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Analisis Varian Gen Arylsulfatase B (ARSB) Ekson 5-8 pada Pasien Mukopolisakaridosis (MPS) Tipe VI di Indonesia = Variant Analysis of Arylsulfatase B (ARSB) Gene Exon 5-8 in Indonesian Mucopolysaccharidosis (MPS) VI Patients

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Abstrak

Mukopolisakaridosis (MPS) tipe VI adalah kelainan genetik langka berupa defisiensi enzim arylsulfatase B (ARSB) akibat kemunculan varian pathogenic gen ARSB. Gejala MPS tipe VI meliputi kornea berkabut, fitur wajah kasar, abnormalitas tulang dan persendian, serta kelainan saluran pernapasan dan pembengkakan organ. Diagnosis MPS tipe VI dilakukan dengan pengukuran aktivitas enzim serta konfirmasi melalui analisis varian gen ARSB. Varian gen pathogenic yang paling umum dilaporkan pada pasien MPS tipe VI terletak di rentang ekson 5—8, yaitu c.962T>C (p.Leu321Pro), c.1197C>G (p.Phe399Leu), dan beberapa varian pada asam amino Arg315 di ekson 5. Analisis varian gen ARSB belum pernah dilakukan di Indonesia walapun sudah ada pelaporan kasus MPS tipe VI. Tujuan dari analisis varian gen ARSB di Indonesia adalah mengidentifikasi dan mengklasifikasi varian gen ARSB serta mendapatkan profil genetik gen ARSB pada pasien MPS tipe VI di Indonesia. Analisis varian gen ARSB dilakukan pada dua pasien MPS tipe VI dan sepuluh individu normal sebagai kelompok kontrol menggunakan sekuensing Sanger. Penelitian tidak menemukan adanya varian pathogenic pada gen ARSB ekson 5—8 pasien MPS tipe VI. Penelitian berhasil menemukan varian benign c.1072G>A (p.Val358Met) pada ekson 5, c.1142+233C>T dan c.1143-27A>C pada intron 5, dan c.1337-32C>G pada intron 7 serta satu varian likely benign c.1213+149C>G pada intron 6 yang sudah pernah dilaporkan sebelumnya. Ditemukan juga satu varian novel c.1142+213C>T pada intron 5 dengan klasifikasi variant of uncertain significance. Penambahan individu dalam kelompok kontrol disarankan agar frekuensi alel dalam populasi lebih tercerminkan dengan baik.

.....Mucopolysaccharidosis (MPS) type VI is a rare genetic disorder due to arylsulfatase B (ARSB) enzyme deficiency caused by the presence of pathogenic variant in ARSB ene. Clinical symptoms of MPS type VI are corneal clouding, coarse facial features, joint and skeletal abnormalities, respiratory problems, and enlarged organs. Diagnosis of MPS type VI is done by evaluating ARSB enzyme activity and is confirmed by ARSB gene analysis. The most commonly reported pathogenic variants in MPS type VI patients are located in exon 5—8, such as c.962T>C (p.Leu321Pro), c.1197C>G (p.Phe399Leu), dan numerous variants involving Arg315 at exon 5. Analysis of ARSB gene has not been done in Indonesia although one MPS type VI case has been reported. Analysis of ARSB gene in Indonesia is done to identify and classify the ARSB gene variants and to also obtain genetic profile of MPS type VI patients in Indonesia. The analysis is done to two MPS type VI patients along with ten normal individuals as control group using Sanger sequencing. This study has found no pathogenic variants in exon 5—8 of ARSB gene. This study have identified benign variants c.1072G>A (p.Val358Met) at exon 5, c.1142+233C>T and c.1143-27A>C at intron 5, and c.1337-32C>G at intron 7 along with one likely benign variant c.1213+149C>G at intron 6 which have been previously reported before. One novel variant c.1142+213C>T at intron 5 was also found and classified as variant of uncertain significance. A larger control group is advised to better reflect the allele frequency in population.