Trichodysplasia Spinulosa Polyomavirus in Respiratory Tract of Immunocompromised Child

Arwa A. Bagasi, Tasneem Khandaker, Gemma Clark, Terry Akagha, Jonathan K. Ball, William L. Irving, C. Patrick McClure

Author affiliations: King Saud University, Riyadh, Saudi Arabia (A.A. Bagasi); University of Nottingham, Nottingham, UK (A.A. Bagasi, T. Khandaker, T. Akagha, J.K. Ball, W.L. Irving, C.P. McClure); Nottingham University Hospitals NHS Trust, Nottingham (G. Clark, W.L. Irving)

DOI: https://doi.org/10.3201/eid2409.180829

Trichodysplasia spinulosa polyomavirus causes trichodysplasia spinulosa, a skin infection, in immunocompromised persons, but the virus is rarely detected in respiratory samples. Using PCR, we detected persistent virus in respiratory and skin samples from an immunocompromised boy with respiratory signs but no characteristic skin spicules. This virus may play a role in respiratory illness.

Trichodysplasia spinulosa is a rare skin disease that occurs exclusively in immunocompromised persons. It is characterized by facial keratotic spicules formed by hyalin accumulation in the inner root sheath cells of affected hair follicles. In 1999, electron microscopy identified a novel polyomavirus, subsequently named trichodysplasia spinulosa polyomavirus (TSPyV) or human polyomavirus 8, in sections of skin spicules of a solid organ transplant patient (1); in 2010, the virus was more completely characterized (2). TSPyV is 1 of 5 polyomaviruses associated with human diseases, particularly those that affect immunocompromised persons (3). Although worldwide seroprevalence of TSPyV antibodies among the general population is estimated at 70% (4) and a respiratory route of infection has been hypothesized (5,6), as of 2015, only 32 cases of trichodysplasia spinulosa had been reported (7), suggesting that other pathologies caused by TSPyV may have gone undiagnosed. We describe PCR detection of TSPyV in an immunocompromised boy with respiratory signs and symptoms.

To elucidate potential causes of undiagnosed viral respiratory infection, during January 2015–February 2016, we used a panpolyomavirus degenerate primer PCR to screen archived samples for polyomavirus. The archived samples were nucleic acid of respiratory specimens from 218 children 6 months to 5 years of age, previously negative for typical respiratory viruses in a panel used for routine diagnosis. Of the 218 samples screened in 22 pools, we obtained positive results for polyomavirus in 1 pool and, subsequently, 1 sample (from the patient reported here). Subsequent Sanger sequencing and BLAST (http://blast.ncbi.nlm.nih.gov/Blast.cgi) analysis of the 274-bp degenerate primer PCR product indicated that the sample contained TSPyV. The complete genome of this TSPyV strain was amplified in 4 overlapping PCR fragments and Sanger sequenced (online Technical Appendix). Phylogenetic analysis of the assembled complete 5,232-nt genome with all available 23 reference sequences revealed that the TSPyV strain was most closely related to TSPyV 1312, which had been isolated in 2012 in Dallas, Texas, USA (online Technical Appendix), but bootstrap support was limited because of the highly conserved nature of TSPyV genomes.

The patient from whom this TSPyV-positive sample was collected was a 4-year-old boy in Nottinghamshire, United Kingdom, who had common acute lymphoblastic leukemia and was receiving maintenance chemotherapy during the study period. Retrospective clinical analysis for March 2014–February 2016 revealed that the child had had frequent cough with fever and coryzal symptoms of varying severity (Table). Concurrently collected nasopharyngeal aspirate and throat swab specimens were negative for bacterial and viral pathogens routinely tested for, except at the start of the study period, when rhinovirus and adenovirus were detected, and the end of the period, when rhinovirus and respiratory syncytial virus were detected (Table). No bacteria were cultured from paired specimens. On this basis, in conjunction with unremarkable physical examination and radiologic findings and stable neutrophil and leukocyte counts (data not shown), the patient’s respiratory signs were treated conservatively on an outpatient basis. However, on 2 occasions (August and November 2015), the child required hospital admission, without and with co-infection, respectively.

