P-085 - THE HFE1 P.HIS63ASP (RS1799945) MUTATION MAY ACT AS A MODIFIER IN GAUCHER DISEASE.

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INTRODUCTION: Gaucher disease (GD) is characterized by the accumulation of glucosylceramide in the lysosomes of reticuloendothelial system cells such as macrophages. The manifestations of GD consist mainly of hepatosplenomegaly, bone pain/deformations, osteonecrosis, anemia, and thrombocytopenia. Abnormalities in iron metabolism may play a central role in some of the clinical and biochemical features of GD. A candidate modifier gene is HFE1, the “causing” gene of hereditary hemochromatosis type I. OBJECTIVES: To analyze the role of HFE1 variants in the phenotype of GD. MATERIALS AND METHODS: Thirty-three GD patients (type I, \(n=30\); type III, \(n=3\)) were enrolled. DNA samples were extracted from peripheral blood and the HFE1 gene was sequenced by next-generation sequencing using IonTorrent-PGM. Two outcomes were derived from clinical data: 1) “altered liver enzymes”, comprising sustained alteration of ALT, AST or GGT while on treatment; and 2) “evidence of iron overload”, comprising increased transferrin saturation, hemosiderosis on liver biopsy, or increased liver iron on MRI. Pearson’s chi-square was used with a level of significance of \(p<0.05\). Patients having and not having the each of the outcomes were compared regarding the frequencies of variants in HFE1. RESULTS: Three known HFE1 variants were found: p.His63Asp (rs1799945; \(n=6\) patients; 18\%), p.Cys282Tyr (rs1800562; \(n=4\); 12\%), and c.340+4T>C (rs2071303; \(n=1\); 3\%). No patient was homozygote or compound heterozygote. Twenty-one patients (63.5\%) were included in the “altered liver enzymes” group and 9 patients (27\%) in the “evidence of iron overload” group. No significant differences of allelic frequency were found between the groups, although the allelic frequency for p.His63Asp, but not for the p.Cys282Tyr (\(p=0.683\)), was found to be borderline significant (altered enzymes: 6/42; normal enzymes: 0/24; \(p=0.063\)). CONCLUSIONS: Although statistical significance was not achieved, the borderline p-value may be due to the low sample size. Therefore, our data suggest that the HFE1 p.His63Asp may be a phenotype modifier in GD.