Ongoing outbreak of aseptic meningitis associated with echovirus type 30 in the City of Novi Sad, Autonomous Province of Vojvodina, Serbia, June – July 2010

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Since June 2010, incidence of aseptic meningitis has increased in Novi Sad, Autonomous Province of Vojvodina, Serbia. From 2 June to 25 July 2010, 80 cases of aseptic meningitis were notified, with an incidence rate ranging from 10 to 366 per 100,000 population in different local communities. The majority of cases (n=64) were aged between two and 15 years. Echovirus 30 was cultured from two of four cerebrospinal fluid specimens. The outbreak, for which no common source has yet been identified, is ongoing.

Background

Aseptic meningitis, which can result from multiple aetiologies, has been a notifiable disease in the Autonomous Province of Vojvodina, Serbia, since 1974. Notification criteria include a syndrome characterised by acute onset of meningeal symptoms (severe headache, vomiting, neck stiffness and fever) and cerebrospinal fluid (CSF) pleocytosis with no laboratory evidence of bacterial or fungal meningitis [1]. Cases of aseptic meningitis in the province are diagnosed throughout the year, with most occurring during the summer months. Incidence rate in years without epidemics have ranged from 1.6 per 100,000 population to 6.3 per 100,000 population; the most common mode of transmission was faeco-oral [2]. There have been several outbreaks in the last 12 years associated with swimming pools, when people probably became infected by swallowing water containing the causative virus. Lack of correct disinfection as well as overcrowding of the pools were factors associated with the infections [3-5]. An outbreak of concurrent echovirus 30 and coxsackievirus A1 infections associated with swimming in the sea among a group of travellers to Mexico was reported recently [6], showing the importance of this mode of transmission. Detection of enteroviruses in water and determining the epidemiology of waterborne diseases are crucial in modern public health and epidemiological and virological survey systems [7].

Descriptive epidemiology

From weeks 22 to 29 (2 June – 25 July 2010), 80 cases of aseptic meningitis were detected in residents of the City of Novi Sad (an administrative unit that includes City of Novi Sad and various surrounding small towns and villages) and reported to the Institute of Public Health of Vojvodina, Serbia (Figure 1). The cumulative incidence for the period was 30 cases per 100,000 population (compared with two per 100,000 population for the same period in 2009 and four per 100,000 population in 2008).

From 2 to 11 June, 10 children aged from six to 15 years were admitted to the University Clinical Centre of Vojvodina, the only hospital treating meningitis in the City of Novi Sad, the capital of the Autonomous Province of Vojvodina. All 10 patients had symptoms of meningitis including severe headache, nausea or vomiting and fever, as well as moderate CSF pleocytosis (white blood cell count $\geq 10/\text{mL}$). The Centre for Disease Control and Prevention of the Institute of Public Health of Vojvodina initiated an outbreak investigation to identify the causative agent, to describe the extent and severity of the outbreak, and to identify and exclude potential risk factors.

Case definitions

A clinical case of aseptic meningitis was defined as any person in the City of Novi Sad with a history of acute onset of severe headache, nausea and/or vomiting and fever, with bacteriologically sterile CSF cultures and moderate CSF pleocytosis (white blood cell count $\geq 10/\text{mL}$) or without CSF culture and/or moderate CCF pleocytosis, but epidemiologically linked with confirmed case, since the beginning of June 2010.

A confirmed case was defined as a clinical case with bacteriologically sterile CSF cultures, CSF moderate pleocytosis (white blood cell count $\geq 10/\text{mL}$) and/or

isolation of enterovirus from CSF or stools, since the beginning of June 2010.

A probable case was defined as a clinically compatible case diagnosed by a physician as aseptic meningitis with a CSF white cell count $<10/\text{mL}$ or unknown CSF cell

FIGURE 1

Cases of aseptic meningitis by date of symptom onset, Novi Sad, Serbia, 2 June – 25 July 2010 (n=80)

Source: Institute of Public Health of Vojvodina, Serbia.

TABLE

Prevalence of clinical features and cerebrospinal fluid abnormalities in cases of aseptic meningitis, Novi Sad, Serbia, 2 June – 25 July 2010 (n=80)

Features	Number of cases
Clinical features^a	
Fever	80
Headache	80
Vomiting	80
Photophobia	64
Diarrhoea	5
Neck stiffness	80
Pharyngitis	13
CSF abnormalities	
White blood cell count $\geq 10/\text{mL}$	70

CSF: cerebrospinal fluid.

^a None of the patients had a rash.

FIGURE 2

Incidence rate of aseptic meningitis per 100,000 population, by age group and sex, Novi Sad, Serbia, 2 June – 25 July 2010 (n=80)

count (lumbar puncture not performed or negative), since the beginning of June 2010.

Clinical and epidemiological data were collected for every case using a structured questionnaire. According to the case definition criteria, there were 70 confirmed cases and 10 probable cases as of 25 July 2010. The prevalence of clinical features and CSF abnormalities in the cases in this outbreak are shown in the Table.

Of the 80 cases, 27 had symptom onset in week 24 (14–20 June). A total of 31 cases came from various districts of the city itself (incidence rate 17 per 100,000 population); the other cases were from neighbouring villages that belong to the City of Novi Sad. The highest incidence rate was in two villages across the Danube River, Ledinci and Sremska Kamenica (366 per 100,000 population and 318 per 100,000 population respectively). Specific incidence rates indicated local community spread mainly among children attending the same preschool or primary schools. In other villages of the City of Novi Sad, the incidence rate was much lower (range: 10 per 100,000 population to 28 per 100,000 population).

