TWO INTERESTING CASES OF DISCORDANT PUBERTY AND SECONDARY AMENORRHOEA

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INTRODUCTION

- Pubertal development is said to be concordant when it follows its usual pattern
- Girls- thelarche → pubarche → menarche
- Boys- increased testicular volume → pubic hair → adult size testicular volume (25ml)
- When the usual pattern is not followed, it is called discordant pubertal development

CASE 1

- 17 years/ Female
- Complaints – secondary amenorrhoea
- HOPI –
  - Child had only one episode of spotting at 15 years of age
  - Breast development noted at 13 years of age
  - No history of pubic hair or axillary hair growth
  - No history suggestive of hypothyroidism/ chronic systemic illness/ head trauma/ CNS infections/galactorrhoea/ acne/ hirsutism
- Past History – nil significant
- Birth History – FTNVD; Birth weight- 2.8kg; cried after birth
- Family History – Non consanguinity; History of hypothyroidism in elder sister. No history of delayed puberty or similar illness in the family

Examination

- GC – Fair
- Vitals – PR – 80/min, BP – 100/70mm Hg
- Height – 134cm (below 3rd centile)
- Weight – 30kg (below 3rd centile)
- BMI – 16.7 kg/m2 (below 3rd centile)
- SMR – A1P1B4
- No dysmorphism
- No acne/ hirsutism
- No goitre
- No Galactorrhoea
- No clitromegaly

Discordant pubertal development with secondary amenorrhoea
? Hypothyroidism
?Polycystic ovarian syndrome

CASE 2

- 12 years/ Female
- Complaints- Secondary amenorrhoea
- HOPI-
  - Attained menarche at 10 years of age and did not resume her cycles after menarche
  - Cycles only occurred with oral progesterone
  - Breast development noticed 1 year prior to attaining menarche
  - No history of pubic or axillary hair growth
  - History of excessive weight gain after attaining menarche
  - No history suggestive of hypothyroidism/ chronic systemic illness/ head trauma/ CNS infections/ galactorrhoea/ Acne/ Hirsutism
- Past History – Nil significant
- Birth History – FTNVD; Birth weight- 2.75kg; Cried after birth
- Family History – Non consanguinity; No history of hypothyroidism , delayed puberty or similar illness in the family

EXAMINATION

- GC – Fair
- Vitals – PR – 82/min, BP – 102/80mm Hg
- Weight – 58.6 kg (90-95th centile)
- Height – 143.2cm (3-10th centile)
- BMI – 28.5 kg/m2 (above 95th centile)
- SMR- A1P1B1
- No dysmorphism
- No acne/ hirsutism
- No goitre
- No Galactorrhoea
- No clitromegaly

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INVESTIGATIONS

INVESTIGATION	CASE 1 (17 year old – A1P1B4)	CASE 2 (12 year old – A1P1B1)
TSH	**>150**	**>150**
FT4	**0.06**	**0.12**
FSH	8.74	0.7
LH	**<0.07**	**<0.07**
OESTROGEN	47	15
TPO ANTIBODY	**5319.4**	**4572.6**
THYROGLOBULIN ANTIBODY	**634.6**	
USG ABDOMEN	Uterus- 7.3x1.6cm ET- 2mm Right ovary- 2.7x1.3x1.4cm Left ovary- 2.2x1x1.2cm	Uterus- 4.4x1.6cm ET- 2mm Right ovary- 1.9x1.7x1.6cm Left ovary- 2.3x1.7x1.8cm
BONE AGE	10 years	11 to 12 years

DIAGNOSIS

- Secondary amenorrhoea with discordant pubertal development due to autoimmune hypothyroidism

TREATMENT

- Both the girls were started on Thyroxine supplementation

FOLLOW UP

- Case 1 – One year after starting Thyroxine, cycles resumed and SMR staging was A2P3B5
- Case 2 – One year after staring Thyroxine, cycles normalised and SMR staging was A1P3B3

DISCUSSION

- Common causes of oligomenorhoea/ menstrual irregularities in adolescents are:
  - Hypothyroidism
  - Hyperprolactinemia
  - Non-classic Congenital Adrenal hyperplasia
  - Polycystic Ovarian Syndrome
- Occurrence of discordant pubertal development in children presenting as secondary amenorrhoea is rare

Hypothyroidism in Children

- Hypothyroidism occurs in 0.3% of school aged children
- Most common cause of acquired hypothyroidism is autoimmune thyroiditis
- Hypothyroidism can cause an entire spectrum of pubertal disorders from precocious puberty to delayed puberty and menstrual disturbances
- In chronic untreated hypothyroidism,
  - precocious puberty is caused due to high circulating levels of TSH (alpha subunit) interacting with FSH receptors.
  - Delayed puberty is caused due to altered/ immature hypothalamo-pituitary gonadal axis.
  - Menstrual Irregularities are due to hyperprolactinemia (caused by elevated TRH), Suppression of gonadotropin secretion (predominant LH suppression) and ovulation.

VAN WYK GRUMBACH SYNDROME

- Van Wyk Grumbach syndrome was first described in 1960 by Van Wyk and Grumbach.
- This syndrome is characterised by (along with long standing hypothyroidism),
  - Breast development (Incomplete precocious puberty)
  - Uterine bleeding
  - Multicystic ovaries
- Probable aetiology:
  - Cross reaction of TSH with ovarian FSH receptors
  - TRH induced hyper prolactinemia- suppresses gonadotropin axis
- Our patients do not fit into this syndrome there is no sexual precocity and USG did not show ovarian cysts
- **?a manifestation of Van wyk Grumbach syndrome spectrum**

CONCLUSIONS

- Incomplete pubertal development with secondary amenorrhoea is a **new** clinical manifestation for a **known** entity - hypothyroidism
- No such case reports are available in literature to our knowledge
- Strong clinical suspicion, careful physical examination and follow up are necessary in order to diagnose and treat discordant puberty associated with hypothyroidism
- Complete pubertal development can be attained with Thyroxine supplementation

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THANK YOU