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Vaccine-associated paralytic poliomyelitis in the Russian Federation in 1998–2014

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ABSTRACT

Objectives: Different polio vaccination schemes have been used in Russia: oral polio vaccine (OPV) was used in 1998–2007 and inactivated polio vaccine (IPV) followed by OPV in 2008–2014. This article presents the characteristics of vaccine-associated paralytic poliomyelitis (VAPP) cases in Russia during this period.
Methods: VAPP cases were identified through the acute flaccid paralysis surveillance system, classified by the National Expert Classification Committee. Criteria for a 'recipient VAPP' (rVAPP) case were poliomyelitis symptoms 6–30 days after OPV administration, isolation of the vaccine virus, and residual paralysis 60 days after disease onset. Unvaccinated cases with a similar picture 6–60 days after contact with an OPV recipient were classified as 'contact VAPP' (cVAPP) cases.
Results: During 1998–2014, 127 VAPP cases were registered: 82 rVAPP and 45 cVAPP. During the period in which only OPV was used, rVAPP cases prevailed (73.8%); cases of rVAPP were reduced during the sequential scheme period (15%). Poliovirus type 3 (39.5%) and type 2 (23.7%) were isolated more often. Vaccine-derived poliovirus types 1, 2, and 3 were isolated from three cases of cVAPP. The incidence of VAPP cases was higher during the period of OPV use (1 case/1.59 million OPV doses) than during the sequential scheme period (1 case/4.18 million doses).
Conclusion: The risk of VAPP exists if OPV remains in the vaccination schedule.

Introduction

In 1996, the Russian Federation (Russia) adopted the National Polio Eradication Programme based on the World Health Organization (WHO) strategy, which included high coverage of the child population with polio vaccination through routine immunization and additional vaccination measures, as well as surveillance of acute flaccid paralysis (AFP) (Hull et al., 1997). Vaccination against poliomyelitis in Russia is carried out within the framework of the national immunization schedule (NIS). From 1959 to 2008, a trivalent oral polio vaccine (tOPV) was used for vaccination. In 2006–2007, certain categories of children (those suffering from oncological diseases, primary immunodeficiency disorders, blood diseases, frequently and chronically ill children) were individually vaccinated with the inactivated polio vaccine (IPV). In 2008, IPV was introduced into the NIS of Russia: the sequential immunization scheme consists of two IPV doses followed by one OPV dose, and revaccination includes three OPV doses.

In 2002, Russia was certified as a polio-free country (CDC, 2002). However, from 1998 through 2014, 146 polio cases were recorded, of which 19 were caused by wild poliovirus type 1 imported into Russia in 2010 (Yakovenko et al., 2014); the remaining 127 were cases of vaccine-associated paralytic poliomyelitis (VAPP). The possibility of

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VAPP is a well-known drawback of OPV (Dowdle et al., 2003). In the USSR (and then in Russia), cases of VAPP were recorded, but their detection was rather accidental. The introduction of the poliomyelitis/AFP surveillance system, which requires identification and then clinical, epidemiological, and virological study, as well as a final classification of each case, made it possible to systematically record cases of VAPP.

This article presents a characterization of VAPP cases in Russia covering a 17-year period (1988–2014), during which different vaccination schedules were used.

Materials and methods

The anti-polio vaccination schedule used in Russia

The complete immunization schedule consists of six vaccine administrations to children aged 3, 4.5, 6, 18, and 20 months, and 14 years. Before 2007, tOPV was used. The sequential immunization schedule was started in 2008. This includes two doses of IPV at age 3 months and 4.5 months and a single dose of OPV at age 6 months, followed by three revaccinations with OPV at age 18 months, 20 months, and 14 years.

Identification and classification of VAPP cases

Cases of VAPP were detected and investigated in laboratory in accordance with the AFP assay algorithm in Russia (Rospotrebnadzor, 2011) and the WHO recommendations (WHO, 1998). Two faecal samples (with 24–48 h between samplings) and two serum samples (with a 3-week interval between samplings) were collected for the primary investigation. In the case of virus isolation, samples of faeces were collected on day 60 and day 90 following the onset of paralysis and then at intervals of 1 month until a negative result was obtained. The final classification of the AFP case was performed by the National Expert Classification Committee as recommended by the WHO (WHO, 1998) and national regulations (Leschinskaya and Latysheva, 1998).

