© Pediatr Med Rodz 2021, 17 (2), p. 148–154
DOI: 10.15557/PiMR.2021.0024

Received: 17.10.2020
Accepted: 10.02.2021
Published: 04.06.2021

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Aseptic meningitis in children: seasonal variation and diagnostic problems as reflected in the authors' experiences from 2017–2018

Aseptyczne zapalenie opon mózgowo-rdzeniowych u dzieci – zmienność sezonowa i problemy diagnostyczne na podstawie doświadczeń własnych z lat 2017–2018

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Abstract

Meningitis is the most common infectious disease of the central nervous system both in children and in adults. The incidence of the disease in Poland, similar to Western Europe, is 6–8 cases per 100,000/year, with the highest figure for children up to 4 years of age. **Aim of the study:** The aim of the study was to make a detailed analysis of aseptic meningitis cases in children, with a focus on aetiology and course of the disease, and laboratory results. **Materials and methods:** A retrospective analysis was performed on a group of 59 children aged between 2.5 months and 17 years in whom aseptic meningitis was diagnosed based on clinical evaluation. **Results:** Between May and October 2018, 44 children aged 7.99 ± 3.93 were hospitalised with the diagnosis of nonpyogenic (aseptic) meningitis. In 9 patients (20.5%), enteroviral neurological infection was found, and in 8 (18.2%) *Borrelia burgdorferi*, in 5 (11.3%) EBV and in 2 (4.5%) HHV-7 neurological infection was diagnosed. For 20 children (45.5%), the cause of infection could not be established. The longest hospitalisation time was associated with Lyme neuroborreliosis. In the same months of 2017, 15 patients were hospitalised at our department with aseptic meningitis. The numbers of cases for different causes were: undetermined – 9 patients (60%), enteroviral – 2 (13%), EBV – 2 (13%), *Parvovirus* B19 – 1 patient (7%) and VZV – 1 patient (7%). **Conclusions:** In 2018, a threefold increase was observed in the number of hospitalisations associated with aseptic meningitis in relation to the same period of 2017, with a lasting predominance of boys. Most frequently, the aetiology was undetermined. Among the cases in which the cause was established, the most common aetiology was enteroviral. In 2018, unlike in 2017, cases of hospitalisation for neuroborreliosis were recorded. Incomplete utilisation of the polymerase chain reaction method was considered to be one of the causes of insufficient identification of neurotropic pathogens. A general examination of the cerebrospinal fluid did not differentiate between causes of aseptic meningitis.

Keywords: aseptic meningitis, neuroborreliosis, children

Streszczenie

Zapalenie opon mózgowo-rdzeniowych jest najczęstszą infekcyjną chorobą ośrodkowego układu nerwowego zarówno u dzieci, jak i u dorosłych. Zapadalność w Polsce, podobnie jak w krajach Europy Zachodniej, wynosi 6–8 przypadków na 100 tys./rok, przy czym największa jest u dzieci do 4 lat. **Cel pracy:** Szczegółowa analiza zachorowań na aseptyczne zapalenie opon mózgowo-rdzeniowych wśród dzieci, ze szczególnym uwzględnieniem etiologii, przebiegu oraz wyników badań laboratoryjnych. **Materiał i metody:** Analizą retrospektywną objęto 59 dzieci w wieku od 2,5 miesiąca do 17 lat, u których na podstawie przeprowadzonej diagnostyki klinicznej rozpoznano aseptyczne zapalenie opon mózgowo-rdzeniowych. **Wyniki:** W okresie od maja do października 2018 roku hospitalizowano 44 dzieci w wieku 7,99 ± 3,93 roku z rozpoznaniem nieropnego (aseptycznego) zapalenia opon mózgowo-rdzeniowych. U 9 (20,5%) pacjentów stwierdzono neuroinfekcję o etiologii enterowirusowej, u 8 (18,2%) *Borrelia burgdorferi*, u 5 (11,3%) EBV, a u 2 (4,5%) HHV-7. U 20 dzieci (45,5%) nie udało się ustalić przyczyny zakażenia. Najdłuższa hospitalizacja wiązała się z neuroboreliozą. W 2017 roku, w analogicznych miesiącach, w Klinice hospitalizowano 15 pacjentów z omawianym rozpoznaniem. Etiologia przedstawiała się następująco: nieokreślona – 9 pacjentów (60%), enterowirusowa – 2 (13%), EBV – 2 (13%), *Parvovirus* B19 – 1 (7%) i VZV – 1 (7%). **Wnioski:** W 2018 roku odnotowano 3-krotnie wyższą liczbę hospitalizacji związanych z aseptycznym zapaleniem opon mózgowo-rdzeniowych w stosunku do analogicznego okresu roku 2017, z utrzymującą się przewagą zachorowań chłopców. Dominowała etiologia nieokreślona. Wśród ustalonych przyczyn najczęstszą były enterowirusy. W 2018 roku,

