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# A clinical case of telomeropathy with heterozygous RTEL1 variant c.3791G>A (p.Arg1264His): discussion of bone marrow transplantation and multisystem management



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## ABSTRACT

Telomeropathies show multisystem phenotypes from dyskeratosis to severe neurological forms caused by genetic variation in genes of the telomerase complex and related proteins, in particular RTEL1.

**THE AIM** of the study was to demonstrate a personal observation of a young adult with telomeropathy and multisystem manifestations associated with RTEL1 variant c.3791G>A (p.Arg1264His) and to analyze the treatment strategy including bone marrow transplantation.

**MATERIAL AND METHODS.** The article presents the personal observation of a patient diagnosed with telomeropathy during his dynamic monitoring by a multidisciplinary team from 2020 to 2025. Common blood analyses, serum amino acid spectrum, serum homocysteine, immunogram, ultrasound investigation, computer tomography, genetic testing were performed on the patient.

**RESULTS.** The patient complained of episodic fever, associated with rash, skin manifestations (hyperkeratosis, telangiectasias), arthralgias and persistent viral infections. Hepato-splenomegaly, cerebellar ataxia, and thrombocytopenia were revealed during examination. Computed tomography showed signs of moderate bronchiectasis of small bronchi in the middle and lower parts of the lungs. Genetic testing identified the heterozygous variant RTEL1 mutation c.3791G>A (p.Arg1264His) and CNV affecting duplication of DOCK8 gene (exons 1-26, CN≈3) as a variant of uncertain significance (VUS). The patient was diagnosed with telomeropathy.

**CONCLUSIONS.** We suggest a personalized approach to bone marrow transplantation in the treatment of telomeropathy, considering not only clinical diagnosis but also individual patient characteristics, hematological, immunological and metabolic profiles.

**KEY WORDS:** RTEL1; telomeropathy; thrombocytopenia; bone marrow transplantation; multisystem management

Telomeropathies or telomere biology disorders (TBDs) involve a wide variety of genetic disorders caused by mutations in the telomerase maintenance mechanism or the DNA damage response system. New data provide an opportunity to reconsider paradigms related to the role of telomeres in human aging. Short telomeres promote clonal hematopoiesis, whereas long telomeres are considered to be the risk factor for cancer in population studies [1, 2].

The spectrum of TBDs includes dyskeratosis congenita (DC), Hoyeraal-Hreidarsson (HH) syndrome, pulmonary fibrosis, pancytopenia and bone marrow aplasia with ectodermal and neurological manifestations. The clinical signs of TBDs differ significantly in children and adolescents. TBDs are severely underdiagnosed in adults. The proper diagnosis is often substantially delayed after the first manifestations. Due to the rarity of adult-onset TBDs, the recommendations for diagnostic algorithms of this pathology remain limited. More data are needed to enhance the diagnostics and management of TBDs for the improvement of the patient outcomes and quality of life. The persons with classical DC were reported to exhibit the triad of typical reticular pigmentation, nail dystrophy, and mucosal hyperplastic leukoplakia. Meanwhile, persons with atypical DC present with one, two or no symptoms [3]. Genetic studies on a large collection of clinically diagnosed cases of DC have demonstrated that approximately 35 % of DC remain uncharacterized at the genetic level [4].

The mutations in *DKC1* (dyskerin), *TINF2*, *TERC*, *TERT*, *C16orf57*, *NOLA2*, *NOLA3*, *WRAP53/TCAB1*, and *RTEL1* (regulator of telomere elongation helicase 1) genes were reported to be linked to DC. Homozygous, compound heterozygous, and heterozygous mutations in *RTEL1* gene on chromosome 20q13 are known to cause autosomal dominant or autosomal recessive DC. Pathogenic variants of the *RTEL1* gene in DC patients were reported as c.2288G>T (p. Gly763Val), c.3791G>A (p. Arg1264His), and p. Arg981Trp [5]. Liver dysfunction was revealed to occur in 7 % of DC patients and includes liver disease progression, cholestasis and portal hypertension.

