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GRISCELLI SYNDROME: MOLECULAR PATHOLOGY, DIFFERENTIAL DIAGNOSIS AND THERAPEUTIC STRATEGIES

Ulug'ov Shuhrat Jabborovich

Asia International University, Bukhara, Uzbekistan

ABSTRACT

Griscelli syndrome (GS) is a rare autosomal recessive disorder characterized by disruption of the intracellular vesicular transport system. This article provides a comprehensive and in-depth coverage of the molecular mechanisms of the disease, its immunopathogenesis, genetic basis, clinical manifestations, differential diagnosis, and modern treatment approaches. Special attention is given to contemporary biomarkers, genetic testing, and transplantation strategies.

INTRODUCTION AND EPIDEMIOLOGY

Griscelli syndrome is a very rare disease that occurs mainly in regions with a high rate of consanguineous marriages. Although the global prevalence of the disease is low, its clinical significance is very high. GS is most often diagnosed in childhood and, if not diagnosed early, leads to severe complications.

MOLECULAR PATHOPHYSIOLOGY

GS is associated with mutations in three main genes: RAB27A, MYO5A, and MLPH. These genes play an important role in intracellular transport mechanisms. Rab27a binds to the organelle membrane, performing the function of a melanophilin adaptor, while Myosin Va ensures movement along actin filaments.

IMMUNOPATHOGENESIS AND HLH

In the GS2 form, a severe impairment of the immune system is observed. The function of cytotoxic T-lymphocytes and NK cells is disrupted. As a result, a cytokine storm develops (IFN-γ, TNF-α, IL-6). This condition leads to the development of hemophagocytic lymphohistiocytosis (HLH).

CLINICAL MANIFESTATIONS

The main clinical signs of the disease include silvery hair, skin hypopigmentation, fever, hepatosplenomegaly, and neurological disorders. GS1 manifests in a neurological form, GS2 in an immunological form, and GS3 in a dermatological form.

DIAGNOSTIC ALGORITHMS

Diagnosis is carried out step by step:

1. Clinical evaluation

2. Trichoscopy (hair structure)

3. Laboratory tests (ferritin, triglycerides, sCD25)

4. Genetic tests (NGS, whole exome sequencing)

5. Bone marrow examination (in cases of HLH)

DIFFERENTIAL DIAGNOSIS

GS must be distinguished from the following diseases:

- Chediak-Higashi syndrome

- Elejalde syndrome

- Hermansky-Pudlak syndrome

Blood smear, hair microscopy, and genetic testing are of great importance in differentiation.

TREATMENT STRATEGIES

For GS2, the HLH-2004 protocol is used:

- Etoposide

- Dexamethasone

- Cyclosporine A

Biological therapy such as emapalumab (IFN-γ inhibitor) may be used.

TRANSPLANTATION

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is considered the gold standard for GS2. Transplantation performed at an early stage has high efficacy.

CONCLUSION

Griscelli syndrome is a complex and life-threatening disease that requires early diagnosis and complex treatment. Modern genetic diagnostics and transplantation methods significantly improve the prognosis of patients.

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