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An outbreak of aseptic meningitis in Podlaskie Voivodeship in 2014

Ognisko epidemiczne zachorowań na aseptyczne zapalenie opon mózgowych w województwie podlaskim w 2014 roku

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Abstract Enteroviruses cause common infections with various clinical course and forms, such as hand-foot-and-mouth disease (Boston exanthem disease), herpangina, myocarditis and pericarditis, widespread myositis (epidemic pleurodynia, Bornholm disease), or aseptic inflammation of the nervous system, among children and adolescents. An increase in aseptic meningitis cases of enteroviral aetiology, including the E30 virus, was occasionally observed in various European countries. In 2014, an outbreak of aseptic meningitis was reported in Podlaskie Voivodeship. A total of 640 cases were reported between June 1 and November 30, 2014, of which 228 had confirmed enteroviral aetiology. Summer and autumn seasons favour the incidence of viral infections of the central nervous system. Symptomatic infections are more common in males than females. Infections with enterovirus show the tendency to form endemic regions.

Key words: enteroviral aseptic meningitis, echovirus 30, enteroviruses

Streszczenie Enterowirusy wywołują częste infekcje wśród dzieci i młodzieży – przebiegają one pod różnymi postaciami klinicznymi, takimi jak choroba dłoni, stóp i jamy ustnej (tj. choroba bostońska), herpangina, zapalenie śródmiąszkowe mięśnia sercowego i osierdzia, nagminne zapalenie mięśni (nagminna pleurodynia, choroba bornholmska) czy też aseptyczne zakażenie układu nerwowego. Incydentalnie odnotowywany jest wzrost liczby powiązanych zachorowań na aseptyczne zapalenie opon mózgowych o etiologii enterowirusowej, w tym ECHO 30, w różnych krajach europejskich. W 2014 roku w województwie podlaskim zarejestrowano ognisko epidemiczne zachorowań na enterowirusowe zapalenie opon mózgowych. W okresie od 1 czerwca do 30 listopada 2014 roku odnotowano 640 zachorowań o etiologii wirusowej, z czego u 228 osób w badaniu płynu mózgowo-rdzeniowego potwierdzono etiologię enterowirusową. Okres letni i jesienny sprzyja występowaniu wirusowych infekcji ośrodkowego układu nerwowego. Objawowe zakażenia częściej dotyczą osób płci męskiej. Zakażenia enterowirusem ECHO 30 wykazują tendencję do tworzenia terenów endemicznych zachorowań.

Słowa kluczowe: enterowirusowe zapalenie opon mózgowych, echowirus 30, enterowirusy

INTRODUCTION

Enteroviruses (EV) are viruses belonging to the family *Picornaviridae*. According to the current classification, 120 types of the human virus are categorised into four groups: A to D (www.picornaviridae.com).

EVs cause common infections of various clinical course and forms among children and adolescents. They are aetiological factors in the course of diseases such as a hand-foot-and-mouth disease (Boston exanthem disease), herpangina, myocarditis and pericarditis, widespread myositis (epidemic pleurodynia, Bornholm disease), or aseptic inflammation of the nervous system. A marked majority of infections are asymptomatic (90%). A human is the only known reservoir of echovirus type 30 (E-30) (Dziubek, 2010; Magdzik *et al.*, 2014).

Enteroviral neuroinfections develop with the symptoms of fever, headaches, vomiting as well as meningeal signs (Dziubek, 2010). Mild forms are accompanied by muscle pains and characteristic rash, while severe forms are manifested by pneumonia, myocarditis and meningitis/encephalitis. In the last 10 years, enteroviruses were the most common cause of all cases of aseptic meningitis in Poland (Magdzik *et al.*, 2014).

Within the EV genus, E-30, with its significant neurotropism and neurovirulence, is the most prevalent serotype in cases of meningitis, both in children and adults (Witek *et al.*, 2011). Additionally, E-30 infections are characterised by the epidemic foci recurring at several-year intervals, covering wide geographical regions (Milia *et al.*, 2013).

In Poland, an epidemic increase in the number of reported cases of enteroviral meningitis was observed in 1982 with more than 24,000 cases caused mostly by E-4, as well as in 1995 and 1996 with 4,000 and 94,000 E-30 related cases, respectively (Majda-Stanisławska *et al.*, 1997).

