MUTATIONS OF *ABCD1* IN 16 VIETNAMESE PATIENTS WITH X-LINKED ADRENOLEUKODYSTROPHY (X-ALD)

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Background

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

• *ABCD1* maps to Xq28, includes 10 exons and codes for a peroxisomal membrane protein that is a member of the ATP-binding cassette transporter superfamily (745 amino acids).

• 1605 causative mutations so far

• X-ALD is panethnic and affects approximately 1:20,000 males.

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

Objectives

To identify mutations of *ABCD1* in Vietnamese patients with X-ALD

Methods

• A case series study: 16 cases from 14 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 3/16 cases; 12/16 cases were cerebral ALD (5 with adrenal insufficiency; 7 with only neurologic symptoms) and 1/16 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) .

❖ **13 different mutations of *ABCD1*** in 16 patients: missense mutations (8/13), deletion (4/13) and splice site mutation (1/13).

❖ Of which, **six novel mutations** including c.1202G>T (p.Arg401Trp); c.1208T>A (p.Met403Lys); IVS8+28-551bp del; c.1668G>C (p.Q556H); c.292_296delTCGGC (p.S98RfsX95); and the extent of deletion included between IVS1+505 and IVS2+1501, containing whole the exone 2 (4243bp), plus insertion of 79bp from BAP31 and 8bp from unknown origin in this deleted region were identified in six unrelated patients.

❖ **Seven reported mutations** including 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.1415_1416delAG (p.Q472RfsX83) and c.46-53del insG were identified in 9 patients from 7 families.

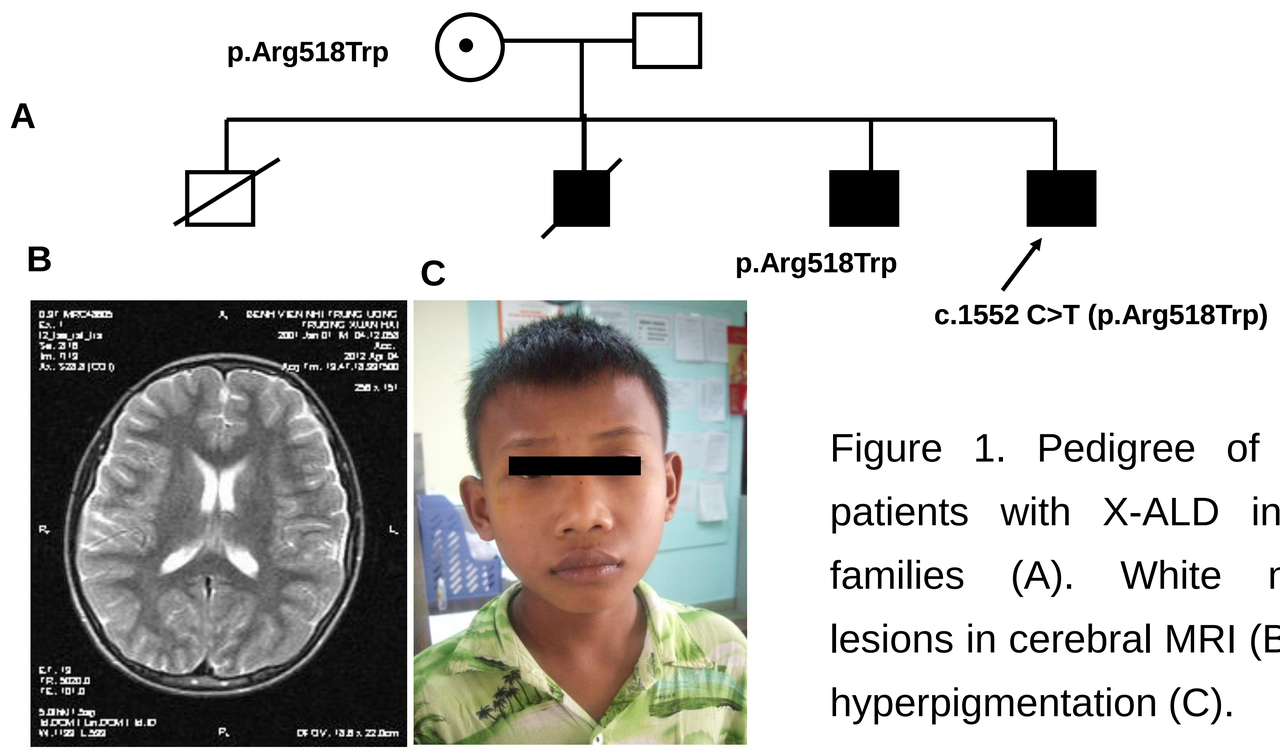

Figure 1. Pedigree of three patients with X-ALD in one families (A). White matter lesions in cerebral MRI (B) and hyperpigmentation (C).

Conclusions

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: dungvu@nhp.org.vn (D.C. Vu).**

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