MPS II DELETION INCLUDING CONTIGUOUS GENES

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Mucopolysaccharidosis type II (MPS II) is a rare lysosomal storage disorder caused by deficient activity of the enzyme iduronate-2-sulphatase. This enzyme is responsible for the catabolism of two different glycosaminoglycans (GAGs), dermatan sulfate and heparan sulfate. The IDS gene spans about 24kb in Xq28 and consists of nine exons. The majority of cases are caused by point mutations and small deletions or insertions, with 20% of cases being the result of major structural alterations, including large deletions and rearrangements. In approximately 6-8% of cases the disease results of a complete deletion of the IDS gene. Some of those patients have additional symptoms not commonly associated with Hunter syndrome, including the occurrence of seizures. These variant phenotypes may be due to involvement of loci adjacent to the IDS. Three patients with severe Hunter syndrome, with and without atypical symptoms, were analyzed to determine whether the mutations in these individuals involved genes located in close proximity to the IDS gene. Exon by exon IDS PCR was routinely performed to generate IDS exon specific amplicons using nine primer pairs each flanking one of the nine exons of the IDS gene. FRAXA and FRAXE amplicons were obtained with primers that flanked the trinucleotide repeat regions used for routine analysis of Fragile X Syndrome The DNA analysis for all three patients demonstrated a complete deletion of the IDS gene. Other genes in the neighbor region of the Xq28 chromosome were analyzed to check for the deletion extension. At least FRAXA and FRAXE gene were also deleted in these patients.