ISSN 2221-2582

UDK 616.24-002-053.2+616.831-009-036.2+615.281.9+579.61
DOI: 10.56871/CmN-W.2023.41.58.011

CLINICAL CASE OF LOWER RESPIRATORY TRACT INFECTION CAUSED BY *ELIZABETHKINGIA MENINGOSEPTICA* IN A CHILD WITH CEREBRAL PALSY

© Elena V. Loshkova[1, 2], Artem V. Lyamin[3], Galina N. Yankina[2], Tatiana S. Lyulka[2]

[1] Research Clinical Institute of Childhood of the Ministry of Health of the Moscow Region. Bolshaya Serpukhovskaya str., 62, Moscow, Russian Federation, 115093
[2] Siberian State Medical University. Moskovsky tract, 2, Tomsk, Russian Federation, 634050
[3] Samara State Medical University. Chapaevskaya str., 89, Samara, Russian Federation, 443099

Contact information:
Elena V. Loshkova — Candidate of Medical Sciences, Associate Professor of the Department of Hospital Pediatrics, Department of Faculty Pediatrics with a Course of Childhood Diseases, Faculty of Medicine, Siberian State Medical University.
E-mail: loshkova@rambler.ru ORCID ID: 0000-0002-3043-8674 SPIN: 9242-5976

For citation: Loshkova EV, Lyamin AV, Yankina GN, Lyulka TS. A clinical case of lower respiratory tract infection caused by *Elizabethkingia meningoseptica* in a child with cerebral palsy. Children's medicine of the North-West (St. Petersburg). 2023;11(4):88-98. DOI: https://doi.org/10.56871/CmN-W.2023.41.58.011

Received: 14.09.2023 **Revised: 27.10.2023** **Accepted: 11.12.2023**

Abstract. The most common cause of morbidity and mortality in patients with cerebral palsy (CP), both in children and adults, is associated with respiratory diseases. Patients with CP are characterized by a decrease in local immunity of the upper and lower respiratory tract, increased viral diseases, a progression of bacterial infection without additional infection or increase in the count of microbial numbers, decrease in lung function, and infection of the respiratory tract with a microbiota, which is atypical for practically healthy children. CP is a disease that occurs with severe comorbid conditions as epilepsy, requiring constant basic therapy, accompanied by standard negative side effects. Both severe gastrointestinal disorders and associated severe disorders of nutritional status, deficient conditions contribute to infectious process against the background of CP. A clinical observation of the patient with CP who had severe community-acquired pneumonia caused by *Elizabethkingia meningoseptica*, which developed while taking glucocorticosteroids, was described. The difficulties of managing of the child who was prescribed empirical antimicrobial therapy, and successful eradication of the pathogen with clinical and radiological recovery after a detection of *Elizabethkingia meningoseptica* in the bronchoalveolar lavage fluid and using the appointment antibiotic therapy based on the results of the obtained antibiogram were described. The authors paid attention to the pathogenetic features of the implementation of respiratory and nutritional disorders in a cohort of patients with CP and the need to personalize diagnostic and therapeutic measures in each case.

Key words: *pneumonia; cerebral palsy; children; Elizabethkingia meningoseptica; nutritional status; antibiotic resistance.*

КЛИНИЧЕСКИЙ СЛУЧАЙ ИНФЕКЦИИ НИЖНИХ ДЫХАТЕЛЬНЫХ ПУТЕЙ, ВЫЗВАННОЙ *ELIZABETHKINGIA MENINGOSEPTICA*, У РЕБЕНКА С ЦЕРЕБРАЛЬНЫМ ПАРАЛИЧОМ

© Елена Владимировна Лошкова[1, 2], Артем Викторович Лямин[3], Галина Николаевна Янкина[2], Татьяна Сергеевна Люлька[2]

[1] Научно-исследовательский клинический институт детства Министерства здравоохранения Московской области. 115093, г. Москва, Большая Серпуховская ул., 62
[2] Сибирский государственный медицинский университет. 634050, г. Томск, Московский тракт, 2
[3] Самарский государственный медицинский университет. 443099, г. Самара, ул. Чапаевская, 89

Контактная информация:
Елена Владимировна Лошкова — к.м.н., доцент кафедры госпитальной педиатрии, кафедры факультетской педиатрии с курсом детских болезней лечебного факультета СибГМУ. E-mail: loshkova@rambler.ru ORCID ID: 0000-0002-3043-8674 SPIN: 9242-5976

Для цитирования: Лошкова Е.В., Лямин А.В., Янкина Г.Н., Люлька Т.С. Клинический случай инфекции нижних дыхательных путей, вызванной *Elizabethkingia meningoseptica*, у ребенка с церебральным параличом // Children's medicine of the North-West. 2023. Т. 11. № 4. С. 88–98. DOI: https://doi.org/10.56871/CmN-W.2023.41.58.011

Поступила: 14.09.2023 **Одобрена: 27.10.2023** **Принята к печати: 11.12.2023**

Резюме. Наиболее частая причина заболеваемости и смертности больных детским церебральным параличом (ДЦП), в том числе в детском возрасте, связана с заболеваниями органов дыхания. Для больных ДЦП характерно снижение местного иммунитета верхних и нижних дыхательных путей, повышение вирусной заболеваемости, прогрессирование бактериальной инфекции без дополнительного инфицирования или увеличения количества микробов, снижение функции легких, инфицирование дыхательных путей с микрофлорой, нетипичной для практически здоровых детей. ДЦП — заболевание, протекающее с тяжелыми коморбидными состояниями: это эпилепсия, требующая постоянной базисной терапии, сопровождающаяся стандартными негативными побочными эффектами, это как тяжелые желудочно-кишечные расстройства и связанные с ними тяжелые нарушения нутритивного статуса, так и дефицитные состояния, способствующие инфекционному процессу на фоне ДЦП. Описано клиническое наблюдение больного ДЦП, перенесшего тяжелую внебольничную пневмонию, вызванную *Elizabethkingia meningoseptica*, развившуюся на фоне приема глюкокортикостероидов. Описаны трудности ведения ребенка при назначении эмпирической антимикробной терапии и успешная эрадикация возбудителя при клинико-рентгенологическом выздоровлении больного после обнаружения *Elizabethkingia meningoseptica* в жидкости бронхоальвеолярного лаважа и назначения антибиотикотерапии по результатам полученной антибиотикограммы. Авторы обращают внимание на патогенетические особенности реализации нарушений дыхания и питания в когорте больных ДЦП и необходимость персонализации диагностических и лечебных мероприятий в каждом случае.

