Case Report

Stuttering: Genetic updates and a case report

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Abstract

Developmental stuttering is a common disorder of speech dissiliency that is characterized by excessive repetitions of sounds, syllables, and monosyllabic words, as well as sound prolongations and complete blockages of the vocal tract. About 60 million people are affected and it is more common between the age of 3 and 6, when children begin forming sentences and connecting thoughts verbally. There are three types of stuttering known as developmental stuttering, neurogenic stuttering, and psychogenic stuttering. The exact pathophysiology of developmental stuttering is unknown; however, various family and twin studies have repeatedly implicated heredity as a major factor in the etiology of stuttering. It is clear that the genetic influence is not in the form of an exact single gene effect such as autosomal recessive, autosomal dominant, or x-linked in all families; however, in all of the inheritance forms it is influenced by sex with higher occurrence in males than females at a ratio of 4:1 in older children and adults. Recently special genetic locus has been determined on several autosomal chromosomes related to developmental stuttering. In this report, the proband is a 20-year-old boy was referred to our clinic for premarriage genetic counseling; he has been affected since 3 years and now is under cure. three generation study of his family show 13 individuals are affected by stuttering. For the first it occurred in the proband's grandfather and after this time about all of affected cases has been seen in consanguineous marriages. Therefore, the genetical inheritance of stuttering is crystal clear in this family and autosomal recessive inheritance pattern is proposed. Totally in such families with repeated occur of stuttering, we cannot account it as a multifactorial disorder.

Key Words: Case report, genetic, inheritance, stuttering

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INTRODUCTION

Stuttering is a puzzling and debilitating disorder that prevents those affected from engaging in effortless and spontaneous conversational interactions. Developmental stuttering is a common disorder of speech disfluency that is characterized by excessive repetitions of sounds, syllables, and monosyllabic words, as well as sound prolongations and complete blockages of the vocal tract that may be associated with additional physical movements of head and neck. This disorder has a prevalence of 5% in children but 1% in adult population because a large number of children will recover before puberty.[1,2] Seventy five percent incidence of stuttering are at the age of 3 to 6 and after 12 years of age almost does not occur[3] that usually with the 1:2 ratio is higher in boys than girls.[4,5]

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Because 80% of affected children, specially girls, recover after 1 to 2 years, eventually the ratio of boys to girls in the older ages will be 1:4.[6,7] The form of stuttering that will be episodic or permanent is inherited in families as children who do not recover are more probable to have affected relatives with permanent and not recovered stuttering. Conversely, children who recover are more probable to have affected relatives with the disorder.[8-10]

Researchers suggest the theory of common genes are involved in both forms of the disorder but there are special genetic factors in addition to common genes which facilitate recovery process in transient form.[11,12]

There are three types of stuttering including developmental stuttering, neurogenic stuttering, and psychogenic stuttering. The exact pathophysiology of developmental stuttering is unknown. Genetic along with environment seems to play a vital role in the onset of transient or permanent stuttering.[13] various family and twin studies indicate that the genetic influence is not in the form of an exact single gene effect such as autosomal recessive, autosomal dominant, or x-linked in all families; however, in all of the inheritance forms it is influenced by sex with higher occurrence in males than females at a ratio of 4:1 in older children and adults. However some studies have repeatedly implicated heredity as a major factor in the etiology of stuttering as: (i) Stuttering in different families shows a cumulative pattern and it rule out the theory that stuttering may be repeated in families because of mimic.[14] (ii) Many similarities have been seen in incidence of the trait in MZ (90%) twins in comparison with DZ twins (3–19%).[15] (iii) In adoption studies, stuttering is more seen in biological relatives of proband than his/her half-siblings. In several studies a high degree of stuttering in the first degree relatives (20–70%) than the general population (3.1% to 42%) is shown.[16]) (iv) phenotypic characteristics of the abnormality, such as excessive repetitions of sounds and primary Floods of words or sound prolongations that are various in different languages and cultures are the same in stuttering patients with different languages. Of course there are some exceptions in each of these reasons as evidences that imply environmental factors are also involved in stuttering. In some studies. Seventy percent contribution of genetic factors along with 30% role of environment are considered.[17-19] Recently special genetic locus has been determined by special genetic markers on several autosomal chromosomes such as chromosome 1, 3, 5, 9, 13, 15, 18, and 12 related to developmental stuttering.[10-12] The study of chromosomes 5 and 15 has been identified in connection with permanent form of stuttering and chromosomes 2, 7, and 9 has been associated with temporary stuttering that can has different patterns in men and women.[13] In a study on 46 Pakistani families with stuttering mutations in GNPTAB gene (GNPTAB encodes the α and β subunits of GlcNAc-phosphotransferase, a protein involved in the lysosomal enzyme-targeting pathway) located on chromosome 12q has been associated with stuttering. Subsequent studies on other European and Asian populations identified other genetic mutations in GNPTG gene in association with stuttering. It seems that these three genes are responsible for 9% of cases of stuttering.[14]

