Outbreak of Poliomyelitis in Gizan, Saudi Arabia: Cocirculation of Wild Type 1 Polioviruses from Three Separate Origins

Huda Alif, Roland W. Sutter, Olen M. Kew, Robert E. Fontaine, Mark A. Pallansch, Mahesh K. Goyal, and Stephen L. Cochi

In 1989, a localized outbreak of 10 cases of poliomyelitis occurred in Saudi Arabia. Wild poliovirus type 1 was isolated from 5 patients. To determine the patterns of poliovirus circulation, partial nucleotide sequences of the poliovirus isolates were compared. These isolates were remarkably diverse. Two isolates were closely related to each other and to viruses isolated during the 1988 epidemic in Oman. Two other isolates were very similar to viruses found in Egypt. The fifth isolate was distantly related to the latter pair. The molecular data suggest that the 10 cases represented three separate outbreaks. The virologic findings underscore the potential for Saudi Arabia, which receives millions of guest workers and their families each year from countries in which polio is endemic, to be exposed to frequent importations of wild polioviruses. To restrict the circulation of imported polioviruses, Saudi Arabia must maintain high poliovirus immunity to poliovirus in all geopolitical divisions.

In 1985, the Pan American Health Organization adopted the goal of regional elimination of indigenous wild poliovirus by the year 1990 [1], and in 1988, the World Health Assembly adopted the goal of global eradication by the year 2000 [2]. Substantial progress toward poliomyelitis eradication has been achieved; the Western Hemisphere recorded its last case in Peru with onset of paralysis in September 1991 [3]. Subsequently, an international commission certified the American region as free of indigenous wild poliovirus in August 1994 [3]. Dramatic progress toward elimination of poliomyelitis has also been documented from other countries and regions [4–7], including China [8, 9], Vietnam [10], and the Philippines [11].

To monitor the progress toward the poliomyelitis eradication objective, a number of process and outcome indicators are used [12, 13]. One of the most important indicators is the number and molecular characteristics of wild poliovirus isolates [14, 15]. As a geographic region makes progress toward eradication of poliomyelitis, poliovirus reservoirs gradually become extinct, and the remaining circulating poliovirus genotypes have reduced biodiversity, indicated by less heterogeneity of the genomic sequences of poliovirus isolates [15].

In 1989, a localized outbreak of 10 cases of paralytic poliomyelitis occurred among highly vaccinated children in the Gizan Emirate of Saudi Arabia. The outbreak was associated with wild poliovirus type 1. The outbreak occurred despite high coverage rates of three doses of oral poliovirus vaccine (OPV) among 1-year-olds in the Emirate in the preceding year. To complement the descriptive epidemiologic [16] and seroprevalence survey [17] investigations of this outbreak, we sought to determine the links among the cases in the outbreak by analyzing the nucleotide sequences relationships among the type 1 polioviruses isolated from the cases. The outbreak turned out to be unexpectedly complex, involving three separate wild poliovirus lineages, two of which could be traced to viruses endemic to neighboring countries.

Methods

Clinical investigations. All patients with suspected cases of poliomyelitis were examined by one of us (H.A. or R.W.S.); in addition, we reviewed medical records and interviewed mothers to obtain information on vaccination history, antecedent illness (including febrile episodes), clinical course of disease, and course of recovery (if any). Vaccination histories were provider- or written vaccination card-verified.

Cases were confirmed using the criteria established by the World Health Organization. In addition, we used the following classification modification: Confirmation of a case also required wild poliovirus isolation.

Characterization of virus isolates. Primary isolation from rectal swabs and stool specimens, serotyping, and characterization of polioviruses as wild or vaccine-related were done at the Centers for Disease Control and Prevention using standard techniques [18], probe hybridization [19], and partial genomic sequencing [14, 15]. Genomic sequences (VP1/2A region, nucleotides 3296–3445) of each isolate from Gizan were compared with a database of nucleotide sequences of contemporary wild polioviruses isolated in many
different areas of the world [15, 20]. A genotype is a group of polioviruses having no more than 15% genomic divergence within the 150-nucleotide VP1/2A interval [14, 15].

