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A Topic Dermatitis and Gastrointestinal Diseases

Mirrakhimova M.Kh., Nishanbaeva N.Yu., Qurbanova D.R.
Tashkent Medical Academy

Resume. One of the peculiarities of chronic diseases of the gastrointestinal tract (GIT) in children is their comorbid course. The link between allergic diseases and the digestive system is of particular interest. It is assumed that direct allergic injury to the mucous membranes of the esophagus, stomach and intestines by various allergens, damage to other organs and simultaneous development of local inflammation may occur with increased permeability of the epithelial barrier of the gastrointestinal tract to allergens. Because the gastric mucosa is in contact with allergens that enter before other digestive organs, the combination of these allergic diseases and AID pathology is attracting the attention of researchers today.

Keywords: children, atopic dermatitis, gastrointestinal tract, intestinal flora, elastase, pancreatitis

Relevance. Numerous cases of atopic dermatitis (AtD) are accompanied by impaired digestive function, leading to exacerbation and complication of the underlying disease. According to Robison RG, Singh AM and Lee MJ, Kang MJ, abdominal pain is observed in 72% of children with AtD, diarrhea - 57%, flatulence - 49%, vomiting - 37%, constipation - 26%, nausea - 22% [11]. N.G. Soboleva and co-authors in their study identified changes in the gastrointestinal tract in a large group of children with atopic dermatitis, in 74.8% of children with AtD hereditary predisposition to gastroenterological pathology was observed mainly by the maternal generation [6]. Signs of damage to the gastrointestinal tract were detected in 81.5% of children. Isolated abdominal pain syndrome was observed in 2.4% of children, abdominal pain with dyspeptic complaints - 30.6%, pain with dyspeptic syndrome and diarrhea - 68.4%. In addition, the authors found a decrease in appetite (41.5%), nausea (37.8%), and belching (23.1%). In the group of children examined, gastrointestinal symptoms often appeared in the first year of a child's life and constipation was considered one of the most common symptoms. The manifestation of gastrointestinal symptoms in these children was often observed against the background of early introduction of additional foods and irrational eating. Undoubtedly, the development of these cases was caused by the fact that the nature of nutrition does not correspond to the functional capabilities of the child's digestive organs. Most often, recurrence was observed in the first year of life in children with AtD (in 28% of children), a condition often associated with the introduction of allergens into the diet, including cow's milk protein. Symptoms of gastroesophageal reflux in 75% of children with relapse in the first year of life persist into adulthood. Based on the data obtained, it can be concluded that in children in the first year of life with food allergies and AtD, a violation of the motility of the digestive system is formed and then worsens.

As for the allergic process, in the first year of a child's life, sensitivity to cow's milk and chicken eggs was observed in 88.2% and 83.0% of children, respectively. A well-known phenomenon associated with gastrointestinal tract damage in AtD is an increase in the permeability of the gastrointestinal tract epithelial barrier. It is assumed that the increase in epithelial barrier permeability is associated with allergic inflammation in the intestine as a sign of an atopic process, in which not only the skin but also the intestine becomes the target organ. As a result of increased intestinal barrier permeability, the entry of antigens from the intestine into the patient's body increases. The mucous layer of OIT is an important barrier that protects the body from environmental antigens that enter the digestive tract. In addition to specific epithelial cells and intercellular connections, this barrier also includes mucus, digestive secretions, intestinal flora, and the immune system of the mucous membrane. Increased sensitivity of young children to food antigens is associated with incomplete mucosal and skin barrier function. Increased permeability of the gastrointestinal mucosa is a major factor in the development of allergic diseases, including atopic dermatitis. The immaturity of this barrier, in some cases an increase in permeability due to inflammation, increases the flow of antigens and leads to an increase in susceptibility.

The decrease in the barrier function of OIT, which leads to an increase in the entry of antigens into the body's internal environment, may be due to a number of nonspecific factors:

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- changes in the composition of mucus,
- Lack of activity of OIT enzymes, primarily proteolytic enzymes that break down proteins,
- Disorders of intestinal metabolism (including associated with changes in the composition of the intestinal microbiocenosis),
- Increased permeability of the epithelial layer.

