ISSN NO: 2770-0003
November 2024

Periodic Disease In Children. Clinical Case

Temirova Oydin Khusan kizi
Assistant of the Department of Propaedeutics of
Children's Diseases and Polyclinic Pediatrics
Faculty of Pediatrics
Andijan State Medical Institute

Abstract. Patients with periodic disease (PD) are quite common in certain ethnic groups. However, the relevance of the topic is also due to the early onset of the pathology and, in most cases, a serious prognosis for the patient's life, provided the disease is detected and treated late. Often, diagnostic errors can lead to unjustified surgical interventions.
Keywords: periodic disease, treatment, method, children.

INTRODUCTION

Periodic disease (PD) is a hereditary autosomal recessive disease that occurs in the form of attacks, the basis of which is spontaneous or provoked degranulation of neutrophils with the release of mediators and the development of aseptic inflammation mainly in the serous and synovial membranes. This pathology is widespread mainly among the ancient peoples of Uzbekistan. It is most often found in Andijan. The high frequency of rare genetic diseases in certain ethnic groups is explained by the founder effect and gene drift in isolated populations. Selection in such cases is of lesser importance. In all cases, we are talking about fairly pronounced marital isolation, sometimes even beyond geographical restrictions.

MATERIALS AND METHODS

The basis of periodic disease is a point mutation in the gene of the protein pyrin, located in the short arm of the 16th chromosome near the genes of autosomal dominant polycystic kidney disease and tuberous sclerosis. Pyrin is a protein of the primary granules of neutrophils, actively participating in the inflammation process. Disruption of the structure of this protein leads to an increase in the production of anti-inflammatory mediators in leukocytes, activation of the microtubular apparatus and spontaneous degranulation of the primary granules of leukocytes, activation of adhesion molecules and increased chemotaxis of leukocytes, resulting in inflammation.

The most common are 3 mutations - M 6801, M 694 V, V 726 A, they are more than 40,000 years old. Mutation M 6801 is found in Armenians, and M 694 V and V 726 A in all ethnic groups. During an attack of periodic disease, the release of mediators and the development of aseptic inflammation causes an increase in the number of neutrophils and the level of acute phase proteins in the peripheral blood. The effect of inflammatory mediators leads to the development of pain syndrome, and a large number of endogenous pyrogens - to the development of fever.

RESULTS AND DISCUSSION

Most often, periodic disease debuts in patients aged 2 to 5 years and is characterized by short-term (from 6 to 96 hours) attacks of fever combined with serositis (peritonitis, pleurisy, arthritis). The onset of attacks is preceded by the presence of provoking factors in the anamnesis - stress, surgery, trauma, vaccination. Abdominal pain is the most common symptom in this pathology (in 95% of patients), often the pain syndrome is so severe that patients undergo unjustified surgical interventions due to the development of acute abdomen. For 75% of patients, damage to large joints (knee, ankle, wrist) is characteristic of monoarthritis. Chest pain caused by the development of unilateral pleurisy is described in 30% of patients. Erysipeloid (erysipelas) skin rashes, localized mainly on the lower extremities, are observed (according to various data) in 7–40% of patients. The frequency of attacks is quite variable.

Acute attacks of the disease are accompanied by polymorphonuclear leukocytosis, increased ESR; during the attack period, an increase in the content of plasma fibrinogen, haptoglobin, C-reactive protein, alpha1-antitrypsin, sialic acids and ceruloplasmin is also noted. As a rule, all these indicators return to normal in the period between attacks [1]. The most common target organs in amyloidosis are the kidneys and heart. Kidney damage is manifested by nephrotic syndrome, hematuria and arterial hypertension are not typical for patients with periodic disease [2].

ISSN NO: 2770-0003
November 2024

Diagnosis of periodic disease includes:

Amnesis

The child's nationality and heredity are of the greatest importance. A typical anamnesis of life and illness of the child: frequent "colds" with fever, abdominal and joint pain, previous surgeries. Clinical picture

• attacks of fever with pain syndrome;
• ineffectiveness of antibiotics and antipyretics;
• good health during the non-attack period.

Laboratory data

• leukocytosis with neutrophilia;
• increased ESR;
• decreased activity of neutrophil myeloperoxidase and increased activity in the blood during an attack: normalization of indicators outside the attack.

Genetic study

Detection of homozygous carriage of mutations M 6801, M 694 V, V 726 A makes the diagnosis of periodic disease 100%. However, sometimes with a typical clinical picture and anamnesis, heterozygous carriage of mutations is detected [2].

Effect of colchicine therapy

The prognosis for this pathology is determined by the development of renal amyloidosis. Amyloid is synthesized from the inflammatory serum protein precursor, AA protein, which is formed as a result of aseptic inflammation of the serous and synovial membranes during spontaneous degranulation of neutrophils during an attack of periodic disease. The AA protein is utilized by macrophages, which synthesize insoluble AA amyloid fibrils from it, which are deposited in the intercellular space.

This causes significant extracellular accumulation of AA amyloid in organs with fixed macrophages (primarily in the kidneys, liver and spleen), which leads to tissue destruction and organ failure. Amyloidosis in periodic disease belongs to the group of AA amyloidoses and is secondary (reactive) and systemic in nature [1–3]. In the absence of renal amyloidosis, a favorable prognosis is possible.

