Modern pediatrics 3 (37) / 2011

FORECASTING HEALTH STATUS OF CHILDREN WITH EARLIEST MANIFESTATIONS OF ATOPIC DERMATITIS

T.L. Protsyuk, N.I. Tocarchuk, L.A. Protsyuk, O. V. Chirka, N.M. Surkova, L.D. Kotsur
National Pirogov Memorial Medical University, Vinnytsya М.И. Пирогова
Vinnytsya Regional Children's Clinical Hospital

Summary. *The prognosis of early manifestations of atopic dermatitis depends on the quality of supervision, the adequacy of the antiallergic activities and severity of clinical manifestations of the pathological process of the skin. Immune status of children with severe and moderate atopic dermatitis is characterized by decreased levels of total IgG, hyperimmunoglobulinemia E, low IgA in patients over the age of 6 months. In severe and moderate atopic dermatitis a significant delay in timing of vaccination in children is observed. In mild atopic dermatitis most of the children's vaccination is timely performed. Vaccination of children with early manifestation of moderate to severe atopic dermatitis should be carried out during the period of remission on the background preparation. Preparations for the vaccination can inculcate children with severe atopic dermatitis without any side-effects and pronounced exacerbation of the pathological process.*

Key words: *atopic dermatitis, children, specific IgE, vaccination.*

INTRODUCTION

Atopic dermatitis (AD) usually occurs in early childhood and is diagnosed in the first year of life in 60-70% of children. Severe forms of AD dramatically reduce the quality of life of the patient and the whole families, contributing to the formation of psycho-somatic disorders. In cases of pronounced hereditary predisposition to atopic and allergic reactions, the disease can develop for many years with the formation of typical clinical criteria of Raika and other attributes of atopy, which defines the classical course of atopic dermatitis. The prognosis of AD is varied. In many respects it not only depends on the presence of family history of allergic heredity, but also on the tactics of management of children suffering from AD, including the vaccination regime.

Objectives of the study: to study the health status of infants of the first year of life with an early manifestation of atopic dermatitis; to determine the prognosis of the disease with different severity of the pathological process; to optimize methods of prevention of exacerbations and preparation for vaccination in this pathology.

MATERIAL AND METHODS OF THE STUDY

90 infants in the first year of life with severe (45 patients) and moderate (45 patients) atopic dermatitis (group 1) and 50 patients in the first year of life with mild forms of atopic dermatitis - (group 2) were examined. Follow-ups of children were carried out during 4 years.

The clinical-anamnestic method was used in the work, including the study of the past medical history (PMH) of children (registration form No. 112 / y) and the questionnaire survey of parents. The following data was taken into account in the questionnaire: hereditary atopy, perinatal risk factors, the age of the parents at the time of childbirth, breastfeeding duration, the age of the child at the time of the first allergic reactions, the presence of background conditions in the first year of life, the timing of preventive vaccination. Objective examination was conducted in accordance with common methods with an emphasis on the skin condition. The presence of skin changes and assessment of the severity of the skin process was carried out in dynamics on the SCORAD scale.

All children underwent general clinical examinations, immunological tests with determination of cellular and humoral immunity parameters, serological methods.

The used allergological methods included the definition of total eosinophilia in calculating the leukocyte formula and evaluating the absolute content of eosinophils. The level of total serum immunoglobulin E (IgE) and allergen-specific IgE antibodies was assessed by the method of semiquantitative ELISA.

A solid-phase enzyme-linked immunoassay was used for the diagnosis of herpesvirus infections.

Secondary prophylaxis was carried out for children with early manifestation of severe and moderate AD to prevent exacerbations of the underlying disease and the formation of bronchial asthma. All discharged infants and breastfeeding mothers were recommended individual hypoallergenic diet, the introduction of supplemental feeding was performed individually with the selection of products that do not cause exacerbation of AD.

All discharged infants were given recommendations on compliance with the elimination diet, with the exception of causative significant allergens for a period of at least 6 months. The courses of enterosorbents (polysorb, enterosgel) were prescribed in individual dosages for 5-7 days each month during 3-6 months. All children were recommended to continue taking the antihistamine drug long-term (1 to 12 months), depending on AD severity. Upon indications - repeated courses of enzyme preparations, pro- and prebiotics. The use of medicinal cosmetics was suggested for regular skin treatment.

To analyze the results, the conventional methods of variational statistics were used on the basis of an analysis of absolute and relative magnitudes, the arithmetic mean, mean square deviation, the t and p Student's criteria. The relationship between the two features was studied by Pearson (r) or Spearman (rs) correlation methods. The correlation degree was determined by means of the correlation coefficient. Differences or interconnection rates were

considered statistically significant at p <0.05. To estimate the relative risk, the odds ratio was calculated according to the I.A. Kelmanson's method (2002).

