Novel mutations in the glucocerebrosidase gene of Indian patients with Gaucher disease

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Gaucher disease (GD) is the most common glycolipid storage disorder resulting from glucocerebrosidase deficiency due to mutations in the GBA gene. Study was performed in 33 unrelated patients with low b-glucosidase activity in leukocytes and/or fibroblasts. The exons and exon–intron boundaries of the GBA gene were bidirectionally sequenced using an automated sequencer. Mutations were confirmed in parents and were looked up in public databases, and in silico analysis was carried for novel mutations. We identified two novel missense mutations G289A (c.866G\textsuperscript{4}C) and I466S (c.1397T\textsuperscript{4}G) in exons 7 and 10, respectively, in two (6.06\%) patients that destabilize the protein structure. L444P (c.1448T\textsuperscript{4}C) was the most common mutation identified in 20/33 (60.60\%) non-neuronopathic and 1/33 (3.03\%) subacute neuronopathic form based on clinical presentation at the time of investigation. Other nine rare mutations were: R463C (c.1504C\textsuperscript{4}T), R395C (c.1300C\textsuperscript{4}T), R359Q (c.1193G\textsuperscript{4}A), G355D (c.1181G\textsuperscript{4}A), V352M (c.1171G\textsuperscript{4}A) and S356F (c.1184C\textsuperscript{4}T) found in each patient (18.18\%). Compound heterozygous mutation L444P (c.1448T\textsuperscript{4}C)/R496C (c.1603C\textsuperscript{4}T) in exon 10/11 and L444P (c.1448T\textsuperscript{4}C)/R329C (c.1102C\textsuperscript{4}T) were observed in exon 10/8 in one each patient (6.06\%). Two patients (6.06\%) from Sri Lanka showed E326K (c.1093G\textsuperscript{4}A) mutation in exon 8. We conclude that L444P is the most common mutant allele with exons 8 and 10 as the hot spot region of GBA gene observed in Indian GD patients.

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