Eye (2009) 23, 1210–1212

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CASE SERIES

Identification of a novel *ALMS1* mutation in a Chinese family with Alström syndrome

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Abstract

Purpose **To report a novel mutation of *ALMS1* in a Chinese family with Alström syndrome.**

Design **Observational case report and results of DNA analysis.**

Methods **A family including one patient and four unaffected relatives was examined clinically. One hundred normal Chinese individuals served as control subjects. Genomic DNA was extracted from venous blood of all participants. Exons 8, 10, and 16 of**

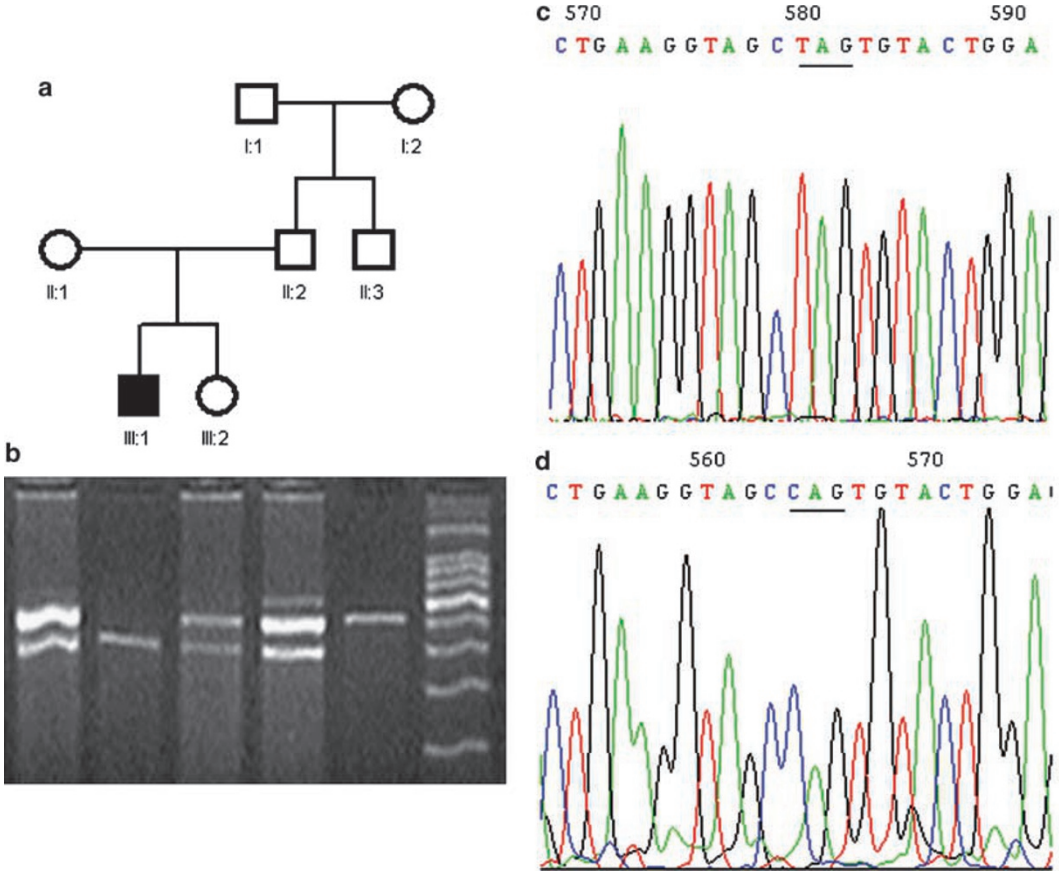

Figure 1 Family structure of the Chinese family, DNA sequence chromatograms, and cosegregation analysis of the Q2471X mutation of *ALMS1* with disease phenotype. (a) Pedigree of Chinese families with Alström syndrome. Squares indicate males; circles indicate females; solid symbols indicate affected; and open symbols indicate unaffected. (b) Restriction fragment length analysis showing the gain of the novel AluI site cosegregated with the proband homozygous for the C→T transition (505 bp only) and the carriers heterozygous the C→T transition (505 bp and 605), but not with the unaffected individual (605 bp only). (c) Sequence (sense strand) showing a homozygous C→T transition in codon 2471 (under line) that changed from glutamine (CAG) to stop codon (TAG). (d) Corresponding normal sequence.

