Smallpox outbreak in Yugoslavia in 1972

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In 1972, former Socialist Federative Republic of Yugoslavia (SFRJ) experienced the largest smallpox (Variola vera) outbreak in Europe after the Second World War, with 175 cases of which 35 (20%) died. This was one of the most dramatic events in the 20th century in the domain of public health in the Balkan region, with enormous social and economic consequences.

Epidemiologic situation before the occurrence of the outbreak

In the 19th century numerous outbreaks of smallpox were registered in Serbia. Between 1896 and 1910, 38,953 persons died of smallpox with over 5,000 deaths in only one year (in 1886 and in 1909). In the first half of the 19th century, immunization against this disease started in Europe with Jenner's vaccine, and in Serbia it became compulsory in 1881. The last death from smallpox was registered in Yugoslavia in 1926, and the last case occurred in 1930. In Belgrade the last 4 cases were noted in a hospital outbreak in 1923 (1). World Health Organization (WHO) proclaimed the plan for the eradication of smallpox in 1967 and started worldwide campaign of vaccination, particularly in endemic area in Asia, Africa, and South America. At that time it was estimated that about 2.5 million of people were affected by smallpox. Large-scale vaccination reduced the number of smallpox cases to only 30,000 in 21 country in 1970. Therefore, further lowering of morbidity rates was expected in the following years. Unexpectedly, in the first 4 months of 1972, the number of the registered smallpox cases suddenly increased for 44% and the disease was imported in 10 countries in which 2,500 persons were affected (2).

Importation of smallpox in Yugoslavia

In such circumstances, a great pilgrimage to Mekka and Medina was carried out in January and February 1972. For that purpose, about 2,700 persons from SFRJ traveled to these destinations. On the way back, one bus with 24 pilgrims from Kosovo and Metohija (KM) visited holy places of Dervish Muslims near Basra and Baghdad in Iraq between February 2 and 6, where the cases of smallpox had already been registered. On February 15, the bus entered SFRJ, and travelers returned to their homes in Orahovac (KM) and other surrounding villages. Retrospective investigation revealed that one of the pilgrims from the village Danjane became ill with non-specific symptoms and signs: malaise, chills, fatigue, and fever 2–3 days after arrival; the disease ended soon with no other clinical manifestations. At that time (February 21), he was on one-day travel to the city of Đakovica (KM). Subsequent serological tests documented that this person was actually infected with smallpox virus and manifested light, atypical clinical picture of this disease (3).

The outbreak in KM was detected on March 14, when the Institute of Public Health of Serbia in Belgrade was informed that 8 patients with suspected smallpox had been hospitalized in Prizren and Đakovica (1, 4). All of them were the relatives of the index case, or had been in contact with him. Samples were taken from them on March 15, and on the next day virological examination confirmed the diagnosis of smallpox. In the meantime, a person from Novi Pazar became severely ill on March 4, after visiting Đakovica where the cases of smallpox had already occurred. With the diagnosis of toxoallergic dermatitis he was transferred to the hospital in Čačak on March 8, and on

March 9 further to the Clinic of Dermatology of the Medical Faculty in Belgrade. On the same day, profuse bleeding urged his transfer to the Emergency Department of the Surgery Clinic, where he died on March 10. Soon after, his brother became ill, as well as 9 patients and medical staff in the hospital in Čačak, 8 persons at the Clinic of Dermatology, and 19 persons at the Emergency Department of Surgical Clinic in Belgrade. Altogether, it was estimated that this patient infected 38 persons, which was the unique example of smallpox transmission ever registered (1, 4). Post-mortem investigation of samples on March 22 revealed that the cause of death was smallpox. Another diseased female in KM with light clinical picture of smallpox transmitted the infection to 16 other persons, and the index case transmitted it to 11 persons. Thus, three cases spread the infection to 65 other persons, which confirmed smallpox as extremely contagious disease.

