

The Different Clinical Phenotypes of Huntington's Disease, About Ten Families

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ABSTRACT

Huntington's disease (HD) is an inherited autosomal-dominant neurodegenerative disorder characterized by motor, cognitive and psychiatric disorders that have a major impact on daily, family, professional and social life. we report the case of ten different families affected by huntington's disease in order to draw attention to the different clinical aspects and modes of revelation of this disease.

Keywords: Huntington's Disease, Psychiatric Disorders, Choreic Movements, CAG Trinucleotide Expansion.

INTRODUCTION

Huntington's disease (HD) is a fully penetrant neurodegenerative disease, which caused by an abnormally expanded CAG repeat near the N terminus of the huntingtin gene (HTT), which leads to the production of mutant huntingtin protein (HTT) on translation. It has now been 25 years since the identification of the genetic mutation [1].

HD is manifested by motor disturbances, psychiatric symptoms, and cognitive impairment, which usually begin in mid-life, with irreversible progression of symptoms over 10–15 years.

OBSERVATION

We report the clinical case of ten different families with Huntington's disease, whose mode of revelation was different, the following table summarizes the case of each patient of each family (Table 1).

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Table 1. Clinical aspect and genetic abnormality of each case.

	Gender	Age	Onset age of the disease	Parental consanguinity	Similar cases	Clinical signs	Cognitive and psychiatric disorders	CAG Trinucleotide Expansion Repeat number
Patient (Family1)	Female	23	19	-	Her Father	Choreic movements	-	60+/-3
Patient (Family2)	Male	40	36	-	Father, uncle, 2cousins, his grand father	Choreic movements	-	46 +/-3
Patient (Family 3)	Female	42	38	-	Her Mother and her sister	Cerebellar ataxia	+	44+/-3
Patient (Family 4)	Female	44	40	-	Her father, her brother, her 3cousins, her grand father	Perioral dyskinesias and choreic movements	+	45+/-3
Patient (Family 5)	Male	42	38	-	His father and his brother	Choreic Movements	-	45+/-3
Patient (Family 6)	Female	43	39	-	Her mother	Choreic movements	+	45+/-3
Patient (Family7)	Male	56	46	-	His brother and his father	Choreic movemnts and cerebellar ataxia	+	46+/-3
Patient (Family 8)	Female	39	36	-	His father	Choreic movements	-	50+/-3
Patient (Family 9)	Male	43	40	-	His brother	Choreic movements	-	45+/-3
Patient (Family10)	Male	45	42	-	His father	Choreic movements	+	46+/-3

-: Without consanguinity or without cognitive and psychiatric disorders.

+: With cognitive and psychiatric disorders.

DISCUSSION

According to the literature, Huntington's disease is a hereditary neurodegenerative pathology, of autosomal dominant transmission. in the huntingtin (HTT) Gene on chromosome 4. This results in the production of a mutant huntingtin (HTT) protein with an abnormally long polyglutamine repeat. Those with greater than 35 CAG repeats are certain to develop the disease, while reduced penetrance is seen between 36 to 39 repeats [2,3]. HD is manifested by motor, cognitive and psychiatric disorders, and usually begins in midlife.

Our clinical cases correspond to the data in the literature, the age of onset of the disease in our patients is between 20 and 40 years old, with no notion of parental consanguinity, with many similar cases in the family, they are even more numerous if we take into consideration the cases followed in psychiatry who just have psychiatric disorders.

The mode of inheritance is autosomal dominant with an expansion of more than 35 repeats of the CAG trinucleotide. Juvenile forms of HD are rare, they start before the age of 20, and they only represent 10% of HD forms. The number of CAG repeats is higher than in adults with MH [2,3], and this is the

case of our first patient who presents a juvenile form with a very high number of expansion (60+/-3) compared to other patients. These juvenile forms are of paternal transmission of paternal, precisely, our two youngest patients have their father affected [2,3].

Cerebellar ataxia is an underestimated sign of HD, due to the predominance of choreic movements especially in the early years of the disease, it is more noticeable in the later stages of the disease. Studies have shown that cerebellar ataxia is a common sign of the disease and should be included in these motor symptoms. Moreover, it may even be the only presenting symptom of the disease masquerading as spinocerebellar ataxia [4,5].

In our series we presented a case of a patient who had just isolated cerebellar ataxia, we were guided by her family pathological history because her mother and sister had choreic movements. The ataxia is more visible late, this is the case of our patient in whom the disease has been evolving for about ten years.

Dyskinesias of the lower half of the face are generally characteristic of neuroacanthocytosis, in particular chorea

acanthocytosis [6] for our series we have a patient who presents with perioral dyskinesia, which is exceptional.

The rest of the patients presented classic forms with choreic movements to the 4 limbs with or without cognitive and/or psychiatric disorders. we haven't received patients with pure psychiatric form, perhaps these patients consult psychiatry without even knowing that it is indeed a neurological disease.

For treatment, Tetrabenazine:(TBZ), a vesicular monoamine transporter (VMAT2) inhibitor, was approved by the US Food and Drug Administration (FDA) for the treatment of chorea in HD in 2008 and is one of two drugs approved for this use [7]. But this treatment is not available in Algeria,twopatients were able to bring it back, but they did not support it because of the worsening of mental disorders and depression, hence their being put on Neuroleptic (haloperidol) with the other patients saw its availability and its good tolerance with a stabilization or even a slight improvement in the(UHDRS) scale of some patients on Haloperidol.

Neuroleptics, they act by blocking dopamine neurotransmission, they treat chorea, agitation and psychosis at the same time. Although the evidence recommendations for the pharmacological treatment of chorea but no sufficient data are currently available to support the use of neuroleptics, according to the International HD Expert Group, antipsychotics were the drugs of choice in patients with both chorea and psychiatric symptoms such as depression, In patients in severe chorea, first-generation neuroleptic drugs such as haloperidol may be useful; however, second-generation neuroleptic drugs are preferred in people with moderate chorea due to lower risk of extrapyramidal symptoms [7-20].

CONCLUSION

Huntington's disease remains a devastating disease for patients and their families, which can pose a diagnostic problem when the signs are atypical and incomplete, hence the importance of knowing the full family history. patients to look for similar cases in the family who could have typical or complementary signs to those of our patient

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