w przeciwieństwie do roku 2017, odnotowano przypadki hospitalizacji związanych z neuroboreliozą. Za jedną z przyczyn niedostatecznej identyfikacji patogenów neurotropowych uznano niepełne wykorzystanie metody łańcuchowej reakcji polimerazy przy ich identyfikacji. Badanie ogólne płynu mózgowo-rdzeniowego nie stanowiło elementu różnicującego etiologię aseptycznego zapalenia opon mózgowo-rdzeniowych.

Słowa kluczowe: aseptyczne zapalenie opon mózgowo-rdzeniowych, neuroborelioza, dzieci

INTRODUCTION

Meningitis is the most common infectious disease of the central nervous system (CNS) both in children and in adults[1].

The incidence of meningitis in Poland, similar to Western European countries, is 6–8 cases per 100,000/year, with the highest figure for children up to 4 years of age (40 cases per 100,000/year). Poorly developed mechanisms of cell-mediated and humoral immunity, and increased permeability of the blood–cerebrospinal fluid barrier are considered to be the cause of increased prevalence of meningitis among infants and small children[2].

Inflammation of the subarachnoid space leads to concurrent irritation of the meninges, which clinically manifests with headache, nausea, vomiting and fever. The presence of meningeal signs on physical examination suggests meningitis in a patient. The signs most commonly used for the diagnosis of meningitis are described in Tab. 1. A definitive diagnosis is made after a biochemical analysis of the cerebrospinal fluid (CSF) collected from the patient is performed in which an elevated leukocyte count compared to the norm for age is observed[2,3].

The widely used division of meningitis is based on establishing the aetiological factor of the disease in classic microbiological studies. This has led to the distinction between pyogenic and nonpyogenic (aseptic) meningitis (AM). Pyogenic meningitis, usually caused by encapsulated bacteria, is characterised by a high granulocyte count in CSF, which determines its pyogenic nature[4]. In Poland, the most common causes of meningitis in older children and adults include *Neisseria meningitidis, Streptococcus pneumoniae* and type B *Haemophilus influenzae*. In newborns and small children, inflammation caused by *Escherichia coli* or *Streptococcus agalactiae*[5] is the most common. AM is characterised by the predominance of lymphocytes in CSF. Viruses, atypical bacteria, fungi and non-infectious factors play a role in the pathogenesis of meningitis (Tab. 2).

The portal of entry for neurotropic pathogens are respiratory, gastrointestinal and genitourinary systems, and damaged skin. After primary microbial replication at the point of entry, CNS can be infected through the bloodstream or peripheral nerves. The agents which spread through the bloodstream during primary or secondary viraemia include, for example, cytomegalovirus (CMV), Epstein–Barr virus (EBV), enteric cytopathogenic human orphan virus (ECHO), *Coxsackie* and influenza virus. Neuronal spread is typical for *Herpes simplex* virus (HSV), *Varicella zoster* virus (VZV), rabies, polio and coronaviruses. The infectious agent is transported inside axons and/or through perineuronal cells[3].

Evaluation for meningitis, regardless of aetiology, is based on the examination of CSF, which is usually collected through lumbar puncture. A typical result indicating AM demonstrates the presence of a few to a few hundred leukocytes, predominantly lymphocytes, in 1 µL of CSF. Protein concentration may be normal or slightly elevated[5].

