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EARLY DIAGNOSIS OF MYASTHENIA IN CHILDREN: CLINICAL FEATURES AND COURSE

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Introduction

Myasthenia in children is a rare neuromuscular disorder characterized by impaired transmission of nerve impulses at the neuromuscular junction, leading to muscle weakness and pathological fatigue. Early diagnosis of this condition is particularly important in pediatric practice, as it helps prevent complications and improves the prognosis. However, diagnosing myasthenia in childhood is a serious clinical challenge due to variable manifestations, polymorphic courses, and difficulties in interpreting symptoms in young children.

Etiology and Pathogenesis

Myasthenia in children is divided into two main groups: congenital myasthenic syndromes (CMS) and acquired autoimmune myasthenia (AAM). Congenital forms are caused by mutations in genes encoding proteins involved in synaptic transmission, including:

• CHAT (choline acetyltransferase)

• CHRNE (ε-subunit of the nicotinic acetylcholine receptor)

• RAPSN, COLQ, and DOK7.

CMS is most commonly inherited in an autosomal recessive manner and is not associated with autoimmune mechanisms [Engel A.G., Shen X.M., Selcen D., Sine S.M., 2015].

Acquired myasthenia in children is caused by the production of autoantibodies against:

• postsynaptic acetylcholine receptors (AChR)

• muscle-specific kinase (MuSK)

• low-density lipoprotein receptor-related protein 4 (LRP4) and other proteins

This form is more commonly diagnosed in adolescents but can also appear in early childhood. The pathogenesis involves disruption of signal transmission at the neuromuscular junction due to the destruction of receptor structures [Gilhus N.E., Tzartos S., Evoli A., et al., 2019].

Clinical Features

The clinical presentation of congenital forms depends on the specific genetic defect. Main symptoms include:

• weakness of facial, swallowing, and respiratory muscles

• ptosis

• fatigue

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• delayed motor development

Manifestations are typically present from birth or emerge within the first few months of life. Apnea episodes, dysphagia, and a weak cry are frequently observed.

Autoimmune myasthenia in children presents similarly but may have a relapsing course, worsening of symptoms in the evening, and a positive response to anticholinesterase medications.

Key features include:

• a fluctuating course

• exacerbations triggered by infections or stress

• possible involvement of respiratory muscles and development of myasthenic crisis [Juel V.C., Massey J.M., 2005]

Transient Neonatal Myasthenia

This special form occurs in 10–20% of newborns born to mothers with myasthenia. Maternal antibodies cross the placenta and temporarily impair receptor function in the neonate. The condition resolves spontaneously as the antibodies are eliminated from the infant's circulation [Vincent A., Palace J., Hilton-Jones D., 2001].

Methods of Early Diagnosis

Diagnosing myasthenia in children requires a comprehensive approach, combining clinical, laboratory, electrophysiological, and genetic methods.

1. Clinical Examination

Early signs physicians should pay attention to:

• poor sucking in infants

• rapid onset of weakness with physical activity

• double vision, ptosis

• fluctuation of symptoms throughout the day

2. Electrophysiological Studies

• Repetitive nerve stimulation (RNS) — a decrease in muscle response amplitude of more than 10% during serial stimulation

• Single-fiber EMG — the gold standard, detecting impaired transmission time between motor unit and muscle [Sanders D.B., Stålberg E.V., 1996]

3. Immunological Diagnostics

Measurement of antibody titers to AChR, MuSK, LRP4

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Antibodies to AChR are detected in approximately 85% of children with generalized myasthenia [Gilhus N.E., et al., 2019]

4. Genetic Testing

Particularly important in suspected congenital myasthenic syndromes. Next-generation sequencing (NGS) technologies allow for precise identification of mutations.

Prognosis and Treatment Approaches

The prognosis for myasthenia in children largely depends on the timeliness of diagnosis and initiation of treatment. Treatment includes:

• anticholinesterase medications (ineffective in some CMS cases)

• glucocorticoids and immunosuppressants (for autoimmune forms)

• intravenous immunoglobulins (IVIG) or plasmapheresis during exacerbations

• thymectomy — in the presence of thymic hyperplasia or thymoma

In congenital forms, treatment must be individualized based on molecular diagnostics. For example, in cases with COLQ mutations, anticholinesterase agents are contraindicated and may worsen the condition [Abicht A., Dusl M., Gallenmüller C., et al., 2012].

Clinical Observation

As part of a clinical-practical observation, 30 children diagnosed with myasthenia were examined and followed at the Multidisciplinary Children's Medical Center of the Andijan region. Among them:

• 18 girls (60%)

• 12 boys (40%)

• Patient age ranged from newborns (0 years) to adolescents aged 17

Distribution of disease forms:

• Congenital myasthenic syndromes (CMS) — 11 children (36.7%)

• Acquired autoimmune myasthenia (AAM) — 17 children (56.7%)

• Transient neonatal form — 2 children (6.6%)

Clinical Data

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• All children with CMS had early symptoms (within the first months of life): lethargy, feeding difficulties, respiratory insufficiency, ptosis

• In AAM, the ocular form (ptosis, ophthalmoplegia) predominated in 10 children; the generalized form occurred in 7 patients and included swallowing and speech difficulties, limb fatigue

• In two newborns with the transient form, symptoms (lethargy, feeding difficulty, hypotonia) resolved by the 3rd–4th week of life

Diagnostic Results

• Electrophysiological studies confirmed a decrease in response amplitude on repetitive stimulation in 22 children

• AChR antibodies were found in 14 patients with the autoimmune form

• Genetic testing confirmed mutations in all children with CMS (most frequently in CHRNE and DOK7)

• Anticholinesterase drug testing showed a positive effect in most children with the autoimmune form, but was ineffective or contraindicated in certain CMS cases

Treatment and Outcomes

• Administration of anticholinesterase drugs (pyridostigmine) led to improvement in 18 children

• 7 patients received corticosteroids and/or intravenous immunoglobulins

• Thymectomy was performed in 2 adolescents with confirmed thymic hyperplasia

• Most patients showed improvement in overall condition, with reduced ptosis and fatigue

Conclusion

The results of observing 30 children with various forms of myasthenia confirm the diversity of clinical manifestations and the importance of a comprehensive approach to early diagnosis. Analysis of clinical cases showed that:

• Early diagnosis is especially crucial in CMS, where symptoms manifest from birth

• Immunological and electrophysiological studies effectively differentiate autoimmune forms

• Genetic testing is essential for accurate diagnosis of congenital forms and for selecting appropriate therapy

Comprehensive diagnostics and individualized treatment allow for stable remission, improved quality of life, and prevention of severe complications, especially respiratory-related ones.