Characteristics of adenovirus associated urethritis

C S Bradshaw, I M Denham, C K Fairley

ORIGINAL ARTICLE

Objectives: To describe the characteristics of adenovirus urethritis in men.
Method: Cases occurred over a 30 month period among men presenting with urethritis to Melbourne Sexual Health Clinic. All cases had a urethral Gram stain and underwent testing for chlamydia, gonorrhoea, herpes, and adenovirus. Cases were empirically treated with a macrolide or doxycycline.
Results: Eight cases of adenovirus associated urethritis were identified in whom no other causative organism was isolated. Cases were clustered in autumn and winter of each year and all reported recent invasive oral sex and seven reported recent invasive vaginal sex. All patients complained of dysuria, seven had meatitis and mucoid discharge, six had conjunctivitis, and four constitutional symptoms. Three sexual contacts were known to be symptomatic.
Conclusion: Adenovirus is an uncommon cause of urethritis in men but it should be considered in all males presenting with dysuria, meatitis, and associated conjunctivitis or constitutional symptoms.

Non-specific urethritis (NSU) is a common presentation to sexual health clinics and in a substantial proportion of cases no pathogen is identified. There are few reports of adenovirus associated with urethritis in men, and it is not usually considered when investigating NSU.

Adenovirus causes a variety of clinical syndromes characterised by inflammation of mucous membranes. There are 47 serotypes; types 8, 19, and 37 (subgenus D) cause keratoconjunctivitis,\(^1\) but have also been infrequently isolated from genital sites in individuals with cervicitis,\(^2\) urethritis,\(^3\) and genital ulcers.\(^7\) We describe characteristic clinical features in eight men presenting with urethritis to a sexual health clinic in whom adenovirus appears to have been the causative agent.

METHOD

All eight cases were collected between April 1999 and September 2001 at Melbourne Sexual Health Centre (MSHC). MSHC services a city of 3.5 million people and sees approximately 15 000 new patients per annum. Adenovirus was tested for in men presenting with urethritis in addition to meatitis or conjunctivitis. Routine screening of all men with urethritis, with additional cervicitis in one, and one male contact had dysuria and pharyngitis.

A urethral Gram stain was performed on all cases. Chlamydia testing was by ligase chain reaction (LCR, Abbott LCX probe system) on a first void urine specimen. Gonococcal testing was performed by culture on gonococcal medium at MSHC. Herpes was excluded by in-house nested polymerase chain reaction (PCR) at the Victorian Infectious Diseases Reference Laboratory (VIDRL). Adenovirus was isolated using viral culture, with confirmation by antibody neutralisation, and in-house nested PCR\(^1\) by VIDRL and four isolates were serotyped by neutralisation assay. HIV 1 and 2 testing was by enzyme immunoassay (Abbott HIV1/2 Go EIA) at VIDRL.

RESULTS

All eight cases that tested positive were suspected clinically of having adenovirus. Cases were clustered between April and September each year, corresponding to the seasons of autumn to winter in Melbourne. Seven men were identified as heterosexual, one as homosexual, and the mean age was 36.4 (table 1).

All eight cases reported a recent history of insertive oral sex (IOS), with six reporting IOS in the 14 days preceding onset of symptoms. Six males reported unprotected vaginal intercourse (UPVI) in the preceding 14 days. Sexual partners were Australian residents except for two Thai partners in Thailand.

All patients complained of marked dysuria, seven had a mucoid urethral discharge and seven had meatitis. Conjunctivitis was present in six cases, constitutional symptoms in four, and pharyngitis was present in one. Three sexual contacts were known to be symptomatic; two females had conjunctivitis, with additional cervicitis in one, and one male contact had dysuria and pharyngitis.

Urethral Gram stain revealed more than four polymorphonuclear cells (PMN) per high powered field in six cases. A further case had no PMNs on initial presentation, but developed a florid discharge subsequently and was not retested. Another had 1–4 PMNs on Gram stain. Cases were considered positive for adenovirus if samples tested positive by culture or PCR (table 1). Adenovirus was identified in all urethral swabs and in the four conjunctival swabs collected. Typing was performed for four urethral isolates; three cases were type 37 and one was type 8. Typing was not performed for specimens tested by PCR alone and was not requested in all patients tested by culture. All patients received empirical treatment for NSU with either doxycycline or azithromycin, and two received additional fampciclovir. No case tested positive for chlamydia, gonorrhoea, or herpes. Six cases were tested for HIV and were negative. Five cases had symptoms persisting for 14 days or more despite antibiotic therapy.