An AFP case was classified as 'recipient VAPP' (rVAPP) when typical clinical symptoms appeared during the period from 6 to 30 days after vaccination with OPV, a virus of vaccine origin was isolated, and residual paralysis remained 60 days after disease onset. A case of AFP in an unvaccinated person with typical clinical symptoms and vaccine poliovirus isolation appearing within 60 days after direct contact with an OPV recipient (or direct contact was not revealed) was classified as 'contact VAPP' (cVAPP). If a disease with a typical clinical appearance occurred between 6 and 30 days after immunization with OPV, but a poliovirus was not isolated despite adequate timing of faecal sampling, the case was classified as 'poliomyelitis of unclear aetiology, possibly rVAPP'. If the poliovirus (either from an OPV recipient or not) was not isolated due to late faecal collection (>14 days after disease onset), the case was classified as 'compatible with polio'. If, at the same time, it was reliably known that the paralysis had developed during the period from 6 to 30 days after an OPV vaccination, the case was classified as rVAPP.

Ethical statement

Samples were collected as a part of the Russian state programme for polio surveillance. Written informed consent was obtained from all subjects or their legal representatives at the primary clinical sites.

Laboratory investigations and epidemiological data collection

Virological studies were conducted in the WHO Polio Regional Reference Laboratory at Chumakov Institute of Poliomyelitis and Viral Encephalitides ("Chumakov FSC R&D IBP RAS") in accordance with the WHO guidelines. The viruses were isolated on RD, L20B, or Hep-2c cell lines. Virus identification was performed in a neutralization assay (WHO, 2004). The intratypic differentiation was conducted using a direct ELISA (van der Avoort et al., 1995; WHO, 2004), RT-PCR, or real-time RT-PCR (Kilpatrick et al., 2009). Isolation of total RNA from the suspension of infected cells, reverse transcription, PCR amplification of the poliovirus genome fragments encoding the VP1 protein, and their purification and sequencing were performed as described previously (Yakovenko et al., 2014).

Serological assays included the determination of poliovirus neutralizing antibodies in serum. This was performed by neutralization assay with Sabin strains types 1, 2, and 3 in Hep-2c cells (WHO, 1997).

Information about the clinical appearance of the disease and the premorbid and immunological statuses of the children was obtained from the case histories.

The estimates of VAPP incidence were obtained using two indicators: the number of doses of OPV administered over a certain period of time per one case of VAPP and the number of cases of VAPP that occurred within a certain period of time per one million newborns. The incidence of VAPP as a whole, for recipients of OPV, for recipients of the first dose of OPV, and for contact patients was assessed. Data on the number of newborns were obtained from the website of the Federal State Statistics Service (1998–2014)Federal State Statistics Service, 1998Federal State Statistics Service (1998–2014).

Data on the number of AFP cases and the number of OPV doses distributed were provided by the Federal Centre for Hygiene and Epidemiology of the Service for Surveillance on Consumer Rights Protection and Human Wellbeing (Rospotrebnadzor); the number of OPV doses included those used for routine vaccination and for additional polio immunization activities.

Statistical methods

The reliability of comparing the results was evaluated as described by Gubler (1978), and using Microcal Origin 8.0 (Student *t*-test after checking samples with a normality test or Fisher's exact test).

Results

During the years 1998–2014, there were 6643 cases of AFP in Russia, 127 of which were cases of VAPP (Table 1, Figure 1). The National Expert Classification Committee classified 82 cases as rVAPP, as follows: 71 cases were fully in compliance with the definition, six cases were 'compatible with poliomyelitis', and five cases were 'poliomyelitis of unclear aetiology'. Forty-two cases that were fully compliant with the criteria for cVAPP, two cases that were 'compatible with poliomyelitis', and one case of 'poliomyelitis of unclear aetiology' were classified as cVAPP. During the period of OPV use (1998–2007), the prevailing cases were rVAPP (73.8%), and during the period in which the sequential scheme was used (2008–2014), cases were mostly cVAPP (85%).

Most of the VAPP patients were male: 80.3% over the entire follow-up period, 79.4% in 1998–2007, and 85% in 2008–2014. Male subjects also prevailed among OPV recipients and among contact patients, 79.3% and 82.2%, respectively, for the entire follow-up period; 78.5% and 82.1% in 1998–2007; 100% and 82.4% in 2008–2014 (Table 1).

The age of VAPP patients ranged from 1 month to 5 years 5 months; children under 1 year comprised 74% (94 of 127). The age of all patients, recipients, and contacts was lower during OPV use