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CLINICAL–EPIDEMIOLOGICAL CHARACTERISTICS OF ASEPTIC MENINGITIS IN CHILDREN OF KHMELNITSKYI REGION (PODILSKYI REGION, UKRAINE): FOURTEEN–YEAR EPIDEMIOLOGICAL OBSERVATION

L.V. Pypa, R.V. Svistilnik, Yu.N. Lysytsia, K.Yu. Romanchuk, I.V. Odarchuk
Vinnytsia National Pyrogov Memorial Medical University, Vinnytsia, Ukraine

Клинико-эпидемиологическая характеристика серозных менингитов у детей Хмельницкой области (Подольский регион, Украина): четырнадцатилетнее эпидемиологическое наблюдение

Л.В. Пыпа, Р.В. Свистильник, Ю.Н. Лисица, К.Ю. Романчук, И.В. Одарчук
Винницкий национальный медицинский университет им. Н.И. Пирогова, Винница, Украина

Abstract

Aim of work — to analyze the etiological structure, epidemiological structure, social-demographic features and the nature of the development of complications of the central nervous system in aseptic meningitis in children in Khmelnitskyi region for the period 2004-2017.

Materials and methods. It was conducted a prospective analysis of 208 cases of aseptic meningitis in children of whom 138 people were boys and 70 people were girls. The etiology of the disease was determined by studying cerebrospinal fluid using PCR method. Complications of the central nervous system were diagnosed on the basis of the clinical picture and CT or MRI scans. The analytical method was used to conduct the analysis of the received data.

Results. The highest seasonal increase of the incidence was from August to October and it was 65.6 % with its peak in September (24.0 %). The clinical picture was characterized by a moderate trend in 71.2 % of cases and in 28.8 % by a severe course. In 100 % of cases the disease began with a fever, headache (83.6 %), vomiting (76.9 %), abdominal pain with diarrhea (6.2 %), epileptic seizures (0.9 %). The average level of cytosis was 269.4 ± 196.7 cells/mm^3 with a predominance of lymphocytes and the average protein level in cerebrospinal fluid was 73 ± 36 mg/dl. The etiological factor was established in 18 (8.6 %) patients.

Conclusions. Enterovirus remains to be the main pathogen which was determined in 72.2 % of cases. The second place was taken by herpes viruses (22.2 % of cases), the third place was given to the mumps virus (5.6 % of cases) (in etiologically verified cases). In most cases the disease ended in complete recovery but in 47 (22.6 %) patients the complications were observed. The prevalence of aseptic meningitis among children in Khmelnitskyi region was 6.2 per 100,000 children, and males outnumbered females by a 2:1 ratio.

Key words: *aseptic meningitis, epidemiology, etiology, children.*

Резюме

Цель — проанализировать этиологическую структуру, эпидемиологические особенности, социально-демографические профили и характер развития осложнений со стороны ЦНС при серозных менингитах у детей Хмельницкой области за период 2004—2017 гг.

Материалы и методы. Проведен проспективный анализ 208 случаев серозного менингита у детей, из которых 138 мальчика и 70 девочек. Этиологию заболевания определяли путем исследования ликвора методом ПЦР. Осложнения со стороны ЦНС диагностировали на основе клинической картины и методом КТ или МРТ. Для проведения анализа полученных данных использовался аналитический метод.

Результаты. Наибольший сезонный рост заболеваемости приходится на период с августа по октябрь и составляет 65,6 % с пиком в сентябре (24,0 %). Клиническая картина характеризовалась среднетяжелым течением в 71,2 % случаев и тяжелым течением — в 28,8 % . В 100 % случаев заболевание начиналось с лихорадки, головной боли (83,6 %), рвоты (76,9 %), боли в животе с расстройствами стула (6,2 %), эпилептических припадков (0,9 %). Средний уровень цитоза составлял 269,4 ± 196,7 клеток в мм^3 с преобладанием лимфоцитов, а средний уровень белка в ликворе составлял 73 ± 36 мг/дл. Этиологический фактор был установлен у 18 (8,6 %) пациентов.