An increase in enteroviral aseptic meningitis cases, including E-30, was occasionally observed in various European countries. In the last decade, numerous outbreaks of epidemics were reported in the European region, e.g. France, Spain, Latvia, Serbia, Finland and Romania (Antona and Chomel, 2005; Ćosić *et al.*, 2010; ECDC, 2012; Juliá *et al.*, 2009; Logotheti *et al.*, 2009; Perevoščikovs *et al.*, 2010, 2006; Savolainen-Kopra *et al.*, 2011).

In moderate climate zone, the increased number of epidemiologically linked cases (direct contact with an infected person) or epidemics occur seasonally or at intervals of 3–5 years. Subsequent outbreaks can occur due to the genetic diversity of strains (Wieczorek *et al.*, 2016).

AIM OF THE STUDY

The purpose of the study was to perform a retrospective analysis of the cases of the epidemic outbreak of viral meningitis reported between June 1 and November 30, 2014 in the Podlaskie Voivodeship.

MATERIAL AND METHODS

Morbidity was analysed with regard to the place of residence, age and sex, based on the data from the reports of 2014 routine public statistics of the Ministry of Health: MZ-57 – *Annual report on chosen infectious diseases according to sex, age, place of residence and their seasonality in 2014 year*; MZ-56 – *Fortnightly/quarterly/annual reports on cases of infectious diseases, infections and poisonings in 2014 and situational reports prepared in the Regional Sanitary and Epidemiological Station in Białystok*. The data from the reports came from the notifications of enteroviral and non-specific meningitis cases (respectively ICD-10 codes: A87.0, A87.9), registered in the units of the State Sanitary Inspection from the Podlaskie Voivodeship in the period of June 1 to November 30, 2014.

All cases of disease and suspected disease are reported on a mandatory basis by doctors to a competent state sanitary inspector. The reports contain information on patients diagnosed with infectious disease (name, date of birth, sex, address, place of residence) and clinical data (clinical diagnosis of infection or infectious disease, the characteristics of the main clinical symptoms, the circumstances of disease or death, with a particular focus on risk factors, biological characteristics of the infectious agent, and other data necessary for the implementation of epidemiological surveillance, in accordance with the principles of modern medical knowledge). This information served as a basis to conduct an epidemiological inquiry to determine the source of infection (e.g. contact with a sick person, main sites of whereabouts – schools and other educational institutions, mass events) and the likely route of infection.

During this period (June to November 2014), 640 cases were reported: 228 patients with enteroviral meningitis (confirmed by molecular testing in cerebrospinal fluid – reverse transcription – polymerase chain reaction, RT-PCR) and 412 patients with non-specific viral meningitis (assessment of cerebrospinal fluid parameters). The group included 500 (70%) children aged up to 18 years and 140 (30%) adults aged over 18 years from 7 counties of the Podlaskie Voivodeship.

RESULTS

Place of residence

The first cases of the epidemic outbreak (7 cases) were reported in the borough of Brańsk in Bielsk County. The subsequent cases occurred in the city of Białystok and the neighbouring borough of Wasilków. In the period between June 1 and 30, 2014, a total of 115 epidemiologically related cases (determining the likely route of infection in the patient's epidemiological history: contact with a person suffering from enterovirus meningitis, main sites of whereabouts – schools and other educational institutions or mass events) were reported in the two counties

of the Podlaskie Voivodeship (Białystok County – 108, Bielsk County – 7 cases) (Fig. 1).

Cases of disease occurred in 7 counties of the Podlaskie Voivodeship. The highest number of cases were reported in Białystok (77%), Sokółka (9%) and Bielsk County (6%). A significant majority of cases occurred among city residents (73%). The analysis of morbidity demonstrated the difference between the city and the rural area. The incidence rate ranged from 83/100,000 in the city to 68/100,000 in the rural area.

In the Podlaskie Voivodeship, new cases in the epidemic outbreaks were related to the residents of Białystok

City and the inhabitants of counties such as Białystok – 507 (79%), Bielsk – 40 (6%), Hajnówka – 16 (2.5%), Mońki – 11 (2%), Siemiatycze – 4 (0.5%), Sokółka – 55 (9%) and Zambrów – 7 (1%) cases.

Number of cases

In the analysed period, 640 cases of aseptic meningitis were reported in the Podlaskie Voivodeship. The first cases occurred in June 2, 2014. The highest number of cases ($n = 268$; 42% of the total number) was observed in July, with a sudden increase in the second half of June.

