Case Report

Genetic Anticipation in Huntington's Disease

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SUMMARY

A case of Huntigton's disease involving several generations is presented with a possibility of early diagnosis. (Rawal Med J 2004;29:92-93)

Key Words: Huntington's Disease, autosomal dominant, mutation

INTRODUCTION

The term anticipation is applied to the phenomenon which children with a genetically influenced illness have the illness recognized at a much earlier age than their parent affected with the same illness. In some instances the illness is more severe in the child than in the parent, especially if the affected parent is the father.[1] There are multiple mechanisms by which apparent anticipation occurs, perhaps due to ascertainment or truncation bias.[2]

Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder. In 1993 the mutation that causes HD was identified as an unstable expansion of CAG (cytosine, adenine, guanine) repeats in the IT15 gene. Although the genetics are mendelian, it manifests some the complexities of psychiatric diseases. Penetrance is age-

dependant, with an average age of onset of approximately 45 years. Although juvenile-onset cases exist, their symptoms differ from those in the adult, with rigidity being more prominent than choreiform movements. We report a case with several generations affected.

CASE REPORT

S, a 23 year old girl presented with a history of a fall 3 days ago which resulted in pain in the hip area radiating to the right leg. This was preceded with the feelings of being depressed for 3 weeks. She had a history of choreiform movements since she was 20 years old. She had a gradual onset of choreiform movements, which was reported to be progressing markedly. Other symptoms included irritability and emotional distress. S was born of normal full term delivery and had normal developmental milestones. She had a very significant family history. Her 38 year old cousin P (paternal uncle's son), was suffering from HD. P was diagnosed as suffering from HD since he was 28 years old. It was reported that P had been manifesting symptoms of psychomotor agitation, depressive mood and sexually disinhibited behavior.

S's father was diagnosed suffering from HD when he was 53 years old. He died 3 years ago. The father was reported to have symptoms of psychomotor retardation, guilt feeling and anhedonia. S's paternal grandmother and great grandmother also had a history of HD. Both her grandmother and great grandmother suffered from HD when they were in their late 50's. S's two paternal uncles were reported to have died from HD when they were 49 and 50 years old respectively. Both of them suffered from HD, which was

diagnosed 5 years before they died. S had two other paternal uncles who were alive, one of them was reported to have been suffering from HD since he was 45 years old.

There was no history of HD or any other neuropsychiatric disorder in S's maternal family. It was reported that HD had its onset in all four generations and the occurrence of HD was gradually regressing towards an earlier age with each generation. S was investigated with thyroid function tests, liver function tests, urea and electrolytes, blood sugar, full blood count, serum caeruloplasmin, urine for routine investigations and copper, EEG, computed tomography (CT) scan and MRI of the brain. MRI revealed marked caudate atrophy. She was treated with Haloperidol 1.5 mg orally three times a day and Fluoxetine 20 mg once a day, to which she made little improvement.

DISCUSSION

All individuals who inherit a mutant Huntington's disease gene will develop signs and symptoms of the condition, if they live long enough. The disorder does not skip generations but the age at which symptoms of the disorder develop can vary widely among individuals, even within the same family.

With the identification of the Huntington's disease gene and the characterization of the CAG trinucleotide[3] repeat expansion that leads to the disorder, there has been a major advance in predictive testing for the condition. Direct testing for the CAG repeat length can not only identify individuals who will develop the disorder, it can identify individuals who have not inherited the mutant gene from a parent. In addition, direct mutation

analysis of the CAG repeat length can be used for prenatal testing[4] for Huntington's disease if parents choose this as an option. For those individuals who are seeking either confirmatory or predictive testing for HD should realize that the number of repeats identified in an expanded allele is not useful for determination of age of onset or clinical course of the disease.[5]

Until research leads to an effective treatment for HD, it is still very difficult for families to learn who carries the HD mutation. Understanding the inter-relationship of the genetic and psychological counseling, neurological counseling and follow up will avoid the pit falls[6] of the past and maximize the chances of optimum standard care.

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