Ключевые слова: *пневмония; детский церебральный паралич; дети; Elizabethkingia meningoseptica; нутритивный статус; антибиотикорезистентность.*

INTRODUCTION

The most common cause of morbidity and mortality in patients with cerebral palsy (CP), both in children and adults, is associated with respiratory diseases [1]. Compared to the general population, adults and children with CP have a 14-fold increased risk of fatal outcome from respiratory diseases [2]. Nowadays, both the duration and quality of life in children with CP are increasing because of the improvement of treatment and rehabilitation technologies. Therefore, long-term follow-up of patients, correction of chronic respiratory disorders and related nutritional status disorders, which largely determine the lung function, become more important [1]. Infectious diseases in children with CP due to impaired immunity, severe gastroesophageal motility disorders, decreased functional activity of mucosal immunity, mucociliary clearance disorders, are atypical, often subclinical. The respiratory failure has been being the main cause of death in this population since the 1970's [3]. In addition, CP is often accompanied by tracheobronchomalacia and other upper and lower airway abnormalities, exacerbating mucociliary transport dysfunction, which increases the need for bronchodilators, antibiotics, anti-inflammatory and mucolytic therapy. Patients with CP are characterized by decreased local immunity of the all respiratory tract, an increased level of viral diseases, progression of bacterial infections without additional infection or increased microbial counts, decreased lung function (FEV1 and VC) and age (catamnesis from 8 to 18 years), and infection of the respiratory tract with atypical microbiota for practically healthy children [4–8]. The course of respiratory tract infection in this category of children has some pathogenetic and clinical features, as well as the associated difficulties of diagnosis and therapy, which are illustrated by the present clinical case.

CLINICAL CASE

The patient K., aged 1 year and 1 month, was under medical observation.

Clinical diagnosis

Main disease. Severe, uncomplicated community-acquired right-sided pneumonia of the upper and middle lobes, Elizabethkingia meningoseptica-etiology, prolonged course.

 ISSN 2221-2582

Concomitant diseases. Epilepsy caused by mutation of the *GNAO1* gene. Cerebral palsy, spastic diplegia. Gross Motor Functional Classification (GMFCS) Level V, Manual Ability Classification System (MACS) Level V, Communication Function Classification System (CFCS) Level V, Drinking Ability Classification System (EDACS) Level V. Dystonic attacks. Bulbar syndrome. Microcephaly. Severe malnutrition. Severe malabsorption. Anemia of chronic diseases, II degree.

Anamnesis morbi The child fell ill acutely, the disease began with a fever up to 38.5 °C, reduced with paracetamol, the maximum temperature was up to 40.0 °C, against this background there was a refusal to eat and drink, parents called an ambulance. The child was taken by the ambulance doctors and hospitalized in the pediatric department of the children's multidisciplinary hospital at the place of his residence.

Anamnesis vitae. The mother is 26 years old, the father is 29 years old, both of them are healthy. A boy is from the second pregnancy. The eldest sib (first pregnancy), aged 2 years, is practically healthy. The present pregnancy occurred with a retrochorial hematoma in the first trimester. Births at term was by caesarean section due to pelvic position. The birth weight was 3470 g and the length was 54 cm. From the second day of life the child has neonatal jaundice and received phototherapy in the maternity hospital. The duration of stay in the maternity hospital was 5 days. The jaundice was ended on its own after three weeks. A breastfeeding was until one month of age. From the 5th day of life, seizures appeared and manifested as shudders and clutching. From 1.5 months of age there were convulsions with spasms and tonic-clonic component, which became more frequent with each month. At the age of 2 months, the child was examined in the psychoneurological department; according to the results of magnetic resonance imaging (MRI) of the brain, congental biventriculomegaly was diagnosed; according to the results of electroencephalography (EEG), diffuse changes in brain activity, diffuse epileptic activity in the background and with elements of suppression were revealed. The diagnosis of epilepsy was verified; molecular genetic examination revealed an amino acid substitution in exome 7 of a GNAO1 gene in a heterozygous variant. During the first and second six months of life, convulsive seizures became more frequent, and anticonvulsant therapy was corrected: doses of valproate acid were increased, and levetiracetam was used. The frequency of epileptic seizures, despite therapy, continued to increase, so a month before the development of the present acute illness, an epileptologist performed pulse therapy with glucocorticosteroids (GCS). At the time of the hospitalization the child received prednisolone (1 mg/kg/day) as a reduction of GCS dosage. In addition to the neurological clinical picture, the child had significant problems with food intake. Against the background of the course of epilepsy and progressive brain damage, pronounced motor disorders and severe difficulties in eating were formed. It corresponded to GMFCS V, MACS V, CFCS V, EDACS V. Pronounced dystonic attacks and pain syndrome persisted. The presence of marked bulbar syndrome was accompanied by persistent lower respiratory tract infections, which were treated on an outpatient basis; antibacterial drugs was used *per os* every month (aminopenicillins with beta-lactamase inhibitor, cephalosporins (CS) II and III generations, macrolides). The parents refused to gastrostomy feeding, which increased malnutrition, and by the age of 1-year patient K. had severe protein-energy malnutrition (PEM). In addition, the intake of food and fluids by mouth constantly provoked and maintained the course of catarrhal-purulent endobronchitis. The patient had been a child with disability since 4 months of age and had palliative status since 8 months of age.