Выводы. Главным возбудителем остается энтеровирус, который определялся в 72,2 % случаях. Второе место заняли вирусы герпеса (22,2 % случаев), третье место занял вирус паротита (5,6 % случаев) (из этиологически определенных). В большинстве случаев заболевание заканчивалось полным выздоровлением, однако у 47 (22,6 %) пациентов наблюдались осложнения. Распространенность серозного менингита среди детей Хмельницкой области составила 6,2 на 100 тыс. детского населения в соотношении между мужским и женским полом — 2:1.

Ключевые слова: *серозный менингит, эпидемиология, этиология, дети.*

Introduction

For many years Aseptic Meningitis (AM) in children occupy a leading place in the structure of infectious diseases of the nervous system, their frequency in the last 5 years was 32%. The annual incidence of AM in the world is 11-15 per 100,000 populations per year [1].

Etiological agents, climatic and epidemiological factors contributing to their occurrence vary according to country and area. Determining these factors is crucial for monitoring and preventing of this problem [2].

Most cases of children meningitis in the etiological structure are viral ones which lead to aseptic inflammation of the membranes [3].

In the etiological structure of AM up to 61% are enteroviruses, up to 7% are herpes viruses (Herpes simplex viruses 1-2, Epstein-Barr virus, Varicella zoster virus), up to 6% are of tick borne encephalitis virus, up to 10% are Borrelia, up to 2% of Yersinia and up to 1% are Mycobacterium tuberculosis [1].

Aseptic meningitis can also cause epidemic mumps, adenoviruses and HIV. Non-pathogenic bacteria (Leptospira, Treponema pallidum, Nocardia, Bartonella, Brucella) can be the causative agents of AM [4].

Enteroviruses of serogroups of ECHO 5, 6, 30 and Coxsackieviruses type 3 are the most common pathogens of aseptic meningitis [5].

According to a study in one of the regions of the Russian Federation with the highest incidence rate for enterovirus meningitis, 2.6 per 1,000 children were aged 3-6 years old, and there was 0.66 per 1,000 of children aged 7-14 years old [6].

In the largest study from 1994 to 2002 made in Greece, the average annual incidence of AM cases was 17 per 100,000 children under the age of 14 years in the Athens region. The highest incidence was observed in the 1-5 years age group (26 per 100,000 children) and the lowest incidence was observed in the 13-14 years old age group (7 per 100,000 children). Although cases of the disease were observed throughout the year, the majority of cases were observed from June to August (38%) and from September to November (24%). The correlation between the male and female sex was 1.8:1 [7].

Objective

The objective is analyzing the etiological structure, epidemiological features, social-demographic profiles and the nature of the development of complications from the central nervous system in aseptic meningitis in children of Khmelnitskyi region during 2004-2017.

Materials and methods

We conducted a prospective analysis of 208 AM cases in children undergoing treatment at the Khmelnytskyi Infectious Diseases Hospital (2004-2017) where 138 people were boys and 70 people were girls.

The diagnosis was established on the basis of clinical data (presence of meningeal, intoxication and cerebral syndromes) and analyzing of cerebrospinal fluid (cytosis with predominance of lymphocytes). The etiology of the disease was determined by detecting the genetic material of the pathogen in the cerebrospinal fluid using the polymerase chain reaction (PCR) method. Complications from the central nervous system were manifested basing on the clinical picture of their development (motor deficits, epileptics seizures, etc.) and additional research methods, mainly CT and MRI scans. During the study we were using an analytical method.

Results and discussion

When analyzing the dynamics of morbidity in children with AM, it can be noted its wave-like nature with the peaks of recovery and decline of infection as shown in figure 1. According to the chart, the peak of incidence was varied in 2008 and the largest — in 2011, while the decline was observed in 2005, 2009, and 2010 with the lowest figures in 2017 which can be primarily due to climate and social demographic factors (especially migration of the population and a decrease in the number of children in the region).

