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Small Anellovirus Infections in Korean Children

To the Editor: Recently, Jones et al. (1) identified circular DNA sequences, classified as Anellovirus genus, in plasma from patients with acute viral infection syndromes. These anelloviruses were then labeled as “small anellovirus (SAV)” because of their smaller genomes when compared with Torque Teno Virus (TTV) and Torque Teno Mini Virus (TTMV), which have small, circular, single-stranded DNA genomes. Although anelloviruses are not associated with any specific disease, TTV has been suggested to play a role in acute respiratory disease (ARD) and in asthma of children (2,3).

Kawasaki disease and Henoch-Schonlein purpura are important vasculitis disorders in children, possibly triggered by unknown infectious agents. Recently, Gergely et al. (4) reported that molecular mimicry involving TTV and the generation of autoantibodies may have a role in the pathogenesis of systemic lupus erythematosus. The purpose of our study was to investigate the prevalence of SAV and its association with various clinical diseases in children.

The study population comprised 81 serum samples from healthy children and 151 serum samples from children hospitalized with hepatitis (81 cases), ARD (40 cases), Kawasaki disease (12 cases), or Henoch-Schonlein purpura (18 cases) during the period January 2002–June 2006. Nasopharyngeal aspirates paired with serum samples were collected from 34 children with ARD, including upper respiratory tract infections, pneumonia, and acute bronchiolitis. Samples were collected after informed consent was obtained at admission from patients’ parents.

PCRs for SAV were performed to amplify a 5′ noncoding region of SAV...
with specific primers, as described previously (5). PCR products were directly sequenced, and nucleotide sequences were registered in GenBank (accession nos. DQ978791–DQ9788810). The \( \chi^2 \) test with Yates correction and Mann-Whitney U-test were used for statistical comparison by using MedCalc (MedCalc Software, Mariakerke, Belgium). A \( p \) value <0.05 was defined as statistically significant.

In our study population, serum SAV DNA was detected in 28 (34.5%) of 81 children in the control group and in 66 (43.7%) of 151 children in the disease group. In the healthy control group, the SAV-positive rate was 7.4% (6/81) in children <12 months of age, 16.0% (13/81) in children 1–4 years of age, and 11.1% (9/81) in children 5–15 years of age. In the disease group, the SAV-positive rate was 35.8% (29/81) in patients with hepatitis, 67.5% (27/40) in ARD, 50% (6/12) in Kawasaki disease, and 22.2% (4/18) in Henoch-Schonlein purpura, respectively (Table). Among 34 nasopharyngeal aspirates collected from children with ARD, SAV DNA was detected in 19 (55.9%). Codetection of SAV and respiratory syncytial virus in nasopharyngeal aspirates was observed in 4 patients.

Percent similarity of nucleotide sequence of PCR products was 99% among SAV isolates. To our knowledge, this is the first report of SAV infections in children. The prevalence and role of SAV in clinical diseases have yet to be determined. Recently, Biagini et al. (5) reported that the prevalence of SAV infection was 20% (12/60) in French blood donors. In an Italian study (6), the positive rate of SAV DNA was 9.1% (5/55) in patients with hepatitis C compared with 8.6% (3/35) in healthy controls. Thus, the prevalence of SAV in Korean children is much higher than that reported in adults from other countries (5, 6). Further studies are needed to confirm this finding.

In our study, the prevalence of SAV did not differ significantly between the hepatitis group and the healthy control group. Our results indicate that SAV presence does not appear to have a defining role in hepatitis, as do TTV or TTMV infection (7). In a previous study, several groups of viruses, including TTV, were ruled out as etiologic agents of Kawasaki disease (8), findings similar to those of our study. We found that the prevalence of SAV was significantly higher in patients with ARD and that SAV-positive results from serum were consistent with those of nasopharyngeal aspirates in 76% (26/34). These findings suggest that the respiratory tract may be a transmission route of SAV in children.

In conclusion, we confirmed the presence of SAV in serum samples and nasopharyngeal aspirates from Korean children. A significantly higher detection of SAV DNA was observed in children with ARD compared with healthy children or children with other clinical diseases.

Table. Prevalence of SAV viremia in the study population, Republic of Korea, January 2002–June 2006*