Under normal conditions, the deposition of antigens through the mucous membranes is mediated by two main mechanisms. Antigens enter through epithelial cells via transcytosis, which are then broken down into smaller fragments in the lysosomes, thereby reducing antigenic stress. The second way is the transport of unchanged antigens and their delivery to the immune system. This pathway is carried out by the cells of Peyer's cells and forms the basis of the body's immunological defense. Both of these processes provide oral tolerance, indicating no response to an antigen previously introduced into the body.

In cases where the barrier function of the OIT mucosa is impaired, the flow of antigens through it, using intercellular spaces, increases many times. The inflammatory process deepens these disorders, but the allergic process itself can also be an inducer of inflammation in the OIT mucosa. Antigen-specific IgE antibodies were detected in the feces and intestinal mucosa of patients with food allergies, and a reliable correlation was found between the degree of degranulation of fat cells in the intestinal mucosa and the response to accidental introduction of the antigen into the stomach.

In a study by McCance KL and co-authors, the concentration of tumor necrosis factor alpha (FNOa), eosinophilic cationic protein, and alpha-1-antitrypsin in feces in response to the introduction of cow's milk into the stomach of children with atopic dermatitis twice under random placebo was identified as a marker of intestinal inflammation. As a result, it was found that in 43% of children who received the allergen, the concentration of alpha-1-atitrypsin increased compared to 1% compared with placebo [9]. Interestingly, the increase in eosinophilic cationic protein concentration was associated with a rapid-type response and a FNOa-delayed response. Numerous studies in children with atopic dermatitis have reported increased intestinal permeability. However, a tendency to high permeability was observed in young children compared to the lactulose / ramnose test. Removal of cow’s milk from the diet of children with allergies to cow’s milk protein decreased permeability, while milk intake resulted in increased permeability.

Permeability was equally increased in patients with skin signs and gastrointestinal symptoms. Increased absorption of macromolecules in patients with allergies to cow's milk has also been shown to be observed at minimal changes in the small intestinal mucosa.

Bogatyreva K.S. and co-authors ’studies showed that the serum trypsin levels in children in the first year of life with AtD increased significantly, the trypsin inhibitor level and the trypsin inhibitor / trypsin ratio decreased, indicating a risk of developing pancreatitis. In addition, an increase in the concentration of carbohydrates in the feces of a large number of children, in particular lactose, has been found to indicate intestinal damage with impaired lactase activity. The severity of these changes decreases during treatment. However, the authors considered it appropriate to use pancreatic enzymes in children with AtD [2].

N.G. Studies by Korotky and co-authors have shown significant disorders of the pancreas and intestines in AtD. The basis of this study was the analysis of the results of a comprehensive clinical and laboratory examination of 122 children with AtD from 5 to 15 years of age. In most cases, the development of ATD was caused by factors such as dietary disorders - 89.3% of children and psychoemotional stress - 40.2%. When analyzing hereditary predisposition, it was found that 75.4% of children with AtD had parents with various allergic diseases, and 47.5% had gastrointestinal tract diseases [4]. Among the comorbid pathological conditions in children with AtD, functional disorders of OIT motility, changes by the pancreas, and neurotic reactions were more common. According to the assessment of the severity of the process on the skin on the SCORAD scale, the observed patients were divided into 3 groups of severity - 54 (44.3%) children (average score of the SCORAD index - 60.6 ± 1.8); average weight - 42 (34.4%) children (SCORAD - 35 ± 1.14); mild degree - 26 (SCORAD - 21.3% of children (19,6x0,5) [8,10].

The study found changes in the digestive system in 97.5% of children. Patients complained of abdominal pain, intermittent nausea, decreased and disturbed appetite, belching, heartburn, unstable stools, constipation, flatulence. Symptoms of intoxication were detected in 69.7% of children: general weakness, hypodynamics, rapid fatigue, increased agitation, inability to concentrate, and sometimes crying. In the anamnesis of 86.9% of the children, the parents reported persistent dyspeptic disorders and diarrhea.

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Examination of pancreatic enzymes in the blood, the amount of triglycerides in the feces, ultrasound examination of the abdominal organs, coprological examinations revealed a significant impairment of pancreatic function in children with AtD. Simultaneous changes in membrane digestion have also been identified with intermittent indigestion.