In order to establish the aetiology of AM, serological and molecular tests are performed on the patient's blood and CSF. Blood tests, which are usually performed using enzyme-linked immunosorbent assay (ELISA), only play an auxiliary role, since they do not provide a definitive confirmation of pathogen transmission to CNS. Examination of CSF has a much higher diagnostic value. It is usually conducted with molecular methods utilising the phenomenon of polymerase chain reaction (PCR), which make it possible to identify the majority of viral pathogens[6]. Due to a lack of standardisation of PCR, serological tests on CSF are recommended in an evaluation for *Borrelia* sp. infection[7]. In addition, in the case of gastrointestinal viral pathogens, particularly polio, the patient's stool samples are tested[8].

Sign	Clinical examination
Nuchal rigidity	Limited passive flexion of the neck towards the chest
Brudzinski neck sign	Reflex flexion of the knees and hips when the chin is brought to the chest to check for nuchal rigidity
Brudzinski symphyseal sign	Reflex flexion of the knees and hips when the pubic symphysis is pressed on
Kernig sign	Limited knee extension over 135 degrees in a supine patient with the leg flexed at the knee and hip; a symmetrical sign
Flatau sign	Pupil dilation during attempted nuchal rigidity test
Amoss sign	Supporting oneself on extended arms placed behind one's back and to the sides when attempting to sit up
Herman sign	Dorsal flexion of the toes in response to attempted flexion of the neck towards the chest

Tab. 1. Meningeal signs checked for in a diagnostic evaluation for AM

 DOI: 10.15557/PiMR.2021.0024

AIM OF THE STUDY

The aim of the study was to make a detailed analysis of AM cases in children, with a focus on aetiology and course of the disease, and laboratory results, based on retrospective data of one centre.

MATERIALS AND METHODS

Medical records were retrospectively analysed of 59 children aged between 2.5 months and 17 years who were hospitalised with the diagnosis of AM at the Department of Infectious Diseases and Child Neurology of the Poznan University of Medical Sciences Teaching Hospital in Poznań, Poland, from May to October 2017 and during the same period of 2018. Medical records were included in the analysis based on the final diagnosis established by the attending physician of a patient staying at the department, confirmed by an infectious diseases consultant. The year 2018 was adopted as the baseline for analysis due to an increased incidence of AM observed in that period. The year 2017 was adopted as a point of reference to confirm the clinical observation of an increase in the number of patients. The diagnosis of AM was established based on clinical signs and symptoms, blood chemistry and serology tests, and chemistry, serology and molecular tests of CSF collected from the patients. A retrospective analysis was performed on data from clinical examination and laboratory tests performed upon admission of a patient to hospital. In every child, thorough paediatric physical examination was performed and blood was collected for complete blood count and differential, C-reactive protein, procalcitonin, creatinine, fibrinogen, international normalised ratio (INR), activated partial thromboplastin time and aminotransferase levels. In addition, blood samples were collected to be used in laboratories mentioned further in the paper to determine the aetiology of infection. Immediately after the suspicion of AM was established, the patients were assessed for lumbar puncture in order to obtain CSF for further laboratory tests. In all children, lumbar puncture was preceded by a computed tomography scan of the head using the 128-slice Siemens SOMATOM Definition AS scanner in order to exclude focal abnormalities in the brain. This neuroimaging study was performed at the Department of Radiology of the Karol Jonscher Teaching Hospital in Poznań. Leukocyte count, and protein and glucose levels were determined in the obtained CSF. In addition, a manual differential of CSF was performed in order to establish the percentage of lymphocytic cells. Blood and CSF chemistry, CSF testing for bacteria and ELISA of blood for CMV and EBV were performed at the Central Laboratory of the Karol Jonscher Teaching Hospital in Poznań, Poland. ELISA-based blood serology tests for *Mycoplasma pneumoniae*, HSV-1 and HSV-2, enteroviruses and tick-borne encephalitis (TBE) were conducted at the Provincial Sanitary and Epidemiological Station in Poznań. Tests to identify *Borrelia burgdorferi* in blood serum and CSF were performed at the Central Laboratory of the Karol Święcicki Teaching Hospital in Poznań based on a two-step diagnostic protocol: ELISA first in all patients, then a Western blot confirmation test for positive samples[7]. Molecular testing of CSF using qualitative real-time PCR (RT-PCR), referred to as meningitis panel for neurotropic pathogens (*Escherichia coli K1, Haemophilus influenzae, Listeria monocytogenes, Neisseria meningitidis, Streptococcus agalactiae, Streptococcus pneumoniae*, CMV, *Enterovirus*, HSV-1, HSV-2, HSV-3, *Human parechovirus*, VZV, *Cryptococcus neoformans/gattii*) were performed at the ALAB Laboratory in Warsaw.

