Presentation of Paired P- and Q-Arm Mosaic Deletions on Chromosome 18 Associated with Neuropsychiatric Symptoms

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Background

In this report, we present a case of an 18-year-old male with a history of ADHD, anxiety, obesity, and autism, as well as unresponsive episodes wherein the patient experiences breath-holding muscle spasms that have been unresponsive to anticonvulsants. He displays muscle weakness, hypotonia, and joint hyperlaxity. The patient has historically received assistance from occupational therapy as well from speech and language pathology services provided by his school to combat social and physical deficits. This report aims to correlate genetic findings with the patient's symptoms.

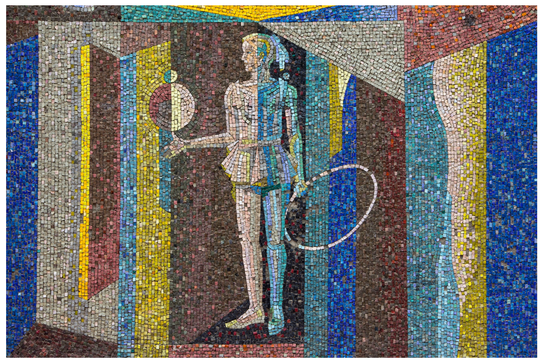

Figure 1. Mosaic artwork
Opensource image obtained from www.upsplash.com/photos

Methods

A buccal swab was collected and used for chromosomal genetic hybridization (CGH) array analysis. Bioinformatic analysis was carried out using the Genome Data Viewer (ncbi.nlm.nih.gov/genome/gdv).

Bioinformatic Analysis

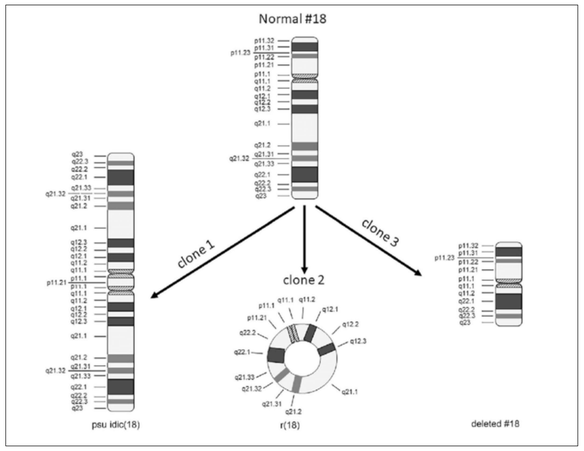

Figure 2. Various interpretations of potential chromosome aberrations, including pseudo-isodicentric, ringed, and independent p- and q- deletion. Due to the unknown degree of mosaicism and the presence of deletions in other tissues of the body, further analysis is needed to determine the type of deletion and its prevalence in various tissues.

Image obtained from Sheth et. al, DOI:10.1186/s12920-020-00796-9

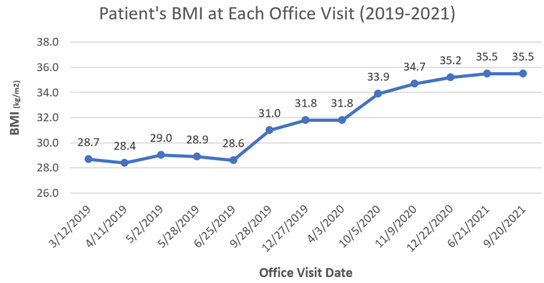

Figure 3. Changes in patient's BMI at each office visit from 2019 (age 15)to 2021 (age 17). Patient's BMI gradually increased from 28.7 to 35.5

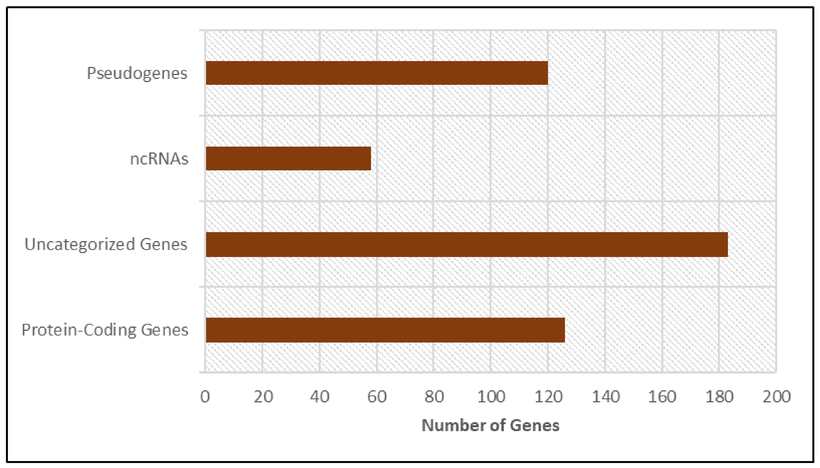

Figure 4. Distribution of deleted genes from 18p11.32-p11.21 and 18q21.32-32-q23. A bioinformatic analysis of mosaic deletions yielded a loss of 487 total genes in affected cells, 126 of which are protein coding. Several of the genes that reside in the mosaic deletion could be associated with the phenotypes presented in the patient. The gene GNAL is associated with dystonia with a teenage onset, and the gene AFG33L2 corresponds to ataxic-like movements and loss of voluntary muscle control, though the implication of the deletion of these genes is still unknown without a known percentage of mosaicism.

Results

CGH revealed a deletion of the distal end of both the p-arm and the q-arm of chromosome 18. The density of reads suggested the deletion to be mosaic, indicating that not all the cells contain a deletion. This technology does not allow for determination of whether the two deletions occur in the same cells. These regions contain 487 total genes. Genes of interest in these regions include GNAL, which is associated with dystonia of teenage onset and AFG3L2, associated with progressive ataxic-like movements and loss of voluntary movement.

Conclusion

The patient presents with a distinct set of neuropsychological phenotypes while chromosomal microarray testing revealed a mosaic loss of portions of both the p- and q-arms of chromosome 18 in buccal skin cells. Further analysis including karyotyping, investigating the mosaicism in peripheral blood mononuclear cells, and FISH to determine the extent of mosaicism in the skin cells and other tissues may be beneficial. Investigation of the deleted genes may also help determine the cause of the presented symptoms and guide treatment options.

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