As a rule, most patients with periodic disease suffer from erroneous diagnoses and associated improper treatment. To exclude such episodes, we would like to present to your attention the following clinical case.

The parents of a 5-year-old girl from an Azerbaijani family contacted the consultative and diagnostic center. Complaints: since the age of 4, the girl began to have periodic temperature increases up to 39°C (1-2 times a month), accompanied by pain in the ankle joints. During examination at the place of residence, changes in blood tests were revealed in the form of an accelerated ESR up to 40 mm per hour. Joint pain over the past 2 months became constant and bothered the child, as a rule, in the evening.

From the anamnesis of life: the child is from the 3rd pregnancy, which was proceeding normally, natural delivery, body weight at birth 3200, length 52 cm. Psychomotor development corresponds to age. It was not possible to clarify the family anamnesis in detail. The child's mother and father consider themselves practically healthy.

On examination: the child's condition is satisfactory. The skin is clean. Breathing through the nose is free. The tonsils are clearly hyperemic, loosened, whitish deposits are noted. Vesicular breathing in the lungs during auscultation, no wheezing. Heart sounds are sonorous and rhythmic. The abdomen is accessible for deep palpation. The liver is at the edge of the costal arch along the midclavicular line.

The spleen is not enlarged. The joints are visually unchanged, the temperature above them is not changed, movements are fully preserved. The genitourinary organs are formed correctly. There is no edema or dysuria. Stool is regular. Results of the examination: immunological blood test: IgG — 1170 mg% (normal — 823–869 mg%), IgM — 265 mg% (normal — 94–100 mg%), IgA — 96 mg% (normal — 77–90 mg%), antistreptolysin O titer — 5 U/ml (up to 100 U/ml), rheumatoid factor 13 U/ml (normal — up to 20 U/ml), circulating immune complexes 702 mV (normal — 109–352 mV). Blood biochemistry: total protein — 79 g/l (normal 60–80 g/l), creatinine — 44 μmol/l (44–88 μmol/l), urea — 3.4 mmol/l (normal 2.5–6.4 mmol/l), alkaline phosphatase — 115 U (60–400 U), amylase — 41 U (25–125 U), glucose — 4.69 mmol/l (3.3–5.5 mmol/l).

In general urine analysis, hematuria — up to 34.1 μl (normal 22.7 μl).

In ultrasound examination of the kidneys and bladder — signs of crystalluria.

ISSN NO: 2770-0003
November 2024

Urine biochemistry: urates 1580.32 μmol/day (normal: up to 2000 μmol/day), calcium 4.06 mmol/day (normal: up to 4.00 mmol/day), phosphates 9.63 mmol/day (normal: up to 21.0 mmol/day).
ENT consultation: grade 2 hypertrophy of the palatine tonsils, candidiasis, grade 2 adenoids.

CONCLUSION

Preliminary diagnosis: periodic disease, arthropathy.
Associated diagnosis: candidiasis of the palatine tonsils. Hypertrophy of the palatine tonsils grade 2. Adenoids grade 2.
Molecular genetic examination of the girl revealed a mutation of the M 694 V gene in a heterozygous state.
Final clinical diagnosis: Periodic disease, articular syndrome, active stage.
Associated diagnosis: Candidiasis of the palatine tonsils. Hypertrophy of the palatine tonsils grade 2. Adenoids grade 2.
This clinical case has some clinical features that may make the doctor doubt the diagnosis. The articular syndrome in this child was not periodic, but permanent. The girl had pronounced changes in the ENT organs, which could complicate the diagnosis. When conducting a differential diagnosis, it is recommended to conduct a genetic examination. In conclusion, I would like to say that periodic disease is quite rare in the general population, but the relevance of the topic is due to the early onset of the pathology and, in most cases, a serious prognosis for the patient's health. Correct diagnosis and selection of adequate therapy can improve the patient's quality of life.

REFERENCES

1. Arutyunyan V. M., Akopyan G. S. Periodic disease (etiopathogenetic and clinical aspects). Moscow: MIA. 2020.
2. Barabanova O. V., Konopleva E. A., Prodeus A. P., et al. Periodic syndromes. Journal "Difficult Patient". Archive No. 2-2007.32. Dolgushin I. I., Bukharin O. V. Neutrophils and homeostasis. Ekaterinburg, 2011.
3. Murray R., Grenner D., Mayes P., Rodwell V. Human biochemistry. M.: Mir, 2013.
4. Kuzmina N. N., Movsisyan G. R. PFAPA (periodic fever, aphthous stomatitis, pharyngitis, cervical adenitis), or Marshall syndrome, in children. Scientific and practical rheumatology / Association of Rheumatologists of Russia (M.), Institute of Rheumatology of the Russian Academy of Medical Sciences (M.). 2015. No. 5. P. 80–83.
5. Fedorov A. M., Tatochenko M. D., Bakradze M. D. et al. Syndrome of periodic fever, aphthous stomatitis, pharyngitis and cervical lymphadenitis (PFAPA) // Medical scientific and educational-methodical journal. 2016. No. 6.