The patient's condition on admission is severe due to neurologic clinical picture, respiratory disorders (saturation 93–94%, tachypnea 70–74 per minute, participation of auxiliary breathing muscles, increased amounts of sputum and frequent cough), intoxication (refusal to eat and drink, fever 39.6 °C, skin pallor), severe malnutrition (an absence of subcutaneous fat, a decreased skin turgor, a weight — 6400 g, a height — 74 cm, the deficiency of weight — 36%). The state of health suffers due to the disease. During the examination there are no seizures, there are some dystonic attacks as a short-term hypertonicity of trunk muscles, limbs, head shaking, at rest a moderately increased tone in extensors of limbs, clonus of feet. Palpebral fissures are equal, pupils S=D, of medium size, no nystagmus, the gaze does not fixate and follow. Nasolabial folds are symmetrical. A feeding was through a baby bottle. A child was sucking slowly and regurgitated 50–60 ml of formula, the choking was frequent. Signs of severe physical and psychomotor delay: the child does not hold his head and sit up. A patient does not react to the surrounding environment. Meningeal signs are negative; the child have severe drowsiness. When

the patient stays awake he has slow reactions as opening of eyes, movements of limbs or short-term dystonic attacks while examination. The skin was pale, dry, there was no rash, but there was an acrocyanosis. A subcutaneous fat layer was practically absent on the limbs, anterior abdominal wall and face. Nasal breathing was difficult, there was a lot of mucous discharge from the nasal passages. There was a moderate hyperemia of the posterior pharyngeal wall, its loosening and there were not plaques. Peripheral lymph nodes were up to 5–7 mm without changes in other properties. The tongue root was moist and covered with white plaque. Mucous membranes of the oral cavity were pink, moist and clean. The voice was sonorous. The cough was frequent with variable productivity. The percussion sound over the lungs was with a bandbox sound, on the right side was total dulled. While auscultation the breathing was bronchial, multicaliberal crackle sounds were on the left, diminished breath sounds were on the right. Heart tones were loud, rhythmic. The abdomen was somewhat sunken, soft and painless. The liver was +1,5+1,5-1/3, its edge was painless, elastic. Spleen was not enlarged. The defecation did not occur independently, it appeared only after microlax. The fecal was yellow, mushy and without pathologic impurities. There were no urination problems, it was free, there was no edema. It should be noted that in addition to oxygen therapy via binasal cannulae, antiviral, antibacterial therapy (ABT) with 3rd generation of CS and continuation of prednisolone *per os* in the previous dose (1 mg/kg/day), infusion therapy with 30 mg of prednisolone was prescribed by the doctor on duty. The patient had been receiving this infusion therapy for 7 days from the moment of hospitalization. It was done for the "detoxification" as indicated in the medical documents. A complete clinical and laboratory examination of the patient was performed; the diagnosis of pneumonia was confirmed by the X-rays result (Fig. 1). On the first day of hospitalization, which coincided with the first day of illnesses, inflammatory infiltration in the projection of the upper and middle lobes of the right lung was detected.

After starting ABT with 3rd generation of CS there was no positive clinical dynamics. Therefore, the first change of ABT (combination of ampicillin/sulbactam, aminoglycoside and macrolide) was performed because of the severe course of pneumonia (Table 1). The results of bacteriologic cultures of sputum and blood were negative. On the 10th day of hospitalization the highest mark-

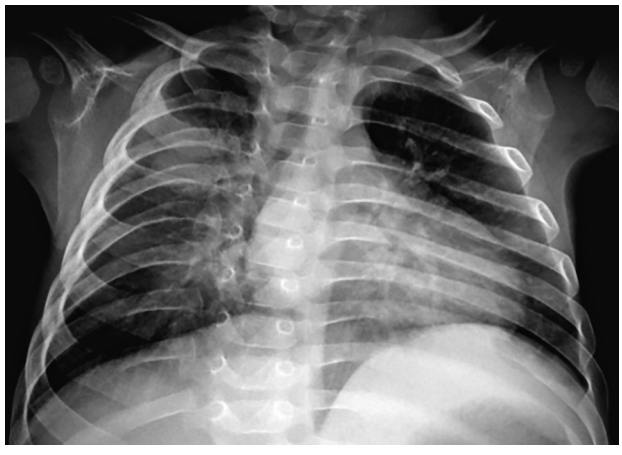

Fig. 1. X-ray picture on day first of hospitalization
Рис. 1. Рентгенологическая картина в первые сутки госпитализации

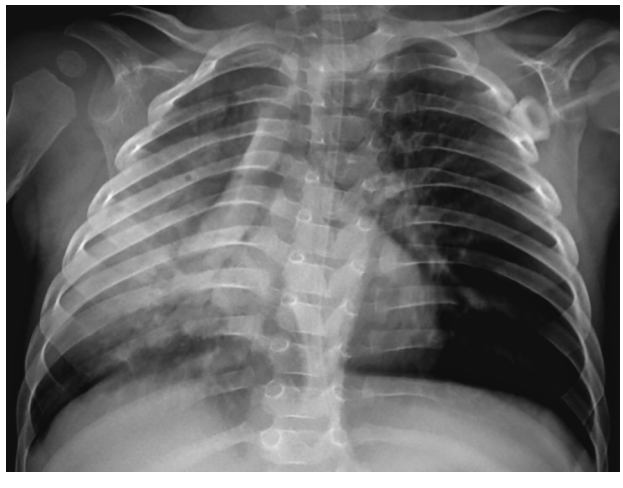

Fig. 2. X-ray picture on the 10th day of hospitalization
Рис. 2. Рентгенологическая картина на 10-е сутки госпитализации

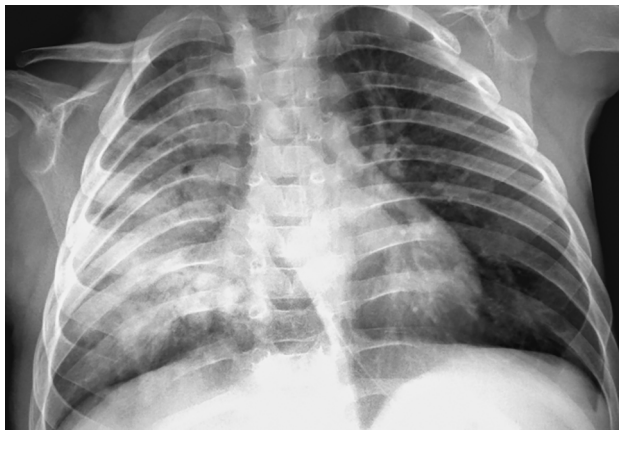

Fig. 3. X-ray picture on the 30th day of hospitalization
Рис. 3. Рентгенологическая картина на 30-е сутки госпитализации

Table 1. Dynamics of clinical and laboratory parameters and antimicrobial therapy during hospitalization

Таблица 1. Динамика клинико-лабораторных показателей и антимикробной терапии в период госпитализации