However, there is a strong strong correlation (R = + 0.76, p <0.01) between serum lipase levels and lactase deficiency, indicating a close association between digestive and absorption disorders. However, the xylose test showed impaired intestinal absorption of carbohydrates and impaired absorption of lipids (noesterified fatty acids according to fecal lipidogram), and the severity of these disorders increased with increasing disease severity (SCORAD scale) [10].

Thus, in children with AtD, in addition to hollow digestion, wall digestion was also observed, and this was associated with impaired multi-stage enzymatic processing required for the assimilation and subsequent absorption of hydrolysis products of nutrients. In AtD, the mechanisms of disruption of intestinal absorption are associated with a massive strain of antigens, leading to an allergic reaction on the principle of "shock organ" damage. Changes in intestinal permeability due to local hypersensitivity reaction were observed as a result of inflammation of the intestinal mucosa caused by exposure to food allergens. Many scientists have cited increased concentrations of IgE-producing cells, tissue eosinophilia, and high concentrations of cytokines, the cationic protein of eosinophils (ESR), a1-antitrypsin, as evidence of local allergic inflammation. In many cases, functional disorders of the colonic motility can be detected in diseases of an atopic nature. Titova N. D. and the co-authors found that affected bowel syndrome (TIS) in atopic adults was statistically more commonly observed (P = 0.015), and this led to the introduction of the term ‘atopic TIS’. Overall, the incidence of TIS symptoms in children with atopy was 3.2 times higher than in patients without AtD (95% II, 1.20–8.50, P = 0.02) [7]. According to the authors, the incidence of TIS among atopic diseases is 2.67 times higher than in the population with allergic rhinitis; 95% confidence interval [II], 1.10-6.49; P = 0.03), allergic eczema (3.85 times ; 95% II, 1.72–8.60; P = 0.001) and depression (2.56 times; 95% II, 1.05–6.14; P = 0.04). Kelly T. and co-authors monitored children aged 3–13 years with allergic disease (compared to non-allergic children) and found that TIS was detected in 6.6% of allergic children and 6.3% of non-allergic children (p = 0.581). Similar results were observed at the level of constipation. According to systematic reviews, inability to tolerate nutrients was observed in 20–65% of patients diagnosed with TIS, and in many cases this was due to immunological disorders. At the same time, significant factors identified using skin prick test had a positive effect on the clinical course of functional impairment of intestinal motility when excluded from the diet. According to the results of the meta-analysis, allergic diseases were the most common in the majority of patients with TIS. Significantly, in addition to allergic diseases, functional dyspepsia (i.e., upper gastrointestinal motility impairment) and depression (i.e., psychoemotional disorders), diabetes mellitus, and diarrhea were also more common in patients with TIS.

According to an analysis of research data from 30,000 patients by the primary care unit, atopic disorders were statistically more likely to be detected in people with FB than in the control group. Atopic disorders in patients with TIS (risk ratio (XN) = 1.43, 1.29-1.58), functional dyspepsia (XN = 1.41, 1.26-1.58) and mixed FB (XN = 1, 92, 1,75-2,12) were observed primarily in patients with atopic asthma. Patients with mixed FB had a higher incidence of allergic rhinitis / pollen allergy (NX = 3.74, 3.32-4.20) and allergic conjunctivitis (NX = 3.00, 2.49-3.62).

According to scientists from the literature, inability to tolerate a variety of foods was observed in 20-30% of adults diagnosed with TIS, according to a well-studied study - 1-7.5%. In terms of pathogenesis, the control group in TIS was wheat (0 IQR ± 285 and 395 IQR ± 1,011p <0.001, respectively), beef (617 IQR ± 435 and 1,079 IQR ± 930 p <0.001), and pork (258 IQR ± 496). and 481 IQR ± 379, p <0.001), increased IgG4 (mug / L) levels against mutton (167 IQR ± 232 and 241 IQR ± 460, p = 0.009) [1,9].

Under stress, which is important in the development of many functional diseases of the digestive tract, fat cells secrete various biologically active substances and mediate the binding of mediators such as anaphylotoxins, neuropeptides and cytokines to receptors, which not only stimulate the inflammatory process but also intestinal motility. also leads to disruption.

