X-LINKED ADRENOLEUKODYSTROPHY IN SOUTH OF TUNISIA

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INTRODUCTION

Adrenoleukodystrophy (ALD) is a rare X-linked disease caused by a mutation of the peroxisomal ABCD1gene. It is a progressive condition with a variable clinical spectrum that includes primary adrenal insufficiency, axonal demyelination and the accumulation of high levels of very long chain fatty acids (VLCFA) in the plasma and tissues.

AIM

The aim of this study was to describe the clinical, biological, radiological and genetic features of Adrenoleukodystrophy (ALD) in children.

METHOD

- We performed a retrospective study of all cases of X-linked ALD who were diagnosed in the pediatrics departement of the university hospital of Sfax between 2004 and 2020.
- Specific data related to epidemiology, phenotype and diagnosis of patients with X-linked adrenoleukodystrophy were collected and analysed.

RESULTS

- Six cases of ALD were included.
- The mean age at first symptoms of ALD was 4 years 3 months old (Range: 16 days- 8 years old)
- Parental consanguinity was noted in one case and a family history of ALD was reported for 4 children.
- For four patients, X- linked ALD started as primary adrenal insufficiency, manifesting with skin hyperpigmentation and vomiting (**Figure 1**).
- For two patients, neurological signs were the first symptoms of the disease (**Table 1**).

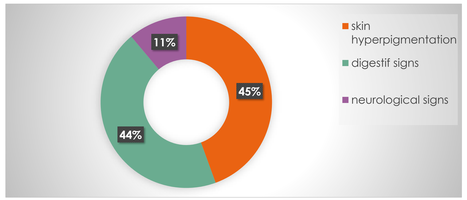

Figure 1: Distribution of children by reason for consultation

Case	Age	Signs of adrenal insufficiency	Neurological signs
1	8 years old	Skin hyperpigmentation-dehydratation-hypoglycimia	_
2	7 years and 2 months old	Skin hyperpigmentation- Deshydratation	_
3	5 years old	Skin hyperpigmentation	-
4	11 years old	Skin hyperpigmentation – Deshydratation	• Epilepsy at the age of 2 years and 2 months old • Pyramidal syndrom at the age of 5 years old
5	16 days	Deshydratation – hypoglycimia	• Delay in psychomotor development • Attention difficulties
6	3 years old	Skin hyperpigmentation	

Table 1: Clinical manifestation at onset of X-linked adrenoleukodystrophy in our study

Case	C24/C22 (Normal: 0,5-1)	C26/C22 (Normal: 0,002-0,02)
1	1,28	0,09
2	1,27	0,04
3	1,58	0,09
4	1,59	0,62
5	1,77	0,16

Table 2: Biochemical results of showing adrenal insufficiency in children with X-linked adrenoleukodystrophy in our study

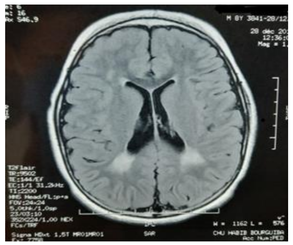

Figure 2: Brain MRI T2 Flair: increased signal in occipital white substance

Case	Serum CORTISOL (normal: 20-200ng/ml)	Serum ACTH (normal: 10-48 ng/l)	Serum Renine (normal: 3,5-20 pg/ml)	Aldosterone (pmol/l)
1	13,8	13700	41,7	87
2	4,27	1480	86,9	61
3	53	3882	35,8	171
4	38	>1000	_	58
5	4,4	1722	20	61
6	2	1250	40,5	640

Table 3: The plasma very long chain fatty acids (VLCFA) levels at onset of X-linked adrenoleukodystrophy in our study

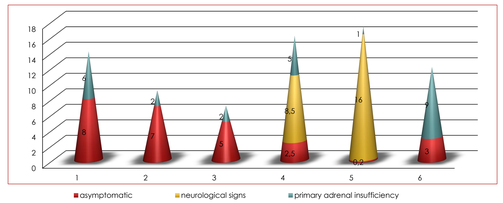

Figure 3: Clinical evolution of children with X-linked adrenoleukodystrophy in our study

- Brain magnetic resonance imaging (MRI) showed signs of leukodystrophy in 2 cases (**Figure 2**).
- The plasma very long chain fatty acids (VLCFA) levels were significantly increased for five children (**Table 2**).
- Genetic testing identified the mutation of ABCD1 gene in 4 cases
- All children developed adrenal insufficiency during the course of the disease (**Table 3**) and 2 children progressed to a cerebral phenotype (**Figure 3**).

CONCLUSIONS

- X-linked ALD should be screened for boys with adrenal insufficiency.
- This disorder is confirmed by serum VLCFA levels and/or genetic testing.
- Confirmation of the diagnosis of X-ALD by analysis of mutations in ABCD1 is particularly recommended to identify heterozygous women and for antenatal diagnosis of ALD.

CONTACT INFORMATION

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