Key Summary of Conference Abstract

Distribution of Mutations Associated With Congenital Myasthenic Syndromes (CMS): Results From the First 54 Specimens Tested at a Clinical Reference Laboratory

Background

- Congenital myasthenic syndromes (CMS) refer to a group of rare inherited disorders that cause muscle weakness. They can present at different ages with varying symptoms and severity.[1]
- Each CMS type is associated with variants in specific genes, and treatment depends on the CMS type.[2] While genetic diagnoses can help in the management of CMS, genetic testing is not widely available.
- The investigators of this study previously developed an assay to test 13 genes associated with CMS.
- **Objective:** In this study, they examined the frequency of CMS-associated variants determined with this test in patient specimens submitted to a clinical reference laboratory.

Methods

- This study included the first 54 patient specimens (deidentified) submitted to Athena Diagnostics® to be tested using the panel described below.
- A next-generation sequencing (hybrid capture) assay targeted the coding regions and at least 10 adjacent noncoding nucleotides for the following genes: *AGRN*, *CHAT*, *CHRNA1*, *CHRNB1*, *CHRND*, *CHRNE*, *COLQ*, *DOK7*, *DPAGT1*, *GFPT1*, *MUSK*, *RAPSN*, and *SCN4A*.
  - In prior validation testing, DNA sequence variations were detected with 99% sensitivity and specificity.

Results

- Of the specimens submitted for testing, 12 (22%) were positive for deleterious variant(s), 16 (30%) had variants of uncertain significance (VUS), and 26 (48%) were negative for CMS-associated variants.
- Among the specimens with deleterious variants, patient age ranged from 3 to 53 years.
- Deleterious mutations were most commonly detected in *CHRNA6* (n=6), followed by *DOK7* (n=2); *COLQ, MUSK*, and *RAPSN* (n=1 each); and *GFPT1* (n=1 carrier).

Conclusions

- The targeted gene-sequencing panel detected deleterious variants associated with CMS in 22% of tested specimens.
- Many VUS were also identified, which may provide insight into CMS in the future.

Poster scheduled for presentation at the American Academy of Neurology Annual Meeting (conference canceled; abstract available online)

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Also selected to be presented at the Grand Finale Science Innovation Lunch

Webpage
https://index.mirasmart.com/AAN2020/PDFfiles/AAN2020-004638.html

References

1. Vanhaesebrouck AE, Beeson D. *Curr Opin Neurol*. 2019;32:696-703.
2. Thompson R, Bonne G, Missier P, et al. *Emerg Top Life Sci*. 2019;3:19-37.