The findings of noncirrhotic portal hypertension, intrahepatic shunting, and angiosarcoma suggest vascular functional pathology as an etiology of hepatic manifestations in DC [6, 7].

The severe variant of DC is HH syndrome. In HH syndrome, clinical manifestations may not always be fully observed. Intrauterine growth retardation, severe microcephaly, cerebellar hypoplasia (manifested by cerebellar ataxia and motor coordination deficiency) and combined immunodeficiency with early development of severe infections are pathognomonic signs for HH syndrome. In newborns and young children, HH syndrome may manifest as a syndrome of physical development delay, frequent infections, and neurological abnormalities. Highly proliferative tissues are primarily affected (bone marrow and the immune system), associated with pulmonary and liver fibrosis [8, 9]. There is significant genetic overlap between HH syndrome and DC, and the genetic defect can be identified in approximately 60 % of the patients with HH syndrome. Mutations in genes *RTEL1* and *DKC1* genes are classically associated with HH syndrome.

The diverse roles of *RTEL1* in telomere stability, replication, inflammation and length regulation have been studied intensively [10]. Biallelic *RTEL1* variants result in childhood onset of DC and Hoyeraal-Hreidarsson syndrome, whereas heterozygous individuals usually present later in life with pulmonary fibrosis or bone marrow failure. Thus, compared with heterozygotes, individuals with biallelic *RTEL1* variants demonstrate an earlier age at diagnosis and worse overall survival [11]. In about half of the patients with HH syndrome, no genetic cause could be found until the role of the *RTEL1* gene was discovered – in 2013, Ballew and Walne were the first to report HH syndrome patients with biallelic *RTEL1* mutations [12].

Hematopoietic stem cell transplantation (HSCT) is the only curative intervention for bone marrow failure. However, initial attempts at stem cell transplantation using conventional myeloablative conditioning in DC have been disappointing due to the severe systemic toxicity of conditioning chemotherapy. Reduced intensity conditioning (RIC) has been

regarded as successful strategy with reasonable outcomes [13]. The recent introduction of RIC regimens has reduced toxicity of chemotherapy. However, long-term mortality after HSCT remains high [14, 15]. Some authors reported that the RIC required for HSCT may lead to accelerated deterioration of the disease comorbidities.

**THE AIM** of the present study was to demonstrate a personal observation of a young adult with a diagnosis of telomeropathy and multisystem manifestations associated with *RTEL1* variant c.3791G>A (p.Arg1264His) and to analyze the strategy of the treatment, including bone marrow transplantation.

## MATERIALS AND METHODS

The diagnosis of telomeropathy in this study was established according to the diagnostic criteria proposed by Niewisch [16]. The informed consent was obtained from the patient. The study has been approved by the Ethical committee of Kharkiv National Medical University.

**Analysis of hematological parameters.** The blood was collected from the person by venipuncture into EDTA tube using a syringe. Red blood cells (RBCs), hemoglobin, leukocytes, neutrophils, lymphocytes, eosinophils, monocytes, erythrocyte sedimentation rate (ESR) and platelets were measured using a complete blood count (CBC) by an autohematological analyzer MYTHIC 3CRP-3 DIFF (*Cormay Diagnostics*, Poland). Plasma was separated by centrifugation at 2000 rpm for 10 minutes and used for further investigation.

Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities were determined through the colorimetric method using multiparametric Photocolorimetric biochemical analyzer ALIZE (*Lisabio*, France). The optical density of the test sample for AST and ALT was measured against a control sample on a photometer at a wavelength of 500 and 340 nm, accordingly.

