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Utilizing Patient-Reported Data to Characterize the Multi-Systemic Landscape of v-ATPase-Related Disorders: Insights from the RARE-X Data Collection Program

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Abstract

v-ATPase-related disorders are ultra-rare genetic conditions with complex multisystem involvement and limited clinical data. This study aimed to characterize their clinical features using patient-reported natural history data collected through the RARE-X Data Collection Program. Data from 21 participants, including genetic reports and standardized surveys, were analyzed to assess neurological, digestive, and muscular manifestations. Neurological symptoms were reported by all participants, with cognitive impairment, coordination difficulties, and seizures being the most common. Digestive involvement was observed in 74% of participants, while 68% reported muscular abnormalities. Many symptoms appeared during early infancy. Patient-reported data provide valuable insights into the multisystem nature of v-ATPase-related disorders and support improved diagnosis, clinical management, and future therapeutic research.

Keywords: v-ATPase-related disorders, Rare diseases, Patient-reported outcomes, RARE-X, Natural history, Genetic disorders-Multisystem disease.

Introduction

Background

v-ATPase-related disorders represent a group of rare genetic conditions with complex, multi-systemic presentations that are often poorly understood. Due to the rarity of these conditions, clinical data is frequently fragmented, leading to diagnostic delays and challenges in clinical management. To address these knowledge gaps, the patient advocacy group v-ATPase Alliance partnered with the RARE-X Data Collection Program to capture comprehensive, patient-reported natural history data.

Methods

This study analyzed aggregate data from a cohort of 21 participants enrolled in the RARE-X platform as of February 2025. Data collection included curated genetic testing reports (n=13) and standardized surveys covering multiple physiological domains, including neurological, digestive, and muscular systems.

Results

The data reveals a significant burden of disease across several domains. 100% of respondents (19/19) reported symptoms within the Brain and Nervous System domain, with high prevalence of cognitive impairment, coordination issues, and seizures (all at 77.8%). Notably, core symptoms like cognitive impairment and hypotonia were frequently identified in the earliest stages of development (0–3 months). The digestive system was affected in 74% of participants, with feeding difficulties and constipation being the most prominent issues. Furthermore, 68% of the cohort reported muscular involvement, primarily characterized by abnormal muscle function and issues with limbs.

Conclusion

These findings highlight the heavy multisystemic impact of v-ATPase-related disorders and emphasize the critical need for early, multidisciplinary intervention. By leveraging patient-reported data, this program provides a clearer phenotype of the disorder, offering a foundation for improved diagnostic protocols and the development of future clinical trial endpoints. This community-led data collection demonstrates the power of patient-driven research in advancing the understanding of ultra-rare diseases.