Parameters	Day of hospitalization										
	1 day	5 day	10 day	15 day	20 day	25 day	30 day	35 day	40 day	45 day	50 day
Dynamics of clinical picture											
Temperature, °C	40,2	39,5	39,3	38,7	38,9	38,5	38,7	37,7	36,5	36,6	36,6
Cough	+++	+++	+++	+++	+++	+++	+++	++	+	+	+
Sputum	+++	+++	+++	+++	+++	+++	+++	++	+	+	+
Refusal to eat or drink	+++	+++	+++	+++	+++	+++	+++	++	–	–	–
Dynamics of laboratory markers											
White blood cells, 10^9/L	18,9	25,6	30,4	27,7	24,3	25,5	29,6	15,6	8,9	7,5	7,3
Neutrophil index	0,24	0,23	0,27	0,25	0,22	0,23	0,24	0,18	0,15	0,14	0,10
CRP, mg/l	78,4	86,4	93,8	77,5	68,9	81,5	88,9	21,2	4,0	3,0	4,0
PCT, ng/l		8,0	12,0	8,0	11,0			2,0	>0,2		
Dynamics of microbiological monitoring											
No colony growth	+	+	+	+		+	+		+	+	+
Staphylococcus aureus, sputum, CFU/mL					10^5						
Elizabethkingia meningoseptica, BAL, CFU/mL								10^7			
Antimicrobial and other treatment											
Cefotaxime	+										
Ampisid +amicacine + sumamed		+									
Meropenem+vancomycin			+								
Immunoglobulins intravenous			+								
Amoxiclav+cephoperazone/sulbactam				+							
Zinforo+fluconazole					+						
Ceftazidime+metronidazol+vifend +vil prafen						+	+				
Ciprofloxacin+ piperacillin/tazobactam+biseptol								+	+	+	+

ers of systemic inflammation, including total leukocytosis, neutrophil index, the highest level of C-reactive protein (CRP) and procalcitonin (PCT) were registered, clinical and radiological dynamics was also negative (Table 1, Fig. 2).

Then, during the hospitalization, a patient K's condition remained stably severe due to respiratory disorders against the background of severe neurological clinical picture with frequent epileptic seizures and dystonic attacks, as well as severe malnutrition. All of that persisted and had no positive dynamics. Furthermore, during the first month of hospitalization the child's inflammatory activity was pronounced without a tendency to decrease, the result of bacteriological cultures was negative. And only on the 20th day of hospitalization the growth of Staphylococcus aureus 10^5 CFU/ml with preserved sensitivity to benzylpenicillin and cefoxitin was detected in the sputum. Anti-staphylococcal antibacterial drugs were already in the ABT, ceftaroline fosamil was given to the child, but there was no positive clinical and X-ray effect (Fig. 3).

Table 2. Antibioticogram of *Elizabethkingia meningoseptica,* 10^7 CFU/ml, obtained as a result of bacteriological culture of broncho-alveolar lavage fluid

Таблица 2. Антибиотикограмма *Elizabethkingia meningoseptica,* 10^7 КОЕ/мл, полученная в результате бактериологического посева бронхоальвеолярной лаважной жидкости

Antimicrobial drug	Minimum inhibitory concentration, mgc/mL	Interpretation
Aztreonam	>32	R
Amikacin	>32	R
Ampicillin/sulbactam	>16/8	R
Ampicillin	>16	R
Gentamicin	>8	R
Imipenem	>8	R
Levofloxacin	<=2	S
Meropenem	>8	R
Nitrofurantoin	>64	R
Piperacillin	>64	R
Piperacillin/Tazobactam	<=16	S
Tobramycin	>8	R
Cefepime	>16	R
Cefotaxime	>32	R
Cefotaxime/clavulanate	4	S
Cefotetan	>32	R
Cefoperazone/ sulbactam	2	S
Ceftazidime	>16	R
Ceftriaxone	>32	R
Cefuroxime	>16	R
Cephalothin	>16	R
Ciprofloxacin	<=1	S
Ertapenem	>4	R
Tetracycline	8	I
Trimethoprim/ sulfometaxazole	<=2/38	S

After 4 weeks of unsuccessful ABT of community-acquired pneumonia, patient K. underwent therapeutic and diagnostic bronchoscopy with collection of bronchoalveolar lavage fluid (BAL) and it sowing on standard nutrient media to detect fungi and Mycobacterium tuberculosis. On the 35th day of the hospitalization, a conclusion was made about the presence of abundant growth of Elizabethkingia meningoseptica (107 CFU/ml) with the results of sensitivity to ABT shown in Table 2. Then, ABT was prescribed according to the obtained antibioticogram (Table 1). After use of combined therapy with ciprofloxacin and piperacillin/tazobactam with trimethoprim/sulfometaxazole for two weeks, a positive dynamics of clinical picture was achieved. It became noticeable on the 2–3 rd day, and complete radiological resolution of the process was achieved on the 50th day of hospitalization (Fig. 4).

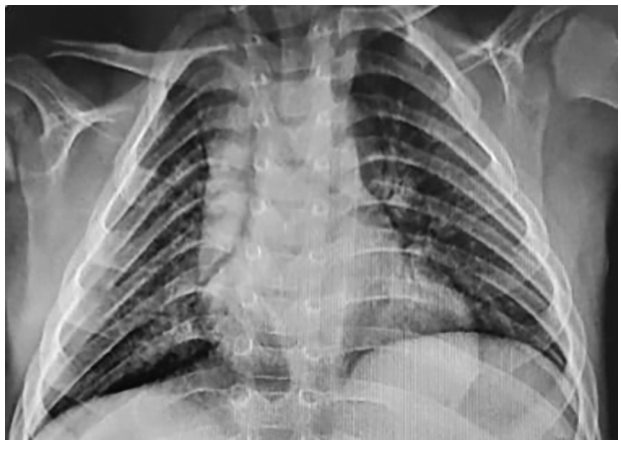

Fig. 4. X-ray picture on the 50th day of hospitalization
Рис. 4. Рентгенологическая картина на 50-е сутки госпитализации

The patient K. was discharged to the outpatient stage on the 58th day with clinical and radiological recovery. Recommendations for treatment of the underlying diseases, including gastrostomy placement, were provided. The result of Mycobacterium tuberculosis (MBT) culture was negative. Currently, the child is a gastrostomy carrier. He undergoes palliative care and rehabilitation every 6 months. There were no episodes of lower respiratory tract infections for the last year. K. receives ABT courses for intercurrent infections no more than 1–2 times a year. Further medical observation of the patient continues.