**Determination of free amino acids in blood serum using high performance liquid chromatography.** Proteins were removed from 200  $\mu$ L of the serum sample by precipitation with a solution of 100  $\mu$ L of 5-sulfosalicylic acid. The supernatant fraction containing amino acids with phenylthioisocyanate in a mixture of methanol and triethylamine was centrifugated. The reaction was carried out at alkaline pH for 25 minutes at room temperature. The excess reagent was removed under vacuum and the residue was dissolved in a small volume of sample solvent. The peak area was integrated for each amino acid.

**C-reactive protein (CRP)** was measured using 10  $\mu$ L of blood serum by an immunoprecipitation assay with the Filicrit-CRP-latex kit (*Filicrit*, Ukraine). The presence of agglutination was regarded as a CRP concentration equal to or more than 6 mg/L. The absence of agglutination indicated the concentration of CRP lower than 6 mg/L.

**Homocysteine** was detected by the Human Homocysteine (HCY) ELISA kit (*MyBioSource*, USA). 100  $\mu$ L of Standards and the studied sample were added to the coated wells. 100  $\mu$ L of PBS (pH 7.0-7.2) was added in the blank control well. 10  $\mu$ L of Balance Solution was dispensed with 100  $\mu$ L of the sample and well mixed. 50  $\mu$ L of Conjugate was added to each well, mixed well and incubated for 1 hour at 37 °C. The microtiter plate was washed and contents of the plate was aspirated into a waste container. This procedure was repeated five times. The plate was inverted and blotted against absorbent paper until no moisture appeared. 50  $\mu$ L of Substrate A and 50  $\mu$ L of Substrate B were added to each well including blank control well, covered and incubated for 15-20 minutes at 37 °C. 50  $\mu$ L of Stop Solution was added to each well. The Optical Density (OD) was determined at 450 nm using a microplate reader immediately. Standard curve was constructed by plotting the concentration on the horizontal (X) axis against the average OD for each standard on the vertical (Y) axis, and a best fit curve using graph paper was drawn. The concentration of the studied sample corresponding to the mean absorbance from the standard curve was calculated.

**Genetic testing.** 4 mL of EDTA blood was used for the analysis. Peripheral mononuclear cells were isolated by density gradient centrifugation using Ficoll-Paque PLUS (GE Healthcare, USA). DNA was extracted using the QIAamp DNA Blood Mini Kit (Qiagen, Germany) according to the manufacturer’s instructions. DNA concentration and purity were assessed with a NanoDrop 2000 (Thermo Fisher Scientific, USA) and a Qubit 4 Fluorometer (Thermo Fisher Scientific, USA). DNA integrity was evaluated by electrophoresis on a 1 % agarose gel. Targeted regions were enriched using a hybridization-based protocol, capturing exonic sequences and 20 bp of flanking intronic regions. Sequencing was performed on the Illumina platform, ensuring an average coverage of  $\geq 50\times$  across all targeted regions. The analysis was performed using the Invitae Autoinflammatory and Autoimmunity Syndromes Panel, which includes sequence and deletion/duplication testing of 156 genes.

Variant classification was conducted according to Invitae’s internal standards. Variants were classified as Pathogenic, Likely Pathogenic, VUS, Likely Benign, or Benign.

**Instrumental investigations.** Ultrasound investigation was performed on a Voluson Expert 22 ultrasound machine. Computer tomography was performed on a SOMATOM go.Now 32 CT scanner (Siemens, Germany).

## RESULTS AND DISCUSSION

A boy was born with body weight of 3500 g and body length of 56 cm. At the age of 9 years, an inexplicable increase in body temperature (38–39 °C) for several days was noted, accompanied by general weakness. The boy was examined for the presence of infection. Positive IgM antibodies to *Toxoplasma gondii* were revealed and the patient underwent a course of anti-toxoplasma therapy.