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Received: 23 April 2008
Accepted in revised form: 27 July 2008
Published online: 25 July 2008

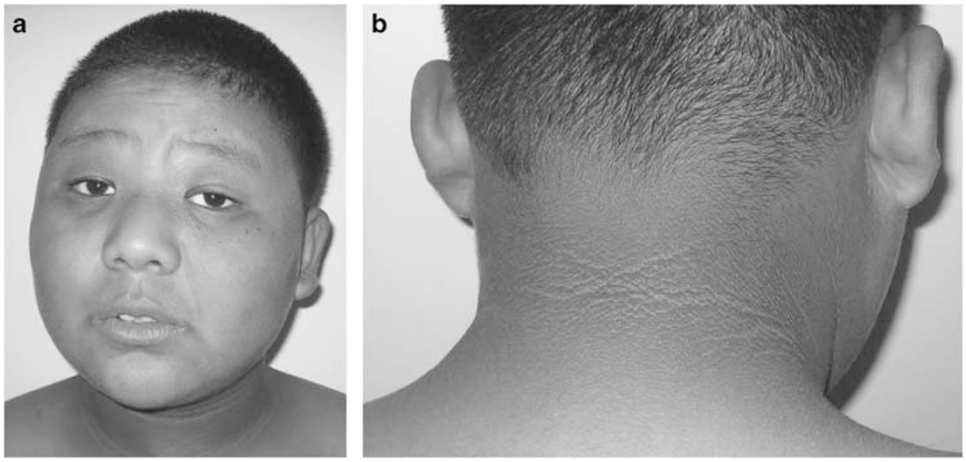

Figure 2 Face and neck features of the proband. (a) The face showing the deep-set eyes. (b) The neck of the proband showing acanthosis nigricans.

the *ALMS1* gene was amplified by the PCR. The PCR products were analysed using direct sequencing.
Results **Clinical examination and laboratory investigations indicate Alström syndrome for the proband of this family. Sequencing of part of the *ALMS1* gene identified one novel homozygous non-sense mutation, c.8335 C>T, resulting in a premature termination signal at codon 2471 (Q2471X).**
Conclusions **Our findings expand the spectrum of *ALMS1* gene mutations causing Alström syndrome and further confirm the role of *ALMS1* gene in the pathogenesis of Alström syndrome.**
Eye (2009) **23,** 1210–1212; doi:10.1038/eye.2008.235; published online 25 July 2008

Keywords: Alström syndrome; *ALMS1* gene; mutation

Introduction

Alström syndrome is a rare and severe autosomal recessive disorder. Alström initially identified five clinical features of this syndrome, such as atypical retinal pigmentary degeneration, sensorineural hearing loss, obesity, type II diabetes mellitus, and normal mentation.[1,2] The disease-causing gene for it was the *ALMS1* gene. The previous works reported 21 ALMS1 mutations that caused premature protein truncation.[3–5]

Methods and results

Case report

A 9-year-old boy from a Chinese third-generation family (Figure 1a) presented with poor vision (20/200 OU), photophobia, nystagmus, and blepharospasm (Figure 2a). Fundus examination showed pale optic discs and narrowed vessels. No pigment spicules were observed. Bilateral sensorineural hearing loss was observed in the proband by audiometry. General physical examination showed that the boy was of short stature and obese (weight 48 kg and height 126 cm). He presented acanthosis nigricans in the neck and axillae (Figure 2b). The testicles and phallus were small. Laboratory investigations indicated that the complete blood count was normal; levels of creatinine, total bilirubin, and conjugated bilirubin were in the normal range. Levels of aspartate aminotransferase (AST, SGOT, 145 U/I; range, 5–40), alanine aminotransferase (ALT, SGPT, 286 U/I; range, 5–40), glucose (9.55 mmol/l; range, 3.9–5.8), and blood urea nitrogen (7.96 mmol/l; range, 2.50–6.30) were elevated; microscopic examination of the urine showed that the levels of glucose (14 mmol; range, 0.72–2.78) and protein (0.3 g/l; range, 0.02–0.06) were elevated.

By direct sequencing of the exons 8, 10, and 16 of *ALMS1* gene, we identified a novel homozygous non-sense mutation in exon 10, c.8335 C>T (Q2471X) in the boy (Figure 1c and d). The boy's parents and his younger sister carried the heterozygous Q2471X change, consistent with carrier status (Figure 1b). The mutation was absent in 100 normal controls.

Comment

Alström syndrome bears some clinical features with other syndromes such as Laurence–Moon syndrome, Edwards disease, and Bardet–Biedl syndrome.[1,2] The diagnosis of it is often difficult. The *ALMS1* gene mutation screen may play an important role for the diagnosis.

Here, we reported an identification of one novel mutation in a Chinese family with Alström syndrome. Our finding expands the spectrum of the *ALSM1* gene mutations in Alström syndrome and provides the genetic counselling for the family.

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