

MENINGOCOCCAL DISEASE IN CHILDREN AT THE PRESENT STAGE: PROBLEMS AND SOLUTIONS

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ABSTRACT

The article reviews the major up-to-date problems meningococcal infection and presents a laboratory analysis of generalized forms of meningococcal infection (MI) in children aged 0 month to 14 years. The age-related features of the disease under the present conditions and a relationship of the frequency serogroup of a meningococcal infections in Almaty.

KEYWORDS

Meningococcal infection, Meningococcus serogroup B, Vaccination, Immunization, Children.

INTRODUCTION

Meningococcal infection is one of the most common invasive bacterial infections in the world which remains highly significant today. High mortality rate reaching up to 10.5% is registered in generalized forms of the disease [1, 2, 3]. In most cases, the disease develops rapidly, thereby requiring urgent need of early diagnosis and emergent therapeutic aid from its onset. Meningococcal disease has various nosological forms that on their turn stipulate the necessity of differential diagnostics. According to WHO, 500 thousand cases of generalized forms of meningococcal infection are registered every year; 50 thousand of them are fatal [3, 14]. The hearing loss, loss of limbs and reduced intelligence are released among the possible after-effects [4, 13].

The epidemiology of meningococcal disease

Meningococcal disease is registered in many countries of the world on different climatic zones. The infection incidence increase is correlated with the wars, disasters and major accidents, which allowed giving it a definition of «war» infection. Agents have a special role in the occurrence of generalized forms of meningococcal infection. If their quantity in closed team reaches up to 20% or more, there occur clinically symptomatic forms of the disease [7, 8, 14].

Currently there are 13 serogroups of meningococci that differ in their immunologic reactivity of the polysaccharide capsule known. Unencapsulated serotypes are less virulent than encapsulated ones. The generalized form of the disease causes limited quantity of meningococcus serotypes. They are mainly A, B, C, W-135, Y serotypes [1, 3].

Serogroup A causes large-scale epidemics, mostly common in sub-Saharan Africa, which is known as meningococcal zone [5, 6, 11, 15].

Serogroup B causes sporadic or endemic cases, is reported in Europe, Cuba, Chile and New Zealand. This serogroup is characterized by disease severity and high mortality rate.

Serogroup C also causes large-scale epidemics which frequently occurs in Africa, Brazil, USA, Canada and Western Europe. This disease is often recorded in adolescents and young adults [5, 6, 7].

Serogroup W-135 became best known in the years 2000-2002 after it was found in majority of people doing the Hajj on places of pilgrimage.

Serogroup Y is common in the United States, Israel, serogroup X in Nigeria and Africa [3, 5, 12]. In Central Asia the exact distribution of individual serogroup are unknown.

In Kazakhstan, meningococcal infection is common in children. According to official statistics of the Republic of Kazakhstan, the highest incidence was registered in Almaty (1.58 per 100 thousand people in 2012) and Astana (1.38 per 100 thousand people in 2012). At the present time, despite the decrease in morbidity, the mortality rate remains high.

In the years 2009-2013 the study between the children of Almaty was conducted to investigate the clinical and epidemiological features of meningococcal disease at the current stage. Its main goal was evaluating the incidence of generalized forms of meningococcal disease in children aged 0-14 years, assessing the distribution of serogroups of *Neisseria meningitidis* among sick children, estimating the proportion meningococcal meningitis and meningitis of unknown

etiology in the overall structure of bacterial meningitis and assessing the treatment frequency, the incidence of complications and mortality at intensive care units,.

The study revealed that in five years the incidence of meningococcal disease ranged from 5.7 per 100 thousand people to 14.7 cases per 100 thousand people. These figures twice exceed the given official information. The lowest incidence was observed in 2009 and the highest in 2012. All these figures demonstrate the ripple effect nature of meningococcal disease epidemic, which on its turn allows predicting an increase of incidence the next two years. The laboratory confirmation of generalized meningococcal infection cases in children younger than 14 years was taken in 70% of cases on average. The study revealed the predominance of serogroup B in 67% of cases, less extent on serogroups A and C and meningococcus of other serogroups were not detected.

The children under the age of 5 years predominated in cases, with the highest incidence observed in children aged younger than 1 year.

In general, all purulent bacterial meningitis incidences over the period 2009-2013 have no downward trend. In its etiological structure the child population in the city of Almaty (between 1993-2007) had dominating meningococcal meningitis (32%) and unfortunately, the percentage of meningitis of unknown etiology remained high (39.8%) as well.

Characters of meningococcal disease in young children (according to Child infections research institute Russia, St. Petersburg)

- The dominance of meningococemia (50%);
- Severity of overall infective and brain symptoms;
- In 70% of cases the disease starts with catarrhal symptoms with the cerebral and meningeal symptoms revealing during the next 2-3 days;
- Cerebral syndrome in 53% of cases is manifested by generalized tonic-clonic seizures;
- On the background of a generalized infection in 65% of cases the dysfunction of the gastrointestinal tract is revealed.

Characters of meningococcal disease in adolescents (according to Child infections research institute Russia, St. Petersburg)

- Prevalence of Mixed forms (50%);
- Moderate overall infective and expressed cerebral and meningeal syndrome;
- High frequency (up to 18%) of extracranial complications (arthritis, myocarditis, heart attack, eye disease);
- Relapsing course in 11% of cases;

- In 26% of cases rash on the 3-5th day of illness.