However, at the age of 15 years, episodes of fever were accompanied by multiforme-like skin rashes and arthralgias. Blood tests showed leukocytosis ( $12\times 10^9/L$ ), neutrophilia, mild anemia (Hb: 110 g/L) and high erythrocyte sedimentation rate (ESR) (30 mm/h). Based on the presence of the set of specific symptoms (fever of unknown origin, serositis, rash, arthralgias, conjunctivitis), the patient was diagnosed with undifferentiated diffuse connective tissue disease. The treatment with methylprednisolone and methotrexate brought improvement and decreased the frequency of episodes of rash, fever, and inflammation.

At the age of 19 years, the increase in the body temperature to 39–40 °C, body aches, arthralgia of the knees were repeated. Hematological and biochemical parameters were investigated to monitor the metabolic status of the patient. Blood test revealed leukocytosis ( $14\times 10^9/L$ ) with neutrophilia (80 %), mild anemia (Hb 115 g/L), increased ESR (28 mm/h) and CRP (24 mg/L). To find out the cause of inflammation the person was examined for the presence of viral infection. High-avidity IgG antibodies to Epstein-Barr virus (EBV) and cytomegalovirus (CMV) have been detected. The patient was diagnosed with active phase of undifferentiated connective tissue disease, with involvement of joints (arthralgia syndrome without X-ray signs of arthritis), eyes (keratoconjunctivitis sicca) and skin (lichen-like rash during fever) (Table 1).

**Table 1.** Summary of the key parameters of the patient with Hoyeraal-Hreidarsson syndrome.

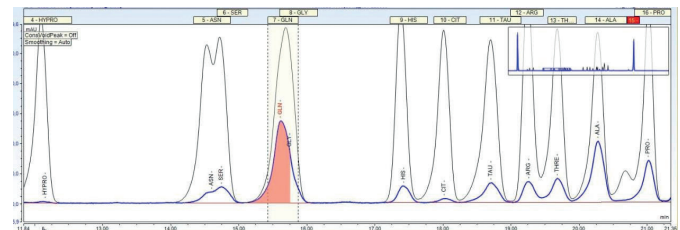
Analysis	Parameter	Value	Normal value	Note
CBC	Platelets	$126.0\times 10^9/L$	$150-400\times 10^9/L$	Decrease
Inflammation	CRP	24 mg/L	$\leq 5.0$ mg/L	High
One-carbon metabolism	Homocysteine	15.0 $\mu\text{mol/L}$	5–15 $\mu\text{mol/L}$	Upper limit
Amino acids	Glutamine	0.94 mmol/L	0.711 mmol/L	Increased
Serology	EBV/CMV/HSV IgG	Positive	-	Persistent immune memory
Bacteriological study	S. aureus	$10^4$ CFU	-	Carrier

**Instrumental examinations.** To find out if there were any structural abnormalities in internal organs ultrasound investigation and computer tomography have been performed. The abdominal ultrasound revealed hepato/splenomegaly. Computer tomography of the chest showed signs of moderate bronchiectasis of small bronchi in the middle and lower parts of the lungs.

**Phenotype.** At the age of 20 years 174 cm tall patient had decreased body weight of 60 kg (BMI 19.8 kg/m<sup>2</sup>). On the mucous membrane of his lower lip leukoplakia up to 3 mm in diameter was revealed. The patient had pale pink skin with marbling, light dryness of the skin, small telangiectasias, rashes on the back and chest, rough skin of the palms, positive phenomenon of reddening of the palms, isolated hyperkeratosis on the big toe of the left foot and on the lateral surface of the right foot, thickening of the skin on the feet; slight swelling of the joints (permanent); early gray hair; conjunctivitis; catarrhal pharyngitis; permanent hepatomegaly, permanent splenomegaly.

**In the neurological status:** muscle tone was slightly reduced in the upper extremities and moderately increased in the lower extremities. Tendon reflexes were of medium liveliness in the hands, lively in the feet, and high in the knees. Achilles reflexes showed clonus of the feet for several seconds. The patient walked independently with a little uncertainty. Mild cerebellar ataxia was detected.

