Deteksi dan analisis varian gen glucosylceramidase beta (GBA) pada penderita penyakit gaucher di Indonesia = Detection and analysis glucosylceramidase beta (GBA) gene variant in gaucher disease patient in indonesia.

Rabbil Pratama Aji, author

Abstrak

Penyakit Gaucher merupakan kelainan metabolik langka yang diturunkan secara resesif pada sel tubuh (autosomal). Penyakit Gaucher disebabkan oleh defisiensi enzim glucosylceramidase (GCase) yang menyebabkan senyawa glucosylceramide (GlcCer) tidak terurai dan terakumulasi dalam sel makrofag sehingga menginduksi perubahan sel tersebut menjadi sel Gaucher. Defisiensi enzim GCase terjadi akibat adanya mutasi pada gen glucosylceramidase beta (GBA) yang terletak di lokus 1q22. Gen GBA memiliki banyak varian patogenik, tetapi terdapat varian yang umum ditemukan yaitu N370S dan L444P. Tujuan dari deteksi dan analisis varian gen GBA yaitu supaya menemukan varian patogenik yang dapat digunakan untuk mengonfirmasi diagnosis secara klinis pada sampel penderita penyakit Gaucher di Indonesia. Varian N370S dan L444P dapat dideteksi menggunakan teknik Restriction Fragment Length Polymorphism (RFLP), sedangkan varian gen GBA lainnya dideteksi dan dianalisis menggunakan teknik automated DNA sequencing. Hasil yang diperoleh adalah sebanyak tiga varian eksonik (R359Q, p.W417W, dan L444P) dan lima varian intronik (c.454+29G>A, c.454+47T>C, c.454+52G>A, c.999+248T>G, dan c.999+271G>A) telah berhasil dideteksi dan dianalisis dari 3 sampel penderita penyakit Gaucher berkebangsaan Indonesia.

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Gaucher disease is an autosomal recessesive metabolic disorder that is caused by a deficiency of the enzyme glucosylceramidase (GCase), leading to accumulation of glucosylceramide (GlcCer) in macrophage cells which transform into Gaucher cells. The GCase enzyme deficiency occurs due to mutations in the glucosylceramidase beta (GBA) gene that is located at locus 1q22. The GBA gene has common pathogenic variants, such as N370S and L444P. The purpose of the detection and analysis of GBA gene variants was to find pathogenic variants that can be used to confirm clinical diagnoses in samples of Gaucher's disease patients in Indonesia. Variants of N370S and L444P could be detected using Restriction Fragment Length Polymorphism (RFLP) technique, while other GBA gene variants were detected and analyzed using automatic DNA sequencing technique. As the result, total of 3 exonic variants (R359Q, p.W417W, and L444P) and 5 intronic variants (c.454 + 29G> A, c.454 + 47T> C, c.454 + 52G> A, c.999 + 248T> G , and c.999 + 271G> A) have been successfully detected and analyzed from 3 samples of Gaucher disease of Indonesian people.