Statistical analysis of the data was performed using GraphPad Prism version 5.01 for Windows, Graph Pad Software Inc.

Infectious causes	Non-infectious causes
Viruses • Enteroviruses – polio, *Coxsackie*, ECHO • HSV-1 and HSV-2 • VZV • CMV • EBV • HHV-6, HHV-7 • adenovirus, rhinovirus, type A and B influenza virus	**Post-infection/post-vaccination** • rubella • varicella • rabies vaccine • pertussis vaccine • influenza vaccine • yellow fever vaccine
Atypical bacteria • *Mycoplasma pneumoniae* • *Mycoplasma tuberculosis* • *Borrelia burgdorferi* • *Treponema pallidum* • *Brucella* • *Leptospirosis*	**Medication** • non-steroid anti-inflammatory drugs • amoxicillin, trimethoprim + sulphamethoxazole • azathioprine • immunoglobulins • methotrexate • allopurinol • carbamazepine • sulphasalazine
Fungi • *Candida* • *Cryptococcus neoformans* • *Histoplasma capsulatum*	**Systemic diseases** • systemic lupus • Wegener's granuloma • CNS vasculitis • rheumatoid arthritis • Kawasaki disease • sarcoidosis
Parasites • *Toxoplasma gondii* • *Bartonella henselae* • *Naegleria*	**Cancer** • leukaemia • brain tumours
Rickettsias • Rocky Mountain spotted fever • typhus	**Infection of neighbouring structures:** brain and meningeal abscesses
	Other • arachnoiditis • migraine • urinary tract infection
CNS – central nervous system; **EBV** – Epstein–Barr virus; **ECHO** – enteric cytopathogenic human orphan virus; **CMV** – cytomegalovirus; **HHV-6** – human herpesvirus-6; **HHV-7** – human herpesvirus-7; **HSV** – *Herpes simplex* virus; **VZV** – *Varicella zoster* virus.	

Tab. 2. Most common causes of AM[4]

RESULTS

Between May and October 2018, 44 children with diagnosed AM were hospitalised at the Department of Infectious Diseases and Child Neurology of the Poznan University of

DOI: 10.15557/PiMR.2021.0024 PEDIATR MED RODZ Vol. 17 No. 2, p. 148–154

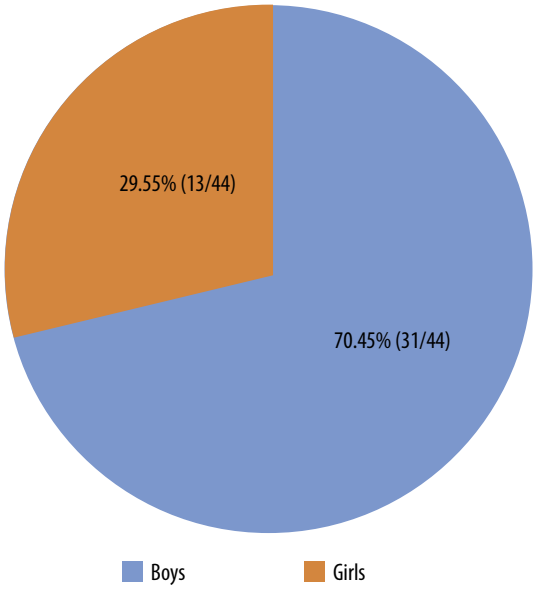

Fig. 1. Gender proportions between patients hospitalised in 2018 (n = 44)

