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Letter to the Editor

Identification of a novel mutation, I403T, in Cuban type 1 Gaucher disease

To the Editor:

Gaucher disease (GD), the most common lysosomal storage disorder, is caused by a deficient activity of the enzyme, β-glucocerebrosidase. Three major forms have been recognized as discrete by virtue of absence (type 1) or presence (type 2 and type 3) of neurological involvement [1]. To date, approximately 300 mutations have been described in the β-glucocerebrosidase gene, although only a few are prevalent in general populations, such as L444P and N370S.

Herein we report a novel mutation in a Cuban patient with type 1 GD.

A 10-year old female of mixed ethnicity (Spanish/Cuban) presented at the age of 6 months with marked splenomegaly for which she underwent partial splenectomy at the age of 3 years. Skeletal complications ensued, including bone crises in the right thigh and fracture of the right elbow. There were no signs of neurological involvement. GD was confirmed by enzymatic assay and molecular analysis initially identified the N370S on one allele. Enzyme replacement therapy (Cerezyme, Genzyme Corporation, Cambridge, MA, USA) at 120 U/kg body weight/infusion was begun at age 7 years with beneficial effects on blood counts, hepatomegaly, and chitotriosidase levels.

To identify the second mutation, a protocol combining Single Strand Conformation Polymorphism (SSCP) and DNA sequence analysis of the β-glucocerebrosidase gene was performed as previously described [2]. A novel missense mutation in exon 9, cDNA nucleotide position 1325 (genomic nucleotide position 5940) was identified. This mutation results in the substitution of isoleucine by treonine at the amino acid 403 (I403T) and does not generate any restriction site at DNA level. Since the wild type amino acid is conserved in mouse and man, this potentially indicates functional/structural relevance of the gene. One may speculate that the substitution of isoleucine, a non-polar amino acid, by the polar treonine, may disrupt the enzyme's hydrophobic characteristics and hence affect its function. No other mutations were found in this patient and the mutation was confirmed in analysis of her mother's DNA. Early signs of the disease in this child may imply a non-mild nature to this mutation.

Three other mutations in 2 single patients and a pair of siblings [3–5] have been described at the 402–403 positions, with phenotypes ranging from very mild to type 3 but none in homozygosity, making it difficult to assess the predictability of a mutation in this domain. In that the ethnicities of these other patients are not Cuban or Spanish, one might conjecture that this area is a hot spot for point mutations.

Conflict of interest

The authors have no conflict of interest to declare.

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References

[1] E. Beutler, G.A. Grabowski, Gaucher disease, in: C.R. Scriver, A.L. Beaudet, W.S. Sly, D. Valle (Eds.), The Metabolic and Molecular Bases of Inherited Disease, McGraw-Hill, New York, 1995, pp. 2641–2669.
[2] M.A. Torralba, J.I. Perez Calvo, G.M. Pastores, et al., Identification and characterization of a novel mutation c.1090 G>T (G325W) and nine common mutant alleles leading to Gaucher disease in Spanish patients, Blood Cells Mol. Dis. 27 (2001) 489–495.
[3] R. Rozenberg, D.C. Fox, E. Sobreira, et al., Detection of 12 new mutations in Gaucher disease Brazilian patients, Blood Cells Mol. Dis. 37 (2006) 204–209.
[4] E. Orvisky, J.K. Park, A. Parker, et al., The identification of eight novel glucocerebrosidase (GBA) mutations in patients with Gaucher disease, Hum. Mutat. 19 (2002) 458–459.
[5] B. Cormand, D. Grinberg, L. Gort, et al., Two new mild homozygous mutations in Gaucher disease patients: clinical signs and biochemical analyses, Am. J. Med. Genet. 70 (1997) 437–443.

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