The course and characteristics of epidemic

In the period March 15–31, the second onset of the outbreak in KM affected 100 persons, and in the third attack (April 1–11), 14 more persons became ill. Altogether, 124 persons suffered from smallpox in KM (including the index case and one person with mild illness detected retrospectively). In KM, 26 (21%) persons died. The affected persons in the first attack were from six villages, in the second from 13, and in the third from 11 localities. Outside KM, the outbreak spread to five localities in Serbia (Novi Pazar, Čačak, Belgrade, Tmavje, Morović - Vojvodina), and one in Montenegro (SR Crna Gora, Plav) (Fig. 1).

![Smallpox epidemic in Yugoslavia, 1972](image)

Fig. 1 – Smallpox outbreak in Yugoslavia in 1972. From Litvinjenko et al. (4)

In these localities, 51 persons contracted smallpox, and 9 died. In Belgrade, the outbreak occurred in two onsets: the first lasted from March 18 to 25, with 27 affected persons, and the second from March 31 to April 11, with 5 cases of smallpox. Out of 32 affected persons, 6 died, with the case fatality rate of 18.7%. The last smallpox case was registered on April 11, and the last patient was released from hospital on May 19 (4).

On March 25, one month after the introduction of smallpox, when 75% of all cases occurred in KM, as well as in other localities, the outbreak was recognized by government authorities and the information was released by media.

Altogether, out of 175 affected persons, 99 (56.6%) were male, and 76 (43.4%) were female. One hundred and five (60%) cases had been previously vaccinated against smallpox, whereas 37.7% had not been immunized; the vaccine status was unknown for 2.3% of the affected persons. The lack of specific immunity was notably registered in the youngest age groups supposed to be best protected by recent vaccination: in the age group of 1–6 years, out of 15 affected persons only one was vaccinated, and in age group 7–14 years, out of 19 cases 6 had been previously vaccinated. Lethality rate was highest in children up to 1 year of age: out of 12 diseased, 8 died (lethality rate 66.7%), in the age group 1–6 years the lethality rate was 20%, in the age group 7–14 years of age - 21%, in persons 15–19 years old - 23%, and in older than 20 years of age - 15%. Lethality rate in previously vaccinated persons was 8%, and in non-vaccinated 35% (4).

There were some differences in epidemiological features of this outbreak between KM and other affected localities in SRFJ (mainly Belgrade): most of the diseased persons, 81 out of 124, (65.3%) in KM acquired infection out of medical institutions (hospitals), whereas in Belgrade
Pazar to the Department of Dermatology in the hospital in that city (5). In total, 91 (52%) of the affected persons were infected in hospitals, and 81 (44%) acquired infection outside these institutions. Furthermore, in localities outside KM, only one person was under 8 years of age, whereas in KM, 30 (24%) of cases were in the age group 1–7 years (6). This increased the lethality rate in KM (21%), when compared to the other affected regions of Yugoslavia (17.6%).

Control measures

At the time of outbreak occurrence, smallpox vaccination against this disease was compulsory for children up to 3 years of age, and revaccination in children of 7 and 14 years of age. Immunization was also compulsory for some professional profiles (medical staff), and for travelers to regions where smallpox was registered. The index case who introduced smallpox, as well as the other 25 pilgrims had also been vaccinated in December 1971, but retrospective serologic investigations revealed that in 20 of them protective titer of antibody was not registered. Furthermore, it was estimated that in the population of SFRJ, 25% of persons had residual immunity against smallpox, 30–40% of persons were partially protected, and 35% were susceptible to this infection, which suggested that the vaccination was not comprehensive, and on the other side, that immunity conferred by vaccination was not long-lasting (10). The vaccination started at the same time on the entire territory of SFRJ. The reasons for mass vaccination were the late detection of the outbreak, the establishment of many secondary foci of epidemic, and intensive movement of population, especially in KM. At the beginning of immunization only 1 000 000 of doses of vaccine was available, but soon 30 million of vaccines were obtained by international aid, and almost all the population was immunized (11). In Belgrade, 1 205 792 persons were vaccinated and 310 380 revaccinated in the period March 23–30 (1). For that purpose, special device for mass vaccination (jet-gun or jet injector) was used, which allowed the vaccination of 1 000 persons for only 1 hour. Adverse reactions and complications after vaccination were registered in 1 of 600 to 1 of 3 000 vaccinated persons in different regions of the country. Most of them were local reactions, vaccinia inoculated and vaccinia accessoria, whereas serious complications such as vaccinia generalisata, eczema vaccinatum, encephalitis, encephalomyelitis and myeloradiculoneuritis postvaccinalis, were rarely encountered (12–15).

