HEXA Gene Analysis in Tay-Sachs Disease

Clinical Features:
Tay-Sachs disease (TSD) is a lysosomal storage disorder with symptoms ranging from an acute infantile form (classic TSD) to subacute juvenile and adult onset forms with later onset and slower disease progression. Infants with classic TSD generally appear normal at birth. At 3-6 months of age motor weakness, myoclonic jerks and an exaggerated startle reaction are usually the presenting features followed by developmental retardation and regression, paralysis, dementia and blindness with death by the second or third year of life. A cherry-red macula is a typical fundoscopic finding and, histologic examination reveals the lysosomal accumulation of GM2 gangliosides represented as distended, ballooned neurons in the central nervous system. The juvenile and adult forms have more variable neurologic findings, including progressive dystonia, spinocerebellar degeneration, motor neuron disease, and in some individuals with the adult onset form, a bipolar form of psychosis.[1] The juvenile and adult onset forms differ from each other primarily by the impact of the disease on intelligence, which is minimal through much of the course of the adult form.[2] The carrier frequency in Ashkenazi Jews is approximately 1 in 30, while the carrier in Sephardic Jews and non-Jews is approximately 1 in 250 to 1 in 300.[1] Other groups that are relatively genetically isolated have also been found to have carrier frequencies similar to or higher than that observed in Ashkenazi Jews including French Canadians from eastern Quebec, Cajuns from Louisiana and the Old Order Amish in Pennsylvania.[1]

Inheritance Pattern/Genetics:
Autosomal Recessive

Test Methods:
Variant analysis of the HEXA gene is performed on genomic DNA from the submitted specimen using bi-directional sequence analysis of coding exons and corresponding intron/exon boundaries. If full sequencing identifies a variant on only one allele of the HEXA gene, and if clinically indicated, reflex deletion/duplication testing (ExonArrayDx) will be performed at no additional charge to evaluate for a deletion/duplication of one or more exons of this gene. Variants found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis or another appropriate method.

Test Sensitivity:
In two studies of non-Ashkenazi Jewish patients with TSD, sequence analysis of the HEXA gene identified variants on 78/78 alleles.[3,4] In another study of non-Jewish TSD unaffected carriers, sequence analysis of the HEXA gene identified variants in 30 of 33 (91%) of cases.[5]

References:

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