Results

The basic clinical, epidemiologic, virologic, and serologic findings for the 10 poliomyelitis cases (5 suspected and 5 confirmed) in Gizan are summarized in table 1 (see also [16]). The cases occurred over an 11-week period from mid-June to late August of 1989. Cases resided within a 50-km² area in Gizan, primarily in towns along the major north-south highway. Eight of the 10 cases were in children <24 months of age. All but 1 of the children had previously received three or more doses of OPV; the exception was a 4-month-old girl who had received only one OPV dose. The cases were associated with poliovirus type 1. High titers of neutralizing antibodies to poliovirus type 1 were found in the convalescent sera of all case-patients (9/10) who provided specimens. Wild poliovirus type 1 was isolated from 5 of the 10 case-patients.

The nucleotide sequences of the 5 isolates were surprisingly diverse. The isolates belonged to two separate genotypic groups (figure 1). Three of the isolates (from patients 5, 8, and 10) were members of the eastern Mediterranean (EMED) genotype. The other 2 isolates (from cases 3 and 6) were members of the SASA (South Asia) genotype, indigenous to the countries of south Asia. Two of the EMED isolates (from cases 5 and 8 from Abu al Qa’id) were closely related to each other (149/150 sequence identity in VP1/2A interval) and to isolates from Egypt. Of interest, the third EMED isolate (from case 10 from Al Haqu) was only distantly related to the other EMED isolates (~15% sequence differences in VP1/2A interval). The separation of the EMED isolates into two clusters in the dendrogram (figure 1) reflects nucleotide sequence differences distributed over the entire VP1/2A interval. Thus, the two clusters appear to represent separate lineages of the EMED genotype that have diverged from a common ancestral infection ~1 decade earlier [14, 15]. Although the poliovirus isolates from Abu al Qa’id are closely related to contemporaneous isolates from Egypt, we have not identified other viruses closely related to the isolate from Al Haqu.

The 2 SASA isolates (from patients 3 and 6 from Salhaba), members of the south Asia genotype, had identical sequences within the VP1/2A interval. They were most closely related (~98% sequence similarities) to isolates from the 1988 epidemic in Oman, suggesting a close (but not necessarily direct) link between cases in the two countries. Viruses of the SASA genotype have been widely distributed in countries along the rim of the Indian Ocean [14, 15, 20]. The limited genetic diversity among recent isolates of the SASA genotype obtained in different regions suggests that all of these viruses are derived from an ancestral infection that occurred in the mid-1980s and whose progeny spread widely along separate lines of transmission.

Another virus, 9366/SAA89, unrelated to the outbreak in Gizan, was isolated in 1988 in Qurayt, near the border with Jordan. This virus appears to be distantly related to some isolates from China and central Asia and is quite different from viruses of the SASA and EMED genotypes (figure 1). However, the endemic source of this virus has not been identified, and with isolate 9366/SAA89 as the only identified representative, the genotype remains unnamed.

Discussion

The 10 cases of poliomyelitis that occurred over an 11-week period in the Emirate of Gizan in 1989 were associated with