Table

PMH data of children with atopic dermatitis of severe and moderate course (%)

PMH data	Group of children with severe AD (n = 45)	Group of children with moderate AD (n = 45)
Pathological labour	45.8	28,0
Breastfeeding in delivery room	52.4	79.1*
Toxic arrythmia in the first three days after birth	9.4	2.8
Duration of breastfeeding exceeds 1 year	24.2	56.0*
First manifestations of atopic dermatitis in infants under 6 months	93.2	87.0
Causes of atopic dermatitis: - diet violation by a breastfeeding mother - introduction of milk mixtures	50.0 38.7***	50.0 7.8
Concomitant pathology: - secondary immunodeficiency state - congenital infection	50.0*** 60.0**	3.2 11.0

Note. Significance of differences between the main group and the comparison group: * - p <0.05; ** - p <0.01, *** - p <0.001.

The results of the studies were processed on a personal computer using Statistica and Microsoft Excel programs.

STUDY RESULTS AND DISCUSSION

During the study, it was found that among infants of up to 1 year old in both groups 1 and 2 (p <0.05) boys suffered from AD more often (65.7% and 55.8%) than girls (34.3% and 44.2% respectively). Positive hereditary PMH of atopy was revealed in 72.9% of patients from group 1 and 67.9% of patients from group 2. A matrilineal allergic anamnesis was noted in 34.7% of infants from group 1 and 25.0% - from group 2. 93.4% of all examined infants were born as a result of a pathological pregnancy. At the same time 63.1% of pregnant women violated the diet, and 52.0% of women received drug therapy during pregnancy. In 22.1% of cases, expectant mothers had various allergic reactions during pregnancy.

76.8% of all infants weighed 3.8 ± 0.3 kg at birth and were born with an Apgar score of 8/9. In the group of infants with early manifestation of mild AD, the majority (94.1%) were first breastfed in the delivery room, whereas in the group of infants with a severe and moderate AD course, - only 48.9%. 55.7% of all infants were breastfed for up to 6 months. Despite this, in 69.4% of cases in infants with severe and moderate course and 68.4% of cases with mild course of the disease the first AD manifestations appeared in infants of up to 3 months of age.

Analysis of possible causes of early development of severe and moderate AD showed that the most frequent were: diet violation by mother during breastfeeding of the child (54.6%), the introduction of milk formulas in the infant's diet, cow milk cereals (39.3%).

In the group of infants with early manifestation of mild AD, the first manifestations of the disease in 74% of infants were associated with a diet violation by mother. Among the concomitant pathologies in this group of children, perinatal CNS involvement and repeated ARVI prevailed.

Laboratory data analysis revealed no changes in the hemogram in 85.9% of children in the first year of life. A slight eosinophilia in the blood was detected only in 14.1% of children suffering from severe and moderate forms of AD. In a subgroup of 10-12-month-old patients, eosinopenia was detected in 89.4% of cases. Biochemical blood indices did not differ from those of healthy children. A coprological examination in most cases showed a steatorrhea. Intestinal biocenosis was disturbed in 85.7% of children, more often there was sowing of *Staphylococcus aureus*, a hemolyzing *E.coli*.

To determine the risk factors for development of severe and moderate AD in the first year of life, a comparative analysis of anamnestic data of patients with different severity of the disease was made. It was found that, in the early manifestation of severe AD, an unfavourable heredity in atopy prevailed, both maternal and paternal (p <0.001), significantly less infants of the main group were breastfed in the delivery room (p<0.05). In severe AD, patients in the first year of life were more often diagnosed with secondary immunodeficiency states (p <0.001) and intrauterine infections (p <0.01). AD in children with severe course of the disease was significantly more often caused by the introduction into the diet of milk formulas (p <0.001), while the duration of breastfeeding for more than a year prevailed (p <0.05) in the group of children with a moderate course of the disease (see the table).

Calculation of the odds ratio (OR) according to the method of I.A. Kelmanson (2002) showed that the probability of the development of severe AD increases 6.7-fold with the early introduction of milk formulas and cereals on whole cow's milk, 4.1-fold - presence of intrauterine virus infection in PMH of the child, 21-fold - secondary immune deficiency.

When assessing the immunoallergological status of children with severe and moderate AD, it was found that practically all patients had a lowered level of total IgG, in infants over 6 months of age a low IgA content was observed, changes in the cellular immunity level were multidirectional.