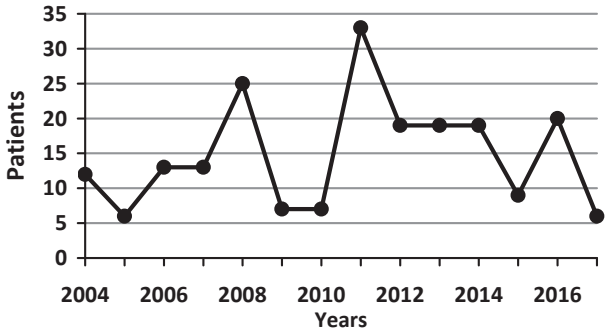

Fig. 1. Dynamics of aseptic meningitis incidence in children of Khmelnytskyi region during 2004 — 2017

Aseptic meningitis occurs in children in all seasons, however the lowest incidence was observed in winter (9.6%) and spring (7.2%) periods (figure 2). Starting from July there is a sharp increase in morbidity which reaches its peak in September (24.0%) and gradually falls in December. In general, the highest seasonal increase of serous meningitis incidence in children accounts for the period from August to October and for 61.5% of the total annual morbidity.

The increase in AM incidence in children in summer-autumn period is mostly due to the seasonal migration of the population. The increase in the number of respiratory diseases and contacts with other children in kindergartens and schools as well as bathing in the surface water bodies and the implementation of the food transmission factor is especially peculiar to the spread of enterovirus infection.

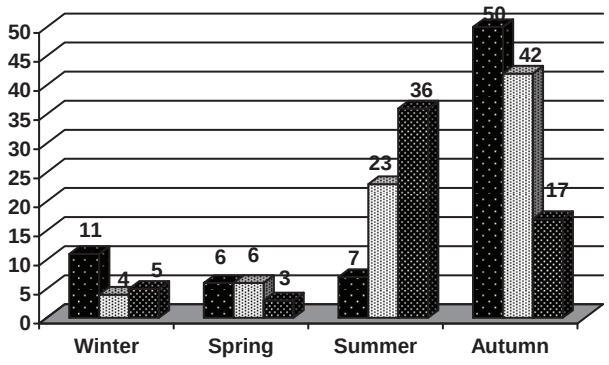

Fig. 2. Seasonal morbidity with aseptic meningitis in children in Khmelnytskyi region from 2004 to 2017

The data which we received almost coincide with the data obtained in other countries. Thus, in a study by J. Kim et al. (2017) about 80% of AM cases were diagnosed from July to September [8]. According to A.A. Agarkova et al. (2015) the peak incidence of AM in children occurred in July-September which was amounted to a total of 77.7% [9].

According to age categories the incidence of AM was distributed as follows: in the first year of life 11 children (5.3%), from 1 to 3 years old — 9 (4.3%), from 4 to 7 years old — 62 (29.8%), from 8 to 12 years old — 63 (30.3%) and from 13 to 18 years old — 63 (30.3%) were ill.

Thus, according to our observation of AM, children of all age groups are affected, but most of all it occurs in children after 4 years without significant fluctuations to 18 years.

According to the data, the number of males who were suffering from AM was 138 (66.3%), while there were 70 females (33.7%), which corresponds to a 2:1 ratio of boys to girls.

In most cases the clinical picture was characterized by a moderate (71.2%) course and in 28.8% of cases the course was severe. Mostly children living in urban areas (72.6%) in comparison with rural children (27.4%), were ill that corresponded to a ratio of 2.6:1.

A similar trend can be attributed to a much larger number of population migrations in the cities crowded by people near reservoirs and in social facilities (kindergartens, schools, etc.) with an increasing contact between them.

More than 85% of patients were hospitalized in the first three days after the onset of the disease. The onset of the disease in most cases was acute and was characterized mainly by manifestations of general-infectious and general brain syndromes of varying degrees of severity.

