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ACUTE OTITIS IMMUNOLOGICAL PROPERTIES IN CHILDREN WITH TYPE 1 DIABETES

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✓ ***Resume***

The purpose of this study is to study the features of the clinic and the course of acute otitis media in children with type- 1 diabetes mellitus. It is shown that with type -1 diabetes mellitus, children under 14 years old with acute otitis media is 60 patients. Of these, 32 patients are boys, and 28 girls. As a result of the analysis of our data, it was found that the most common signs of acute otitis media in children are: ear pain, suppuration, fever, toxicosis, exsicosis. The peculiarity of the clinical manifestation of acute otitis media in children, in our opinion, is primarily associated with both the biological properties of the virus (damage to immunocomponent cells) and the anatomical and physiological characteristics of the child's body. Summarizing, it should be noted that the clinic and the course of acute otitis media in children with type -1 diabetes mellitus are similar to those in uninfected children, that is, when choosing antibiotic therapy, doctors should follow the same recommendations as in the treatment of acute otitis media in immunocomponent children.

Key words: acute otitis media, diabetes mellitus, children, antibiotic therapy.

ИММУНОЛОГИЧЕСКИЕ ОСОБЕННОСТИ ОСТРОГО ОТИТА У ДЕТЕЙ С САХАРНЫМ ДИАБЕТОМ 1 ТИПА

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✓ ***Резюме***

Целью данного исследования является изучение особенностей клиники и течения острого среднего отита у детей с сахарным диабетом 1 типа. В результате анализа наших данных было установлено, что наиболее распространенными признаками острого среднего отита у детей являются: боль в ухе, нагноение, лихорадка, токсикоз, эксикоз. Особенность клинического проявления острого среднего отита у детей, на наш взгляд, в первую очередь связана как с биологическими свойствами вируса (повреждение иммунокомпонентных клеток), так и с анатомо-физиологическими особенностями детского организма. Следует отметить, что клиника и течение острого среднего отита у детей с сахарным диабетом 1 типа аналогичны таковым у неинфицированных детей.

Ключевые слова: острый средний отит, сахарный диабет, дети, антибактериальная терапия.

1-TOIFA DIABET BILAN OG'RIGAN BOLALARDA O'TKIR OTITNING IMMUNOLOGIK XUSUSIYATLARI

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✓ ***Rezyume***

Ushbu tadqiqotning maqsadi 1 – tip qandli diabet bilan kasallangan bolalarda kasallikning klinikasi va kechish xususiyatlarini o'ziga xosligini o'rganishdir. Ma'lumotlarimizni tahlil qilish natijasida bolalarda o'tkir otitning eng keng tarqalgan belgilari: quloq og'rig'i, yiringlash, isitma, toksikoz, ekssikoz ekanligi aniqlandi. Bolalarda o'tkir otit vositalarining klinik namoyon bo'lishining o'ziga xos xususiyati, bizning fikrimizcha, birinchi navbatda virusning biologik xususiyatlari (immunokomponent hujayralarning shikastlanishi) va bola tanasining anatomik va fiziologik xususiyatlari bilan bog'liq. Xulosa qilib shuni ta'kidlash kerakki, -1-toifa qandli diabet bilan og'rigan bolalarda o'tkir otit klinikasi va kechish xususiyati infektsiyalanmagan bolalarnikiga o'xshaydi.

Kalit so'zlar: o'tkir otitis media, diabetes mellitus, bolalar, antibakterial terapiya.

Relevance

The problem of type 1 diabetes mellitus (DM) in children is urgent due to the ongoing development of the pandemic of this disease among the children's population around the world [1,8].ENT disease- is one of the most common and dangerous diseases of childhood, it occurs as a complication of viral, respiratory, bacterial, fungal infections. One of the serious complications From childhood is the lesion of the ENT organs, where the risk of intracranial complications increases sharply, leading to an unfavorable outcome of the underlying disease [2,6].

Recently, middle ear diseases have been leading in the structure of childhood morbidity worldwide. According to the World Health Organization (WHO), approximately 15-20% of the world's adult population and 10-150.4 children suffer from some form of otitis media.Among the clinical forms of otitis, acute otitis media accounts for 50-59% in children, while the frequency of chronic otitis media ranges from 5 to 20%, which leads to a high burden on the healthcare system[3,4,9]. Currently, an average of about 400 million people are infected with diabetes, more than 15 0/6 of whom are children. With the combination of AOM and DM, prerequisites are created for the persistence of a purulent infection focus, as well as for the progression of spleen damage in children. Timely detection and early treatment of middle ear diseases in children with DM will provide a favorable prognosis for both diseases, taking into account their mutually aggravating influence. At the same time, the identification of common syndromes and their pathogenesis in DM and AOM is a priority in the field of pediatrics and otorhinolaryngology [5,7].

Another classic manifestation of DM that an otorhinolaryngologist may encounter is the development of acute otitis media. This dictates the urgent need to carry out the study.

In this regard, **the purpose** of this study was to study the clinical and immunological features of acute otitis media in children with type 1 diabetes mellitus.