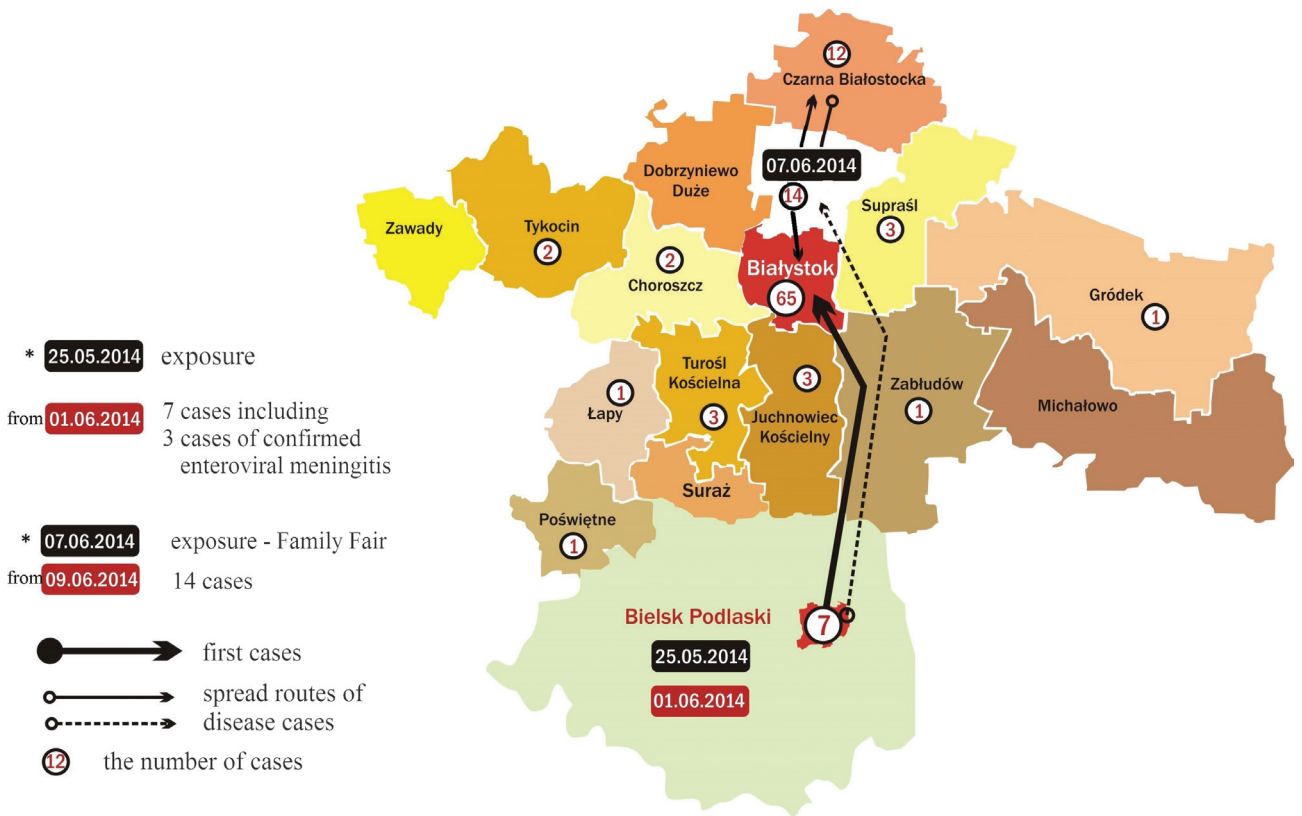


Fig. 1. Disease spread in the epidemic outbreak between June 1 and 30, 2014 (Białystok and Bielsk counties) (source: WSSE in Białystok after modification)

Place of residence	Number of cases	%	Morbidity in 100,000
City	466	73%	83
Below 20 thousand inhabitants	115	18%	
20–99 thousand inhabitants	28	4%	
Above 100 thousand inhabitants	323	50%	
Rural area	174	27%	68
Total	640	100%	78