Depending on the prevalence of the skin process, analysis of the immune status indicators showed that the prevalent AD was characterized by lymphocytosis and elevated T-lymphocyte level, while diffuse AD - by leukocytosis, eosinophilia, low IgA level. The content of total IgE did not depend on the prevalence of skin lesion and significantly ($p < 0.001$) exceeded the normative values.

The immune status of patients with severe AD differed from that in the case of moderate course of significant eosinophilia (28.44 ± 3.60% vs. 10.00 ± 1.41%, respectively, $p < 0.001$), hyperimmunoglobulinemia E (550.70 ± 113.90 IU/ml vs. 52.76 ± 15.67 IU/ml, respectively, $p < 0.001$), low IgG level (3.07 ± 0.52 g/l versus 5.30 ± 0.69 g/l, respectively, $p<0.001$).

The total IgE in serum was increased in most patients (95.6%), and in 35.0% it exceeded the age norm by more than 10-fold. A weak direct correlation between the severity of the skin process and the level of total IgE ($rs = 0.277$, $p < 0.05$) and a weak inverse correlation between the serum IgA and the severity of skin allergic inflammation ($rs = 0.264$, $p < 0.05$) were found.

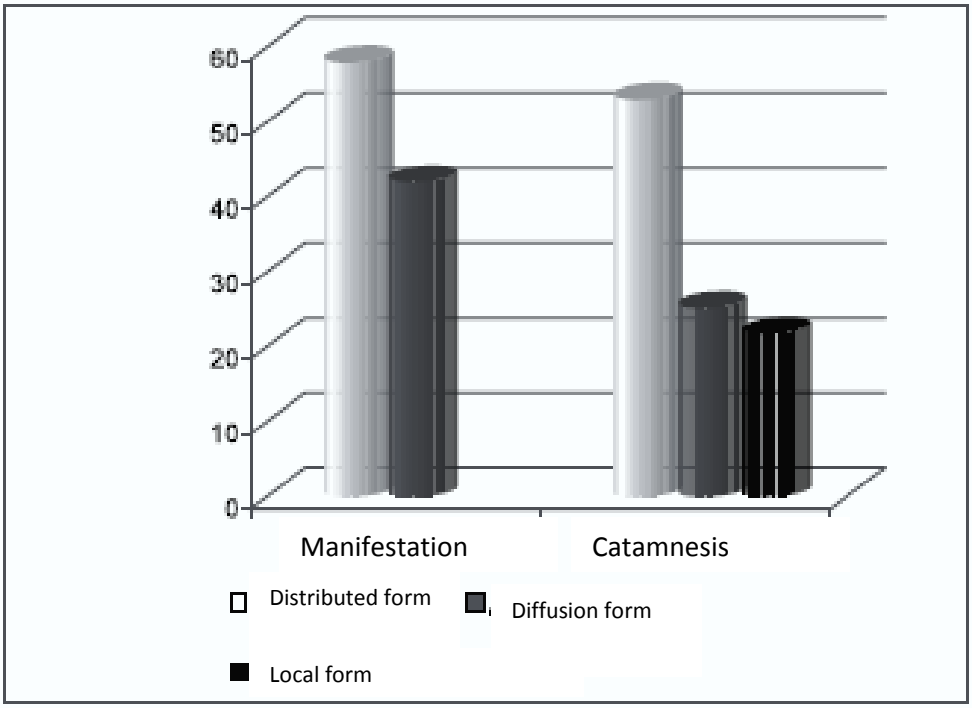

Figure The prevalence of the skin process when atopic dermatitis is manifested and in the catamnesis

The incidence of allergen-specific IgE antibodies varied from 11.7% to 41.2%. The average level of IgE antibodies was also different. Curious is the fact that sensitization to cow milk allergens was noted only in 11.7% of cases, and its level was low (0.40 ± 0.12).

In the hospital, children received combined therapy, including an individual hypoallergenic diet, enterosorbents, antihistamines, local therapy, according to indications - antibiotics, pancreatic enzymes, pre- and probiotics. At discharge, it was recommended to continue breastfeeding, and mothers were prescribed a hypoallergenic diet. In the case of artificial feeding the child was prescribed therapeutic mixtures with complete hydrolysis of cow's milk proteins, it was advised not to expand the range of foods in the nutrition of infants for 6-9 months. Hypoallergenic lifestyle recommendations were provided. All children were prescribed a long course (3-12 months) of antihistamines. To reduce dryness and restore the lipid layer of the skin, all discharged patients were recommended a long-term use of medicinal cosmetics.