DISCUSSION

The presence of severe motor disorders on the background of cerebral palsy regardless of its cause determines the formation of chronic lung diseases, atypical and subclinical course of acute infectious bronchopulmonary inflammation due to different factors (Fig. 5, 6). Muscle control impairment, dystonic attacks increase dysphagia and microaspiration [6–8].

In turn, gastrointestinal dysfunction appears due to motor and neurological problems and is

 ISSN 2221-2582

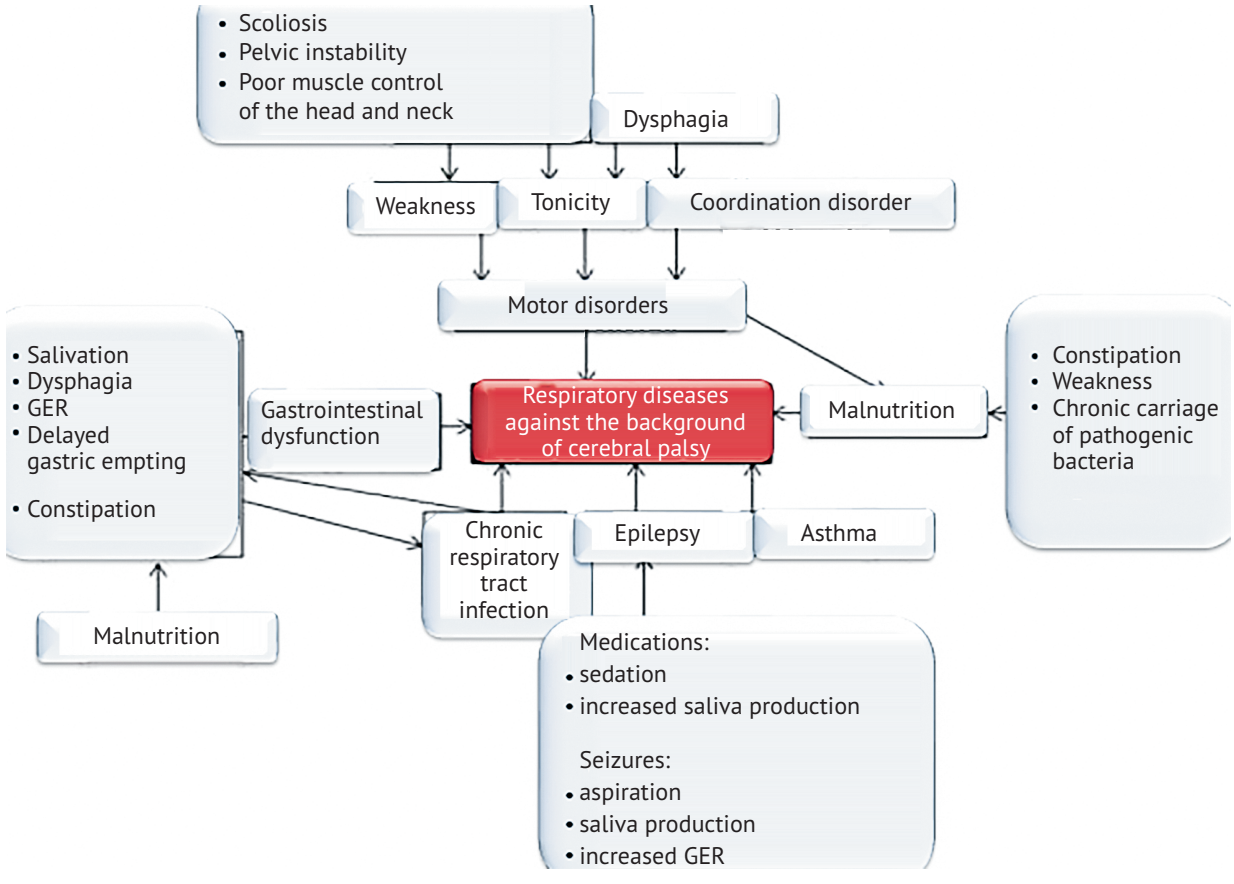

Fig. 5. Pathogenesis of the development and progression of respiratory disorders against the background of cerebral palsy
Рис. 5. Патогенез развития и прогрессирования респираторных нарушений на фоне церебрального паралича

common in both upper gastrointestinal (GI) tract (it manifests by hypersalivation, choking, aspiration, gastric hypomotility, gastroesophageal reflux) and lower GI tract. There it is shown as chronic constipation, bacterial overgrowth syndrome, malnutrition and malabsorption [6–8]. Moreover, taking medications, including anticonvulsants and cholinergic blocking drug, has certain classical side effects that increase a count of functional GI disorders [6–8].

All patients suffering from CP with class V in motor disorders have malnutrition, associated severe nutritional status disorders and severe malabsorption (Fig. 6). All this conditions are expressed not only in delayed physical development, growth and body weight delay, but also in the formation of numerous deficiency states including disorders of calcium-phosphorus homeostasis with changes in bone mineral density. In turn, a patient has a severe chronic pain syndrome, which presented in children due to dystonic attacks. Disorders of iron metabolism affect the immune system, and the developing hypoxia due to an iron deficiency aggravates respiratory failure, associated with bronchopulmonary diseases [6–8]. The patient we observed had severe protein-energy malnutrition and anemia, as well as osteoporosis, which is well visualized by X-ray.

Patient K. had severe motor disorders on the background of CP, and therefore, he had all pathogenetic and clinical factors affecting the onset and progression of respiratory and nutritional disorders. Thus, it should be noted that chronic colonization of atypical microbiota and/or bacterial overgrowth syndrome should be considered as an independent risk factor for severe infectious process in this category of patients. The use of GCS repeatedly increases infectious complications, if a patient has severe diseases. The classic example is GCS therapy for severe bronchopulmonary dysplasia to reduce the dependence on respiratory support at the stage of neonatal intensive care units [9]. Patient K. received pulse therapy with GCS for refractory seizure syndrome before the pneumonia, and then continued to receive GCS in the standard dose. In addition, treatment with prednisolone was continued both orally and parenterally despite the detection of pneumonia after chest

radiography. This fact aggravated the existing immunosuppression, and probably played a role in the progression of bronchopulmonary inflammatory infiltration and worsening of the patient's condition. Respiratory disorders were increased.

