commercial test kits

<table>
<thead>
<tr>
<th>Serotype of adenovirus</th>
<th>Protein concentration of viral suspension (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IC test</td>
</tr>
<tr>
<td>3</td>
<td>0.15a</td>
</tr>
<tr>
<td>4</td>
<td>0.055</td>
</tr>
<tr>
<td>7</td>
<td>0.054</td>
</tr>
<tr>
<td>19</td>
<td>0.046</td>
</tr>
<tr>
<td>37</td>
<td>0.053</td>
</tr>
</tbody>
</table>

*Number indicates the lowest protein concentration at serial twofold dilution of purified viral suspension with positive test result  
*aNumbers in parenthesis indicate relative sensitivity of the immunochromatographic (IC) test (SA Scientific) against the other test  
*bAdenoclone (Cambridge BioScience)  
*cIDEIA Adenovirus (Dako Diagnostics)

Discussion

The IC test kit is more sensitive and results are obtained more rapidly than with EIA test kits for detection of adenovirus. Further, the IC test does not require any special equipment. We can obtain results within 10 min following a simple one-step procedure, although it takes at least 70 min for other tests based on EIA. Therefore we can use this one-step test at an outpatient clinic for patients with upper respiratory tract infection, and we can then withhold the prescription of unnecessary antibiotics for patients with adenoviral infection. Moreover, the rapid detection of this viral agent enables us to recognize nosocomial spread of infection early and institute cross-infection control measures promptly. The sensitivity of 88.5% in the one-step test against virus isolation by cell culture is acceptable and similar to that of rapid group A streptococcal antigen detection tests against throat culture. The monoclonal antibody against the capsid hexon antigen, which is common to all known adenovirus serotypes, is used in the IC test, so we may not miss any serotypes of this etiologic agent. Although PCR may have superior sensitivity, the IC test still shows great advantage because of its simple procedure, short time requirement, and lack of equipment requirement. In summary, this one-step test is more rapid and easier to perform than EIA tests, and it has high specificity. Therefore it is very useful in the rapid diagnosis of adenoviral infection in pediatric patients.

References