1-3 years after discharge, a follow-up of children with an early manifestation of AD was carried out. It was revealed that in severe and moderate disease during the first year of life, a total regression of skin changes occurred in 27.6% of patients. The remaining children had AD manifestations, but the structure of the disease changed in severity: the subgroup of infants with moderate AD significantly decreased ($p < 0.05$) due to transformation into a mild form of the disease. 46% of patients had severe manifestations of the disease. Localized form of AD appeared (53.6%), the number of patients with a common ($p < 0.05$) and diffuse ($p < 0.01$) forms significantly decreased (Fig.). Skin changes in the children examined in the catamnesis differed from those in AD manifestation: significantly less ($p < 0.001$), dry skin and skin hyperemia were noted ($p < 0.001$). The pathological process was reliably less often located on the facial skin ($p < 0.001$), the skin of the body and extremities was more often affected.

At an early manifestation of severe and moderate AD, 39.3% of patients subsequently showed signs of obstructive bronchitis, bronchial asthma, pollinosis, allergic rhinitis. Correlation analysis revealed a strong direct correlation between the development of the "atopic march" and the allergic heredity of mother ($r_s = 0.625$, $p < 0.001$), perinatal CNS damage ($r_s = 0.640$, $p < 0.001$), total eosinophilia ($r_s = 0.632$, $p < 0.001$), an increase in the total IgE level of more than 800 IU/ml ($r_s = 0.701$, $p < 0.001$), the presence of specific IgE antibodies to household allergens ($r_s = 0.664$, $p < 0.001$).

A direct weak correlation was observed between the presence of severe AD and the formation of respiratory allergy ($r_s = 0.392$, $p = 0.020$).

In patients with severe AD manifestations, complete regression of skin manifestations was noted in 15.6% of cases, and in the remaining patients the severity of the disease changed: in 37.5% of cases it acquired a mild course, in 46.9% - moderate.

In the group of children with early manifestation of mild AD, complete regression of skin allergic changes was noted in 40% of patients, which is significantly more frequent ($p < 0.05$) than in the main group.

Thus, the prognosis for early AD manifestation depends to a large extent on the quality of observation, the adequacy of antiallergic activities and the severity of the clinical manifestations of the pathological skin process. Significant risk factors for the formation of respiratory allergy in children with severe and moderate AD are general eosinophilia, an increase in the total IgE level of more than 800 IU/ml, the presence of specific IgE antibodies to household allergens, family history of maternal allergic inheritance, perinatal CNS damage.

The follow-up immunological examination showed a significant reduction in the number of patients with a total IgE level, 2-10-fold higher than the age standard ($p < 0.05$).

The timing of vaccination of children with AD of varying severity was analyzed. At an early manifestation of severe and moderate AD, there was a significant delay in the timing of vaccination. Quite often vaccination of this group of children was started at the age of over 1 year (against hepatitis B - in 7.2% of cases, DPT vaccine and against poliomyelitis - in 49.2%, against measles and epidemic poliomyelitis - in 75.6% of cases).

In the early manifestation of mild blood pressure in most of the children, the vaccination was carried out within standard time limits. Over the age of 1 year, only 12.0% of patients received DPT vaccine and against poliomyelitis, against measles, epidemic parotitis, and rubella - in 9.8% of cases.

Unlike children with severe AD in the comparison group, the completion of DPT vaccine, against poliomyelitis ($p < 0.001$), measles, epidemic parotitis and rubella ($p < 0.001$) was significantly more frequent in the first year of life, as well as significantly more children with a mild AD were vaccinated with BCG at the maternity hospital ($p < 0.001$).

DPT vaccine and vaccination against poliomyelitis in the comparison group were delayed by 2-3 months from the standard dates, and in the main group the delay of vaccination exceeded 6 months ($p < 0.01$).

We have proposed a scheme of preparing for vaccination of children with severe and moderate AD. We recommend to follow diet with the exception of obligate allergens (fish, eggs, honey, chocolate, nuts, cocoa, citrus fruits, strawberries, wild strawberries), as well as abstain from the products that had previously caused allergic reactions or new foods in the diet. The diet was recommended to be observed for at least 1 week before the vaccination and 1 to 3 months after it. The scheme of individual preparation included enterosorbent, which was prescribed 1-1.5 hours before meals for 5 days. Antihistamines were given for 10 days before and 10 days after vaccination, and the daily dose was divided into two intakes. Given the presence of intestinal dysbiosis of varying severity in 81.2% of patients, a probiotic was introduced into the vaccination preparation schedule. This scheme of preparation for vaccination was used in 20 children with moderate AD and 7 patients with severe AD. Remission of the skin process in the group of infants suffering from a moderate degree of disease lasted from 1 to 6 months and averaged 4.6 ± 0.5 months. Children were vaccinated against measles, parotitis and rubella, DPT revaccination and against poliomyelitis. Against a background of vaccination against measles, parotitis and rubella, 3.1% of patients showed an exacerbation of the skin allergic process in the form of hyperemia, flaking of the skin in the elbows and popliteal pits. The value of total IgE before vaccination was 102.2 ± 65.26 IU/ml, after vaccination - 174.4 ± 119.4 IU/ml.