The other control measure in fighting against smallpox outbreak was quarantine. Several kinds of quarantines were established: hospital, hotel, home quarantine, and quarantine of the entire village. The total number of quarantined persons was 15 595; out of them, 1 218 were in hospital quarantines, 803 in a hotel, 388 at home, and 13 186 at village quarantines. Fifty percent of all the persons were quarantined in KM, 36% in Serbia, 13% in Vojvodina, and 0.2% in Montenegro. Among the quarantined persons, smallpox was registered in 105; out of them, 52 in hospital quarantines, 7 in hotel quarantines, 44 in village quaran-

Clinical features

The incubation period ranged from 7 to 16 days, average 11.3. Clinical forms of smallpox were presented as following: hemorrhagic form (purpura variolosa) developed in 8% of cases, flat type in 10.8% (Fig. 2), ordinary form in 41.2%, modified form in 38.3%, and variola sine exanthe- late in 1.7% of cases.

Diagnosis

Diagnostic procedures included the isolation of smallpox virus on chorioallantoic membrane or on chicken embryos, electronic microscopy, detection of viral antigen by agar gel precipitation test, and determination of antiviral antibody titer by the method of haemagglutination-inhibition test. The best results were obtained by electron microscopy (sensitivity 90%), and by the method of virus isolation (sensitivity 94%), but the former was faster, and therefore more convenient for rapid etiologic diagnosis (9).

Fig. 2 – Flat type of smallpox. From Kecmanović et al. (7)
times, and 2 in home quarantines. Daily surveillance of these quarantines comprised physical examination and temperature control of all quarantined persons once or twice daily. These measures were effective in preventing further spreading of smallpox, since only 3 persons acquired infection while staying in quarantine; all the others had been infected before entering the quarantine. The treatment of the quarantined persons with antiviral drug methisazone or with gamma-globulin had no obvious impact in preventing the development of the disease (16).

Epilogue

Some of the reasons that contributed to the occurrence of this large outbreak were: the "silent" importation of smallpox (light and atypical clinical picture of the disease in the index case), late detection of the outbreak and late establishment of control measures. Further reasons were the lack of the most effective strategy of immunization in those circumstances, i.e., "ring vaccination" starting with vaccinating contacts in the focus of the outbreak and further progressing in concentric rings, difficulties in performing vaccination (delay, lack of vaccine, as well as of specific immunoglobulin, high percentage of unsuccessful vaccination). Lack of doctrine for epidemic containment, and the delay of release of accurate information to the population were also the reasons for the large outbreak (17).

The outbreak of smallpox had a great impact on health and economic situation in SFRJ, and also caused a certain degree of disruption of social life, since many persons were quarantined with no opportunity to contact their families, which provoked the stress and dissatisfaction. Direct cost of this outbreak was 6 billion SFRJ dinars (600 million US dollars in 1972) (1).

Fortunately, the battle against this severe disease ended in a triumphal success for modern preventive medicine, since the last case was registered in 1977 in Somalia, and in 1980 WHO proclaimed the eradication of smallpox. Yet, the experience of this outbreak may contribute to the education of healthcare workers in the prevention and control of the spread of this "mother of all plagues", especially in the light of the arising threat of the use of smallpox virus as a biological weapon (18).

REFERENCES


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