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Case report

Exploring the role of genetics in autism: A sibling case study

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ABSTRACT

Autism is a neurodevelopmental disorder characterized by social impairment, communication problems, and repetitive behaviors. Autism and genetic link is still controversial. So far about 5-10% of children with Autism seem to have a genetic link. Some of the genes associated with an autism risk appear to be clustered in a region on chromosome 11, according to the study of families with a predisposition to the condition. This case report is about the two siblings with autism who have the identical contiguous region of allele homozygosity totaling 33.3 Mb observed in chromosome 11. The large contiguous block of homozygosity confers a relative risk of a recessive disorder for the genes with in that interval. Genetic linkage studies are designed to identify the genomes shared by the family members. In the case report described in this article, both the siblings share the same changes in the genome [1,2]. As both the siblings show features of Autism and have identical chromosomal changes, the case supports the unified genetic model [1] for inherited autism.

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1. Introduction

Autism is a neurodevelopmental disorder characterized by social impairment, communication problems, and repetitive behaviors. Although the relationship between autism and heredity (genetics) is still controversial, about 5-10% of children with Autism seem to have a genetic link. According to a study of families with a predisposition to the condition, some of the genes associated with an autism risk appear to be clustered in a region on chromosome 11. Using genetic linkage analysis, the authors in the journal nature genetics, found that the 11p12-p13 region of chromosome 11 was most closely linked to neuroligins, transmembrane proteins expressed on the postsynaptic cell that bind to presynaptic transmembrane proteins called β-neurexins[3].

This autism case report is regarding the two siblings of Mexican origin who have the identical contiguous region of allele homozygosity totaling 33.3 Mb observed in chromosome 11. The large contiguous block of homozygosity confers a relative risk of a recessive disorder for the genes within that interval. As the symptoms in the brothers appear similar, the cause could originate from a recessive allele pairing in the 33.3 Mb homozygotic intervals – creating a 25% recurrence risk.

Even though there are a number of cases with autism associated with chromosomal abnormalities, this may be a unique case in which both the siblings, show the same changes in the specific chromosome.

2.Case Presentation

The case study involves two siblings.

1st case: 4 year, 9 month old little boy whose parents came from a small town in Mexico. He presented with developmental delay, especially in regards to speech and behavioral concerns, with decreased eye contact and social reticence noticed since he was 2 years of age.

He was evaluated in our office by the speech and language pathologist and the occupational therapist. Based on the E-LAP (Early Learning Accomplishment Profile)

Chronological age	**57 months**
Cognitive skills	24 months
language skills	15 months
personal/social skills	24 months
Self-help skills	30 months

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As he also exhibited spinning, eye gazing, hand flapping and other repetitive behaviors during the evaluation, he was evaluated using Childhood autism rating scale (CARS) and was placed in the mild autism spectrum category after receiving a total score of 33.

As part of the work-up, genetic testing was ordered, including CGH (Comparative genomic hybridization) array. This showed a contiguous region of allele homozygosity, totaling 33.3 Mb in chromosome 11.

He was recommended to continue the "speech and occupational therapies" through the county program and "private therapies" through our program. Parents were also given a list of local agencies and resources for wrap-around services, including ABA therapy.

2nd case: 2 year, 8 month old little boy (Younger brother of 1st case), presented with a history of developmental delay and behavioral concerns with decreased eye contact and social reticence observed since he was 12 months of age.

He was evaluated in our office by the speech and language pathologist and the occupational therapist.

Based on the E-LAP (Early Learning Accomplishment Profile)

Chronological age	32 months
Cognitive skills	5 months
language skills	6 months
personal/social skills	7 months

He also exhibited a lot of clapping, spinning finger flicking, visual gazing and other self-stimulatory behaviors, and seemed to be more impaired than his brother. He was also evaluated using the Childhood Autism Rating Scale (CARS) and was placed in the severe autism spectrum disorder category after receiving a total score of 43.5.

As his brother exhibited specific homozygosity in chromosome 11, the genetic work-up was sent to see if he had the similar changes. The CGH array showed contiguous region of allele homozygosity, totaling 33.3 Mb in chromosome 11.

3.Conclusion

Chromosome 11 spans about 134.5 million base pairs (the building material of DNA) and represents between 4 and 4.5 percent of the total DNA in cells. It is one of the most gene- and disease-rich chromosomes in the human genome. Chromosome 11 likely contains between 1,300 and 1,700 genes. A recent study showed that 11.6 genes per megabase, including 1,524 protein-coding genes and 765 pseudogenes can be found on chromosome 11 [4,5].

In data derived from the AGP (Autism Genome Project) study, linkage and copy number variation analyses implicated chromosome 11p12-p13 and the genes for the neurexins, among other less significant genetic candidates. The site on chromosome 11, to which this study is also strongly linked, includes a gene that aids in the process of regulating glutamate, one of the most common chemical signals in the brain [6].

Genetic linkage studies are designed to identify the genomes shared by the family members. In the case report described above, both the siblings share the same changes in the genome [2]. As both the siblings show features of Autism and have identical chromosomal changes, this case report supports the unified genetic model* for inherited autism.

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