214 Tab. 1. The number of patients by place of residence

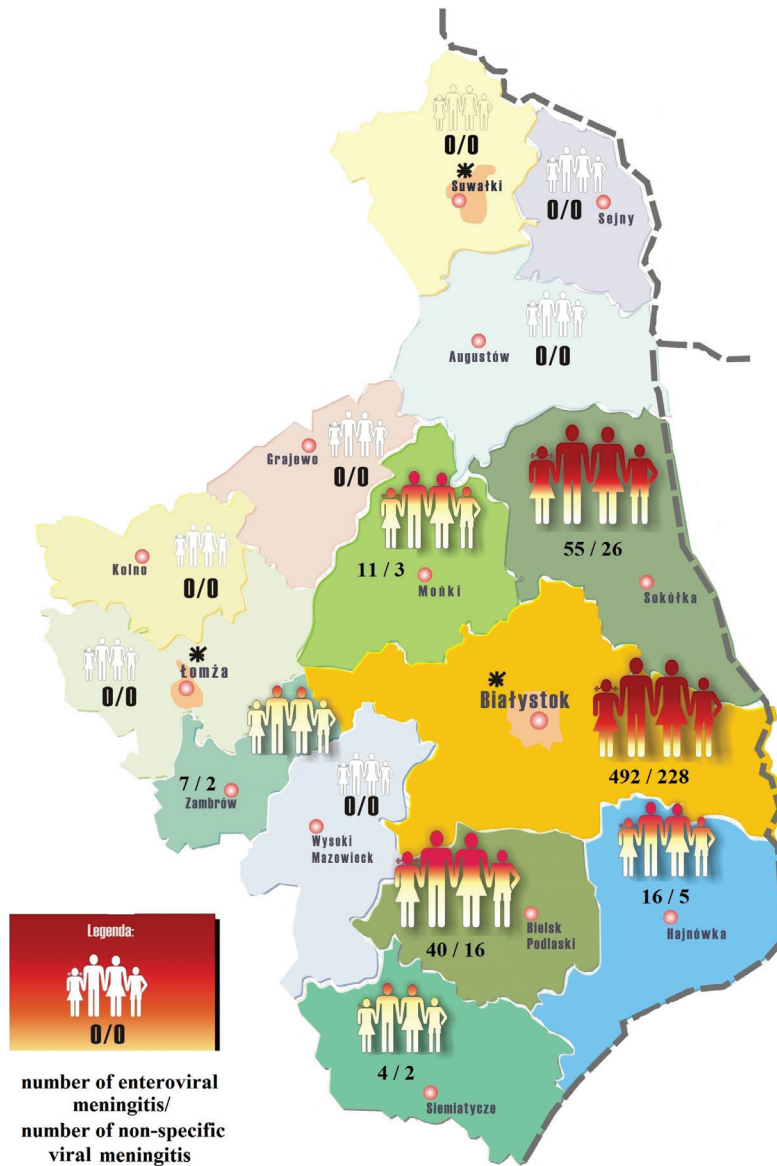


Fig. 2. The number of aseptic meningitis cases in the counties of the Podlaskie Voivodeship from June 1 to November 30, 2014 (source: WSSE in Białystok after modification)

Age groups	The number of cases of enteroviral, other viral and non-defined meningitis		Incidence rate per 100,000 population			Total	%
	Male	Female	Male	Female	Total		
0–4	48	29	516	339	431	77	12
5–9	102	66	1021	679	852	168	26
10–14	86	52	883	548	718	138	22
15–19	69	34	588	308	452	103	16
>19	85	69	16	12	14	154	24
Total	390	250	99	59	78	640	100

Tab. 2. The number of cases of enteroviral, other viral and non-defined meningitis and the number of cases in 100,000 population in the age groups

As the epidemic curve (Fig. 2) shows, the number of cases decreased significantly at the beginning of September 2014.

Age groups

Nearly half of cases (48%) occurred among children and adolescents aged between 5 and 14 years. The highest number of cases in both sex groups were observed in the age group of 5–9 years. In the study period, the incidence of aseptic meningitis reached 78 per 100,000 population, in the study region. In the age group of 5–9 years, it was 852 cases per 100,000 population. In adults, the incidence rate was 14 per 100,000 population.

Gender

An analysis of cases with regard to the sex showed differences in morbidity. Of 640 cases, 390 (61%) were males (Tab. 2). Similarly, morbidity among males was higher in each age group.

DISCUSSION

In the current study (June 1 to November 30, 2014), 640 cases of viral aetiology were reported, including 228 patients with enteroviral aetiology, which was confirmed by cerebrospinal fluid testing using molecular methods. Cerebrospinal fluid examination in 10 patients in all assays showed a type of E-30 virus (EV were isolated using RD cells and isolates were sequenced and characterised by phylogenetic analysis of partial VP1 region – 793 nt) (Wieczorek *et al.*, 2016).