References

1. Li, D., & Donohue, M. C. (2018). Disease progression models for dominantly-inherited Alzheimer's disease. Brain, 141(5), 1244–1246. https://doi.org/10.1093/brain/awy089
2. Guerrini, R., Mei, D., Kerti-Szigeti, K., Pepe, S., Koenig, M. K., Von Allmen, G., ... Fassio, A. (2022). Phenotypic and genetic spectrum of ATP6V1A encephalopathy: A disorder of lysosomal homeostasis. Brain, 145(8), 2687–2703. https://doi.org/10.1093/brain/awac160
3. Ma, J., Zhang, H., Lv, Y., Gao, M., Gai, Z., & Liu, Y. (2024). Clinical and genetic characteristics of two cases with developmental and epileptic encephalopathy 93 caused by novel ATP6V1A mutations and literature review. Human Mutation, 2024, Article 4678670. https://doi.org/10.1155/2024/4678670
4. Sirchia, F., Taietti, I., Donesana, M., Bassanese, F., Clemente, A. M., Barbato, E., ... Foiadelli, T. (2024). Expanding the spectrum of autosomal dominant ATP6V1A-related disease: Case report and literature review. Genes, 15(9), 1219. https://doi.org/10.3390/genes15091219
5. Tian, Y., Zhai, Q. X., Li, X. J., Shi, Z., Cheng, C. F., Fan, C. X., ... Wang, J. (2022). ATP6V0C is associated with febrile seizures and epilepsy with febrile seizures plus. Frontiers in Molecular Neuroscience, 15, Article 866776. https://doi.org/10.3389/fnmol.2022.866776
6. Mattison, K. A., Tossing, G., Mulroe, F., Simmons, C., Butler, K. M., Schreiber, A., ... Escayg, A. (2023). ATP6V0C variants impair V-ATPase function causing a neurodevelopmental disorder often associated with epilepsy. Brain, 146(4), 1357–1372. https://doi.org/10.1093/brain/awac328
7. Selvanathan, A., Macintosh, R., Johnson, A., Sarkozy, V., Neville, K., & Sachdev, R. (2023). Challenges in seizure control in ATP6V0C deficiency: A longitudinal case report. Epileptic Disorders, 25(5), 783–786. https://doi.org/10.1002/epd2.20054
8. Aoto, K., Kato, M., Akita, T., Nakashima, M., Mutoh, H., Akasaka, N., ... Saitsu, H. (2021). ATP6V0A1 encoding the a1-subunit of the V0 domain of vacuolar H+-ATPases is essential for brain development in humans and mice. Nature Communications, 12(1), Article 2107. https://doi.org/10.1038/s41467-021-22389-5
9. Bott, L. C., Forouhan, M., Lieto, M., Sala, A. J., Ellerington, R., Johnson, J. O., ... Rinaldi, C. (2021). Variants in ATP6V0A1 cause progressive myoclonus epilepsy and developmental and epileptic encephalopathy. Brain Communications, 3(4), fcab251. https://doi.org/10.1093/braincomms/fcab251
10. Yuan, Y., Zhang, J., Chang, Q., Zeng, J., Xin, F., Wang, J., ... Dai, P. (2014). De novo mutation in ATP6V1B2 impairs lysosome acidification and causes dominant deafness-onychodystrophy syndrome. Cell Research, 24(11), 1370–1373.
11. Zhao, W., Gao, X., Qiu, S., Gao, B., Gao, S., Zhang, X., ... Yuan, Y. (2019). A subunit of V-ATPases, ATP6V1B2, underlies the pathology of intellectual disability. EBioMedicine, 45, 408–421.
12. Menendez, I., Carranza, C., Herrera, M., Marroquin, N., Foster, J., Cengiz, F. B., ... Tekin, M. (2017). Dominant deafness–onychodystrophy syndrome caused by an ATP6V1B2 mutation. Clinical Case Reports, 5(4), 376–380.
13. Beauregard-Lacroix, E., Pacheco-Cuellar, G., Ajeawung, N. F., Tardif, J., Dieterich, K., Dabir, T., ... Campeau, P. M. (2021). DOORS syndrome and a recurrent truncating ATP6V1B2 variant. Genetics in Medicine, 23(1), 149–154.
14. Veltra, D., Kosma, K., Papavasiliou, A., Tilemis, F. N., Traeger-Synodinos, J., & Sofocleous, C. (2022). A novel pathogenic ATP6V1B2 variant: Widening the genotypic spectrum of the epileptic neurodevelopmental phenotype. American Journal of Medical Genetics Part A, 188(12), 3563–3566.
15. Amore, G., Calì, E., Spanò, M., Ceravolo, G., Mangano, G. D., Scorrano, G., ... Di Rosa, G. (2023). ATP6V1B2-related disorders featuring Lennox–Gastaut syndrome: A case-based overview. Brain and Development, 45(10), 588–596.
16. Ma, T. C. N., Shih, F. Y. C., Ou, M., Wu, K. W. P., Yiu, W. C., Ho, S. K. L., ... Luk, H. M. (2026). Exploring ATP6V1B2-related disorders: A case report-based literature review. Clinical Dysmorphology, 35(2), 85–88.

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