Thus, based on the above, it can be assumed that the violation of antigen transport from the barrier of the small intestinal mucosa in children with AtD occurs due to:

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1) decreased secretion of enzymes of the small intestine and pancreas, decreased blood flow to the small intestine and pancreas, impaired their trophism, increased contraction of smooth muscle in the small intestine;
2) insufficient enzymatic processing of food products and depolymerization due to wall digestion along with cavitation, resulting in increased formation and accumulation of allergens in the small intestine;
3) dysfunction of the small intestinal mucosa due to a hypersensitivity reaction developed in response to a massive attack of food allergens;
4) signs of inflammation in the small intestinal tissue (due to food allergies, infection) and atrophy of intestinal villi and decreased enzyme synthesis.

The state of the autonomic nervous system significantly determines the function of all systems of the body, including the digestive organs. Vegetative disorders in AD are detected in a large proportion of children, so it can be assumed that these changes affect the performance of OIT functions.

Mixaylova O.D. and co-authors in a study of 30 children aged 8–14 years with AtD, sympathotonia in 40% of children with AtD, asympticotonic vegetative reactivity in 81.1% of children as a result of clinoortostatic testing. In addition, the authors found a higher incidence of psychoemotional disorders, including sleep disorders in 64.7% of children, and increased anxiety - 53% [5]

Benn S.S. and co-authors conducted cardiointervalography (KIG) in 82 children with ATD (under 3 years - 28, 4-7 years - 54) and found a statistically significant decrease in the stress index, indicating the predominance of vagotonia. In these children, this condition was clinically manifested in the form of excessive sweating, redness of the skin, red dermographism, bradycardia. In addition, abdominal pain was more common in children. According to the authors, along with an increase in the tone of the parasympathetic division of the autonomic nervous system, a decrease in the activity of the sympathetic division.

This situation can be explained by an increase in the level of autonomous contour of the body's functions management and a decrease in the central contour, which leads to a decrease in the body's adaptability and resistance to stress [1,12].

Hypersympathotonic vegetative reactivity was observed in a large proportion of the children in the follow-up, and this was more pronounced in older children. Normal reactivity has been observed in many cases in young children. During remission of atopic dermatitis, normalization of the indicated parameters and restoration of vegetative balance were observed.

The result is an incorrect pathogenetic circle connection. The allergic process is accompanied by damage to the intestinal epithelium and an increase in the permeability of the intestinal mucosa, which leads to an increase in the entry of antigens into the bloodstream and deepens the course of the underlying disease. Disorders of intestinal digestion and absorption, which occur due to the atopic process, further increase the antigenic strain, which further exacerbates atopy. Thus, allergy causes the development of malabsorption, which in turn deepens the allergic process. By correcting the function of the digestive organs and carrying out the basal treatment in parallel, it is possible to achieve a breakdown of this misaligned circuit.

The basis of the etiopathogenesis of AtD is a combination of triggers such as food allergies, stress-induced conditions, changes in the intestinal microflora, pancreatic (OOB) deficiency, disruption of environmental microecology, hereditary predisposition.

Functional disorders of the digestive system lead to the absorption of incompletely digested food components, especially proteins, thereby increasing the body's sensitivity to various allergens. Correction of non-secretory pancreatic insufficiency (PE) is of great importance in the treatment of AtD.

Chronic pancreatitis is a dynamic disease that is difficult to diagnose, requires a number of laboratory instrumental tests, is characterized by the development of pancreatic tissue destruction and the development of complications.

Often, chronic pancreatitis manifests itself as a complication of another disease (for example, atopic dermatitis, bronchial asthma, biliary tract dyskinesia, etc.) and as a result leads to a severe course of the primary disease. In such cases, chronic pancreatitis is overlooked by primary arthritic physicians.

Dynamic observation of such patients allows them to be monitored in a timely manner, to identify factors influencing the rate of development of the pathological condition, the nature of the stages and course,

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as well as the effectiveness of treatment measures [10,11]. Therefore, the above aspects determine the next direction of research, which opens up new possibilities for the treatment of AtD in children.

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