Materials and methods

During the period from may 2021 to july 2023, 60 children with a diagnosis of type 1 diabetes mellitus were under our supervision. The study was conducted on the basis of the regional children's multidisciplinary hospital. The diagnosis of DM was established on the basis of Order No. 542 of the Ministry of Health. The material of the study was 60 sick children for 2021-2023 up to 14 years with diabetes. Boys make up 32 (53.3%) of patients, and girls 28 (46.7%).

The children were examined regardless of the presence of complaints. In addition to standard methods of examination (general blood, urine, bacteriological and biochemical studies), we conducted a thorough otorhinolaryngological examination (otoscopy, anterior rhinoscopy, laryngoscopy, accumetry, impedance measurement, audiometry, vestibulometry) for all children, and X-ray examination in 8 (13.4%).

Results and their discussions

As a result of the analysis of the data obtained by us, it was found that the most common signs of acute otitis media in children are: ear pain (100%), suppuration (100%), fever (100%), Tweezer symptom (30%), Wache symptom (47%), sepsis (43%), the phenomenon of meningism (17.7%), convulsions (42%), breast rejection (29.4), toxicosis (12%), exicosis (56%), nasal discharge (29.4%) and malaise (5.6%). Most of the children had candidiasis lesions of the middle ear.

The peculiarity of the clinical manifestation of acute otitis media in children, in our opinion, is primarily due to both the biological properties of the virus (rapid replication, damage to

immunocomponent cells, high genetic variability) and the anatomical and physiological characteristics of the child's body. These include the inability to develop an adequate immune response against diabetes mellitus, a large number of target cells for the virus, physiological immaturity of various systems and organs, including the middle ear.

As a result, children have a more rapid formation of a deep immunodeficiency state (ID) and severe multiple organ pathology, including a wide range of virus-associated (basic symptoms), opportunistic infections, malignant tumors, which causes difficulties in the clinical diagnosis of diabetes in childhood.

It is important to note that with the duration of the disease in the spectrum of clinical manifestations, our patients had a lesion of the middle ear, the symptoms of which are indicated in

Table No. 1.

Clinical manifestations of acute otitis media in children with type 1 diabetes mellitus

Symptoms of the disease	Children with diabetes mellitus (n=17)	Children with out diabetes (n= 15)
Ear pain	17(100%)	1(6,7%)
Suppuration	17(100%)	8(53,3%)
Increase in body temperature	17(100%)	12 (80%)
Prince's Symptom	5(29,4%)	1(6,7%)
The symptom is yours	8(47%)	7(46,7%)
Sepsis	15(88%)	-
Throwing back the head	2(11,7%)	-
Is a phenomenon of meningism	3(17,7%)	-
Convulsions	15(88%)	7(46,7%)
Breast rejection	5(29,4%)	2(13,3%)
Toxicosis	2(11,7%)	-
Exicosis	15(88%)	12(80%)
Nasal discharge	5(29,4%)	-
Vomiting	15(88%)	1(6,7%)
Diarrhea	11(64%)	-
Malaise	1(5,8%)	1(6,7%)

Children with diabetes mellitus had AOM symptoms in the form of Penza symptom (29.4%), Vash symptom (47%), sepsis (88%), suppuration (100%).

When analyzing the severity of immunosuppression in patients of the compared groups, significant differences were also revealed. In prenatally infected children, pronounced immunosuppression was shown in comparison with parenterally infected children. The average value of CD4+ lymphocytes in children with congenital pathology was 23.25 ±6.04%, in children with acquired pathology this indicator was slightly higher than 24.6 ±2.3%.

Similar changes were observed on the part of CD8 lymphocytes, which manifested themselves in a sharp decrease in this indicator in patients of group 2 compared with patients of group 1. An increase in the level of IgG and IgM immunoglobulins was noted in individuals of both groups compared with those in healthy children, however, group differences in the compared groups were not expressed. A characteristic feature of immune disorders in our children is the absence of statistically significant changes in Ig A in comparison with healthy children (table 2).

Table 2

Indicators of immunological status in children with AOM on the background of type 1 diabetes mellitus

Indicator	Healthy	Children with diabetes mellitus	Children without diabetes
Leukocytes, cl/mcl	6100±0,6	5600±912,69	4375±35б,7
Lymphocytes, %	40,9±1,9	31,4±7,15	30,25±7,2
Lymphocytes, abs.	2452,4±211,9	1905,2±67б,82	1075,75± 112,87
T-lymphocytes, %	58,8±2,0	48,4±7,6	42±4,7
T-lymphocytes, abs.	1393,5±110,5	762,6±178,72	527±53,19
CD 4, %	34,б±1,8	24,6±2,3	23,25±6,04
CD 8, %	22,9±1,0	34,6±4,8	2б,5±4,7
CD 4/ CD 8	1,5±0Д	0,82±0,14	0,965±0,27
CD 19, %	24,3 ±1,22	29,62±5,4	29,75+7,68
CD 19, abs..	583,5±49,7	514,2±130,8	155,75±17,5
Ig A, мг%	1047,3±35,7	94,4±8,7	93,75±23,29
Ig M, мг%	90,1±6,6	150,4±14,1	146,25±13,13
Ig G, мг%	129,2±10,8	1085,6±45,19	988,75±57,18
CD 16, %	15,10,8	26,2±4,5	30,25±3,77

The results of studying the level of anti-inflammatory cytokines in peripheral blood serum against the background of type 1 diabetes mellitus are presented in table 3.

