Здоров'я дитини

Випадок із практики / Case Report

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Difficulties in diagnosing gastrointestinal allergy in paediatric practice: a clinical case

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Abstract. *Since allergy pathology in the structure of general somatic diseases occupies a significant niche in both adult and child populations and is accompanied by a number of unresolved issues, it represents a major medical and social problem. The use of modern diagnostic techniques has made it possible to broaden scientists' knowledge of the in-depth mechanisms of the pathogenesis of allergic diseases with the subsequent development and implementation of new diagnostic, therapeutic and prophylactic recommendations. However, the multidisciplinary aspects of paediatric allergy continue to be studied; among them, the problems of specific diagnosis of food allergy are of particular importance. Recently, the study of allergic lesions in the various parts of the gastrointestinal tract has received increasing attention in paediatric practice. Since in most cases the mucosa of the digestive system is the first to contact with allergens of various nature, the gastrointestinal form ranks second in the overall structure of clinical symptoms of food allergy. Gastrointestinal symptoms of food allergy are characterized by polymorphic manifestations, making timely verification of the diagnosis difficult. This leads to prolonged differential analysis and requires the exclusion of concomitant organic and functional gastrointestinal pathology, which delays early diagnosis and timely therapeutic recommendations for patients with food allergy. The relevance of the above-mentioned problem is highlighted by the following clinical case.*

Keywords: *food allergy; diagnosis; children*

Introduction

Food allergic reactions have an ever-increasing trend and remain the most debated problem encountered by physicians at all levels of care, but are of greatest interest to paediatricians, general practitioners — family physicians, paediatric allergists and gastroenterologists. Of all the possible side effects of food intake, food allergy (FA) deserves special attention, as it is characterized by immunologically mediated food hypersensitivity mechanisms and is accompanied by the development of systemic lesions. This leads to a variety of clinical symptoms, including gastrointestinal, cutaneous, respiratory, systemic and anaphylaxis [1, 2]. Because the gastrointestinal mucosa is in most cases the first to contact with various allergens, the gastrointestinal form ranks second (48–67 %) in the overall structure of clinical symptoms of FA [3–5], which therefore explains the interest of scientists to investigate its course and early diagnosis in greater depth. Wide variability of clinical manifestations, concomitant sensitization to household and pollen allergens, lack of unified diagnostic algorithms, difficulties in verification of allergic gastrointestinal lesions in children at primary contact with food allergens, high risk of developing anaphylactic reactions when carrying out oral provocation test as the gold standard of FA diagnosis determine prospects for further research, finding noninvasive diagnostic markers of allergy and creating standardized recommendations [6, 7]. Thus, food allergy remains an urgent problem of modern medicine both in Ukraine and abroad, due to its widespread occurrence, difficulties in early diagnosis and timely organization of therapeutic and prophylactic measures.

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Clinical case

A 13-year-old boy P. (born 08.08.2004) was admitted to Pediatric Unit 1 (gastroenterological beds) of Poltava Regional Clinical Hospital in May 2018 with complaints of frequent moderate abdominal pain disturbing mostly after food, sometimes nausea, sour taste in the mouth, throat scratch, heartburn, diarrhea, sometimes alternating with constipation. Recently, rapid fatigue, intermittent dizziness and sleep disturbances have been noted.