The other cases of meningitis (412) were reported to the units of sanitary inspection as other viral or non-specific infections (A87.9). Epidemiological investigation (an epidemiological history confirming a direct contact with a diagnosed person, staying in the area of an increased incidence of infection) classified these cases as related cases in the epidemic outbreak. In the countries where prophylactic vaccinations against epidemic parotitis are conducted – also in Poland, it is estimated that enteroviruses are aetiological agents in about 90% of all cases of aseptic meningitis (Witek *et al.*, 2011). The circulation of enteroviruses in the human population decreases with improved sanitary conditions, which is directly connected with an increase in the percentage of people without antibodies against the individual types of enteroviruses (Magdzik *et al.*, 2014).

As shown in the epidemiological investigation, the first cases initiating the outbreak of the epidemic were reported after an event the citizens of Belorussia participated in. The phylogenetic analysis of strains from the epidemic outbreaks in Poland demonstrated that the meningitis outbreaks caused by E-30 from Podlaskie (2014) was associated with an outbreak in an adjacent region

of Mazowieckie (2013) as well as it showed the closest correlation to Russian and Chinese echoviruses. On the basis of detected isolates it was revealed that the virus had spread from Russia to Poland and from China to Russia (Wieczorek *et al.*, 2016).

Epidemic outbreaks of enteroviral neuroinfections described by other authors in the last decade in the European region included between 44 and 258 cases and showed a similar proportion of affected children compared to our study (about 80%) (Antona and Chomel, 2005; Ćosić *et al.*, 2010; ECDC, 2012; Juliá *et al.*, 2009; Logotheti *et al.*, 2009; Österback *et al.*, 2015; Perevoščikovs *et al.*, 2010, 2006; Savolainen-Kopra *et al.*, 2011).

High EV-associated morbidity among early school age children was confirmed in this study. In the Podlaskie Voivodeship, the morbidity in the age group of 5–9 years reached 852/100,000 and constituted 26% of all cases in the epidemic outbreak in 2014. A significant proportion of cases in this age group was also reported in the outbreaks described in Latvia in 2010 – 26% of all cases, in Serbia in 2010, where morbidity among boys and girls aged 5–9 years reached 250/100,000, and 110/100,000, respectively (Ćosić *et al.*, 2010; Perevoščikovs *et al.*, 2010, 2006). The analysis of cases in the epidemic outbreaks in Europe in the last 10 years showed the highest morbidity in early school age children, which was probably caused by a lower percentage of children with active immunity against the defined type of a virus compared to older children, and also more intensive social contacts compared to children below the age of 5 years.

A difference in the morbidity with regard to sex is described by other authors of E-30 infection cases, which means that boys and men are affected by this infection more frequently than girls and women (Ćosić *et al.*, 2010; ECDC, 2012; Juliá *et al.*, 2009; Logotheti *et al.*, 2009; Perevoščikovs *et al.*, 2010, 2006). In the Podlaskie Voivodeship, this proportion referred to each age group and was higher in men.

The analysis of cases with enteroviral aetiology in Europe indicates their seasonal occurrence. Summer and autumn seasons favour the spread of E-30 meningitis in moderate climate zone. So far, the occurrence and seasonality of this phenomenon have not been fully explained (Antona and Chomel, 2005; Ćosić *et al.*, 2010; ECDC, 2012; Österback *et al.*, 2015; Perevoščikovs *et al.*, 2010, 2006).

The analysis of cases demonstrated features of an epidemic. In 2014, a significant increase in the number of viral neuroinfection cases was observed in the Podlaskie Voivodeship, i.e. from 50 cases in 2013 (morbidity 4/100,000 cases) to 640 cases in 2014 (morbidity 54/100,000). In 2015, also in the summer, an increase in the number of viral neuroinfection cases was reported in Białystok County, i.e. 117 cases, of which 45 had a confirmed enteroviral aetiology (NIZH-PZH, 2016). Epidemiological inspection should be intensified to react immediately (e.g. by introducing sanitary regime or temporary closure of nurseries,

kindergartens and schools, reduction of mass events) to the formation of endemic regions with cases of infections caused by E-30 virus (Österback *et al.*, 2015; Witek *et al.*, 2011). Our findings indicate that the epidemic of enteroviral neuroinfections in the Eastern Europe may pose a challenge for public health in the future.

CONCLUSION

1. An epidemic increase in the number of aseptic meningitis cases was reported in Podlaskie Voivodeship between June 1 and November 30, 2014.
2. In 2015, an increase in the number of viral meningitis cases was reported again. Infections with E-30 enterovirus showed a tendency to recur.
3. Symptomatic infections are more common in boys than in girls.
4. An epidemic of enteroviral neuroinfections may in the future pose a challenge to public health in the Eastern Europe.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations which might negatively affect the content of this publication and/or claim authorship rights to this publication.

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