Table 3.

The content and anti-inflammatory cytokines in the background of type 1 diabetes mellitus in the dynamics of treatment

Indicator	Control group	Main group
IFN-γ, pg/ml	23,70 ± 5,38	82,80 ± 25,07
		21,93 ± 5,28
IL-10, pg/ml	10,95 ± 3,65	86,08 ± 25,72
		52,04 ± 15,06
Note: in the numerator, the data before treatment, in the denominator - after treatment; * - P< 0.05 compared to the control group;		

The analysis of the results revealed the presence of significant differences between the values of the main group and the control group. So, for example, if in healthy children the level of IFN-γ was 23.70 ± 5.38 pg/ml, then in children with diabetes mellitus with AOM, the same parameter was 3.5 times higher and was at the level of 82.80 ± 25.07 g/ml (table №3).So, a high level of IFN-γ in children with diabetes mellitus with AOM testified to the severity of the degree of inflammatory reaction.

It is known that the source of IFN-γ is activated T-lymphocytes and natural killers.Among T-lymphocytes, IFN-γ producers are both cytotoxic CD8+ and helper CD4+ cells, however, when the latter differentiate into Th1 and Th2, only Th1 cells retain the ability to produce IFN-γ.

The most important function of IFN-γ is its participation in mediating the relationships between lymphocytes and macrophages, as well as in regulating the ratio of cellular and humoral components of the immune response.Being the main product of Th1 cells, IFN-γ reduces the secretory activity of Th2 cells.Thus, IFN-γ enhances the development of cellular immunity and suppresses the manifestations of humoral immunity.Therefore, IFN-γ plays an important role in immunoregulation, being a key cytokine of the cellular immune response and an inhibitor of the humoral immune response.

The level of IL-10 in the group of children with diabetes mellitus with AOM was approximately 8 times higher than those of the control group. It is known that IL-10 is described as a factor stimulating B lymphocytes, since it causes the proliferation of B cells.

The main producers of IL-10 are Th2 cells. IL-10 suppresses the functions of macrophages and their

secretion of IL-1, TNF and IL-6, while having an anti-inflammatory effect. IL-10 causes the proliferation and differentiation of B and T lymphocytes, affects the development of hematopoietic cells, macrophages, natural killers, basophils, being a functional antagonist of cytokines produced by Th1 cells. IL-10 promotes the development of allergic reactions, has a pronounced antiinflammatory effect. Comparative analysis showed that the ratio of IFN-γ/ IL-10 (pro-inflammatory/anti-inflammatory cytokines or Th1/Th2) in healthy children was 2.2. In the presence of a pronounced inflammatory process, that is, in children of the main group, this indicator was 0.96.A pronounced imbalance in the functioning of the main regulatory cytokines was revealed, which was expressed by a sharp rise in the level of anti-inflammatory cytokines and suppression of pro-inflammatory cytokines, which are the main regulators of acute inflammatory conditions.

Thus, in AOM there is a pronounced stimulation of the production of both pro-inflammatory and anti-inflammatory cytokines. Such processes can be a necessary condition for protection against an infectious agent and the systemic damaging effect of high concentrations of proinflammatory cytokines. After treatment in the group with diabetes mellitus with AOM, the level of IFN-γ approached the control values, and the level of IL-10 in the dynamics of treatment decreased, but still remained at a high level, 5.5 times exceeding those parameters in children of the control group. The ratio of IFN-γ/IL-10 in the main group tended to decrease even more, amounting to 0.42.

Conclusions

The presented data indicate the features of the clinical and immunological course of AOM in children with type 1 diabetes mellitus.

1.All children have symptoms of AOM, bacterial infections, generalized lymphadenopathy, hepatomegaly, sepsis, disseminated cytomegalovirus infection, severe herpetic infection against the background of a deep underlying disease. In children, Pinsa symptom, Vash symptom, convulsive manifestations were noted in smaller numbers.

2. Children with type 1 diabetes have pronounced immunosuppression compared to children without diabetes, whose immune system was in a more mature state at the time of the disease.

3. On the part of the immune system, the absence of statistically significant changes in the SHPA indicator compared to the control group was characteristic.

4. Under the influence of the treatment, there was a noticeable improvement in the clinical condition of the children of the main group, which, along with the suppression of the proinflammatory cytokine IFN-γ, was accompanied by the disappearance of clinical symptoms of AOM.However, it should be emphasized that the revealed change in the level of IL-10 and the violation of the quantitative ratio of pro- and anti-inflammatory cytokines indicates the presence of a pre-existing immunodeficiency condition, which, apparently, manifested itself in the form of complications against the background of type 1 diabetes mellitus.

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