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

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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

References