According to the medical history, the boy is known to be ill since infancy, when he was first disturbed by abdominal pain, bloating and stool disorders, which were accompanied by pronounced crying and restlessness. As general clinical and coprological investigations did not reveal any pathological changes, the child was observed for a long time for various gastrointestinal functional disorders, in particular intestinal colic and functional diarrhea. From the second half of life onwards, the boy's condition gradually deteriorated, symptoms worsened and persisted almost continuously, despite dietary advice to restrict consumption of certain foods and symptomatic therapy. Occasionally, there were brief latent phases of conditioned well-being and improvement of well-being. During dynamic anthropometric examinations, insufficient weight gain and a moderate delay in physical development were detected. Over time, the child's parents began to monitor a worsening of well-being in the presence of dairy and cereal products in the diet. The consumption of milk, irrespective of the state of thermal processing (raw/boiled), caused exclusively gastrointestinal complaints, which in the first year of life were accompanied by pronounced crying and refusal to eat that explained a poor weight gain. Therefore, the child had been on a gluten-free diet for a while prior to the clinical examination and had received enzyme replacement therapy with lactase preparations. During the outpatient examination, a genetically determined autoimmune T-cell-mediated enteropathy with a malabsorption syndrome characterized by persistent gluten intolerance (ie, celiac disease) and congenital deficiency of β-D-galactosidase hydrolase responsible for the metabolism of dietary lactose (ie, lactase deficiency) was ruled out in the first year of boy's life. A follow-up visit to the paediatrician revealed symptoms of atopic dermatitis in the form of rash, dry skin and itching. Therefore, the child was referred for consultation to a paediatric allergist who, after analyzing the history and features of the clinical symptoms, confirmed gastrointestinal and skin signs of food allergy. After further investigations (including positive results of skin allergy testing), according to the International Classification of Diseases 10th revision, the diagnosis was "atopic dermatitis, erythematous-squamous form, localized, mild severity, period of unstable remission. Food allergy is in question" followed by protocol therapy, which resulted in long-term remission of the disease. The absence of data from endoscopic and morphological examination of the gastrointestinal tract and the impossibility of conducting oral provocation tests due to parental refusal did not allow for the verification of allergic gastrointestinal lesions and confirmation of a gastrointestinal form of food allergy. The food diary data analyzed indicated that food hypersensitivity to milk and cereals continued to be of concern at later ages, but its severity decreased significantly. Tolerance to these food allergens developed with age, and further consumption did not cause clinical symptoms from different organs and systems.

According to ***the anamnesis data***, in the subsequent age periods, the boy was repeatedly examined and treated both at the outpatient phase and in the paediatric hospital for various gastroenterological nosologies, both functional (functional dyspepsia, irritable bowel syndrome, pancreatopathy) and organic (chronic gastroduodenitis). He was under constant supervision of a paediatrician, followed all therapeutic recommendations, received enzyme, antisecretory, reparative drugs, probiotics to correct various gastrointestinal disorders that cause a short-term improvement of well-being, but complete regression of complaints was not observed. In order to clarify the diagnosis, perform a complete clinical and paraclinical examination, and to determine further treatment tactics, the child was admitted to the indicated specialised department.

It is known from ***the life history*** that the boy was born from the first pregnancy at 40 weeks gestation, his mother had a first trimester miscarriage and signs of intrauterine fetal hypoxia. The birth was physiological against the background of weak contractions. Weight of the child at birth was 3,460 g, height was 54 cm. From birth the boy was on artificial feeding, from 5 months of age vegetable and fruit puree supplementation was introduced, at 6 months of age semolina, then buckwheat, rice and wheat porridge were introduced into the child's diet, which provoked the development of the first symptoms. The introduction of cow's milk into the diet at 6.5 months was accompanied by the development of symptoms of gastrointestinal allergy (colic, bloating, repeated loose stools with mucus and sometimes blood streaks, and consequent refusal to eat, malnutrition and lack of body weight gain). Vaccination was carried out according to the immunization schedule. The patient had no childhood infectious diseases (chickenpox, measles, rubella, scarlet fever). Rare acute respiratory viral infections occurred. Allergic anamnesis was aggravated by maternal medication allergy and atopic dermatitis. An in-depth study of aggravated heredity revealed the presence of atopic dermatitis in the boy's mother and maternal aunt who also had food hypersensitivity to chicken eggs and fish. The paternal grandfather had a history of peptic ulcer disease, highlighting the fact of a hereditary predisposition to gastroduodenal pathology.

At the initial phase of the examination, a questionnaire based on the Allergoscope international allergy test was used during the clarification of the clinical and anamnestic data of this patient. The answers to the questionnaire allowed the identification of products that caused gastrointestinal symptoms. Thus, the presence of intermittent allergic reactions to egg in the early childhood was found, characterized by oropharyngeal (sore throat), gastrointestinal (stomach pain, nausea, belching) and sometimes upper and lower respiratory tract symptoms (sneezing and coughing). Clinical manifestations against the background of peanut consumption were observed in the preschool period and were accompanied by the development of Quincke's edema. According to the European Food Safety Authority, thermal processing of peanuts can increase their allergenic properties due to the heat-stable antigens Ara h 1 and Ara h 2. Therefore, to prevent the risk

of allergic reactions, the Food Allergen Labelling and Consumer Protection Act requires food manufacturers to indicate this ingredient in a marked and clear print and persons sensitized to peanuts should avoid them in the diet. However, according to the boy's parents, it was not always possible to follow these recommendations as the child grew and became independent, which could have made the course of the disease much more difficult. The onset of FA following the consumption of nuts (primarily hazelnuts) has been noted in primary school age, but symptoms occur intermittently, mostly after consuming a full serving of the ingredient.

