P-040 - MUCOPOLYSACCHARIDOSSES TYPE IIID: REPORT OF THE FIRST PATIENT IDENTIFIED BY THE MPS BRAZIL NETWORK

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INTRODUCTION: Mucopolysaccharidosis type IIID (MPS IIID) or Sanfilippo syndrome type D is caused by deficiency of the lysosomal enzyme N-acetylglucosamine-6-sulfatase. Among the four subtypes of Sanfilippo syndrome, this is the least frequent. OBJECTIVE: To investigate a patient with clinical suspicion of mucopolysaccharidosis type III, in whom the more common types IIIA, IIIB and IIIC were previously excluded. MATERIALS AND METHODS: Blood and urine were collected for biochemical tests (enzyme assays, glycosaminoglycans – GAGs - measurement by dimethylmethylene blue – DMB - colorimetric method, identification of GAGs species by electrophoresis, and analysis of GAGs by liquid chromatography/tandem mass spectrometry–LC/MS/MS) and molecular analysis (gene sequencing by next-generation sequencing – NGS - using a customized panel which includes the GNS gene). A few other sulfatases were assayed to exclude multiple sulfatase deficiency. Age-matched controls were used for the quantitative measurements of GAGs. RESULTS: The patient had deficient activity of N-acetylglucosamine-6-sulfatase (0,55 nmol/24h/mg of protein; normal range: 7-22) in leukocytes. Increased levels of urinary GAGs (374 µg/mg of creatinine; normal age-range: 67-124) were detected by DMB assay, and presence of heparan sulfate in urine was observed in the electrophoresis. LC/MS/MS of urinary GAGs revealed high levels of heparan sulfate (HS-0S: 85 ng/mg of creatinine [average age-matched controls: 2 ng/mg of creatinine], HS-NS: 35 ng/mg of creatinine [average age-matched controls: 0.5 ng/mg of creatinine]). NGS identified the variant c.624+1G>T in homozygosis in the GNS gene. CONCLUSIONS: To the best of our knowledge, we are reporting the first Brazilian patient with MPS IIID.