Persistent Elevation of Gonadotropins In A Girl with Aromatase Deficiency Despite Adequate Estradiol Supplementation- A Case for Reset Hypothalamic-Gonadal Axis

GROW India
Growth & Obesity Workforce

Neha Agarwal, Chetan Dave, Riddhi Patel, Rishi Shukla, Anurag Bajpai
Department of Pediatric Endocrinology, Regency Center for Diabetes and Research, Kanpur

REGENCY HEALTHCARE
ENSURING WELLNESS - ENRICHING LIVES
Center for Diabetes Endocrinology Research

Background

Aromatase deficiency associated with atypical genitalia in infancy and delayed puberty later

Normalization of gonadotropin levels and pubertal development with estrogen replacement

Case Report

A 16-year old girl with novel *CYP19A1* mutations, misdiagnosed as CAH, with persistently elevated gonadotropin levels despite adequate estrogen treatment

Clinical Details

Delayed Puberty at 13.5 y age

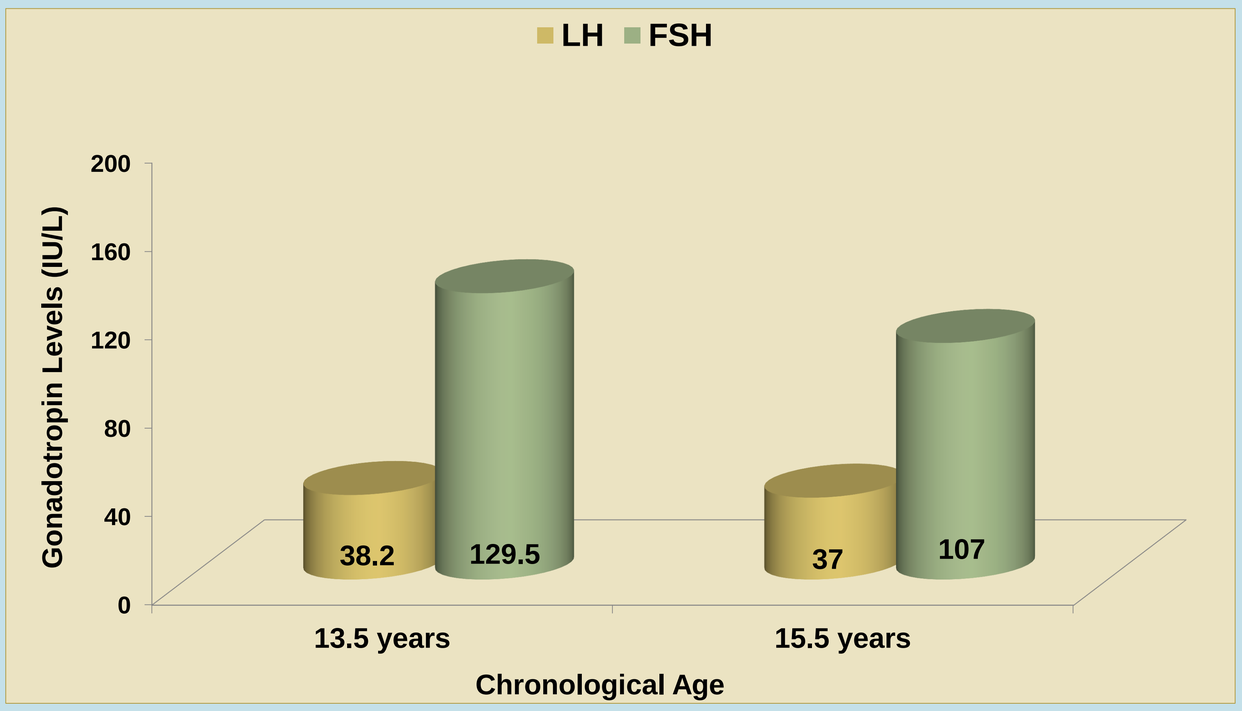
- Neonatal presentation- clitoromegaly, labial fusion
- No palpable gonads, Ultrasound showed uterus; 46 XX,
- Mildly elevated 17OHP
- Diagnosed as 21OHD; HC ;Persistently low 17OHP at low HC doses
- Gene study for 21OHD normal; HC stopped at 11 years