Thus, interviewing this child, analysing peculiarities of allergic reactions to food made it possible to determine specific clinical criteria, structure, dose dependence, frequency, rate of development of allergic reactions and to evaluate recurrence of clinical manifestations against the background of exclusion of etiologically significant products, which had extremely important diagnostic value for further differentiating true manifestations of food allergy and non-immune food intolerance reactions with post-allergic reaction. This allowed for the next correct organization of elimination measures to avoid contact with relevant allergens. The identification of all causative elements ensured an optimal further diagnostic algorithm with precise selection of the allergen spectrum for skin prick testing and sIgE determination to clarify the structure of sensitization.

According to ***the objective examination*****,** the child's general condition is satisfactory. The child has a normosthenic constitution. Height — 165 cm, body weight — 51 kg. Body mass index is 18.1 (according to centile charts, it corresponds to normal values by age and sex). Skin surface is of pale pink colour, dry. Visible oral mucous membranes are pale pink, with visualization of an aphtha on the right side of the palate. The tonsils are not enlarged and the lymph nodes were not palpated. The musculoskeletal system has no features. Free nasal breathing is observed, respiratory rate is 18 per minute. During auscultation, the breathing is vesicular, on percussion clear lung sounds are heard. The heart rate is 82 beats per minute. Blood pressure is 110/70 mmHg. The boundaries of the heart are not expanded. Heart rhythm is correct, tones are sound. The tongue is moist, covered with a white coating. The abdomen is of regular shape, symmetrical, participates in the act of breathing. Superficial palpation is painless, there are no pathological formations; at deep palpation, the abdomen is soft, not tense, there is moderate tenderness in the epigastric region and gastroduodenal area. The gallbladder is not palpable, biliary symptoms are negative. The liver is painless on palpation, not enlarged, the edge is rounded. The spleen is not palpable. Peritoneal irritation symptoms were negative. Auscultation — peristalsis is satisfactory, rhythmic. The kidneys are not palpated. The tapping symptom is negative on both sides. The external genital organs are without features. Physiological excretions are characterized by alternating constipation and diarrhea with mucus. Urination is not impaired. Based on the patient's complaints, medical and life history, the results of the interview, objective examination, the preliminary clinical diagnosis was established: *chronic gastritis, with unspecified acid-producing function of the stomach, period of exacerbation. Chronic duodenitis, period of exacerbation. Food allergy is in question.*

Results of laboratory and instrumental examinations

General blood count: red blood cells — 4.23 • 10^{12}/l, haemoglobin — 136 g/l, erythrocyte sedimentation rate — 11 mm/h, leucocytes — 6.3 • 10^{9}/l, stab cells — 4 %, segm. cells — 64 %, eosinophils — 1 %, basophils — 0 %, lymphocytes — 28 %, monocytes — 4 %, thrombocytes — 235 • 10^{9}/l.

General urinalysis is without pathological changes.

Biochemical blood count: total protein — 75.6 g/l, urea — 4.2 mmol/l, uric acid — 234 mmol/l, creatinine — 67 μmol/l, a slightly increased level of bilirubin: total — 22 μmol/l, direct — 5 μmol/l, indirect — 17 μmol/l, alanine aminotransferase — 18 U/L, aspartate aminotransferase — 25 U/L, gamma-glutamyl transpeptidase — 14 U/L, alpha-amylase — 51 U/L, thymol, an increased level of alkaline phosphatase — 624 U/L, creatin phosphokinase — 116 U/L.

Stool for helminth eggs: no eggs were detected.

Enterobiasis test: negative.