Gram-negative non-fermenting bacteria are frequent causative agents of chronic respiratory tract infection in children with severe CP [5]. Gram-negative bacteria of the genus *Elizabethkingia* are actual causative agents of hospital-acquired infections and are usually associated with high mortality [10, 11]. Recent publications have reported several cases of severe infection caused by this bacterium. The most common variant of disease was neonatal meningitis with septicemia and bacteremia. In addition, cases of osteomyelitis [15], urinary tract infections [16, 17], endogenous endophthalmitis [18], endocarditis [19], epididymo-orchitis [20], lung abscess [21], necrotizing fasciitis [22], cystic fibrosis [23], hydrocephalus [24], and secondary infections with high mortality, especially in immunocompromised patients [25], have been described. *Elizabethkingia meningoseptica* infections have also been in patients with COVID-19 [26]. *E. meningoseptica* affects not only immunocompromised individuals but also immunocompetent people [27]. Historically, the first report of human infection with *E. meningoseptica* was about 19 cases of meningitis in infants in the United States [28].

Our report shows that *E. meningoseptica* is specific to immunocompromised patients.

Both whole genome sequence analysis and optical mapping, MALDI-TOF mass spectrometry, led to a composition revision of the genus *Elizabethkingia* with the isolation of 8 species, named *E. meningoseptica*, *E. miricola*, *E. anophelis*, *E. bruuniana*, *E. ursingii*, *E. occulta* [29], *E. argenteiflava* [30] and the newest *E. umeracha* [31]. It is necessary to know that the identification of *Elizabethkingia* using traditional microbiological methods is difficult [32]. It accounts for the low detectability of this pathogen.

In case of the patient K., *E. meningoseptica* was detected only in the BAL, despite abundant sputum discharge. It occurred only on the 35th day of hospitalization, what confirms the difficulty of

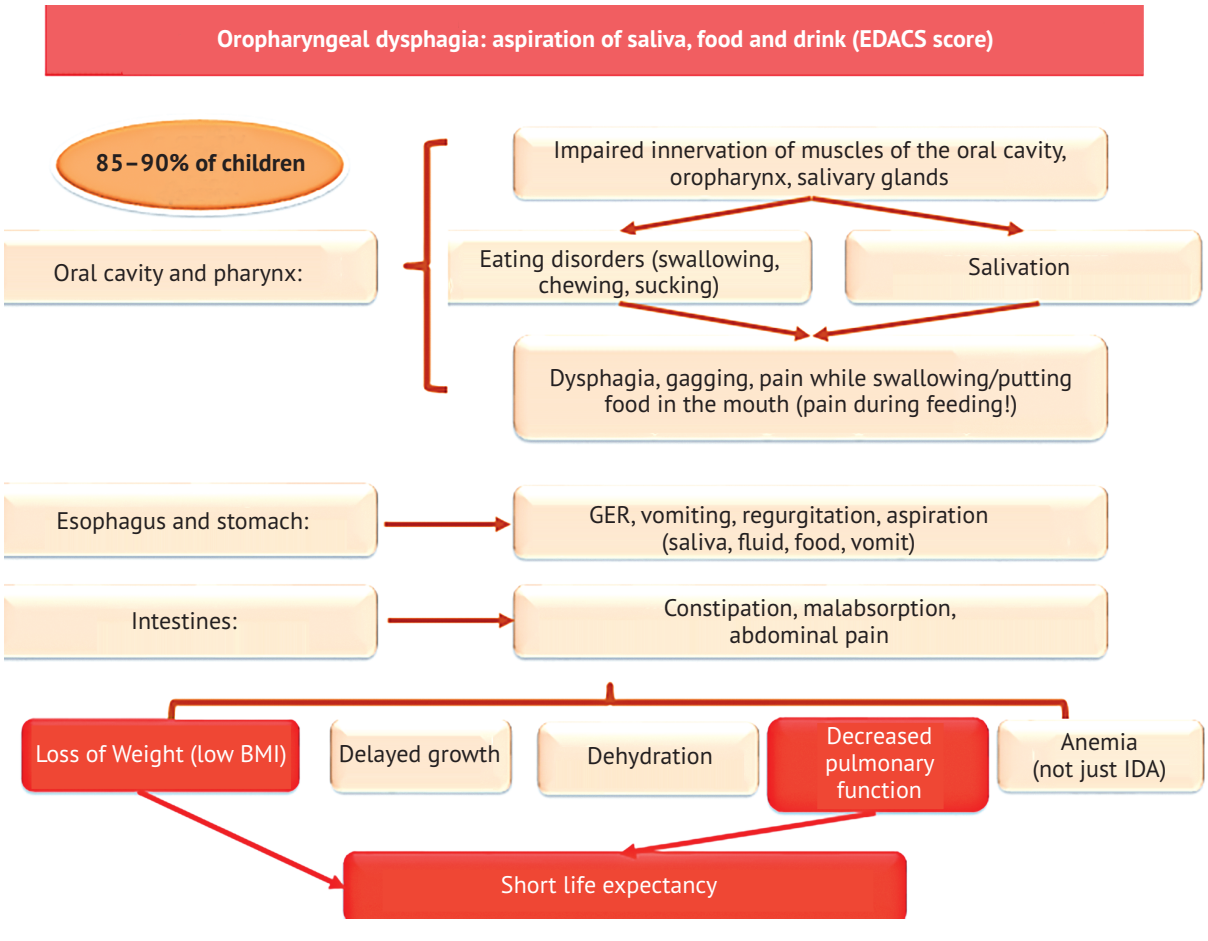

Fig. 6. Pathogenesis of the development and progression of nutritional disorders against the background of cerebral palsy
Рис. 6. Патогенез развития и прогрессирования нутритивных нарушений на фоне церебрального паралича

identification of this pathogen. This consists to already published data [32].

Members of the genus *Elizabethkingia* are resistant to most β-lactams, inhibitor-protected β-lactams and carbapenems because of the presence of two unique class B metallo-β-lactamases (MBL), namely blaBlaB and blaGOB, and also a class A extended-spectrum β-lactamase (ESBL) — blaCME [33].