CASE REPORT

Proband is a 20-years-old boy who is affected by Stuttering since 3 years and now is under treatment. He was born in a 3 degree consanguineous marriages and were originally from the Ardakan in Yazd province of Iran. The proband was referred to our genetic counseling center for Genetic counseling before marriage. In addition to proband, his mother and two of his brother had been also affected by stuttering since 3 to 7 years. Study of three generations of this family pedigree showed that 13 individual in this family were affected by stuttering; the first onset was in his maternal grandfather and about all of patients were born in consanguineous marriages [Figure 1]. Patients VI-7 and VI-17 show transient stuttering at the age of 2–3 and recovered at the age of 6–7. In addition to proband the other patients had permanent stuttering; however, none of them were under speech therapy. Therefore, stuttering in this family seems to be genetically and autosomal recessive pattern of inheritance is recommended for them. However, the hypothesis of influenced by sex for this trait is evident in this family pedigree.

CONCLUSION

Developmental stuttering is a common disorder of speech with prevalence of 5% in children that incidence in boys are twice than girls and the recovery in boys is less than girls (1, 2, 4, and 5) Genetics may play a vital role in the onset of permanent or transient stuttering, cumulative pattern of stuttering and various family

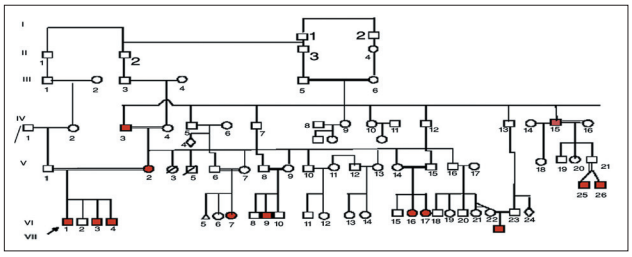

Figure 1: Family pedigree of the proband who is affected by stuttering

and twin studies repeatedly implicated heredity as a major factor in the etiology of stuttering.[20,21] Recently, researchers have identified special genetic locus on several autosomal chromosomes by special genome scanning, genetic markers, and comparison between chromosomes of normal individuals and abnormal ones.[10-14] Usually geneticists consider stuttering as a multifactorial disorder in determining risk in a family tree that has several occurrences of the stuttering; however, according to recent progress in determining the genes involved in this disorder, in patients with familial history of the disorder it is necessary to draw the pedigree of the family to determine the exact inheritance pattern of it. In this study, the primary investigation of proband and his family suggested an autosomal dominant or x-linked recessive inheritance but drawing the family pedigree for more than three generation of this family revealed the occurrence of about all of the cases in consanguineous marriages, suggested the autosomal recessive pattern for the family. Patients VI-7 and VI-17 show transient stuttering at the age of 2–3 and recovered at the age of 6–7. In addition to proband the other patients had permanent stuttering and most of them were male; therefore, that is in accordance with these two facts that all of the inheritance forms of stuttering is influenced by sex with higher occurrence in males than females and girls are more likely than boys to outgrow stuttering. Linkage analysis can be used to prove the hypothesis of autosomal recessive inheritance pattern in this family.

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