Stool test (coprogram): unformed, light brown, pH-neutral, moderate amounts of mucus, single muscle fibres, no starch or neutral fat, few vegetable fibres, fatty acids and a small amount of soap. No leucocytes or erythrocytes were detected.

Urine test for diastase: 112 U/L.

Skin allergy testing: histamine solution +++, oat cereal –, chicken egg yolk ++, beet –, tomato –, soy +++, chicken egg protein +++, rice cereal –, cocoa –, wheat cereal +, buckwheat flour –, wheat flour +, potato –, rye flour +, milk +++, hake –, pork –, chicken –, carrot –, cabbage –, apple –, tangerine –, beef –, carp –, cow's milk casein ++, banana –, raspberry –, cucumber –, watermelon –, beans –, orange –, lemon –, pumpkin –, pollock –, buckwheat groats –, barley cereal +, corn flour –, peanuts +++, walnut ++, hazelnut ++, honey –.

ELISA (blood test for helminths): no antibodies against antigens of giardia, ascarids, toxocaras, opisthorchis, trichinellas, echinococcus, anisococcus, strongyloides were detected.

ELISA (immunoglobulin blood test): an increased level of total IgE — 269 IU/ml, a reduced level of IgA — 3.7 g/l, normal level of IgM — 0.98 g/l, normal level of IgG — 12.36 g/l.

ELISA (cytokine blood test): an increased level of IL-4 — 1.2 pg/ml, a reduced level of IL-10 — 2.0 pg/ml, an increased level of an immunologically mediated marker of allergic inflammation — serum thymus- and activation-regulated chemokine TARC/CCL17 — 408.5 pg/ml.

ELISA (blood test for specific immunoglobulin E): sIgE to milk — 1.29 IU/ml (class 2 — moderately elevated level (0.70–3.49)), sIgE to α-lactalbumin — 1.32 IU/ml (class 2 — moderately elevated level (0.70–3.49)), sIgE to casein — 0.95 IU/ml (class 2 — moderately elevated level (0.70–3.49)), sIgE to egg (protein) — 2.24 IU/ml (class 2 — moderately elevated level (0.70–3.49)), sIgE to wheat — 1.67 IU/ml (class 2 — moderately elevated level (0.70–3.49)), sIgE to hazelnut — 1.06 IU/ml (class 2 — moderately elevated level (0.70–3.49)), sIgE to peanuts — 10.0 U/ml (class 3 — significantly elevated level (3.5–17.49)), sIgE to chicken egg (yolk), soy, potatoes and carrots were not detected.

Fibroesophagogastroduodenoscopy: esophageal mucosa is normal, cardiac sphincter is closed. Stomach is of normal

shape, gastric mucosa is hyperemic, moderately edematous, folds are normal. There was a small amount of mucus in the gastric cavity. Duodenal mucosa was moderately hyperemic, postbulbar section had no features. Intragastric pH-metry is 1.3–1.5 units.

Histological characterization of a biopsy specimen of the gastric mucosa showed preservation of the histostructure, but signs of chronic inflammation were detected. The surface epithelium was represented by smaller cells, whose shape was close to cubic both on the surface of the mucosal folds and in the fossae. In addition, there was no clear differentiation of the cell poles due to the absence of a mucous secretion in the apical part and the presence of dystrophic changes. A narrow rim of light cytoplasm, presumably resulting from the development of hydropic dystrophy, was observed around the cell nuclei. There was a thin layer of mucus on the mucosal surface or it was absent. Desquamation of single epithelial cells or their layers was found. In almost all sections of the biopsy sample, there was a pronounced polymorphocellular inflammatory infiltration in the mucosal plate with predominance of lymphocytes, plasmocytes and comparatively larger number of neutrophils, eosinophils, macrophages. In some locations of the studied material, a marked eosinophilic infiltration with their focal accumulation and pronounced stromal edema was detected. Many eosinophils were degranulated. Along with eosinophils, there were also lymphocytes and plasmocytes. Eosinophilic infiltration was evaluated with determination of the number of eosinophils and lymphocytes in 5 random fields of view of high magnification in a section of histological preparation of gastric and duodenal mucosa: eosinophils of the stomach — n = 54, eosinophils of the duodenum — n = 59; lymphocytes of the stomach — n = 39, lymphocytes of the duodenum — n = 39. The presented mucosal changes indicate a chronic immune-allergic inflammatory process of the gastroduodenal area.