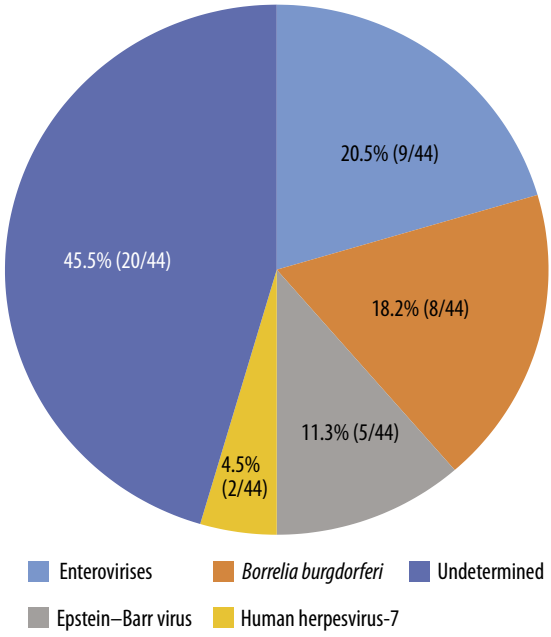

Fig. 2. AM aetiology in 2018 (n = 44)

Medical Sciences, Poland. In the study group, girls accounted for 29.5% (13 individuals) and boys for 70.5% (31 individuals) of the subjects (Fig. 1). The mean age was 8 years (7.99 ± 3.93). In the same period of 2017, only 15 patients with diagnosed AM were hospitalised at the department: 4 girls (27%) and 11 boys (73%).

Based on diagnostic evaluation, it was established that enteroviral aetiology dominated among children hospitalised in 2018: it was confirmed in 9 patients (20.5%). In 8 patients (18.2%) *Borrelia burgdorferi*, in 5 (11.3%) EBV and in 2 (4.5%) human herpesvirus-7 (HHV-7) were indicated as the cause of AM (Fig. 2). For 20 children (45.5%), the cause of infection could not be established (undetermined aetiology) (Fig. 2). Among the children treated in 2017, the numbers of cases for different causes of AM were the following: undetermined – 9 patients (60%), enteroviral – 2 (13%), EBV – 2 (13%), *Parvovirus* B19 – 1 patient (7%) and VZV – 1 patient (7%) (Fig. 3).

Detailed analysis was performed on the records of children hospitalised in 2018. It was determined that the main symptoms reported by the patients were strong headache (71%), fever (60%) or low-grade fever (14%), vomiting (44%) and asthenia (23%). Other symptoms present on admission included nausea (18%), photophobia (5%) and decreased mood (4%).

In children with a diagnosis of Lyme neuroborreliosis, subacute complaints dominated (prolonged headache, low-grade fever, malaise, weak meningeal signs or absence thereof). In 3 out of 8 patients, erythema migrans was observed and 1 patient presented with peripheral facial nerve paralysis. A tick bite was found in the medical history of only 1 child.

The analysis of the methods used for microbial identification in 2018 (Tab. 3) reveals that enteroviral infection was confirmed in 3 children exclusively based on an ELISA blood test an in 4 children exclusively with a PCR CSF test. Concurrent positive results of both tests were obtained only in 2 patients. For EBV infection, a positive blood serum result (ELISA) was found in 4 patients. One child had positive results of both blood serum and CSF testing. HHV-7 infection was identified exclusively with molecular methods in CSF (PCR). In 4 patients with AM caused by *Borrelia burgdorferi*, only blood tests were positive. In 4 other patients, the diagnosis was confirmed with a CSF examination (Tab. 4).

In this study, an attempt was made to determine the relationship between AM aetiology and the patients' age and certain laboratory values. The results of this analysis are presented in Tab. 5.

