

Triple A syndrome : the second most common cause of chronic adrenal insufficiency in North Africa

Kahina Mohammedi^a, Asmahane Ladjouze^b, Ammar Tebaibia^c, Leila Kedji^b, Abdelmajid Maoudj^b, Karima Berkouk^b, Manoubia Bensmina^b, Souhila Amoura^d, Mohamed El Amine Boudjella^a & Abdennour Laraba^b

^aDepartment of Paediatrics, EPH AinDefla, Ain-Defla, Algeria; ^bDepartment of Paediatrics, Bab El Oued Teaching Hospital, Algiers, Algeria; ^cDepartment of Gastroenterology, Kouba Hospital, Algiers, Algeria; ^dDepartment of Immunology, Mustapha Teaching Hospital, Algiers, Algeria



Background

The triple AAA syndrome (AAAS, OMIM#231550), is a very rare inherited disease characterized by the association of:

- Chronic Adrenal insufficiency,
- Achalasia,
- Alacrima
- Plus central and peripheral neurological disorders.

The condition is caused by mutations in the AAAS gene which encodes the nuclear pore complex scaffolding protein ALADIN .

The relative prevalence and genotype of AAAS in the Maghreb countries has not been ascertained.

Material and Methods

Clinical data were collected retrospectively from the medical records of patients attending a single centre of Paediatric Endocrinology in Algiers between 2007 and 2015.

Written informed consent for genetic testing was obtained from patients and family members.

Objectives

To estimate the prevalence, clinical features and genetic findings of triple A syndrome among children with chronic adrenal insufficiency in Algeria

Results

Of 160 children and adolescents with chronic adrenal insufficiency identified between 2007 and 2015, 25 (15.6%) were diagnosed with Triple A syndrome, rendering it the second most common cause of chronic adrenal insufficiency after congenital adrenal hyperplasia (see Fig.1).

The 25 patients with AAAS syndrome were from 20 families.

- Parents were consanguineous in 17 cases (68%).
- There was a family history of unexplained sibling death in 7 cases.
- The sex ratio was 1.5M/1F
- Mean± (range) age at diagnosis was 4.34±2.80 (1-10.8) years
- The clinical findings of the AAAS patients are shown in Figure 2.
 - ✓ Height at diagnosis (WHO 2007 data) was -1.26 ± 1.5 SDS (cf. Fig.3)
 - ✓ BMI at diagnosis (WHO 2007 data) was 0.74 ± 1.36 SDS.
- All patients were initially diagnosed because of adrenal insufficiency,
- 19 had isolated glucocorticoid deficiency,
- 6 had combined glucocorticoid and mineralocorticoid deficiency.
- All patients had alacrima,
- 24 patients had achalasia
- 9 patients had neurological disorders (cf. Table.1)
- Genetic analysis of the AAAS gene was performed for seven families.

The previously reported IVS14+1G>A splice donor mutation was found in six patients, the EVS9 mutation in one patient.

