UPDATES ON GENOTYPE AND PHENOTYPE OF 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.
• 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
• 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_296delTCGGGC (p.S98RfsX95); c.1946_1947insA (p.Aspl649fsX733), 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

References
• Durmaz A et al. 2014. Metab Brain Dis. 29(3):809-12
• Cai YN et al. 2015. J Pediatr Endocrinol Metab. 28(5-6):725-9

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