**Blood test** revealed leukocytosis ( $11.2\times 10^9/L$ ), neutrophilia (72 %), lymphopenia (18 %), increased AST (58 U/L), ALT (60 U/L), LDH (480 U/L), CRP (18 mg/L), ferritin (350 ng/mL), interleukin-6 (15 pg/mL). To explore the metabolic status of the person the level of vitamins and amino acids was investigated. The levels of vitamins B2, B5, B9 were decreased: 8, 20 and 2 ng/mL, respectively (normal values > 10, > 30 and > 4 ng/mL). Analysis of blood amino acids showed an increase of glutamine (820  $\mu\text{M}$ ; normal value 600  $\mu\text{M}$ ) (Fig. 1) with slightly increased ammonia (50  $\mu\text{M}$ ; normal value < 50  $\mu\text{M}$ ).



**Fig. 1.** Detection of increased glutamine in the patient’s sample. The studies were performed by high-performance liquid chromatography using a Chromatographic Complex based on a high-performance liquid chromatograph Ultimate 3000 Dionex (USA) using Chromeleon 6.7 Thermo Fisher Scientific software.

**Immunological study** showed an increased level of IgE: 220 IU/mL (normal value < 100 IU/mL), decreased CD19<sup>+</sup> B lymphocytes: 5 % (normal value 10 %), natural killers CD3<sup>+</sup>CD16<sup>+</sup>CD56<sup>+</sup>: 4 % (normal value 10 %); CD3<sup>+</sup> T lymphocytes: 75 % (normal value 70 %).

**Genetic studies.** To find out if the patient had any genetic disease genotyping has been performed. The patient underwent whole exome sequencing (WES) that demonstrated several clinically significant variants in different genes:

- RTEL1: heterozygous mutation c.3791G>A (p.Arg1264His), a pathogenic variant associated with autosomal recessive dyskeratosis and HH syndrome.
- DOCK8 (Dedicator of Cytokinesis 8): CNV, with a duplication of exons 1–26 in one allele (gain with copy number 3 for region 9p24.3), variant of undetermined significance (VUS), as there is currently no evidence of a pathological effect of such a duplication in the available sources.
- NOS1 (neuronal NO synthase): a heterozygous variant.

**Interpretation.** Patient's complaints (recurrent episodes of fever since childhood; exacerbations with rashes); systemic manifestations (hepatomegaly, splenomegaly); skin signs (hyperkeratosis of palms, teleangiectasias); conjunctivitis; neurological signs (cerebellar ataxia, decreased reflexes); signs of viral infections (EBV/CMV/HSV); bacterial findings (*Staphylococcus aureus* carrier); hematological and biochemical findings (thrombocytopenia:  $126.0 \times 10^9/L$ , increased serum glutamine; high CRP; homocysteine) and the heterozygous RTEL1 variant have been consistent with a diagnosis of telomeropathy of the Hoyeraal-Hreidarsson spectrum.

**Treatment and further course.** After bilateral tonsillectomy the frequency of fever episodes significantly decreased. A course of immunomodulatory and antioxidant therapy was prescribed. The diet with a high protein and vitamin content was adjusted, and vitamins B and vitamin D were additionally prescribed. After 2 months, subfebrile temperature almost disappeared, body weight slightly increased (+3 kg), complaints of joint pain and conjunctivitis decreased. The neurological status did not change significantly. However, the patient felt greater stability when walking.

The presented clinical observation is an example of telomeropathy. Biallelic mutations of the telomere-regulating gene are required for the development of the complete manifestation of HH syndrome, whereas in the presented patient only one pathogenic variant of RTEL1 gene was detected. The mutation c.3791G>A (p.Arg1264His) in the RTEL1 gene is clearly pathogenic: it has been repeatedly described in DC and HH syndrome [17].