In 100% of cases the disease began with a fever, headache (83.6%), vomiting (76.9%), abdominal pain with diarrhea (6.2%), epileptic seizures (0.9%). Meningeal syndrome was detected in 97.6% of patients where the nodular muscles were rigid and less commonly characterized by the symptom of Kernig and hyperesthesia.

Hyperesthesia was observed in 19.7% of patients and was manifested as a general excitation on sensory and tactile incentives during examination and in the form of photophobia or phonophobia. Meningeal signs were determined within 2-7 days of the disease. The development of similar clinical symptoms characteristic of AM is also noted in the studies of other authors [9, 10].

The diagnosis of AM was based on the study of cerebrospinal fluid. At the same time the level of cytosis and cellular composition of the cerebrospinal fluid differed significantly in the variability. In general, the average level of cytosis was 269.4 ± 196.7 cells/mm^3 with a predominance of lymphocytes and the mean protein level in cerebrospinal fluid was 73±36 mg/dl. The level of protein in cerebrospinal fluid was within the norm in 35.5% of cases. The content of glucose and chlorides was within normal limits.

The etiological factor of AM was established in 18 (8.6%) patients (fig. 3). It can be due to the fact that the study of cerebrospinal fluid using PCR method is not investigated for all possible pathogens of AM, mainly due to technical and economic factors. According to N.V. Skrypchenko et al. (2016) aseptic meningitis in children is characterized by etiological polymorphism with the prevalence of enteroviruses (up to 64%), a tick-borne encephalitis virus (4%), and parvovirus B19 (7%) [1]. Corresponding pathogens (besides enterovirus) are usually not determined by screening in Podilskyi region and therefore their frequency and contribution to the structure of AM in children as well as other possible pathogens in Khmelnytskyi region remains unknown.

Figure 3 shows that enterovirus remains to be the main pathogen in AM which was determined in 13 (72.2%) cases.

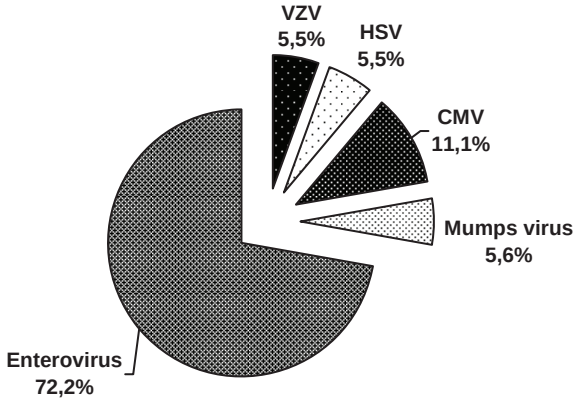

Fig. 3. The etiological structure of aseptic meningitis in children in Khmelnytskyi region from 2004-2017 (n = 18)

Herpesviruses which were determined in 4 patients (22.2%) were ranked the second place among the verified etiological factors of AM in children of Khmelnitskyi region. The third place was taken by mumps virus which was detected in 1 patient (5.6%) (from etiologically verified ones).

According to the published data, the detectability of AM pathogens is in the range of 40-50% which is significantly higher compared to our data, possibly due to technical and economic opportunities.

Just as in our study, other observations demonstrated that the key etiological factor of AM is enterovirus, and according to A.A. Agarkova et al. (2015) it was detected in 44% of cases and according to M.S. Sasan et al. (2012) enterovirus was detected in 12.7% of cases and conceded only to mumps virus which was found in 19.6% of patients with AM [3, 9].

According to modern literature AM is a self-limiting state that requires only symptomatic treatment and usually ends with recovery without the development of significant neurological complications both during the course and during the early reconvalescence [10, 11, 12].

However, some authors believe that the insidiousness of AM is in the fact that with a relative ease of the course during the acute period of the disease in the future in the absence of proper catamnestic observation during the convalescence there are formed neurological disorders. It has been established that the AM reconvaliscents before the clinical recovery (up to 20 days since the start of the disease) had the cerebral-asthenic symptomatology occurring in 60-85% cases, which persisted for 6 months in 20-40% cases, as well as an increase of memory impairment in 24-68% of cases [1].