According to given recommendations "Determination of susceptibility of microorganisms to antimicrobial agents" version 2021-01, *E. meningoseptica* has natural resistance to the antibacterial drugs: ampicillin, amoxicillin, amoxicillin/clavulanic acid, ampicillin/sulbactam, ticarcillin, ticarcillin/clavulanic acid, piperacillin, cefazolin, cephalothin, cephalexin, cefadroxil, cefuroxime, ceftriaxone, cefotaxime, ceftazidime, cefepime, aztreonam, ertapenem, imipenem, meropenem, and polymyxin. *Elizabethkingia* spp. isolates are often resistant to aminoglycosides, macrolides, tetracycline, and vancomycin, but can remain sensitivity to piperacillin/tazobactam, fluoroquinolones, minocycline, tigecycline, trimethoprim/sulfamethoxazole [34, 35] and levofloxacin [36]. Nowadays, there are no established criteria for assessing antimicrobial sensitivity for members of the genus Elizabethkingia. In our study the results were interpreted in terms of borderline MIC values by the EUCAST 2022 criteria for Pseudomonas spp. and Enterobacteriaceae, due to the lack of defined borderline values for *E. meningoseptica*.

The isolate of E. meningoseptica was sensitive to fluoroquinolones, piperacillin/tazobactam, cefoperazone/sulbactam and trimethoprim/sulfamethoxazole, therefore a combination of three antibacterial drugs was prescribed taking into in view of the possible production of MBL and ESBL. The child was prescribed off-label ciprofloxacin, piperacillin/tazobactam and trimethoprim/sulfamethoxazole.

CONCLUSION

Thus, the clinical observation demonstrates a severe course of community-acquired pneumonia caused by the infrequently diagnosed pathogen *E. meningoseptica* in a patient with severe comorbid pathology in the form of cerebral palsy and its complications, as well as risk factors for generalization of the infectious process associated with the usage of glucocorticosteroids against the background of active bacterial infection. This clinical observation pays attention of practitioners to the peculiarities of microbial colonization of the respiratory tract in children with severe cerebral palsy. It shows a need for earlier usage of invasive diagnostic procedures (bronchoscopy) with targeted microbiological diagnosis of bronchoalveolar lavage fluid for identification of pathogens by microbiological routine methods.

ADDITIONAL INFORMATION

Author contribution. E.V. Loshkova — patient management and preparation of extracts from medical records, analysis of literature data and their interpretation, structuring of the material and writing of the article; A.V. Lyamin — interpretation of the results of microbiological studies and their discussion, verification and structuring of the article; G.N. Yankina — discussion of the article; T.S. Lyulka — technical support and discussion of the manuscript. All authors read and approved the final version before publication.

Competing interests. The authors declare that there have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Consent for publication. Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Е.В. Лошкова — ведение пациента и подготовка выписки из медицинской документации, анализ данных литературы и их интерпретация, структурирование материала и написание статьи; А.В. Лямин — интерпретация результатов микробиологических исследований и их обсуждение, проверка и структурирование статьи; Г.Н. Янкина — обсуждение статьи; Т.С. Люлька — техническое сопровождение и обсуждение рукописи. Все авторы прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Информированное согласие на публикацию. Авторы получили письменное согласие пациента на публикацию медицинских данных.

REFERENCES / ЛИТЕРАТУРА

1. Rakocevic G., Alexopoulos H., Dalakas M.C. Quantitative clinical and autoimmune assessments in

stiff person syndrome: evidence for a progressive disorder. BMC Neurol. 2019; 19(1): 1.
2. Ryan J.M., Peterson M.D., Ryan N. et al. Mortality due to cardiovascular disease, respiratory disease, and cancer in adults with cerebral palsy. Dev Med Child Neurol. 2019; 61(8): 924–8.
3. Himmelmann K., Sundh V. Survival with cerebral palsy over five decades in western Sweden. Dev Med Child Neurol. 2015; 57(8): 762–7.
4. Myers L.L., Nerminathan A., Fitzgerald D.A. et al. Transition to adult care for young people with cerebral palsy. Paediatr Respir Rev. 2020; 33: 16–23.
5. Gerdung C.A., Tsang A., Yasseen A.S. 3rd. et al. Association Between Chronic Aspiration and Chronic Airway Infection with Pseudomonas aeruginosa and Other Gram-Negative Bacteria in Children with Cerebral Palsy. Lung. 2016; 194(2): 307–14. DOI: 10.1007/s00408-016-9856-5. Epub 2016 Feb 16. PMID: 26883134.
6. Marpole R., Blackmore A.M., Gibson N. et al. Evaluation and Management of Respiratory Illness in Children With Cerebral Palsy. Front Pediatr. 2020; 8: 333. DOI: 10.3389/fped.2020.00333. PMID: 32671000; PMCID: PMC7326778.
7. Blackmore A.M., Bear N., Blair E. et al. Prevalence of symptoms associated with respiratory illness in children and young people with cerebral palsy. Dev Med Child Neurol. 2016; 58(7): 780–1.
8. Blackmore A.M., Bear N., Blair E. et al. Factors Associated with Respiratory Illness in Children and Young Adults with Cerebral Palsy. J Pediatr. 2016; 168: 151–7.e1.
9. Bonadies L., Zaramella P., Porzionato A. et al. Present and Future of Bronchopulmonary Dysplasia. J Clin Med. 2020; 9(5): 1539. DOI: 10.3390/jcm9051539. PMID: 32443685; PMCID: PMC7290764.
10. Govindaswamy A., Bajpai V., Trikha V. et al. Multidrug resistant Elizabethkingia meningoseptica bacteremia — Experience from a level 1 trauma centre in India. Intractable Rare Dis Res. 2018; 7(3): 172–6. DOI: 10.5582/irdr.2018.01077. PMID: 30181936; PMCID: PMC6119665.
11. Lau S.K., Chow W.-N., Foo C.-H. et al. Elizabethkingia anophelis bacteremia is associated with clinically significant infections and high mortality. Sci. Rep. 2016; 6: 26045. DOI: 10.1038/srep26045.
12. Dziuban E.J., Franks J.L., So M. et al. Elizabethkingia in children: A comprehensive review of symptomatic cases reported from 1944 to 2017. Clin. Infect. Dis. 2018; 67: 144–9. DOI: 10.1093/cid/cix1052.
13. Opota O., Diene S.M., Bertelli C. et al. Genome of the carbapenemase-producing clinical isolate Elizabethkingia miricola EM_CHUV and comparative genomics with Elizabethkingia meningoseptica and Elizabethkingia anophelis: Evidence for intrinsic multidrug resistance trait of emerging pathogens. Int. J. Antimicrob. Agents. 2017; 49: 93–7. DOI: 10.1016/j.ijantimicag.2016.09.031.
14. Swain B., Rout S., Otta S., Rakshit A. Elizabethkingia meningoseptica*:* An unusual cause for septicaemia. JMM Case Rep. 2015; 2: e000005. DOI: 10.1099/jmmcr.0.000005.
15. Lee C.-H., Lin W.-C., Chia J.-H. et al. Community-acquired osteomyelitis caused by Chryseobacterium meningosepticum: Case report and literature review. Diagn. Microbiol. Infect. Dis. 2008; 60: 89–93. DOI: 10.1016/j.diagmicrobio.2007.07.009.
16. Gupta P., Zaman K., Mohan B., Taneja N. Elizabethkingia miricola: A rare non-fermenter causing urinary tract infection. World J. Clin. Cases. 2017; 5: 187. DOI: 10.12998/wjcc.v5.i5.187.
17. Raghavan S., Thomas B., Shastry B. Elizabethkingia meningoseptica*:* Emerging multidrug resistance in a nosocomial pathogen. Case Rep. 2017; 2017: bcr-2017-221076. DOI: 10.1136/bcr-2017-221076.
18. Young S.M., Lingam G., Tambyah P.A. Elizabethkingia meningoseptica Engodenous Endophthalmitis — A Case Report. Antimicrob. Resist. Infect. Control. 2014; 3: 35. DOI: 10.1186/2047-2994-3-35.
19. Yang J., Xue W., Yu X. Elizabethkingia meningosepticum endocarditis: A rare case and special therapy. Anatol. J. Cardiol. 2015; 15: 427. DOI: 10.5152/akd.2015.6014.
20. Chi S., Fekete T. Epididymo-orchitis. In: Schlossberg D., editor. Clinical Infectious Disease. 2nd ed. Cambridge University Press; Cambridge, UK. 2015: 401–5.
21. Gonzalez C., Coolen-Allou N., Allyn J. et al. Severe sepsis and pulmonary abscess with bacteremia due to Elizabethkingia miricola. Med. Mal. Infect. 2015; 46: 49–51. DOI: 10.1016/j.medmal.2015.10.011.
22. aufiq Kadafi K., Yuliarto S., Aji Cahyono H. et al. Cerebral Salt Wasting Due to Bacteremia Caused by Elizabethkingia meningoseptica: A Case Report. Arch. Pediatr. Infect. Dis. 2020; 8: e44832. DOI: 10.5812/pedinfect.88432.
23. Kenna D.T., Fuller A., Martin K. et al. rpoB gene sequencing highlights the prevalence of an E. miricola cluster over other Elizabethkingia species among UK cystic fibrosis patients. Diagn. Microbiol. Infect. Dis. 2018; 90: 109–14. DOI: 10.1016/j.diagmicrobio.2017.10.014.
24. Amir A., IC Sam J., Nawi S. Elizabethkingia meningoseptica neonatal meningitis in a premature infant. Asian J. Med. Biomed. 2018; 2(Suppl. 1): 22.