The male:female sex ratio of cases was 1.9:1. The median age was 12.8 years (range: two to 46 years); 64 of the 80 cases were under 15 years of age. All adult cases (confirmed and probable) were epidemiologically linked to confirmed child cases. Age-specific incidence rates are shown in Figure 2. All patients were immunocompetent and had good outcomes without sequelae.

Microbiological findings

Bacterial meningitis was excluded in all cases. In 74 patients with lumbar puncture, bacteriological cultures were sterile. Lumbar puncture was not performed for the other six cases as their clinical manifestation was very benign. Bacterial meningitis was therefore excluded in these six cases on that basis; all six were epidemiologically linked to confirmed cases. The presence of enterovirus was confirmed by serological test (Virion-Serion) in samples from 16 patients. Four CSF samples and one stool sample were sent to the National Reference Laboratory for Poliomyelitis and Enteroviruses at the Torlak Institute for Virology, Vaccines and Sera, Belgrade, for viral culture. Enterovirus with apparent cytopathic effects was cultured from two of the four CSF samples. Enteroviruses are among the most common human viral pathogens causing the wide variety of diseases including aseptic meningitis. These RNA viruses are members of the picornavirus family and include coxsackieviruses A and B, echoviruses, numbered enteroviruses and polioviruses. The predominant agents identified in enteroviral meningitis outbreaks are echoviruses serotypes 6, 9, 11, 13, 19 and 30 [15,21,26]. In this outbreak, neutralisation with type-specific antisera established the identity of the virus as echovirus type 30.

Control measures

As a result of the outbreak, a number of control measures have been put in place. As in similar outbreaks [8], enhanced surveillance has been implemented – case definitions and a questionnaire were developed for the purposes of outbreak investigation. All cases were reported by infectious disease specialists to the Centre for Disease Control and Prevention on a daily basis and general practitioners and paediatricians in the area were informed about the outbreak and warned of a possible further increase in the number of cases. Early diagnosis of aseptic meningitis helps to avoid unnecessary antibiotic treatment and additional testing [9].

Following experience from other outbreaks [10], as public alarm was expected, a proactive media communication plan was put in place. Epidemiological reports were updated and published on a weekly basis on the website of the Institute of Public Health of Vojvodina.

Information leaflets on the main control measures were distributed to preschool facilities in the affected region. As the school year ended on 11 June, primary and secondary schools were already closed when the outbreak started.

Discussion

Outbreaks of aseptic enteroviral meningitis are notified in the Autonomous Province of Vojvodina every four to five years [3-5,11]. The largest previous outbreak occurred in 2000, with 461 cases reported that year (the incidence rate in the province was 23 per 100,000 population and incidence rate in the City of Novi Sad was 28 per 100,000 population). Outbreaks of aseptic enteroviral meningitis were notified in all neighbouring countries (Croatia, Hungary and Romania) in the last two decades [11-13]. In Kosovo under United Nations Security Council Resolution 1244, an outbreak with a total of 878 cases of acute neurological syndrome was reported in 2006 to the World Health Organization Regional Office for Europe: enteroviral origin was detected [14]. Enteroviral meningitis outbreaks involved many communities throughout other countries within Europe and also other continents [8,15-22].

As expected in temperate climate, the ongoing outbreak has occurred in hot summer months, spreading by direct or indirect contact. Although none of the common sources (contaminated food or water) has yet been implicated, since viral meningitis outbreaks are sometimes associated with recreational use of water, the use of public swimming pools had been considered a potential source of infection in this outbreak but no such exposure of cases has been identified.

Previously reported outbreaks of enteroviral meningitis have demonstrated a predominance of males in child cases, with a sex ratio of 2:1 [8,14,15,21]. Our findings are consistent with this. They are also in line with these reports that find a large proportion (70%) of cases under 15 years of age, but there was a higher

incidence rate (149 per 100,000 population) in children aged 5–15 years [8,14,15,21].

According to its epidemiological features, this outbreak is likely to continue towards the autumn months [23]. No specific control measures are available for non-polio enteroviruses [9]. Good personal and communal hygiene is recommended (thorough hand washing as a routine practice, prompt and safe disposal of waste and faeces, and prompt washing or disposal of the soiled articles in preschool and nursery facilities), as well as disinfection of contaminated surfaces with household cleaning products, and avoidance of shared utensils and drinking containers [9]. All susceptible people and parents of young children are advised to ask for medical help immediately when there is onset of sudden headaches, fever, nausea and vomiting.

A three-step model has been suggested for diagnostic procedures in order to ensure comprehensive diagnostic investigation [24], including local medical investigation and usual analysis (polymerase chain reaction (PCR) and serology) of acute cases, then as a second step, extended analysis of suspected cases by a reference laboratory for commonly recognised causative agents (or less common agents if indicated, e.g. in returning travellers), and finally identification of specific pathogens in cases with unknown aetiology.

Monitoring circulating enteroviruses is important because individual serotypes have different temporal patterns of circulation and the changes in predominant serotypes can be accompanied by large-scale outbreaks of enteroviral illnesses [25]. Environmental surveillance has been used successfully in monitoring enterovirus circulation and assessing the extent or duration of epidemic non-poliovirus enteroviruses in specific populations [26].

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