Table 1. Characteristics of poliomyelitis cases, Gizan, 1989.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age</th>
<th>Sex</th>
<th>Village</th>
<th>Onset of paralysis</th>
<th>Residual paralysis</th>
<th>No. of OPV doses</th>
<th>Virus isolated</th>
<th>Convalescent titer* to poliovirus type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18 m</td>
<td>F</td>
<td>Sabya</td>
<td>6/14/89</td>
<td>LLE</td>
<td>3</td>
<td>NS</td>
<td>≥1024 3 2048 &lt;8</td>
</tr>
<tr>
<td>2</td>
<td>23 m</td>
<td>F</td>
<td>Goz Jaafra</td>
<td>6/21/89</td>
<td>RLE</td>
<td>4</td>
<td>NS</td>
<td>≥1024 NS NS NS</td>
</tr>
<tr>
<td>3</td>
<td>14 m</td>
<td>M</td>
<td>Salhaba</td>
<td>7/06/89</td>
<td>BLE</td>
<td>3</td>
<td>PV1 (SASA)</td>
<td>&gt;1024 &gt;1024 9 &lt;8</td>
</tr>
<tr>
<td>4</td>
<td>11 m</td>
<td>M</td>
<td>Abu al Qa’id</td>
<td>7/12/89</td>
<td>BLE</td>
<td>3</td>
<td>Echo 13</td>
<td>≥1024 &lt;8 &lt;8</td>
</tr>
<tr>
<td>5</td>
<td>13 m</td>
<td>M</td>
<td>Abu al Qa’id</td>
<td>7/13/89</td>
<td>BLE</td>
<td>3</td>
<td>PV1 (EMED)</td>
<td>≥1024 &gt;1024 &lt;8</td>
</tr>
<tr>
<td>6</td>
<td>3 y</td>
<td>F</td>
<td>Salhaba</td>
<td>7/27/89</td>
<td>BLE</td>
<td>4</td>
<td>PV1 (SASA)</td>
<td>≥1024 &gt;1024 576</td>
</tr>
<tr>
<td>7</td>
<td>8 y</td>
<td>M</td>
<td>Abu al Qa’id</td>
<td>8/03/89</td>
<td>RLE</td>
<td>3</td>
<td>Negative</td>
<td>≥1024 &gt;1024 9 &lt;8</td>
</tr>
<tr>
<td>8</td>
<td>18 m</td>
<td>F</td>
<td>Abu al Qa’id</td>
<td>8/07/89</td>
<td>RLE</td>
<td>3</td>
<td>PV1 (EMED)</td>
<td>&gt;1024 &gt;1024 &gt;1024</td>
</tr>
<tr>
<td>9</td>
<td>4 m</td>
<td>F</td>
<td>Sabya</td>
<td>8/16/89</td>
<td>LLE</td>
<td>1</td>
<td>NS</td>
<td>724 &lt;8 &lt;8</td>
</tr>
<tr>
<td>10</td>
<td>11 m</td>
<td>M</td>
<td>Al Haqu</td>
<td>8/28/89</td>
<td>LLE</td>
<td>3</td>
<td>PV1 (EMED)</td>
<td>455 &lt;8 &lt;8</td>
</tr>
</tbody>
</table>