CSF chemistry results were significantly different depending on AM aetiology. The mean cell count was the highest for enteroviral infections: 486.11 cells/μL (±509.43) and the lowest for HHV-7: 96 cells/μL (±57.98). The mean protein content in CSF was 40.67 mg/dL (±14.93) for infections with enteroviruses, 40.38 mg/dL (±18.63) for *Borrelia burgdorferi*, 38.8 mg/dL (±17.98) for EBV, 45 mg/dL (±9.89) for HHV-7 and 51.3 mg/dL (±27.62) for undetermined aetiology. The percentage of lymphocytes in CSF was the highest for EBV infection: 85.25% (the highest value being 96% and the lowest 67%) (Tab. 5).

The mean duration of treatment for an enteroviral infection was 8 days (±3), for EBV 11 days (±3), for HHV-7 also 8 days (±1) and for undetermined aetiology 9 days (±2). The longest hospital stay was associated with Lyme neuroborreliosis: the mean duration of treatment was 18 days (±4) and this time was statistically significantly different from the treatment time for other aetiologies (Fig. 4).

DISCUSSION

The analysis of the study material revealed a threefold increase in the number of hospitalisations associated with AM in 2018

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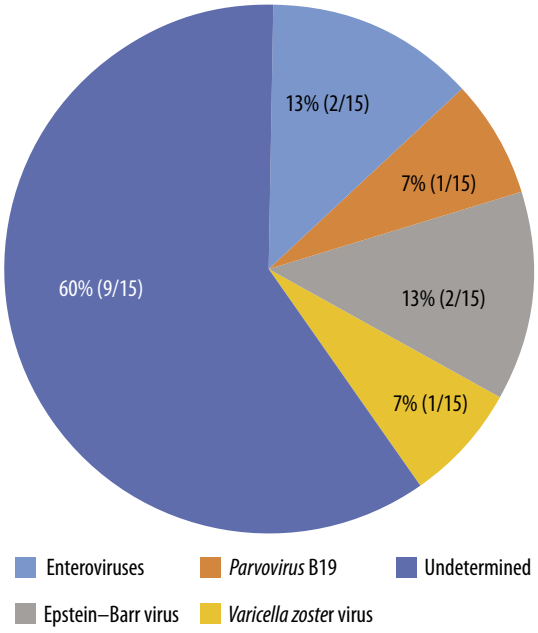

Fig. 3. AM aetiology in 2017 (n = 15)

Aetiology	Serum (ELISA)	CSF (PCR)	Serum + CSF
Enteroviruses ($n = 9$)	3	4	2
EBV ($n = 5$)	4	0	1
HHV-7 ($n = 2$)	0	2	0

CSF – cerebrospinal fluid; **EBV** – Epstein–Barr virus; **ELISA** – enzyme-linked immunosorbent assay; **HHV-7** – human herpesvirus-7; **PCR** – polymerase chain reaction.

Tab. 3. Distribution of positive results based on which the diagnosis of AM aetiology was made in 2018

Aetiology	Serum		CSF
	ELISA (+)	Western Blot (+)	ELISA (+)
Borrelia burgdorferi	3	1	4

CSF – cerebrospinal fluid; **ELISA** – enzyme-linked immunosorbent assay.

Tab. 4. Lyme neuroborreliosis identification methods in 2018 (n = 8)

	Enteroviruses	*Borrelia burgdorferi*	EBV	HHV-7	Undetermined	*p*
Number of cases	9	8	5	2	20	
Age (years)	7.13	6.88	6.07	9	8.97	0.6312
Cell count (CSF) [cells/µL]	486.11	185.25	333.6	96	139.60	0.0527
Protein (CSF) [mg/dL]	40.67	40.38	38.8	45	51.3	0.6375
Lymphocytes (CSF) [%]	70.98	79	85.25		71.42	0.6213
Leukocytes (blood) [10^3/µl]	9.46	10.4	11.4	10.16	9.4	0.6069
Lymphocytes (blood) [%]	66.13%	65.38%	67.62%	68.2%	70.15%	0.8849
CRP [mg/dl]	1.52	1.01	4.03	2.86	1.49	0.7079
Duration of treatment [days]	8	18	11	8	9	<0.0001
Girls	4 (44.4%)	4 (50.0%)	1 (20%)	0	4 (20%)	
Boys	5 (55.6%)	4 (50.0%)	4 (80.0%)	2 (100%)	16 (80%)	

CRP – C-reactive protein; **CSF** – cerebrospinal fluid; **EBV** – Epstein–Barr virus; **HHV-7** – human herpesvirus-7.

