BIALELIC PATHOGENIC (C.830G>A (P.R277Q)) VARIANT DISRUPTING THE *GNE* GENE FUNCTION AND CAUSES NONAKA MYOPATHY PHENOTYPE

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Nonaka myopathy (MIM 605820) is caused by homozygous pathogenic variants in the GNE gene. It is a recessively inherited early adult-onset myopathy that usually preserves the quadriceps and presents with bilateral foot drop, usually caused by anterior tibialis weakness. In patients with Nonaka myopathy, serum creatine kinases are slightly elevated, muscle weakness progresses slowly, and ambulation loss develops after 15–20 years. The current study aims to raise awareness of Nonaka myopathy that occurs as a rare phenotype due to pathogenic variants in GNE gene. Detailed family histories and clinical data were recorded. Whole exome sequencing was performed and co-segregation analysis of the family were done by Sanger sequencing. Also the homology model of the mutant protein was created with the ProMod3 algorithm. We identified a bialelic pathogenic variant (c.830G>A) in GNE gene, which explain the patients' clinical status. We present the main findings of two siblings with Nonaka myopathy together with detailed clinical and genetic profiles of the patients together with a three-dimensional mutant GNE protein model. We think that the clinical characteristics and the effect of the (c.830G>A) variant will facilitate our understanding of GNE gene in Nonaka myopathy pathogenesis.

Key words: *GNE myopathy, distal myopathy, sialic acid, Nonaka disease, rare diseases.*

ДІАЛЕЛЬНИЙ ПАТОГЕННИЙ (C.830G>A(P.R277Q)) ВАРІАНТ, ЩО ПОРУШУЄ ФУНКЦІЮ ГЕНУ *GNE* І ВИКЛИКАЄ ФЕНОТИП МІОПАТІЇ НОНАКА

Міопатію Нонака (MIM 605820) викликають гомозиготні патогенні варіанти в гені *GNE*. Це міопатія з раннім початком розвитку в дорослих, яка успадковується рецесивно та за якої зберігаються чотириголові м'язи і виникає двостороннє обвисання стіп, що зазвичай спричинено слабкістю переднього великогомілкового м'язу. У пацієнтів із міопатією Нонака дещо вищий рівень креатинкінази сироватки, повільне прогресування м'язової слабкості та втрата здатності самостійно переміщатися розвиваються через 15–20 років. Поточне дослідження спрямоване на підвищення обізнаності про міопатію Нонака, яка виникає як рідкісний фенотип через патогенні варіанти в гені *GNE*. Проводиться детальна реєстрація історій хвороби та клінічних даних. Було проведено повне секвенування екзому і косегрегаційний аналіз родин за допомогою секвенування Сенгера. Також було створено модель гомології мутантного білка за використання алгоритму ProMod3. Ми ідентифікували діалельний патогенний варіант (c.830G>A) у гені *GNE*, який пояснює клінічний стан пацієнтів. Ми представляємо основні результати двох дітей із однієї родини, які мають міопатію Нонака, а також детальні клінічні та генетичні профілі пацієнтів і тривимірну модель мутантного білку GNE. Ми вважаємо, що клінічні характеристики та вплив варіанта(c.830G>A) сприятимуть нашому розумінню ролі гена *GNE* у патогенезі міопатії Нонака.

Ключові слова: міопатія *GNE*, дистальна міопатія, сіалова кислота, хвороба Нонака, рідкісні захворювання.

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