NOTE. Ages are given in months (m) or years (y). Dates of onset of paralysis are month/day/year. Residual paralysis: LLE, left lower extremity; RLE, right lower extremity; BLE, both lower extremities. Genotype abbreviations: EMED, eastern Mediterranean; SASA, south Asia. NS, no specimens available for testing.
* Using results of specimen with highest dilution if several specimens were tested.
† Specimen taken 9 days after onset of paralysis.
Figure 1. Dendrogram summarizing sequence relatedness among 40 type 1 polioviruses across interval of nucleotides 3296–3445 (VP1/2A region). Dendrogram was constructed by neighbor-joining method using PHYLIP 3.5c program package of Felsenstein [21]. Differences between any 2 sequences can be estimated by comparing horizontal lengths of connecting lines with reference scale. Included are sequences of isolates obtained since 1985 from Saudi Arabia and neighboring countries plus representative isolates from other geographic regions. Case numbers of isolates from Gizan are indicated in parentheses; isolate 9366/SAA89 is from Quriyat, near Jordan. Isolate 9825/USA89 is representative type I vaccine-related poliovirus. Country abbreviations: ANG, Angola; AZB, Azerbaijan; BRA, Brazil; CHN, China; EGY, Egypt; ETH, Ethiopia; GEO, Georgia; GUT, Guatemala; IND, India; ISR, Israel; JOR, Jordan; MAA, Malaysia; MMR, Myanmar; NIE, Nigeria; OMA, Oman; PAK, Pakistan; SAA, Saudi Arabia; SYR, Syria; THA, Thailand; TKM, Turkmenistan; TUN, Tunisia; TUR, Turkey; UAE, United Arab Emirates; USA, United States. Poliovirus genotype (members of genotype share ~85% nucleotide sequence similarity in VP1/2A interval) abbreviations: BRAZ, Brazil; CAMR, Central America; CHJX, China, Xinjiang; CHSC, China, Sichuan; CHSC, China, Sichuan; CHSC, China, Sichuan; CHXJ, China, Xinjiang; EMED, eastern Mediterranean; NAFR, north Africa; SAB1, Sabin 1–related; SASA, South Asia; SEAS, Southeast Asia; SWAF, southwestern Africa; WAFF, West Africa; WASA, western Asia; ?, unnamed (only 1 recognized isolate of this genotype).
at least three separate lineages (two of the EMED genotype and one of the SASA genotype) of poliovirus type 1. What had appeared from the temporal and geographic clustering of the cases to be a single outbreak was shown by molecular analyses of the virus isolates to be three overlapping outbreaks. Cocirculation of separate independent lineages of the same serotype has been described previously (e.g., in South Africa [14], China [15, 22], and Pakistan [20]) but not before in such a small geographic area. Seroprevalence surveys [17] relying on standard methods for neutralization assays [23] done by the Centers for Disease Control and Prevention suggested that type 1 seroprevalence was significantly higher but type 3 seroprevalence significantly lower in Gizan compared with two reference areas in Saudi Arabia. These results were interpreted as indications that wild type 1 polioviruses had circulated widely in Gizan but not in the reference areas and that a comparatively wide gap in immunity to polioviruses had developed in Gizan. This gap appears to have been the result of vaccine failures rather than from failure to vaccinate. Except for the youngest patient (who had received one OPV dose), all of the case-patients had received at least three OPV doses, yet neutralizing antibody titers to poliovirus types 2 and 3 were generally very low. Whether the low OPV immunogenicity in Gizan is due to specific cold-chain failures or other factors could not be critically assessed.

Taken together, the epidemiologic, virologic, and serologic findings suggest that the clustering of polio cases in Gizan in the summer of 1989 reflected the accumulation of children in the community who, despite high reported OPV coverages, remained susceptible to poliomyelitis. The diversity of the case isolates in Gizan illustrates the high risk in Saudi Arabia for importation of wild polioviruses from many different endemic reservoirs, a point further underscored by the isolation during the previous year of a representative of another type 1 poliovirus genotype in the northern part of the country. We cannot determine from the data currently available whether the imported viruses had circulated locally in the months before the appearance of cases. However, because importations are most frequent during the summer peak for poliovirus circulation, it seems most likely to us that the outbreak viruses were recent imports into the Gizan area.

Despite the outbreak in 1989, Saudi Arabia has made great progress toward achieving and maintaining poliovirus elimination. Acute flaccid paralysis surveillance was implemented in 1992, and completion of the recommended immunization series is now required for school entry. In 1995, Saudi Arabia conducted national immunization days with OPV. Supplemental immunization activities (such as national immunization days), together with enhanced surveillance for poliomyelitis, should preclude any resurgence of poliomyelitis and hold promise that Saudi Arabia will be able to document the absence of wild poliovirus disease for eventual certification of polio-free status. However, only the eradication of the reservoirs of wild poliovirus remaining in countries in which polio is endemic, especially the neighboring countries of Yemen, Egypt, and those on the Indian subcontinent, will ensure that Saudi Arabia can permanently maintain its polio-free status [24].

Acknowledgments

We gratefully acknowledge the assistance of Melinda Wharton and Stephen Hadler in critically reviewing the manuscript.

References