CONGENITAL ADRENAL HYPERPLASIA IN MALE AND FEMALE SIBLINGS LEADING TO PRECOCIOUS PUBERTY

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ABSTRACT

CAH in male and female siblings leading to isosexual and heterosexual precocious puberty is extremely rare and not very well reported in the paediatric age group, but it is reported among female siblings.(1) CAH is mainly seen in infants and young children with the major enzyme defect being 21-hydroxylase, the loss of which maybe complete or partial; 21-hydroxylase deficiency accounts for 90% of CAH cases, whereas other enzyme deficiencies such as 11-beta hydroxylase, 17-alpha hydroxyls and 3-beta hydroxysteroid dehydrogenase account for minority of the cases; 70% of affected infants present with the salt losing form; 30% of them present with simple virilising form. Present case study is about a pair of male and female siblings affected by simple virilising form of CAH.

KEYWORDS

Male and Female Siblings, CAH, Precocious Puberty.

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INTRODUCTION/CASE REPORT 1

A 9-year-old male child from rural South India presented to the Emergency Room with episodes of vomiting, fever and altered sensorium.

Child was agitated with violent behaviour. He could not be restrained by parents. Mother does not report similar complaints in the past or other complaints related to altered sensorium such as seizures, headache, head trauma, etc.

Clinical examination was negative. All lab reports were normal.

Child was born to non-consanguineous parents. Mother suffered two miscarriages in the past. Mother noticed development of pubic hair at the age of 3 years and hair over upper lip at 5 years in both the siblings. History of accelerated growth in height for the past 1 year.

Clinical Examination

- Child was hyperpigmented.
- He was restless.
- Vitals were normal.

CNS and other system examination revealed no abnormality.
Anthropometry: (Male child). Height - 151 cms (Expected 137 cms. More than 97th percentile). Weight - 45 kgs (Expected 33 kgs. More than 97th percentile) US/LS - 1.09.

Height age	-	12.5 years.
SMR staging	-	Pubic hair stage 5.
SPL	-	Stage 5.
Orchidometry	-	3 mL (TV); SMR stage 1.

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Investigations for Male Child

1. CBP : Hb - 12 gm%
   WBC - 4,800 cells/cumm,
   DLC-WNL
2. **Serum Electrolytes**
   - S. Na+ - 117 mEq/L.
   - S. K+ - 5.6 mEq/L.
   - S. Cl- 112 mEq/L.
3. Blood Urea: 26 mg%.
4. Serum creatinine: 1 mg%.
5. CSF: Normal.
6. Fundus: Normal.
7. CT brain – Normal.
8. USG Abdomen – Normal.
9. X-Ray upper tibia and wrist for bone age >16 years.
10. MRI brain and abdomen – Normal.
11. Karyotype - XY (Male).

CASE REPORT 2

6-year-old female sibling brought with complaints of clitoral prominence since birth, development of pubic and axillary hair since 3 years of age. Hair over upper lip and change in voice since 1 year. Accelerated growth in height since 1 year. Child had masculine facies and low pitched voice.

Anthropometry: (Female child).
Height - 135 cms (Expected - 119 cms).
Weight - 35 kgs (Expected 22 kgs).
US/LS - 1.07.
Height age -
SMR staging - Breast: Prepubertal.
Pubic hair - Stage 4.
Axillary hair – Present.
Clitoromegaly - 4 cms.

Investigations for Female Child

All routine tests' reports were within normal limits.
X-Ray wrist for bone age >12 years.

USG Abdomen - Hypoplastic uterus with bilateral normal ovaries.
MRI Brain – Normal.
Karyotype - XX (Female).

