UPDATES ON GENOTYPE AND PHENOTYPE OF VIETNAMESE PATIENTS WITH X-LINKED ADRENOLEUKODYSTROPHY(X-ALD)

Ha Nguyen Thu[1], Khanh Nguyen Ngoc[1], Thao Bui Phuong[1], Dung Vu Chi[1]
[1]National Children's Hospital , Hanoi, Vietnam

Background

• X-linked adrenoleukodystrophy (X-ALD) is caused by a defect in the gene *ABCD1.*

• Impairment peroxisomal beta-oxidation of very long-chain fatty acids leads an accumulation of VLCFA in plasma and all tissues, including the white matter of the brain, the spinal cord and adrenal cortex.

• The frequency is about 1:42000 in male

•This disease characterized by progressive neurologic dysfunction, occasionally associated with adrenal insufficiency.

•There was no correlation between genotype and phenotype

Objectives

To describe phenotype and genotype in affected male patients in Vietnamese patients with X-ALD

Methods

• A case series study: 24 cases from 20 unrelated families

• Phenotype diagnosis bases on clinical features, cerebral MRI lesions and biochemical finding (plasma elevated VLCFA).

• Genomic DNA from these patients was extracted using standard procedures from the peripheral blood leukocytes.

• Mutation analysis of *ABCD1* was performed using Polymerase chain reaction (PCR) and DNA direct sequencing.

Results

❖ Age of onset was 1.5 – 14 years; Age of diagnosis was 4.7 – 22 years.

• Addison only were observed in 5/24 cases; 18/25 cases were cerebral ALD (11 with adrenal insufficiency; 7 with only neurologic symptoms) and 1/24 case was adrenomyeloneuropathy.

Results

❖ Plasma cortisol levels at 8 AM of AO were 0.2 → 50 nmol/l ; 7 – 41.5 nmol/l in CALD. Plasma ACTH levels were 17,2 – 416,7 pmol/l.

❖ 8/8 cases showed increased plasma: C24:0/C22:0 (1.32 – 2.18) (normal range 1.05 ±0.16); C25:0/C22:0 (0.059 – 0.26) (normal range: 0.024 ± 0.006); C26:0/C22:0 (0.049 – 0.22) (normal range : 0.012 ±0.005) .

❖ **20 different mutations of *ABCD1*** in 24 patients: missense mutations (14/20), deletion (4/20),), nonsense mutation (1/19) and splice site mutation (1/20).

❖ Of which, **8 novel mutations** including c.1202G>T (p.Arg401Trp); c.1208T>A (p.Met403Lys); IVS8+28-551bp del; c.1668G>C (p.Gln556His); c.292_296delTCGGC (p.S98RfsX95); c.1946_1947insA (p.Asp649fsX733), c.46-53del insG and the extent of deletion included between IVS1+505 and IVS2+1501, containing whole the exon 2 (4243bp), plus insertion of 79bp from BAP31 and 8bp from unknown origin in this deleted region were identified.

❖ **12 reported mutations** including c.796G>A (p.G266R); c.1628C>T (p.Pro543Leu); c.1553G>A (p.Arg518Gln); c.1552 C>T (p.Arg518Trp); c.854G>C (p.R285P); c.1825G>A (p.E609K); c.1978C>T(p.Arg660Trp), c.1849C>G (p.Arg617Gly); c.1552C>T (p.Arg518Trp); c.1415_1416delAG (p.Q472Rfs*83), c.1849C>G (p.Arg617Gly) and c.311G>A (p.Arg104His) were identified in 16 patients from 12 families.

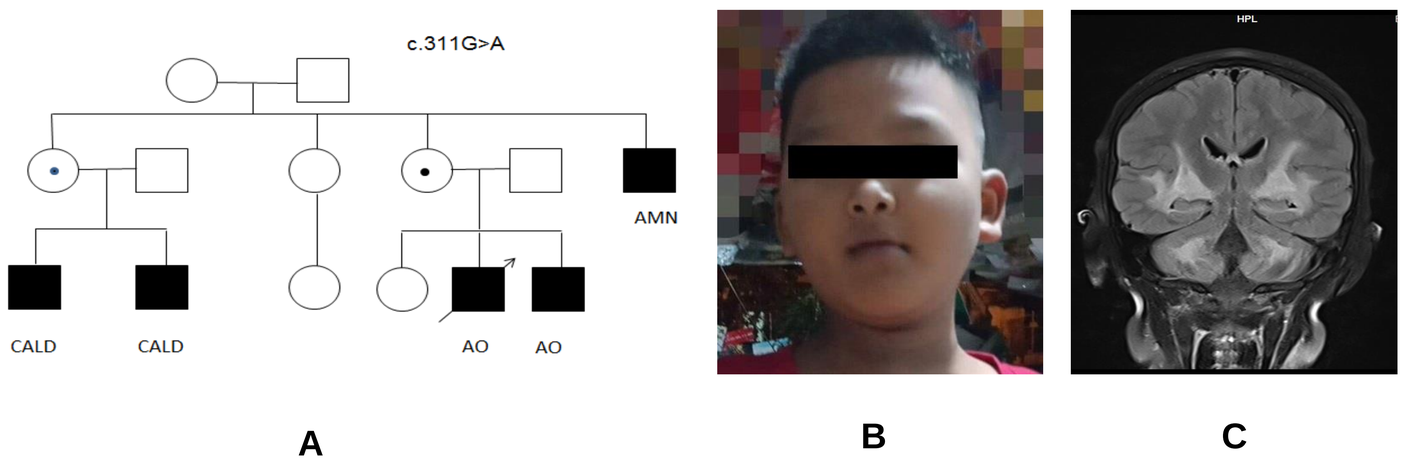

Figure 1. Pedigree of three patients with X-ALD in one families (A). Hyperpigmentation (B). White matter lesions in cerebral MRI (C).

Conclusions

Heterogeneity of genotype in X-ADL in small cohort of Vietnamese patients. Mutation analysis of *ABCD1* helped confirmation of diagnosis of X-ALD, genetic counselling and prenatal diagnosis.

References

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Conflicts of interest: None declared; **E-mail address: dr.nguyenha88@gmail.com (Nguyen Thu Ha).**

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Thu Ha Nguyen
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