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Clinical and Genetic Heterogeneity of Wolfram Syndrome.

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Wolfram syndrome, sometimes referred to as DIDMOAD (Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness) (MIM # 222300) is an autosomal recessive disorder in which insulin dependent DM and bilateral progressive optic atrophy are necessary to make the diagnosis. Previous reports have mapped DIDMOAD to 4p16.1, close to the dopamine receptor D5 gene. We have identified 19 patients from 7 different families and have observed a previously unreported clinical picture. There is an absence of diabetes insipidus in all affecteds. In addition, several patients have defective platelet aggregation to collagen and some have profound upper gastrointestinal ulceration. Sixteen of the patients are from 4 families with notable consanguinity. Utilizing 3 microsatellite markers (D4S432, D4S3023, and D4S2366) reported to be linked to the 4p16.1 locus, we significant'y excluded linkage in 3 out of the four families.

The two affecteds in the 4th family showed homozygosity for all three markers from the region of linkage on 4p16.1. In conclusion, we report here the unique clinical findings and linkage analysis results of 19 patients with DIDMOAD providing further evidence for both clinical and genetic heterogeneity of this disorder.

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