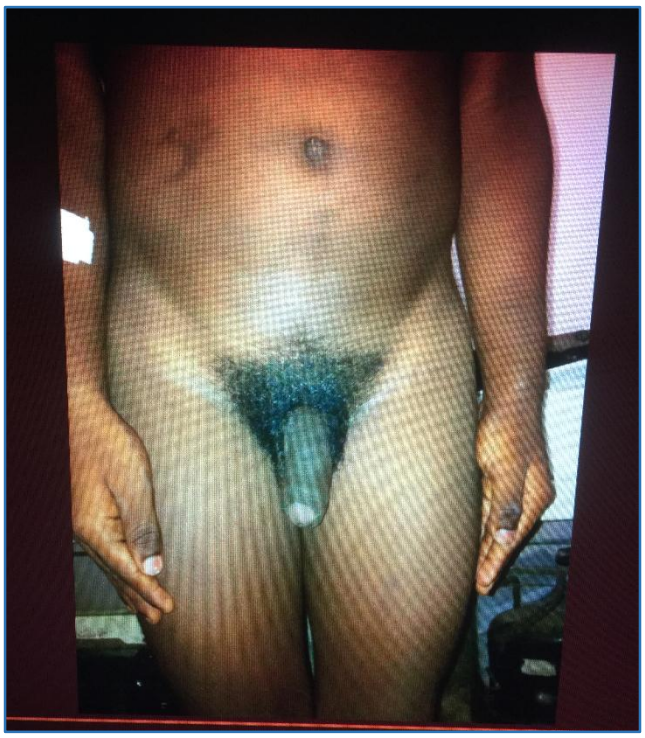

Fig. 1: 9 year old boy with SMR stage 5

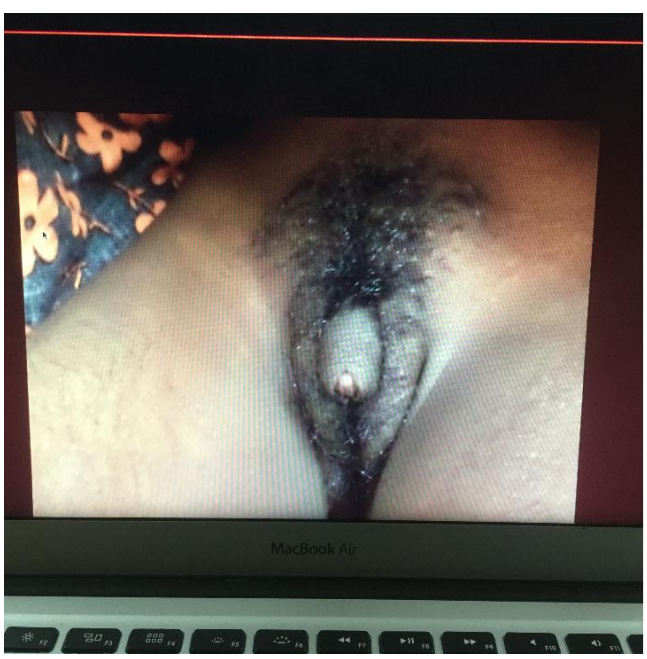

Fig. 2: 6 year old girl with pubic hair and clitoral enlargement

DISCUSSION

CAH is a group of autosomal recessive disorders characterised by impaired cortisol synthesis. Incidence is 1:10,000 to 1:20,000, but it is more prevalent in some ethnic groups in which consanguineous marriage practices are prevalent.

The most common form of CAH is caused by mutations in C4P21A2, the gene encoding the adrenal steroid 21-hydroxylase enzyme. The cortisol synthesis block leads to ACTH stimulation of adrenal cortex with accumulation of cortisol precursors that are directed to sex hormone synthesis.[2]

Present study was done on two siblings, both who are affected with simple virilising form of CAH with the parents being recessive carriers of the gene. Chance of 1 child being affected in consanguineous marriage (Parents being related and unaffected carriers) is 1:25 and 2 kids being affected is 1 in 12.5. Chance of both kids being affected in a non-consanguineous marriage is 1:20,000. Incidence of CAH in India has been found to be 1 in 2575 from a small sample survey.[3] Extensive search of literature revealed no such reported case of untreated CAH leading to isosexual precocious puberty in male child and virilisation/pseudo-hermaphroditism/intersex in the female child. Hence, this could be the first of its kind in medical literature.

CONCLUSION

In view of the extreme rarity of the case, this case study was reported. Early diagnosis and treatment with steroids could have prevented development of precocious puberty in these siblings. Male child had frequent rage attacks.[4] due to androgen excess. Social stigma might have prevented the parents and the children from seeking medical help.

As neonatal screening.[5] for metabolic disorders is not established even in teaching hospitals, this case serves as an example for mandatory screening in the second child when the first sibling is affected with CAH, which could prevent many deaths in the severe form.[6,7]

REFERENCES

1. Bin-Abbas B, Al-Humaida D, Al-Sagheir A, et al. Divergent gender identity in three siblings with 46 XX karyotype and severely virilising congenital adrenal hyperplasia caused by a novel CY11B1 mutation. Endocrine Practice 2014;20(10):e191-7.
2. New MI. An update of congenital adrenal hyperplasia. Annals of the New York Academy of Sciences 2004;1038:14-43.
3. Devi AR, Naushad SM. Newborn screening in India. Indian Journal of Paediatrics 2004;71(2):157-60.
4. Rushworth RL, Falhammar H, Munns CF, et al. Hospital admission patterns in children with CAH: admission rates and adrenal crises decline with age. International Journal of Endocrinology 2016;2016:1-7.
5. White PC. Neonatal screening for congenital adrenal hyperplasia. Nature Reviews Endocrinology 2009; 5(9): 90-8.
6. Grosse SD, Vliet VG. How many deaths can be prevented by neonatal screening for congenital adrenal hyperplasia. Hormone Research 2007;67(6):284-91.
7. Carlson AD, Obeid J, Kanellopoulou N, et al. Congenital adrenal hyperplasia: update on prenatal diagnosis and treatment. The Journal of Steroid Biochemistry and Molecular Biology 1999;69(1-6):19-26.