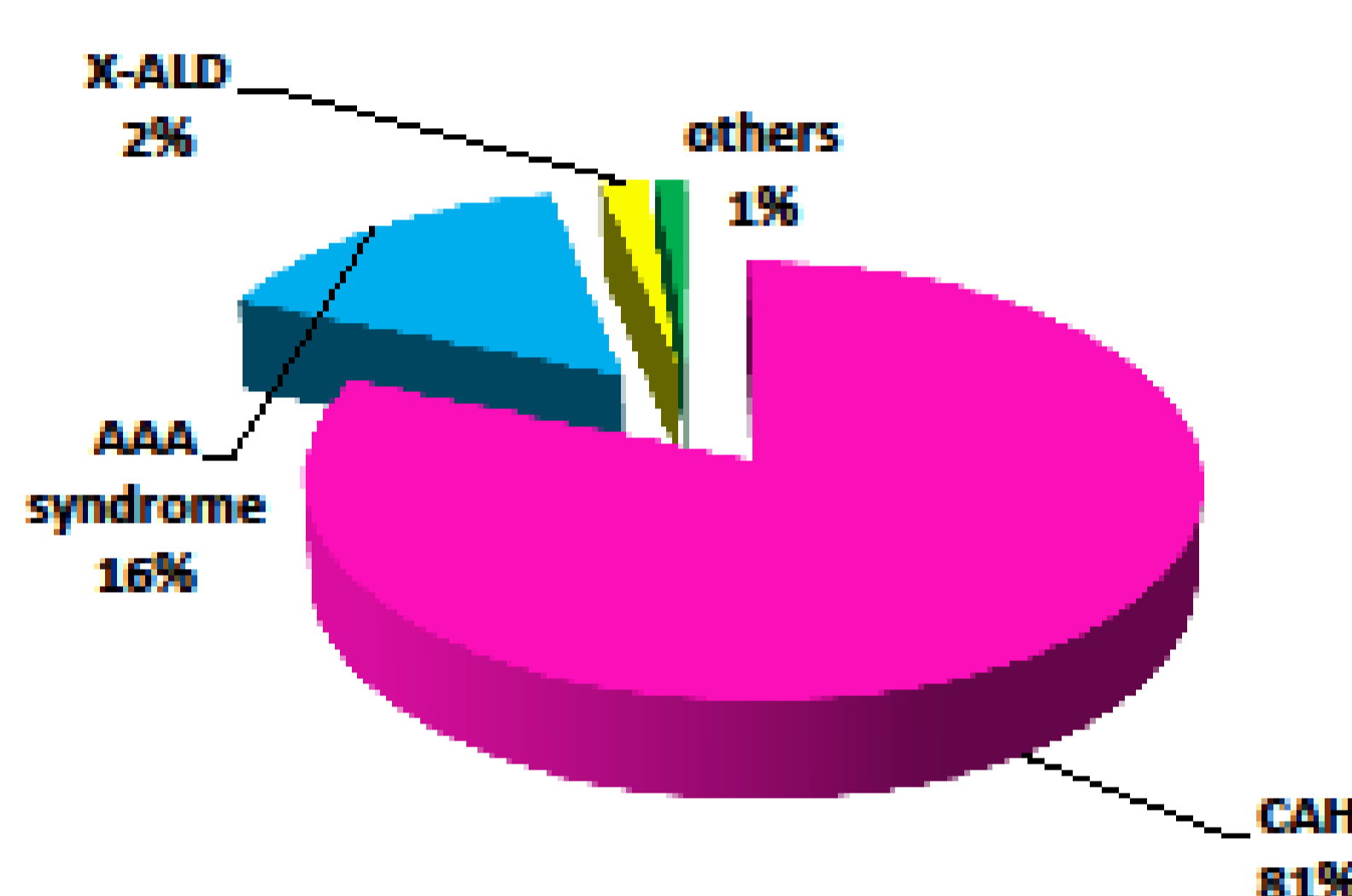


Fig.1.Etiologies of chronic adrenal insufficiency (N=160)

X-ALD: X-linked Adrenoleukodystrophy
AAAS: Triple A Syndrome
CAH: Congenital Adrenal Hyperplasia

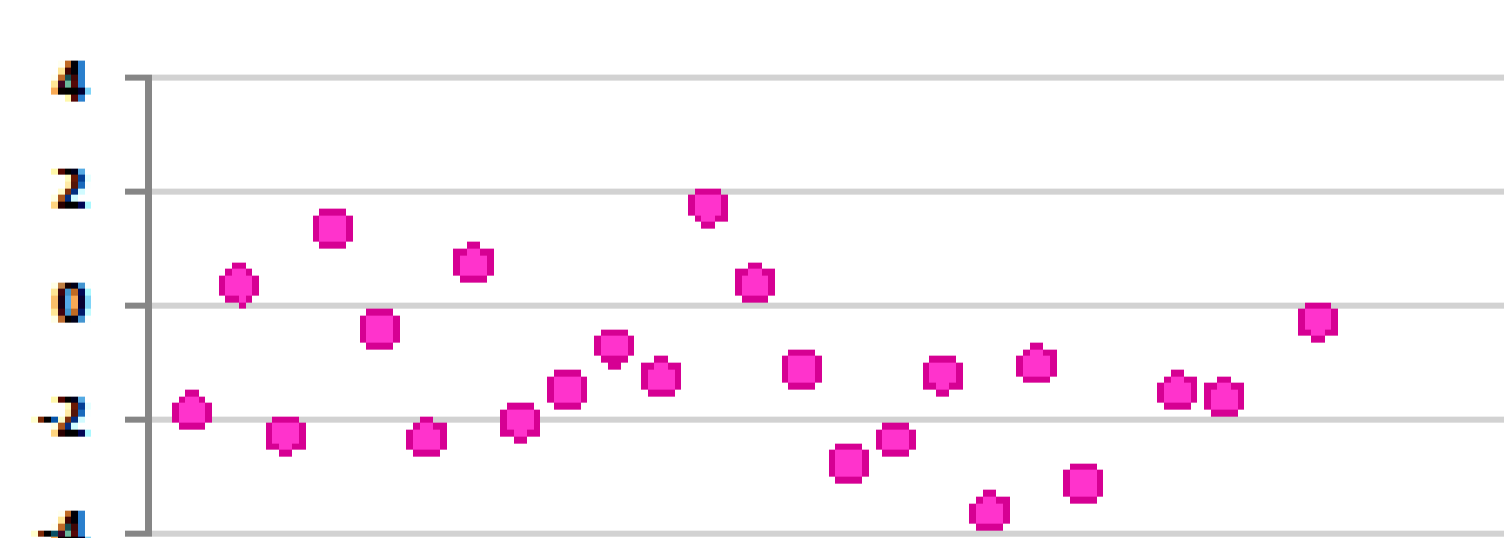


Fig. 3. Height (SDS) of patients at diagnosis (WHO 2007)