On Evaluation

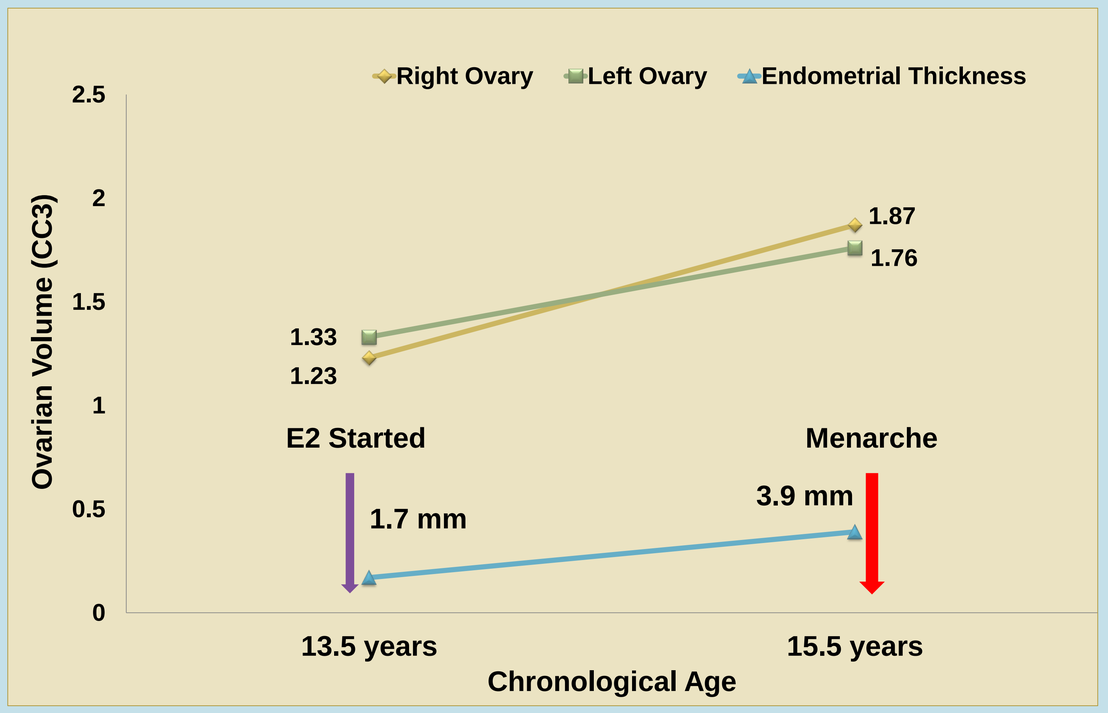
- Delayed Bone Age; Breast stage II, Pubic hair V
- Elevated gonadotropin levels; undetectable estrogen levels
- Perinatal history of maternal virilisation
- Genetic study - two novel heterozygous mutations on exon 4 (p.Arg115Ter) and exon 5 (p.Tyr184Ter) of *CYP19A1*
- Estrogen Replacement Started

Post Estrogen Replacement

Gonadotropin Levels



Ovarian Volumes and Endometrial Thickness



High Gonadotropins In Presence Of Adequate Pubertal Progress

Ovarian Cysts Not Observed At Any Time Point

Conclusion

- Novel heterozygous mutation in *CYP19A1* identified
- Gonadotropin levels did not decrease with estrogen replacement
- Absence of ovarian cysts despite high FSH levels
- Indicates abnormal pituitary responsiveness to estradiol

References

- Akçurin S, Türkkahraman D, Kim WY, Durmaz E, Shin JG, Lee SJ. A Novel Null Mutation in P450 Aromatase Gene (CYP19A1) Associated with Development of Hypoplastic Ovaries in Humans. J Clin Res Pediatr Endocrinol. 2016 Jun 5;8(2):205-10
- Janner M, Flück CE, Mullis PE. Impact of estrogen replacement throughout childhood on growth, pituitary-gonadal axis and bone in a 46,XX patient with CYP19A1 deficiency. Horm Res Paediatr. 2012;78(4):261-8

58ESPE P3-227
Sex differentiation, gonads and gynaecology or sex endocrinology
Neha Agarwal
Poster presented at: ESPE 2019 VIENNA
PosterSessionOnline.com