Further retrospective laboratory investigation found that all 11 additional samples collected from this patient during November 2014–2015 were positive for TSPyV, with co-infection at the 4 time points (November and December 2014, September and November 2015); testing showed fluctuating cycle threshold (Ct) levels on quantitative PCR (Table; online Technical Appendix). Of note, various forms of rashes appeared in different anatomic regions of the patient but did not resemble the characteristic appearance of trichodysplasia spinulosa and, thus, did not raise any clinical suspicion for this condition. Indeed, retrospective testing found that a single skin swab sample taken from a suspected viral rash (site undocumented) that looked like blisters and...
was queried as chickenpox was positive for TSPyV with a low C\textsubscript{t} value of 24.97 (Table). Thus, it is conceivable that this rash represented the early papular stages of a trichodysplasia spinulosa lesion that did not progress to the characteristic spicules.

Previously, TSPyV has almost exclusively been associated with pathology of the skin (4); but 4 reports indicate its isolation from blood (6) and respiratory samples, suggesting a potential transmission route (5,8–10). However, respiratory signs and symptoms were observed only in patients co-infected with another virus. In contrast, the patient we report had persistent respiratory signs and symptoms and concomitant TSPyV-positive (by PCR) respiratory samples in conjunction with varying forms of skin lesion lacking the characteristic spicule form of trichodysplasia spinulosa. However, it is difficult to assess the virus pathogenicity in the absence of any supportive cell culture results. Hence, the potential of TSPyV to cause respiratory signs and symptoms needs further investigation and surveillance. The relatively low C\textsubscript{t} values (and thus high viral loads) of TSPyV DNA obtained from this patient in the absence of positive results for any other microbial agents may suggest an etiologic role of the TSPyV in respiratory pathogenesis. The fact that TSPyV skin disease can be effectively treated with antiviral medication, such as cidofovir (6), presents potential for treatment of respiratory manifestations of TSPyV infection.

This study was funded internally by the University of Nottingham, UK, as part of a master of science degree project.

About the Author
Ms. Bagasi is a PhD student at the University of Nottingham. Her research interests are epidemiology and cellular entry of viral infections.

References

Table. Clinical and laboratory data from TSPyV-positive patient, Nottinghamshire, United Kingdom, November 2014–2015*

<table>
<thead>
<tr>
<th>Collection date</th>
<th>Sample type</th>
<th>Signs and symptoms at time of sample collection</th>
<th>Documented skin lesion</th>
<th>Hospital admission</th>
<th>Viral/bacterial co-infection</th>
<th>TSPyV C\textsubscript{t} value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014 Nov</td>
<td>Throat swab</td>
<td>Cough, sore throat, fever</td>
<td>Tiny skin colored pustules on hand</td>
<td>Not required</td>
<td>Rhinovirus</td>
<td>31.83</td>
</tr>
<tr>
<td>2015 Dec</td>
<td>NPA</td>
<td>Cough, fever</td>
<td>None</td>
<td>Not required</td>
<td>Adenovirus</td>
<td>31.17</td>
</tr>
<tr>
<td>2015 Jan</td>
<td>Skin swab</td>
<td>None recorded</td>
<td>Suspected varicella zoster virus rash</td>
<td>Not required</td>
<td>None</td>
<td>24.97</td>
</tr>
<tr>
<td>2015 Feb</td>
<td>NPA</td>
<td>Dry cough, fever</td>
<td>None</td>
<td>Not required</td>
<td>None</td>
<td>31.23</td>
</tr>
<tr>
<td>2015 Mar</td>
<td>Throat swab</td>
<td>Dry cough, corystaliform symptoms</td>
<td>None</td>
<td>Not required</td>
<td>None</td>
<td>21.43</td>
</tr>
<tr>
<td>2015 Jul†</td>
<td>Throat swab</td>
<td>Cough with runny nose</td>
<td>None</td>
<td>Not required</td>
<td>None</td>
<td>23.90</td>
</tr>
<tr>
<td>2015 Jul‡</td>
<td>NPA</td>
<td>Cough with runny nose</td>
<td>None</td>
<td>Not required</td>
<td>None</td>
<td>22.70</td>
</tr>
<tr>
<td>2015 Jul‡</td>
<td>NPA</td>
<td>Dry cough, fever</td>
<td>Few blisters on fingers</td>
<td>Not required</td>
<td>None</td>
<td>22.30</td>
</tr>
<tr>
<td>2015 Aug</td>
<td>Throat swab</td>
<td>Cough, fever (high)</td>
<td>Erythematous rash with tiny white center on face</td>
<td>Hospitalized 4 d</td>
<td>None</td>
<td>21.47</td>
</tr>
<tr>
<td>2015 Sep Nov</td>
<td>NPA</td>
<td>Cough, wheeze, fever</td>
<td>None</td>
<td>Hospitalized 5 d</td>
<td>Respiratory syncytial virus</td>
<td>26.87</td>
</tr>
</tbody>
</table>