Tab. 5. Detailed analysis of AM cases in 2018 depending on aetiology

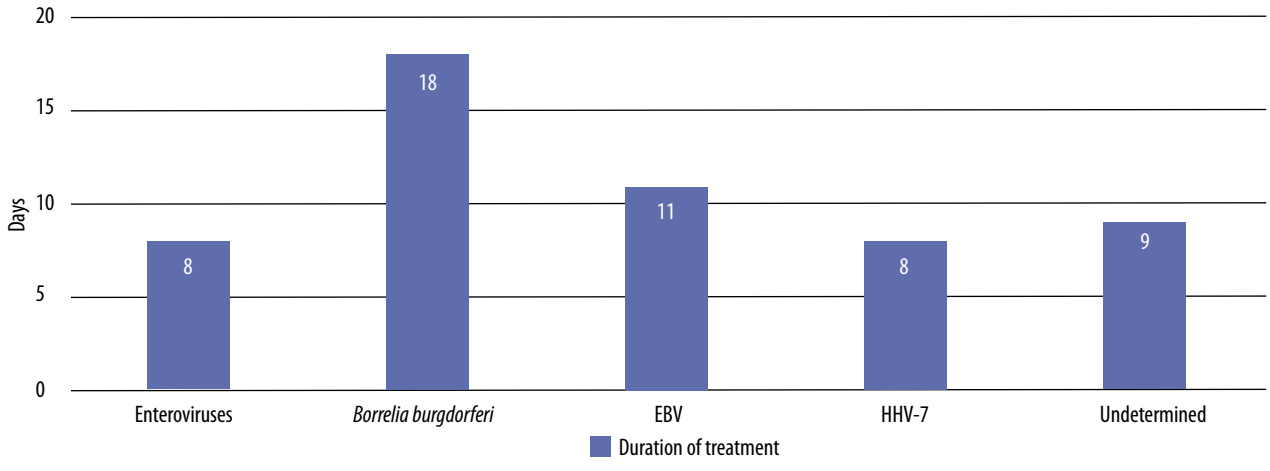

Fig. 4. Mean duration of AM treatment in 2018 depending on aetiology

DOI: 10.15557/PiMR.2021.0024

in relation to the same months of 2017. Epidemiological data of the Polish National Institute for Hygiene and Public Health for the second and third quarter of 2017 reveal 49 cases of AM in the Greater Poland Province[9], where the city of Poznań is situated [*translator's note*]. To date, no data for 2018 on the number of cases in Polish provinces have been published. The significant increase in the number of hospitalisations in only one centre that was covered in this study allows one to assume that there was an AM incidence rate increase in the paediatric population of Greater Poland in 2018. In 2017, no *Borrelia burgdorferi* infection was recorded for the studied patients, unlike in 2018, when this agent was identified as the second most common cause of AM. For a few years, a constant increase in the number of cases of Lyme disease has been recorded. Its seasonal variation with predominance in the summer has also been observed[10]. In addition, an even further increase in the number of cases is being projected for the coming years[11].

In both periods analysed with regard to disease incidence, it was confirmed that AM is over twice as common in boys than in girls. Literature sources also point to an increased susceptibility to aseptic meningitis among males[8].

In the study group, the predominant symptom was a severe headache. According to the literature, a severe stabbing headache located behind the eyes is particularly characteristic of enteroviral infections, which remain the most common cause of AM. Additional manifestations such as rash and symptoms of gastroenteritis may also suggest an enteroviral neurological infection[11]. In the group of children with aseptic meningitis with an established aetiology, enteroviruses were the most common cause of the disease. Enteroviral AM had a mild course with no complications, which is corroborated by literature data[12]. Incidence periodicity has been observed in the population, which may be associated with a lack of antibodies against the different viral serotypes. The epidemics recorded are caused by high-neurovirulence serotypes; in the case of low-neurovirulence serotypes, there are no identification and diagnostic evaluation due to a subclinical course[13]. A link between a population's epidemic status and the occurrence of enteroviral epidemics has been reported. In populations with a low socioeconomic status, people are infected in infancy[14]. Molecular techniques are believed to be the most useful ones for diagnostic evaluation; they make it possible to detect small amounts of viral genetic material. A disadvantage of such techniques is the lack of possibility to identify serotypes circulating in the population[15,16].