<table>
<thead>
<tr>
<th>Group</th>
<th>Sex, M/F</th>
<th>Age range (mean age)</th>
<th>No. tested</th>
<th>No. positive (%)</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>48/33</td>
<td>1 mo–15 y (47 mo)</td>
<td>81</td>
<td>28 (34.5)</td>
<td></td>
</tr>
<tr>
<td>Hepatitis</td>
<td>44/37</td>
<td>1 mo–15 y (58 mo)</td>
<td>81</td>
<td>29 (35.8)</td>
<td>1</td>
</tr>
<tr>
<td>HBV</td>
<td>8/12</td>
<td>0–15 y</td>
<td>20</td>
<td>10 (50)</td>
<td>0.30</td>
</tr>
<tr>
<td>HCV</td>
<td>11/0</td>
<td>0–10 y</td>
<td>11</td>
<td>5 (45.4)</td>
<td>0.71</td>
</tr>
<tr>
<td>Others</td>
<td>10/9</td>
<td>0–13 y</td>
<td>19</td>
<td>7 (36.8)</td>
<td>0.93</td>
</tr>
<tr>
<td>Unknown</td>
<td>15/16</td>
<td>0–13 y</td>
<td>31</td>
<td>7 (22.5)</td>
<td>0.3</td>
</tr>
<tr>
<td>ARD</td>
<td>22/18</td>
<td>0–5 y (18 mo)</td>
<td>40</td>
<td>27 (67.5)</td>
<td>0.001†</td>
</tr>
<tr>
<td>Vascuaitis</td>
<td>22/8</td>
<td>1–10 y (46 mo)</td>
<td>30</td>
<td>10 (33.3)</td>
<td>0.51</td>
</tr>
<tr>
<td>KD</td>
<td>9/3</td>
<td>1–9 y</td>
<td>12</td>
<td>6 (50)</td>
<td>0.47</td>
</tr>
<tr>
<td>HSP</td>
<td>13/5</td>
<td>2–10 y</td>
<td>18</td>
<td>4 (22.2)</td>
<td>0.46</td>
</tr>
<tr>
<td>Total</td>
<td>136/96</td>
<td>1 mo–15 y</td>
<td>232</td>
<td>94 (40.5)</td>
<td></td>
</tr>
</tbody>
</table>

*SAV, small anellovirus; HBV, hepatitis B virus; HCV, hepatitis C virus; ARD, acute respiratory tract disease; KD, Kawasaki disease; HSP, Henoch-Schonlein purpura.

†\( p < 0.05 \), statistically significant.

References

Antibodies against Leptospira spp. in Captive Collared Peccaries, Peru

To the Editor: Leptospirosis is endemic to tropical South America and is a major public health problem for persons living in some regions of the Amazon Basin (1–3). For local inhabitants, the collared peccary (Tayassu tajacu) represents a major source of meat and income and is one of the most hunted species. As a result, several farms are attempting to produce captive collared peccaries (4). Although spirochetes have been isolated from bats, marsupials, and rodents in the Peruvian Amazon (5), local popular game animals have not been tested.

From May through December 2003, 96 collared peccaries from 4 experimental farms in 2 Amazonian provinces of Peru (Loreto and Ucayali) were surveyed for antibodies against Leptospira spp. Although the initial stock of each farm came from the wild, most animals had been born in captivity, remained on their respective farms, and had no contact with animals from the different farms. Blood samples were taken from animals that were born or maintained on the farm for ≥6 months, were in good physical condition, and showed no signs of disease. Samples that had been hemolyzed or otherwise contaminated were discarded, leaving optimal samples from 96 animals (sex ratio 1:1, 71% ≥1 year of age).

The microscopic agglutination test was performed with a panel of 24 antigens belonging to 17 serogroups of Leptospira spp. used for screening surveys at the National Leptospirosis Reference Laboratory. An additional distinct strain, obtained from a febrile human patient in the Peruvian Amazon and provisionally designated as Var10, was added (2). Serum samples were considered positive if they had 50% agglutination and titers >100 (6). Chi-square tests were used for statistical comparisons of sex and age; significance was set at p<0.05.

Among the screened samples, 64.6% reacted to 15 serovars (strains) that belong to 11 serogroups of Leptospira spp. used for screening surveys at the National Leptospirosis Reference Laboratory. An additional distinct strain, obtained from a febrile human patient in the Peruvian Amazon and provisionally designated as Var10, was added (2). Serum samples were considered positive if they had 50% agglutination and titers >100 (6). Chi-square tests were used for statistical comparisons of sex and age; significance was set at p<0.05.

Seroprevalence on the farm in Loreto (n = 27) was 100%. At this farm, peccaries are kept near aquatic species and numerous ponds of stagnant water, which provide an ideal environment for the development of Leptospira spp. Because of recent human leptospirosis outbreaks in the area (2), 3 of the peccary caretakers were tested for antibodies against Leptospira spp.; their results were negative.

Although similar to animals described in previous reports (7,9), none of the sampled animals showed evidence of disease at the time of sampling; however, absence of clinical disease does not exclude the possibility of subclinical or past infections. Furthermore, the high prevalence of antibodies to multiple serotypes suggests a wide exposure to Leptospira spp. Despite reports that suggest the collared peccary could act as a reservoir for Leptospira spp. (7,9), the finding of high antibody titers in some individual animals could indicate that collared peccaries are incidental rather than reservoir hosts. However, the prevalences found at 4 distant farms also indicate that this species could play some role in the maintenance and spread of leptospirosis in the Amazon Basin.

Multiple titers to different serovars or serogroups in the same serum sample are common with serologic testing and difficult to interpret. Multiple titers can result from cross-reactions between different serovars or from true multiple infections (10). Regardless, serologic tests are only indicative of exposure to leptospires. Further efforts are necessary to isolate leptospires from the urine or renal tissue of collared peccaries to confirm the presence of spirochetes and their potential dissemination into the environment.

Our findings indicate that persons who have contact with collared peccaries and their products, particularly animal caretakers, researchers, hunters, and game traders, are at risk for