Children with severe AD were vaccinated against measles, parotitis and rubella and underwent DPT revaccination and against poliomyelitis. The remission stage in 68% of patients lasted from 1 to 3 months, in 32% the remission was incomplete.

Exacerbation of the underlying disease was recorded only in AD patients who were vaccinated at the stage of incomplete remission. The frequency of AD exacerbation was 4.5% after the introduction of DPT vaccine, 10.3% after vaccination against measles and epidemic parotitis. The average level of total IgE before vaccination in these patients was 970.0 ± 27.5 IU/ml, in the post-vaccination period - 1641.0 ± 453.6 IU/ml. The content of total IgE in the post-vaccination period increased briefly, and after 1.5-2 months its level was comparable to the baseline values.

Exacerbations of the skin allergic process after vaccination of children with severe and moderate AD were short-lived and corrected by prescribing antihistamines and local therapy.

CONCLUSIONS

Infants with mild forms of AD in the first year of life should be consulted by an allergologist-immunologist in order to identify risk factors for aggravation of skin process and the formation of respiratory allergy, in order to timely prescribe an adequate therapy. The immune status of children with severe and moderate AD is characterized by a decrease in the level of total IgG, low IgA in patients over 6 months of age. Changes in the cellular and phagocytic links of immunity are multidirectional.

Severe AD differs from the moderate course of the disease with reliable eosinophilia, hyperimmune-globulinemia E, low IgG ($p < 0.001$).

The development of the "atopic march" is predisposed by the aggravated allergic heredity along the maternal line, the presence of secondary immune deficiency, perinatal lesion, general eosinophilia, an increase in the total IgE level of more than 800 IU/ml, and the presence of specific IgE antibodies to household allergens.

The regime of preventive vaccination of children with early AD manifestation depends on the severity of the course of the disease. Preparation for vaccination according to the proposed scheme does not replace basic therapy, but it allows vaccinating children with severe AD without side reactions and pronounced exacerbations of the pathological process.

REFERENCES

1. Атопический дерматит в практике педиатра / Аряев Н. Л., Клименко В. А., Кожемяка А. И., Феклин В. А. — К., 2007. *[Atopic dermatitis in pediatric practice / Aryaev N.L., Klimenko V.A., Kozhemyaka A.I., Feklin V.A. - K., 2007. – in Russ.]*
2. Банадига Н. В. Атопічний дерматит з позиції педіатра / Н. В. Банадига // Здоровье ребенка. — 2008. — № 4. — С. 86—89. *[Banadiga N.V. Atopic dermatitis from the position of the pediatrician / N.V. Banadiga // Child's health. - 2008. - No. 4. - P. 86-89. – in Ukr.]*
3. Баранов А. А. Аллергология и иммунология / А. А. Баранов, Р. М. Хаитов. — М. : Союз педиатров России, 2008. — С. 35—74. *[Baranov A.A. Allergology and Immunology / A.A. Baranov, R.M. Haitov. - M.: Union of Pediatricians of Russia, 2008. - P. 35-74. – in Russ.]*
4. Намазова Л. С. Аторический дерматит у детей" проблемы и решения /Л. С. Намазова, Н. И. Вознесенская, Л. П. Мазитова // РМЖ. —2006. — Т. 14, № 19. —С. 44—46. *[Namazova L.S. Atoric dermatitis in children "problems and solutions / L.S. Namazova, N.I. Voznesenskaya, L.P. Mazitova // RMJ.-2006 .- P. 14, No. 19.-p. 44 -46. – in Russ.]*
5. Moore M. M. Perinatal predictors of atopic dermatitis occurring in the first six months of life / M. M. Moore, S. L. Rifas"Shiman, J. Rich-Edwards //Pediatrics. — 2008. — Vol. 113, № 3. — P. 468—474.
6. Palmer C. N. Common function variant of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis / C. N. Palmer, A.D. Irvine, A. Terron"Kwiatko // Nat Genet. — 2006. —Vol. 38. — P. 441—446.
7. Wright A. L. The epidemiology of the atopic child: who is at risk for what? / A. L. Wright // J. Allergy. Clin. Immunol. — 2007. — Suppl. 113. — P. 2—7.