In a temperate climate, seasonal variation of AM is observed; its incidence peaks in the summer and autumn[17].

Viral AM often involves two phases. In the first period of the disease, symptoms associated with the inflammation of the upper respiratory tract (sore throat, cough) or gastrointestinal tract (vomiting, diarrhoea) appear. After that, the patient's condition often seemingly improves, but then the patient develops malaise and a characteristic headache. Fever, vomiting, irritability, sensory hypersensitivity, particularly to light and touch, and circadian rhythm sleep disorders can also occur[18]. In the case of Lyme disease, CNS symptoms may be preceded by the appearance of the characteristic erythema, although it does not have to occur for the disease to be diagnosed. Meningitis develops in only 30% of children with Lyme neuroborreliosis, a disease which much more commonly manifests with facial nerve paralysis (60%)[18–20]. The course of AM caused by *Borrelia burgdorferi* seems to be milder, more chronic than in other types of aseptic meningitis. Facial nerve paralysis, particularly bilateral, which is characteristic of Lyme neuroborreliosis (not reported for other aetiologies in the literature)[21], requires verification in a CSF examination. For such a clinical presentation, even a lack of meningeal signs requires the performance of lumbar puncture[22].

The largest group of patients in this study had AM with an undetermined aetiology. Incomplete utilisation of PCR for the most common viruses is considered to account for the failure to identify the pathogens responsible for the disease. This technique may be underused due to the generally mild clinical cause and a lack of causal treatment for the majority of viral neurological infections[18].

At the Department of Infectious Diseases and Child Neurology of the Teaching Hospital in Poznań, extensive diagnostic evaluation was performed in order to identify the neurotropic pathogens. Tabs. 3 and 4 present the detection figures for neurotropic pathogens in the study group. Enteroviruses were detected in blood serum or CSF. In a small number of children, the presence of enteroviruses was demonstrated both in blood serum and CSF. For other viruses, for instance EBV, the diagnosis was established only in serology tests. The analysis of the study material indicates a need to search for infection aetiology using both serological and molecular methods in parallel, preferably in every diagnostic material available[18]. Such patient management increases the chances for detection of the AM causal factor. The diagnostic investigation of a neurological infection is a significant challenge since similar symptoms may be caused by many different pathogens. A lack of pathognomonic signs and symptoms makes it impossible to establish the disease aetiology solely on the basis of clinical presentation. In addition, a general examination of CSF does not reveal any characteristic features that could help determine the aetiology of AM; in particular, it is unable to confirm a *Borrelia* sp. infection, which requires antibiotic therapy. Due to a high risk of serious complications caused by bacterial AM and *Herpes* viral infection, empirical treatment is applied[23]. A possibility to perform tests confirming the aetiology of AM in the shortest time possible would help one to avoid unnecessary antibiotic therapy and thus make significant savings and reduce the duration of a patient's hospital stay.

CONCLUSIONS

1. In 2018, a threefold increase was observed in the number of hospitalisations associated with AM in relation to the same period of 2017, with a distinct predominance of boys.

 DOI: 10.15557/PiMR.2021.0024

2. In both periods under analysis, most of the infections were of undetermined aetiology, while in the case of AM with an established aetiology, enteroviruses were the most common cause. For 2018, hospitalisations associated with Lyme neuroborreliosis were additionally reported.
3. A general CSF examination does not differentiate between different aetiologies of AM.

Conflict of interest

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

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DOI: 10.15557/PiMR.2021.0024 PEDIATR MED RODZ Vol. 17 No. 2, p. 148–154