



Clinical and Immunological Features of The Course of Acute Otitis Media in Children with Type 1 Diabetes Mellitus

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Article History	Abstract
Received: 06 June 2023 Revised: 05 Sept 2023 Accepted: 13 Oct 2023	<p><i>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, exsiccosis. 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.</i></p>
CC License CC-BY-NC-SA 4.0	<p>Keywords: <i>Acute otitis media, Diabetes mellitus, Children, Antibiotic therapy.</i></p>

1. Introduction

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 [1.3.7.9].

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 [2.4.6.8].

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.

2. 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%).

3. Results and Discussion

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 [11.13.15.17.19.21].

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 1.

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 $23.25 \pm 6.04\%$, in children with acquired pathology this indicator was slightly higher than $24.6 \pm 2.3\%$.

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 N 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±356,7
Lymphocytes, %	40,9±1,9	31,4±7,15	30,25±7,2
Lymphocytes, abs.	2452,4±211,9	1905,2±676,82	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, %	34,6±1,8	24,6±2,3	23,25±6,04
CD 8, %	22,9±1,0	34,6±4,8	26,5±4,7
CD 4/ CD 8	1,5±0,1	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, mΓ%	1047,3±35,7	94,4±8,7	93,75±23,29
Ig M, mΓ%	90,1±6,6	150,4±14,1	146,25±13,13
Ig G, mΓ%	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 No.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
		82,80 ± 25,07
IFN-γ, pg/ml	23,70 ± 5,38	21,93 ± 5,28
		86,08 ± 25,72
IL-10, pg/ml	10,95 ± 3,65	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.

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 anti-inflammatory 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 [10.12.14.16.18.20.21].

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.

4. Conclusion

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.

References:

1. Azova E.A. Complications of type 1 diabetes mellitus in children and adolescents: regional monitoring, optimization of medical care // *International Endocrinological Journal*. 2019. - No. 4.-P. 24-28.
2. Kosyakov S.Ya., Lopatin A.S. Modern principles of treatment of acute moderate, prolonged and recurrent acute otitis media // *RMZH*.-2002.-No. 20.-P.903–909.
3. Kryukov A. I., Turovsky A. B. Clinic, diagnosis and treatment of acute inflammation of the middle and outer ear // *www.MedLinks.Ru*.-2010.-P.43-45.
4. Narzullaev N.U. Clinical and epidemiological characteristics of acute otitis media in HIV-infected children. *Tibbiyda yangi kun*. No. 2 (26). Tashkent 2019.-P.227-229.
5. Narzullaev N.U. Cytokine profile of children with acute inflammation of the middle ear in acute respiratory disease on the background of treatment. *Dr. akhborotnomasi*. №2. Samarkand. 2019.-P.80-83.
6. Daly KA, Brown JE, Lindgren BR et al. Epidemiology of otitis media onset by six months of age. *Pediatrics* 2019; 103: -P.1158–66.
7. Dowell, S. F., Butler, J. C., Giebink, G. S. et al. Acute otitis media: management and surveillance in an era of pneumococcal resistance – a report from the Drug-resistant *Streptococcus pneumoniae* Therapeutic Working Group. *Pediatr. Infect. Dis. J.* 18 (2009).-P.1–9.
8. Healy GB. Otitis media and middle ear effusions. In: Ballenger JJ, Snow JB, Ed. *Otorhinolaryngology: Head and Neck Surgery*. 15th edition. Baltimore: Williams & Wilkins, 2006.-P.1003–1009.
9. Marchisio, P., Principi, N., Sorella, S., Sala, E. & Tornaghi, R. Etiology of acute otitis media in human immunodeficiency virus-infected children. *Pediatr. Infect. Dis. J.* 15 (2016).-P.58–61.
10. Нарзуллаев Н.У. Опыт лечения отоанtritов у ВИЧ-инфицированных детей // *Журнал теоретической и клинической медицины*. - Ташкент, 2010. - №6. - С. 86-88. (14.00.00; №3).
11. Гариб В.Ф., Хасанов С.А., Нарзуллаев Н.У. Особенности антибактериальной терапии у ВИЧ-инфицированных детей с острым средним отитом // *Журнал теоретической и клинической медицины*. - Ташкент, 2010. - №5. - С. 115-118. (14.00.00; №3).
12. Нарзуллаев Н.У., Нуров У.И., Пардаев М.С. Эпидемиологическая характеристика заболеваемости ЛОР-органов у ВИЧ-инфицированных детей // *Стоматология*. – Ташкент, 2010. - №3-4, - С. 29-31. (14.00.00; №12).
13. Нарзуллаев Н.У., Вохидов Н.Х., Раджабов Р.Р. Особенности течения острого среднего отита у детей инфицированных вирусом иммунодефицита человека // *Стоматология*. - Ташкент, 2010. - №3-4. - С. 89-90. (14.00.00; №12).
14. Нарзуллаев Н.У. Стартовая антибиотикотерапия при остром среднем отите и остром синусите у ВИЧ-инфицированных детей // *Инфекция, иммунитет и фармакология*. - Ташкент, 2010. - №5. - С.45-48. (14.00.00; №15).
15. Нарзуллаев Н.У. Клинико-иммунологические особенности течения острого среднего отита у ВИЧ-инфицированных детей в зависимости от путей инфицирования // *Инфекция, иммунитет и фармакология*. – Ташкент, 2010. - №5. - С. 49-51. (14.00.00; №15).
16. Нарзуллаев Н.У., Ахмедов А.Т., Хомидов Ф.К. Микозы в структуре оппортунистических заболеваний полости рта и глотки у ВИЧ-инфицированных детей // *Журнал теоретической и клинической медицины*. – Ташкент, 2011. - №3. – С. 115-117. (14.00.00; №3).
15. Нарзуллаев Н.У., Хомидов Ф.К., Ахмедов А.Б. Местная терапия воспалительной патологии глотки у ВИЧ-инфицированных детей // *Инфекция, иммунитет и фармакология*. – Ташкент, 2011. - №1-2. - С. 249-253. (14.00.00; №15).
16. Нарзуллаев Н.У., Хасанов С.А., Хомидов Ф.К. Иммунные нарушения у новорожденных и грудных ВИЧ-инфицированных детей с острым средним отитом // *Инфекция, иммунитет и фармакология*. – Ташкент, 2011. - №1-2. - С. 254-258. (14.00.00; №15).
17. Narzullayev N.U., Suleymanov S.F., Ismailova A.A., Sabitova R.Z. Immune Status of HIV-positive Children with Acute Rhinosinusitis // *International Journal of Public Health Science (IJPHS) USA*. – 2013. - Vol. 2, №3. - P. 83-88. IF- 1,966.
18. Нарзуллаев Н.У., Вохидов Н.Х., Раджабов Р.Р., Адилова Г.М., Нуров У.И. Эффективность применения амоксициллина с рокситромицином при лечении воспалительных заболеваний ЛОР-органов у ВИЧ-инфицированных больных // *Биология ва тиббиёт муаммолари*. – Самарқанд, 2013. - № 4.1. - 72-73б. (14.00.00; №19).
19. Narzullayev N. U. The characteristic of the immune status at HIV-infected children with acute rhinosinusitis // *European Science Review*. - Austria, 2015. -№ 7-8. - P. 85-89. (14.00.00; №19)
20. Нарзуллаев Н.У., Сулейманов С.Ф. Параметры иммунного статуса у ВИЧ-инфицированных детей с острым риносинуситом // *Журнал инфектологии*.- Санкт-Петербург, 2017.-С.24-28. (14.00.00; №162).
21. Narzullayev N.U. FarGALS efficiency in complex treatment of HIV-infected children with acute purulent sinusitis // *European Science Review* . Austria, 2017 №1-2 P.86-88.(14.00.00; №19)