In our observation, 47 (22.6%) children were observed with acute neurological complications of the disease and late neurological complications of the disease, many of which were not difficult and did not require appropriate correction and were self-limiting over time.

Acute neurological complications of the disease were observed in 5 (2.4%) patients of whom epileptic seizures were observed in 3 patients and cerebral edema and hydrocephalus was observed in 1 patient. The pathogens of the disease in these patients have not been established.

Late neurological complications were observed in 42 (20.2%) patients. The main complication that arose during the early reconvalescence was the asthenic syndrome which was detected in 36 (85.7%) patients and the autonomic disorders syndrome was detected in 6 (14.3%) patients. The outcome of the disease with complete recovery was observed in 166 (79.8%) patients.

On average the duration of treatment for patients with AM was 20.9 ± 4.5 days and depended on the severity of the condition and the development of complications.

Taking into account epidemiological data over the course of the study, the prevalence of AM among children in Khmelnitskyi region was determined that in total there were 6.2 per 100,000 children per year. The largest prevalence of AM in the region was 13.6 per 100,000 children per year in 2011 and the lowest prevalence was 2.5 per 100,000 children per year. It can be noted that the obtained index is slightly less than the global index which is probably related to the climatic conditions of the region, the annual decrease of the population of the region and the effectiveness of the planned vaccination against major infantile measles virus (measles-rubella-parotitis) and a decrease in their share in the structure of AM.

The tendency to reduce the incidence of AM in children over the last decade has been observed in Britain which is most likely due to the introduction of vaccination programs (measles-rubella-parotitis) and accordingly a decrease in the proportion of meningitis-induced pathogens of controlled viral infections and the use of more sensitive methods of diagnosis of the disease [13].

Conclusions

The annual dynamics of AM morbidity has a wavelike character with its peaks in the rise and fall of infection. The highest seasonal increase in the incidence of aseptic meningitis in children occurs in the period from August to October and it is 61.5% of the total annual incidence with the peak in September (24.0%).

The etiological factor of AM was established in 18 (8.6%) patients. Enterovirus remains the main causative agent of AM which was determined in 13 (72.6%) cases. Herpesviruses which were determined in 4 patients (22.2%) took the second place among the verified etiological factors of AM in children. The third place was taken by mumps virus which was detected in 1 patient (5.6%).

In most cases AM ended with complete recovery, however 47 (22.6%) patients had complications of the disease, most of them (91.3%) were non-severe (asthenic syndrome, autonomic disorders) and self limiting over time. Severe complications such as epileptic seizures, cerebral edema and hydrocephalus occurred only in isolated cases where the disease has not been identified.

In our study, the prevalence of AM among children in the Khmelnytskyi region averaged 6.2 per 100,000 children per year with a ratio of 2:1 between males and females.

Конфликт интересов: *отсутствует.*

Conflicts of Interest: *authors don't have any conflict of interest to declare*

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Information about authors:

Pypa L. V., MD, PhD, DSci, Professor, Head of the Department of Pediatrics, Faculty of Postgraduate Education, Vinnytsia National Pyrogov Memorial Medical University, Ukraine.

Svistilnik R. V., MD, PhD, Assistant, Department of Neurology and Neurosurgery, Faculty of Postgraduate Education, Vinnytsia National Pyrogov Memorial Medical University, Ukraine.

Lysytsia Yu. N., Assistant, Department of Pediatrics, Faculty of Postgraduate Education, Vinnytsia National Pyrogov Memorial Medical University, Ukraine.

Romanchuk K.Yu. MD, PhD, Assistant, Department of infectious diseases with the course of epidemiology, Vinnytsia National Pyrogov Memorial Medical University, Ukraine. 21000, Vinnytsia, Khmelnytskyi shosse st., 96, tel: 432-51-12-33

Odarchuk I. V., Assistant, Department of Pediatrics, Faculty of Postgraduate Education, Vinnytsia National Pyrogov Memorial Medical University, Ukraine