The structure of the after-effects of generalized forms of meningococcal infection (GFMI)

Among 128 children under observation, 60.5% were treated in the ICU while the mean residence time was 9 days.

According to the results of our own research, dominating after-effects of generalized forms of meningococcal infection were infectious toxic shock of I-II degree, disseminated intravascular coagulation syndrome I, II, acute heart failure; the convulsive syndrome, myocardial and intestinal bleeding could be observed as well.

The outcomes of meningococcal disease

11% of cases ended lethally, the impact of serotype on outcome could not be reliably determined, in one case it was meningococcus of serogroup A, in four other cases serogroup B.

89% of patients were discharged from the hospital, further supervision of a neurologist recommended, because of after-effects of different degrees in the psychoneurological status.

Ways of meningococcal disease prevention:

One of the main methods for the prevention of meningococcal disease is vaccination. Vaccines are of two types - conjugate and polysaccharide.

The polysaccharide meningococcal vaccine:

- Contain freeze-dried encapsulated polysaccharide of appropriate meningococcal serogroups;
- Indicated for immunization of children older than 2 years, adolescents and adults;
- Epidemiological efficiency reaches up to 85-95%;
- Re-vaccination is recommended not earlier than 3 years. For the children vaccinated before the age of 5, if at high risk, revaccination is recommended after 2-3 years.

For the children under the age of 2 years, that are infected more than in half of all cases of meningitis, these vaccines like all polysaccharide vaccines cause a weak immune response.

The conjugated meningococcal vaccine:

- Contain relevant meningococcal serogroup polysaccharides conjugated to a carrier protein that allows the start of T-cell responses at any age;
- Induce a strong immune response in all age groups;
- Indicated for immunization to 9 months. (FDA) up to 55 years;
- Vaccination regimen for children 9-23 months: 2 doses at an interval of 3 months (FDA);
- Vaccination regimen for the people aged from 2 to

55 years: a single regimen;
 - Booster vaccination: once at the age of 15-55 years (according to epidemiological indications) [8, 9, 10, 12].

CONCLUSION

The epidemic meningococcal process in Kazakhstan has ripple effect character today. The figures of child morbidity by meningococcal disease in Almaty exceed the country by more than 4 times, and overall morbidity rate in Kazakhstan for 13 times, indicating a high risk of infection of the child population of the city.

In the structure of generalized forms of meningococcal infection serogroup B remained dominant for years 2009-2013, showing 66.7%.

In 40% of cases had after-effects during generalized forms of meningococcal infection. The most frequent after-effects were toxic shock, disseminated intravascular coagulation and acute cardiovascular failure.

Children under the age of 5 years are at highest risk, which is the basis for the development of specific measures for specific immunization of meningococcal disease in this age group.

REFERENCES

1. Dinleyici EC., Kurugol Z. 6th World Congress of the World Society for Pediatric Infectious Diseases (WSPID). *Expert Rev Vaccines*. 2010; 9(3): 261-272.
2. Vestergard D., David KP. Global spread of meningococcal serogroup W135. *Ugeskr. Laeder*. 2008; 170-39: 3044—3047.
3. WHO. Meningococcal meningitis. *Weekly Epidemiological Record*. 2003; 78-33: 285-296. Available from <http://www.who.int/wer/en/> [accessed on June 15, 2015].
4. Harrison LH., Trotter CL., Ramsay ME. Global epidemiology of meningococcal disease. *Vaccine*. 2009; 27: 51-63.
5. Tan LK., Carlone GM., Borrow R. Advances in the development of vaccines against *Neisseria meningitidis*. *N. Engl. J. Med*. 2010; 362-16: 1511-1520.
6. Parkhill J., Achtman M., James KD. et al. Complete DNA sequence of a serogroup A strain of *Neisseria meningitidis* Z2491. *Nature*. 2000; 404-6777: 502—506.
7. Shyshov AS. Purulent meningitis as a syndrome, a clinical marker of generalized bacterial infections and an indicator of their severity. *Journal of Neurology and Psychiatry*. 2009; 5: 92-96.
8. Trotter CL., Ramsay M E. Vaccination against meningococcal disease in Europe: review and recommendations for the use of conjugate vaccines. *FEMS Microbiol. Rev*. 2007; 31-1: 101-107.
9. Vidarsson G., Overbeeke N., Stemerding AM. et al. Working mechanism of immunoglobulin A1 (IgA1) protease: cleavage of IgA1 antibody to *Neisseria meningitidis* PorA requires

- de novo synthesis of IgA1 Protease. *Infect. Immun*. 2005; 73-10: 6721-6726.
10. Rosenstein NE., Parkins BA., Stephens DS., Popovic T., Hughes JM. Meningococcal disease. *N Engl J Med*. 2001; 344-18: 1378—1388.
 11. Prevention and control of meningococcal disease. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2000; 49-RR-7: 1-10.
 12. Shyshov AS. About the system of registration and account of «Acute neuroinfections». *Epidemiology and Infectious Diseases*. 2006; 2: 56-61.
 13. Lobzin YV., Pilipenko VV., Gromyko YN. Meningitis and encephalitis. Monograph. Foliant, St. Petersburg. 2006: 2-54.
 14. Rtishchev AYu., Shamsheva OV. The Problem of Prophylaxis of Meningococcal Disease at Children: Ways of The Decision. *Childhood infections*. 2009; 3: 31-35.