Hemoglobin Presbyterian [β108 (G10) ASN>LYS] in a Nicaraguan family

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ABSTRACT

Hemoglobin (Hb) is the protein responsible for oxygen transportation. It is a tetrameric protein comprising two α- and two β-globin subunits. In the literature, a large number of mutations in the α- and β-globin genes have been documented. Among these mutations, Hb Presbyterian (Hb Pres) is a naturally occurring mutant exerting low oxygen affinity. C to G exchange (AAC>AAG) in codon 108 of the β-globin gene (β108) results in the substitution of asparagine (Asn) by lysine (Lys). Objective: detection and identification of abnormal hemoglobin in a 6-year-old female patient and her family. Hemoglobin lysate from peripheral blood from the patient and her family was analyzed. Detection of the abnormal hemoglobin was performed by cellulose acetate electrophoresis and HPLC. Genomic DNA from leucocytes was extracted and genomic DNA sequencing analysis were conducted. A variant hemoglobin fraction migrating near HbA, between HbA and HbS, was found by the cellulose acetate electrophoresis. The hemoglobinopathy was also confirmed by HPLC analysis. The β-globin gene sequences for both, father and daughter, disclosed the heterozygous mutation in codon 108 for Hb Pres. Herewith, we document the identification of Hb Pres in a 6-year-old female patient from Nicaragua. The hemoglobinopathy was also detected in her father, a 28-year-old Cuban, who never showed any symptoms indicating anemia or other hematologic pathologies.

The mutant Hb Pres has been previously reported for four families from North America, Germany, Japan, and Spain. This is the fifth family with HbPres described to date, and the first report in Latin America.

Keywords: Hemoglobin Presbyterian; Unstable hemoglobin; DNA sequencing

INTRODUCTION

Hemoglobin (Hb) is the protein responsible for oxygen transportation. It is a tetrameric protein comprising two α- and two β-globin subunits. In the literature, a large number of mutations in the α- and β-globin genes have been documented.[1] Among these mutations, Hb Presbyterian (Hb^{Pres}) is a naturally occurring mutant exerting low oxygen affinity. C to G exchange (AAC>AAG) in codon 108 of the β-globin gene (β108) results in the substitution of asparagine (Asn) by lysine (Lys).

OBJECTIVE

Detection and identification of abnormal hemoglobin in a 6-year-old female patient and her family.

METHOD

Hemoglobin lysate from peripheral blood from the patient and her family was analyzed. Detection of the abnormal hemoglobin was performed by cellulose acetate electrophoresis and HPLC. A heat stability test and p50 measurement were accomplished.Genomic DNA from leucocytes was extracted and genomic DNA sequencing analyses were conducted.

RESULTS

A variant hemoglobin fraction migrating near HbA, between HbA and HbS,was found by the cellulose acetate electrophoresis (figure).Furthermore, a flocculent precipitate was detected in a heat stability test on the propositus' hemolysate.The hemoglobinopathy was also confirmed by HPLC analysis. The β-globin gene sequences for both, father and daughter, disclosed the

heterozygous mutation in codon 108 for Hb^{Pres}(figure). Correspondingly, p50 of the propositus' blood was determined by using a blood gas analyzer (Nova-biomedical) and found to be 31.1 mmHg which is increased compared to the normal range of 25-29 mmHg.

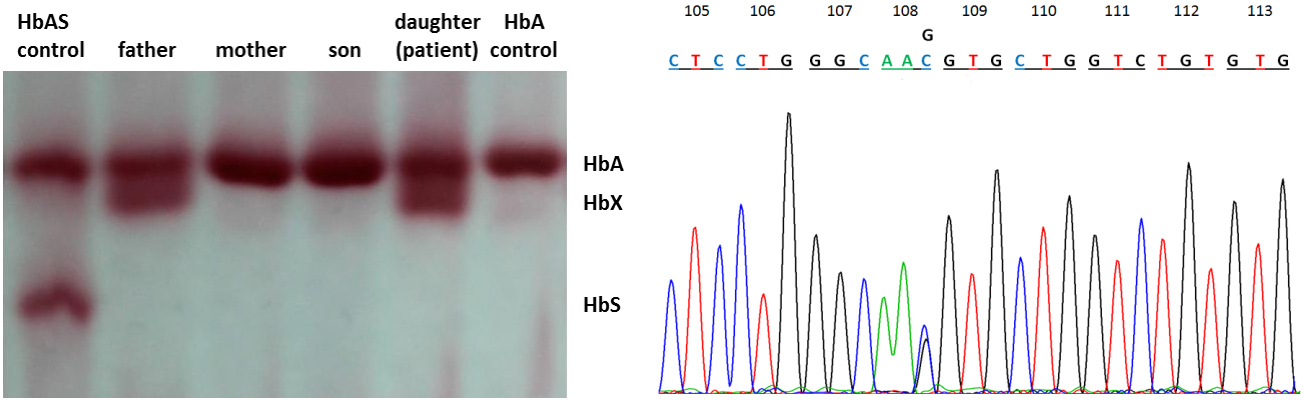

Figure. Identification of Hb^{Pres} in a 6-year-old female patient and her family.
A: Cellulose acetate electrophoresis of hemolysates (TBE-buffer, pH 8.4) indicating presence of abnormal hemoglobin in the propositus (daughter) and her father. From left to right: HbAS control, father, mother, son, daughter, HbA control. **B** Nucleotide sequencing of the proband´s β-globin gene, codons 105 – 113 revealing codon 108 with C>G heterozygosity (AAC>AAG).

CONCLUSION

Herewith, we document the identification of Hb^{Pres} in a 6-year-old female patient from Nicaragua. The hemoglobinopathywas also detected in her father, a 28-year-old Cuban, who never showed any symptoms indicating anemia or other hematologic pathologies. The mutant Hb^{Pres}has been previously reported for four families from North America, Germany, Japan, and Spain. This is the fifth family with Hb^{Pres} described to date,[2-5]and the first report in Latin America

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