Homozygous variant of RTEL1 gene, exon 24, c.2060C>T (p.Ala687Val) in a patient with DC presenting with leukoplakia, dystrophic nails, reticulate pigmentation, and a positive family history of a similar phenotype was reported in the literature [18]. Incomplete penetrance has been observed in carriers of this allele (c.3791G>A): heterozygotes are phenotypically healthy and develop isolated pulmonary fibrosis in adulthood. In contrast, homozygotes or combined heterozygotes for the mutant allele manifest classical DC in childhood.

Why did our patient, being a heterozygous, demonstrated the HH syndrome phenotype? One possible reason is the phenomenon of synergistic heterozygosity (oligogenic inheritance) that has been increasingly recognized as symptomatic. Additional mutations identified in the patient (DOCK8 duplication and GAD1 variant) could modify the manifestations of the main telomeric mutation, impairing immune function and neurological development. This gene interaction led to the fact that even the presence of only one defective RTEL1 allele, the patient's bone marrow stem cell reserve and immunity become significantly reduced that causes a clinical picture compatible with HH syndrome. According to ClinVar, TEL1 p.Arg1264His mutation has been found in at least 5 independent families with DC/HH worldwide.

The impact of the DOCK8 duplication on the patient's phenotype remains hypothetical. Heterozygous mutations or duplications of DOCK8 do not cause disease per se, as complete loss of function (two mutations) is required for immunodeficiency to occur. On the other hand, DOCK8 is a large gene, and in the presented person exons 1–26 were duplicated (a significant part of the protein). It can be assumed that as a result of this duplication, one of the alleles is incorrectly spliced or expresses a truncated protein, not causing the classic hyper-IgE syndrome, but suppressing lymphocyte function. This is supported by the fact that our patient had persistently low B-cells and

NK-cells, frequent viral infections (EBV, CMV), and chronic tonsillitis and furunculosis of the skin in childhood (*Staphylococcus* infections). These manifestations can be interpreted as immune vulnerability, although not as pronounced as in DOCK8 deficiency. Currently, in clinical genetics, DOCK8 duplications are considered as variants of uncertain significance – there are studies describing them in carriers without immunopathology. Nevertheless, we suggest that the presence of this variant in our patient could modify the severity of HH syndrome, increasing susceptibility to infections.

**Management of patients with telomeropathies.** The Guidelines for TBDs systematize approaches to the diagnosis and management of TBDs, including considerations for HCT preparation and monitoring of extramedullary lesions [19]. New technologies have been shown to elongate telomeres by recombination [20]. HCT with reduced conditioning regime in a case of progressive bone marrow aplasia might be considered. Personalized vaccination and infection prevention plan and immunoglobulins may be applied if needed, as well as pulmonary/hepatic/endocrine monitoring, dental support, neurological rehabilitation and genetic counseling.

**Hematopoietic cell transplantation (HCT)** represents the only known cure for BMF in DC, but poses significant toxicities. The patients with allogeneic HCT and novel nonmyeloablative conditioning regimes were reported. HCT demonstrated reactivation of CMV infection [21–23]. The researchers demonstrated the safety and feasibility of haploidentical HCT using a RIC regime [24]. However, some authors reported a poor outcome after HCT. Pulmonary disease, infection, and graft failure were the leading causes of death. Multivariate analysis identified the age of > 20 years at HCT and an alternate donor source to be poor prognostic markers. RIC was not significantly found to be associated with improved survival. The researchers reported 66 % overall survival at 3 years after HCT. These findings emphasize the high risk of mortality associated with pulmonary and hepatic complications post-HCT in DC.

The allogeneic HCT, a promising option to overcome impaired hematopoiesis in patients with telomeropathies, does not correct nonhematological defects and may enhance the risk of secondary malignancies. Disease-specific management is necessary, since TBDs are associated with complications after HCT. Long-term follow-up is essential to detect complications related to HCT [25]. Challenges include the treatment of adults with bone marrow aplasia [26].

