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FASTER AND ROBUST PROTOCOL FOR THE PRENATAL DIAGNOSIS OF MUCOPOLYSACCHARIDOSIS TYPE II

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Introduction: Hunter disease or Mucopolysaccharidosis type II (MPSII) is an X-linked recessive lysosomal disorder caused by deficiency of iduronate-2-sulfatase (*IDS*; EC 3.1.6.13), which is involved in the catabolism of glycosaminoglycans (GAGs). Objectives and Methods: We aimed to develop a new and faster protocol to apply in pregnant women who had previous cases of MPS II in the family. These patients are normally anxious and demand an urgent result to know how to manage their risky pregnancy. In this study, 4 pregnant carriers of MPS II were referred for prenatal diagnosis. The strategy used for the identification of the MPS II disease was based on cytogenetic, biochemical and molecular analysis. The molecular analysis was performed according to the mutation found in the family's index case. Results: Cytogenetic and biochemical analyses were performed after a 12 days period of cell culture, indicating a normal karyotype (46, XY) in all samples and normal enzyme activity in 3 cases. Gene analysis was performed with cells suspended in culture, not attached to the flasks' wall, after first medium change. These cells were used for DNA extraction and amplification of the region of interest, by PCR, followed by sequencing or RFLP. This new protocol, using the cells not attached to the flask, allowed a faster result. The analysis indicated absence of mutation in 3 samples, suggesting that the fetus was not affected by MPS II. In one case, enzyme activity was below the lower reference limit; a result which was confirmed by molecular analysis, which detected the same mutation found in the index case, confirming that the fetus had MPS II. Conclusion: These cases illustrate the importance of a comprehensive prenatal diagnostic protocol to provide more robust results and a safer genetic counseling, and suggest that free amniotic fluid cells could be used as a source of fetal material to allow a faster alternative for prenatal diagnosis. We also propose the use of free fetal DNA (ffDNA) in maternal circulation in order to perform a non invasive procedure.