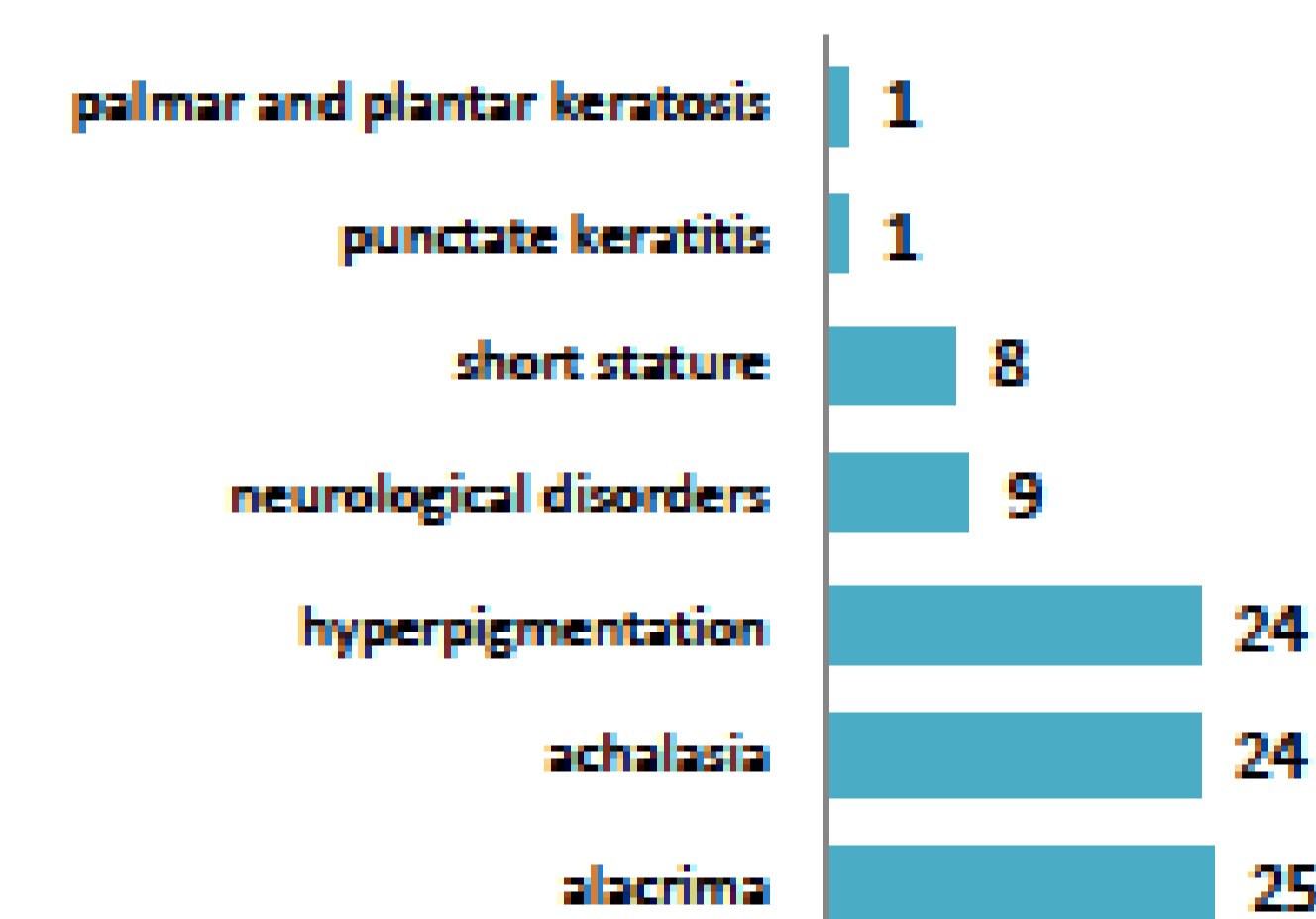


Fig.2. Clinical findings in patients with AAAS (n=25)

Neurological features	N
Intellectual disability	5
Polyneuropathy	3
Dysarthria	1
Autonomic dysfunction	0
Ataxia	0

Table 1. Neurological features (N=9)

Genetic analysis

Mutation	N
IVS14 + 1G>A	6
EVS9	1

Conclusion

Although rare, Triple A syndrome is the second most common cause of chronic adrenal insufficiency in our patients. Because it's not so rare in our region, it is very important to ask the parents about alacrima in all patients with adrenal insufficiency.

Unfortunately, it remains a cause of unexplained death in young undiagnosed children. Systematic early recourse to blood glucose testing in sick children may help to an early diagnosis of adrenal insufficiency and prevent those evitable deaths.