Urease breath test: basal level — 2 mm, loading level — 4 mm, growth index — 2 mm (normal is up to 3 mm).

Abdominal ultrasound: the liver is normally located, the shape is unaltered, the contour is clear, the lower edge is rounded. Dimensions: left lobe: anteroposterior — 12.0 cm; right lobe: anteroposterior — 3.4 cm. Echostructure of the parenchyma is not changed, the structure is homogeneous. Vascular architectonics: slight perivascular infiltration. Diameter of the portal vein was 0.7 cm. Gallbladder is located normally, oval, with inflection in the upper third, contours are smooth, wall is not changed, low-level echo signals are found layered in the adjoining part of the gallbladder without acoustic occlusion. Pancreas: size — 1.7 × 0.8 × 1.7 cm; shape is not changed, contours are clear, medium echogenic, homogeneous structure. Spleen and kidneys correspond to the age norm. Conclusion: ultrasonic findings show insignificant reactive changes in the liver. Biliary sludge.

Based on complaints, medical and life history, results of interview, objective examination, data of laboratory and instrumental methods of research, the final clinical diagnosis was made: *allergic gastroenteritis, gastrointestinal form of food allergy. Functional disorder of the gallbladder.*

Therapy: hypoallergenic elimination diet with exclusion of causal food allergens; probiotics and reparants for 10 days; enzyme, antisecretory and hepatoprotective drugs for 3 weeks; omega-polyunsaturated fatty acids for 1 month.

Conclusions

The above clinical and paraclinical characterization of a patient with gastrointestinal symptoms clearly demonstrates the difficulties in timely verification of food allergy in paediatric practice. A lack of positive clinical dynamics from the protocol therapy for functional and inflammatory diseases of the digestive tract, delays in physical development is the basis for expanding the diagnostic panel in order to clarify the pathogenesis of persistent gastrointestinal symptoms and timely verification of allergic lesions of the digestive tract. Therefore, when a food allergy is suspected and a patient with an undifferentiated abdominal syndrome is managed, the doctor's tactics require a multidisciplinary approach, popularization and wide implementation of Allergoscope questionnaires for early detection of the relationship between the consumption of certain food products and the occurrence of clinical symptoms. Consideration of all the specific data of the allergological anamnesis will allow personifying the recommendations for elimination of specific causative elements both in pure form and in the composition of other foods, followed by extension of the diagnostic algorithm, which involves in-depth study of allergological-immunological and endoscopic-morphological characteristics necessary for the diagnosis of food allergy and prevention of a systemic response to food allergens.

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Труднощі діагностики гастроінтестинальної алергії в педіатричній практиці: клінічний випадок

Резюме. Оскільки алергопатологія в структурі загальних соматичних захворювань займає одну з вагомих ніш як в дорослій, так і в дитячій популяції і супроводжується низкою невирішених питань, вона становить собою велику медичну та соціальну проблему. Використання сучасних діагностичних методик дозволило розширити знання науковців про поглиблені механізми патогенезу алергічних захворювань з наступною розробкою та впровадженням нових діагностичних, терапевтичних та профілактичних рекомендацій. Однак до цього часу продовжують вивчатися багатопрофільні аспекти алергології дитячого віку, серед яких особливе місце належить проблемам специфічної діагностики харчової алергії. Останнім часом у педіатричній практиці все більше уваги приділяється алергічним ураженням різних відділів шлунково-кишкового тракту. Оскільки слизова оболонка травної системи в більшості випадків першою контактує з різними за природою алергенами, гастроінтестинальна форма посідає другу позицію у загальній структурі клінічних симптомів харчової алергії. Гастроінтестинальні симптоми харчової алергії характеризуються поліморфними проявами, що, у свою чергу, утруднює своєчасну верифікацію діагнозу. Це призводить до затяжного диференційного аналізу й потребує виключення супутньої органічної та функціональної патології шлунково-кишкового тракту, що відстрочує ранню діагностику та своєчасні терапевтичні рекомендації в пацієнтів із харчовою алергією. Актуальність вищезазначеної проблеми наглядно підкреслює представлений клінічний випадок.

Ключові слова: харчова алергія; діагностика; діти