* C\textsubscript{t}, cycle threshold; NPA, nasopharyngeal aspirate; TSPyV, trichodysplasia spinulosa polyomavirus; VZV, varicella zoster virus.
† Collected on the same date.
A swab culture of the ulcer site grew *Wohlfahrtiimonas chitiniclastica*, and this species has been a gram-negative, short, facultative anaerobic, straight-rod gammaproteobacterium that was first isolated from the parasitic fly, *Lucilia sericata* (Tokyo, Japan). He had a necrotic lesion on his left shoulder of the National Center for Global Health and Medicine by a passerby and admitted to the emergency department. An unidentified patient was found unconscious on the ground in a 75-year-old man in Japan who had squamous cell carcinoma on his shoulder. In September 2016, an unidentified patient was found unconscious on the ground and was later discharged to another hospital.

After saline infusion and intravenous cefazolin (3 g/d) were initiated, the patient’s condition improved. A blood culture taken at the time of admission grew *Pepotoniphilus harei*. A swab culture of the ulcer site grew *Proteus mirabilis*, *Morganella morgani*, and *Kerstersia gyiorum*. A biopsy was performed on day 3, and the patient was diagnosed with squamous cell carcinoma. Enhanced computed tomography scanning revealed an ulcer and ring-enhancing lesion on his left shoulder (which was suspected of being a tumor or abscess) and multiple enlarged lymph nodes and 10-mm pulmonary nodules in the right lung.

On day 20, the patient had fever and disturbance of consciousness; therefore, he was transferred to the Infectious Disease department of the hospital. Intravenous therapy with vancomycin (1.5 g/d), cefepime (3 g/d), and metronidazole (1,500 mg/d) was initiated, and the patient’s fever and consciousness improved. Two cultures of blood taken on day 20 grew *P. mirabilis*, *M. morganii*, *Streptococcus anginosus*, *Streptococcus agalactiae*, *Bacteroides fragilis*, and gram-negative rods. After we obtained the culture results, vancomycin was stopped in accordance with the susceptibility test results. We identified the gram-negative rods as *W. chitiniclastica* by using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonics, Billerica, MA, USA), which showed scores of 2.239. We further confirmed the isolate to be *W. chitiniclastica* by using 16S rRNA sequencing; the isolate was 99.08% identical to strain S5 (GenBank accession no. AM397063). We assessed the isolate’s antimicrobial susceptibility profile (Table). The patient improved and was later discharged to another hospital.

*W. chitiniclastica* is a gram-negative, short, facultative anaerobic, straight-rod gammaproteobacterium that was first isolated from the parasitic fly *Wohlfahrtia magnifica* (1). This fly has not been reported in Japan. However, *W. chitiniclastica* has also been isolated from the parasitic fly *Chrysomya megacephala*, and this species has been reported in Japan (2), and from from the parasitic fly *Lucilia sericata* housefly, which is widely distributed all over the world (3). Campisi et al. reported that the *Lucilia sericata* housefly might be a vector for *W. chitiniclastica* (4); this fly is common and widely distributed throughout Japan, and a