The presented patient was recommended to continue observation and perform the following set of examinations: control common blood test, biochemical profile, determination of vitamins B2, B3, B9, homocysteine and ammonia levels, amino acid analysis; PCR/ELISA for EBV and CMV to monitor viral activity. The patient was also offered a course of sanatorium-resort treatment for rehabilitation (exercise therapy, swimming, massage to improve coordination). Since 2025, the patient has been under the supervision of a multidisciplinary team. Hematological parameters remain relatively stable: mild cytopenia alternates with periods of normal tests, there are no signs of progressive aplastic anemia (the bone marrow compensates for hematopoiesis).

Currently we conduct an observation of another patient with telomeropathy and a rare genetic environment. The diverse spectrum of clinical manifestations of TBDs in pediatric and adult patients, their correlation with pathogenic variants, and considerations during their management should increase physician awareness and improve a multidisciplinary approach [27].

## CONCLUSION

**Telomeropathies do not always present with classical symptoms. Physicians should be aware of the presence of one or no symptoms of telomeropathy. Clinicogenetic data of the presented patient are compatible with Hoyeraal-Hreidarsson spectrum of telomeropathy associated with RTEL1 c.3791G>A (p.Arg126 p.Arg1264His) variant. Genetic analysis is needed to establish an atypical course of telomeropathy. Treatment strategy should include a multidisciplinary approach and strict indications to the bone marrow transplantation.**

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# Клінічний випадок теломеропатії з гетерозиготним варіантом RTEL1 c.3791G>A (p.Arg1264His): обговорення трансплантації кісткового мозку та мультисистемного ведення патології



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## РЕЗЮМЕ

Теломеропатії мають мультисистемні фенотипи від дискератозу до тяжких неврологічних форм, обумовлених варіантами генів теломерозного комплексу та споріднених білків, зокрема RTEL1.

**МЕТА ДОСЛІДЖЕННЯ:** продемонструвати особисте спостереження молодої людини з теломеропатією та мультисистемними проявами, пов'язаними з мутацією гена RTEL1 c.3791G>A (p.Arg1264His), та проаналізувати стратегію лікування, зокрема, трансплантацію кісткового мозку.

**МАТЕРІАЛ ТА МЕТОДИ.** Представлено власне спостереження пацієнта з діагнозом теломеропатії в процесі його динамічного моніторингу мультидисциплінарною командою з 2020 по 2025 роки. Пацієнту було проведено клінічні та біохімічні аналізи крові, визначення амінокислотного спектру сироватки, рівню гомоцистеїну в сироватці, імунограма, ультразвукове дослідження, комп'ютерна томографія, генетичне тестування.

**РЕЗУЛЬТАТИ.** Пацієнт звернувся зі скаргами на епізодичну лихоманку, що асоційована з висипом на тілі, шкірні прояви (гіперкератоз, телеангіектазії), персистуючі вірусні інфекції. При обстеженні виявлено гепато-спленомегалію, мозочкову атаксію, тромбоцитопенію. Комп'ютерна томографія визначила ознаки помірної бронхоектазії дрібних бронхів у середніх та нижніх відділах легень. Генетичне дослідження встановило гетерозиготність за мутацією гена RTEL1 c.3791G>A (p.Arg1264His) та CNV гена DOCK8 (екзони 1-26, CN≈3) як варіант невизначеного значення (VUS). Хворому був встановлений діагноз теломеропатії.

**ВИСНОВКИ.** Ми пропонуємо персоналізований підхід до трансплантації кісткового мозку при лікуванні синдрому Хойсрала-Хрейдарсона, враховуючи не лише клінічний діагноз, а й індивідуальні характеристики пацієнта, гематологічні, імунологічні та метаболічні профілі.

**КЛЮЧОВІ СЛОВА:** трансплантація; RTEL1; кістковий мозок; теломеропатія; тромбоцитопенія; мультисистемне ведення.