DISCUSSION

We have described eight cases where adenovirus was isolated in men presenting with NSU associated with marked dysuria, meatitis, and conjunctivitis. There were strong similarities in the clinical presentations of the cases. Oral sex preceded the onset of symptoms in all cases and vaginal sex was a common exposure. There was seasonal clustering of cases in autumn and winter each year. The four isolates typed were of subgenus D (types 8 and 37), an established cause of keratoconjunctivitis.\(^5\)

Testing was not performed for Trichomonas vaginalis given the low prevalence in the population attending our clinic, or for Ureaplasma urealyticum because of high rates of asymptomatic urethral colonisation. Testing was not performed for Mycoplasma genitalium as PCR is required and is not routinely available in most clinic settings. U urealyticum and M genitalium
Table 1 Clinical and laboratory findings

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Season</th>
<th>Sexual history</th>
<th>Genital symptoms and signs</th>
<th>Associated symptoms</th>
<th>Contact symptoms &amp; signs</th>
<th>Urethral PMN count</th>
<th>Urethral isolate</th>
<th>Conjunctival isolate</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28</td>
<td>Winter 1999</td>
<td>IOS and PVI with CSP</td>
<td>Severe D, MUD, and MT, resolved by day 22</td>
<td>CNJ and CS</td>
<td>Unknown</td>
<td>0</td>
<td>NT</td>
<td>Ad 37†</td>
<td>Doxy and famv</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>Winter 1999</td>
<td>IOS and UPVI with RSP—regular sexual activity but no dates of contact documented</td>
<td>Severe D, MUD, and MT, ongoing day 14</td>
<td>CS</td>
<td>CNJ and cervicitis (chlamydia and gon negative)</td>
<td>8–20</td>
<td>Ad†</td>
<td>NT</td>
<td>Doxy and famv</td>
</tr>
<tr>
<td>3</td>
<td>44</td>
<td>Autumn 2000</td>
<td>IOS and UPVI with CSP 3 days before onset of D</td>
<td>Severe D, MUD, and MT, resolved by day 18</td>
<td>CNJ and CS</td>
<td>Well</td>
<td>8–20</td>
<td>Ad 37††</td>
<td>Ad††</td>
<td>Doxy and roxi</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>Autumn 2000</td>
<td>IOS and UPVI with CSP in Thailand 9 days before onset of D</td>
<td>D and MT, ongoing day 5</td>
<td>CNJ and CS</td>
<td>Unknown</td>
<td>5–8</td>
<td>Ad††</td>
<td>Ad††</td>
<td>azith</td>
</tr>
<tr>
<td>5</td>
<td>33</td>
<td>Autumn 2000</td>
<td>IOS and UPVI with a CSP 14 days before onset of D</td>
<td>D and MUD (altered urinary stream), resolution by day 14</td>
<td>CNJ</td>
<td>CNJ</td>
<td>1–4</td>
<td>Ad 37††</td>
<td>NT</td>
<td>azith</td>
</tr>
<tr>
<td>6</td>
<td>47</td>
<td>Winter 2001</td>
<td>IOS and UPVI with CSP 6 days before onset of D</td>
<td>Severe D, MUD, and MT, ongoing d5</td>
<td>Nil</td>
<td>Unknown</td>
<td>8–20</td>
<td>Ad 8††</td>
<td>NT</td>
<td>azith</td>
</tr>
<tr>
<td>7</td>
<td>35</td>
<td>Winter 2001</td>
<td>IOS with RSP 10 days before D, IOS and IAS with CSP 28 days before onset of D</td>
<td>D, MUD, and MT, ongoing d5</td>
<td>Nil</td>
<td>Unknown</td>
<td>8–20</td>
<td>Ad††</td>
<td>Ad††</td>
<td>azith</td>
</tr>
<tr>
<td>8</td>
<td>49</td>
<td>Winter 2001</td>
<td>IOS and UPVI with RSP in Thailand—regular sex but no dates specified</td>
<td>Severe D, MUD, and MT, present for &gt;9 days</td>
<td>CNJ</td>
<td>CNJ</td>
<td>5–8</td>
<td>Ad††</td>
<td>Ad††</td>
<td>azith, doxy, and roxi</td>
</tr>
</tbody>
</table>

*Homosexual, all other cases heterosexual. Insertive oral sex (IOS), vaginal intercourse (V), condom used (P), unprotected (UP), regular sexual partner (RSP), casual sexual partner (CSP), dysuria (D), mucoid urethral discharge (MKUD), malodorous urethral discharge (MUD), conjunctivitis (CNJ), constitutional symptoms (CS), polymorphonuclear cells per high power field (urethral PMN count). Chlamydia (chl), gonorrhea (gon), adenovirus (Ad), adenovirus type 37 (Ad37), culture positive (†), PCR positive (††), not tested (NT), azithromycin (azith), doxycycline (doxy), roxithromycin (rox), and fumariclovir (famv)
C S Bradshaw, I M Denham, C K Fairley, Melbourne Sexual Health Centre, Carlton, Victoria, 3053, Australia

C K Fairley, Department of Public Health, University of Melbourne, Victoria, Australia

REFERENCES


WEBSITE REVIEW

www.chlamydiae.com

This is arguably the most comprehensive medical website to host information on chlamydial infections. It is set up and designed by Michael Ward, professor of medical microbiology at the University of Southampton. The site boasts not only a multilingual (12 languages) textbook on chlamydiae but also a calendar of relevant scientific meetings, conference, and news reports. The website caters to health professionals as well as the general public and covers factual information in the form of FAQs focused on genital tract infections.

Only about half of the “health professionals” area requires (free of charge) registration initially for log-in (albeit that section of most interest to STI readers), but the wealth of accurate and up to date information contained within should make this site a compelling reason for putting it on your list of websites to be bookmarked. Excellent.

R Lau
Courtyard Clinic, St George’s Hospital, London SW17 0QT, UK; Richard.Lau@stgeorges.nhs.uk