25. Seong H., Kim J.H., Kim J.H. et al. Risk factors for mortality in patients with elizabethkingia infection and the clinical impact of the antimicrobial susceptibility patterns of elizabethkingia species. J. Clin. Med. 2020; 9: 1431. DOI: 10.3390/jcm9051431.
26. Nori P., Cowman K., Chen V. et al. Bacterial and fungal coinfections in COVID-19 patients hospitalized during the New York City pandemic surge. Infect. Control Hosp. Epidemiol. 2021; 42: 84–8. DOI: 10.1017/ice.2020.368.
27. Yang C., Liu Z., Yu S. et al. Comparison of three species of Elizabethkingia genus by whole-genome sequence analysis. FEMS Microbiol. Lett. 2021; 368: fnab018. DOI: 10.1093/femsle/fnab018.
28. King E.O. Studies on a group of previously unclassified bacteria associated with meningitis in infants. Am. J. Clin. Pathol. 1959; 31: 241–7. DOI: 10.1093/ajcp/31.3.241.
29. Nicholson A.C., Gulvik C.A., Whitney A.M. et al. Revisiting the taxonomy of the genus Elizabethkingia using whole-genome sequencing, optical mapping, and MALDI-TOF, along with proposal of three novel Elizabethkingia species: Elizabethkingia bruuniana sp. nov., Elizabethkingia ursingii sp. nov., and Elizabethkingia occulta sp. nov. Antonie Van Leeuwenhoek. 2018; 111: 55–72. DOI: 10.1007/s10482-017-0926-3.
30. Hwang J.-H., Kim J., Kim J.-H., Mo S. Elizabethkingia argenteiflava sp. nov., isolated from the pod of soybean, Glycine max. Int. J. Syst. Evol. Microbiol. 2021; 71: 004767. DOI: 10.1099/ijsem.0.004767.
31. Hem S., Jarocki V.M., Baker D.J. et al. Genomic analysis of Elizabethkingia species from aquatic environments: Evidence for potential clinical transmission. Curr. Res. Microb. Sci. 2022; 3: 100083. DOI: 10.1016/j.crmicr.2021.100083.
32. Zajmi A., Teo J., Yeo C.C. Epidemiology and Characteristics of Elizabethkingia spp. Infections in Southeast Asia. Microorganisms. 2022; 10(5): 882. DOI: 10.3390/microorganisms10050882. PMID: 35630327; PMCID: PMC9144721.
33. Breurec S., Criscuolo A., Diancourt L. et al. Genomic epidemiology and global diversity of the emerging bacterial pathogen Elizabethkingia anophelis. Sci. Rep. 2016; 6: 30379. DOI: 10.1038/srep30379.
34. Lin J.-N., Lai C.-H., Yang C.-H., Huang Y.-H. Elizabethkingia infections in humans: From genomics to clinics. Microorganisms. 2019; 7: 295. DOI: 10.3390/microorganisms7090295.
35. Kwambana-Adams B., Laxton C., Foster-Nyarko E. et al. Isolation of Methicillin-resistant Staphylococcus aureus and Multidrug-resistant Elizabethkingia meningoseptica from Neonates within Minutes of Birth. Pediatric Infect. Dis. J. 2017; 36: 123–4. DOI: 10.1097/INF.0000000000001368.
36. Huang Y., Huang Y., Lin Y. et al. Risk factors and outcome of levofloxacin-resistant Elizabethkingia meningoseptica bacteraemia in adult patients in Taiwan. Eur. J. Clin. Microbiol. Infect. Dis. 2017; 36: 1–8. DOI: 10.1007/s10096-017-2942-7.