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Excellence In Health Care

DEPARTMENT OF GENOMICS AND MOLECULAR DIAGNOSTICS

Patient Name	Mrs. JAMUNA RANI	**Visit ID**	--	**Collection Date**	16-03-2024 03:42 PM
Age / Gender	58 Y / FEMALE	**UHID**	--	**Registration Date**	17-03-2024 03:31 PM
Ref Doctor	Dr. SELF	**Hospital Name**	--	**Received Date**	17-03-2024 09:26 AM
Barcode	24037109	**Sample Type**	WHOLE BLOOD EDTA	**Reported Date**	22-03-2024 04:57 PM

HUNTINGTON - CAG REPEAT ANALYSIS

Referral Reason

I/V/O clinical suspicion for Huntington disease she was referred for genetic testing of CAG triplet repeats in HTT gene .

Test Result

Screen positive for Huntington CAG triplet repeats

Interpretation

As a result of heterozygous expansion of CAG repeats corresponding to nearly 58 repeats in exon 1 of HTT gene confirmed by end point PCR , this individual was classified as "**full penetrance or HTT screen positive**".

Recommendations

Genetic counselling and clinical correlation

Method

Polymerase chain reaction (PCR) followed by size analysis using agarose gel electrophoresis to determine HTT CAG repeat length along with defined control.

Background

Huntington disease is a neurodegenerative disease characterized by atrophy of the caudate nucleus and the putamen which leads to involuntary movements (chorea), progressive dementia, and psychiatric disturbances (Hayden and Kremer 2014). The average age of onset for Huntington disease is 40 years, but can range from late teens (juvenile onset) to over 60 years. The first signs to appear are a general slowing of intellectual ability, and a small personality change. These symptoms eventually lead to the major signs of the disease: chorea, hyopkinesia, rigidity, and dystonia. Chorea symptoms are defining to the disease. It is characterized by involuntary muscle movements, and they increase in severity throughout the course of the disease. Gait disturbances, global cognitive decline, and dysphagia are also common as the disease progresses (Hayden and Kremer 2014). There are currently no long-term treatment options to slow disease progression.

Huntington disease is inherited in an autosomal dominant manner, caused by a CAG repeat expansion in the HTT gene which occurs in the first exon, and encodes a polyglutamine tract beginning at residue 18. The exact function of the huntingtin protein is unknown (Zuccato et al. 2010). The polyglutamine region has been shown to be an essential regulator for binding partners Repeat copynumbers can be categorized into 4 different categories: < 27 repeats – normal, 27-35 – normal mutable, 36-39 – reduced penetrance, > 39 full penetrance Huntington disease (Jama et al. 2013). Typically, the more repeats in an individual, the earlier

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symptoms will develop. The largest repeats, ranging above 60 repeats to around 250 repeats (Bean & Bayrak-Toydemir, 2014) are causative of juvenile-onset Huntington disease (Warby et al. 2014). Huntington disease does not necessarily follow classical Mendelian inheritance patterns. Mosaicism of the HTT-CAG repeat has been reported and seems to be more prominent in juvenile- onset cases. However, according to the ACMG, the degree of mosaicism is not substantial enough to affect the interpretation of results obtained from peripheral.

Remarks/Limitations

- DNA analysis is limited to the requested test and cannot rule out all other genetic conditions or mutations. The methods
- described detect >99% of carriers of Huntington syndrome.
  Rarely, carriers of fragile X syndrome may have a non-expansion type mutation (e.g., point mutation) not detected by this assay.
- Other than HTT triplet repeats no other variants are been analysed. The
  correct clinical diagnosis is important for accurate DNA results.
  Results should be correlated with clinical history, Biochemical and pathological findings of the individual.
  It is presumed that the specimen used to perform the test belongs to the patient specified above, such verification having been carried out at the collection level of sample.
  Although all precautions are taken while conducting the tests, there is a standard error rate of approximate 1% in all genetic tests and this should be taken into consideration before any clinical decision. 1

References

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***** End Of Report *****

Suggested clinical correlation & follow up