



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

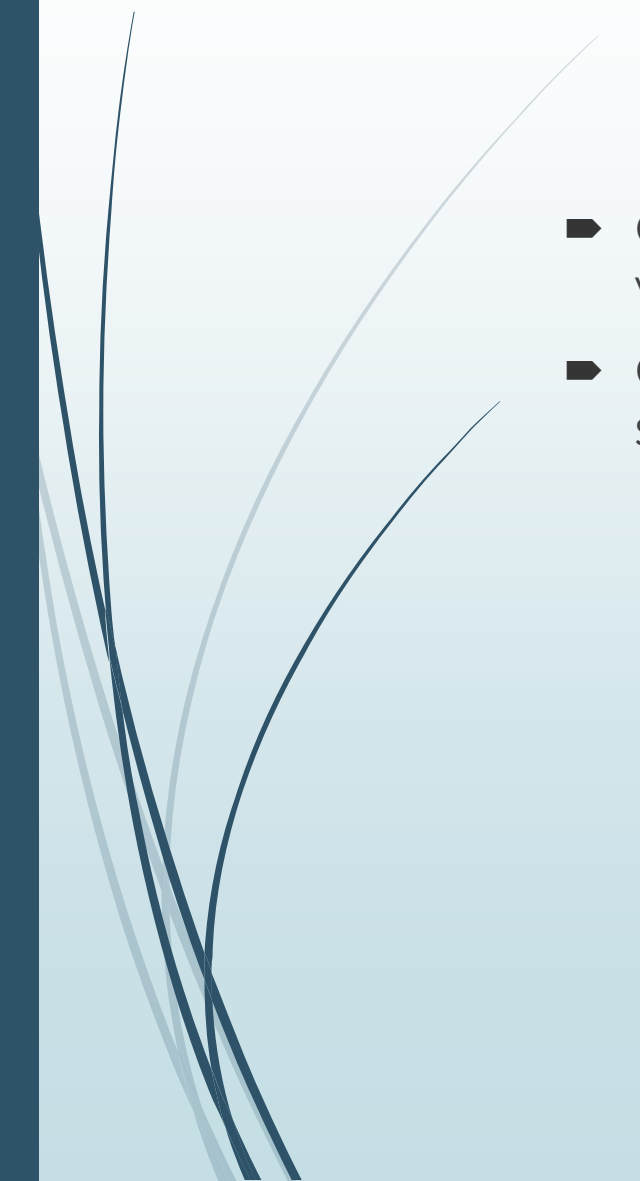
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TREATMENT

- ▶ Both the girls were started on Thyroxine supplementation

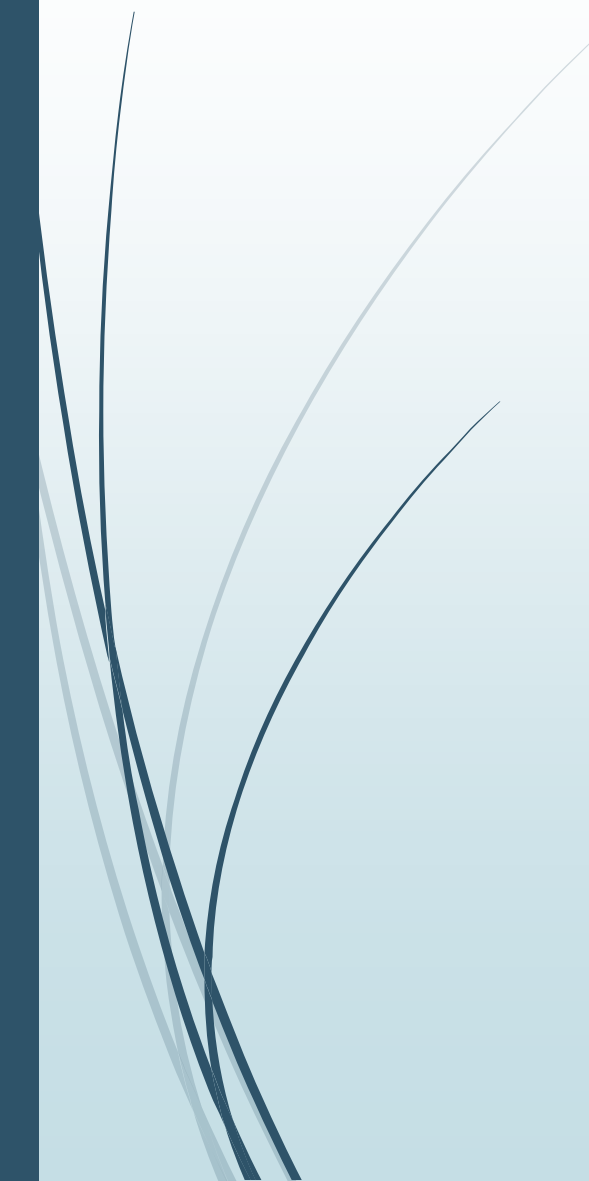



FOLLOW UP

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



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- ▶ Common causes of oligomenorrhoea/ 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**



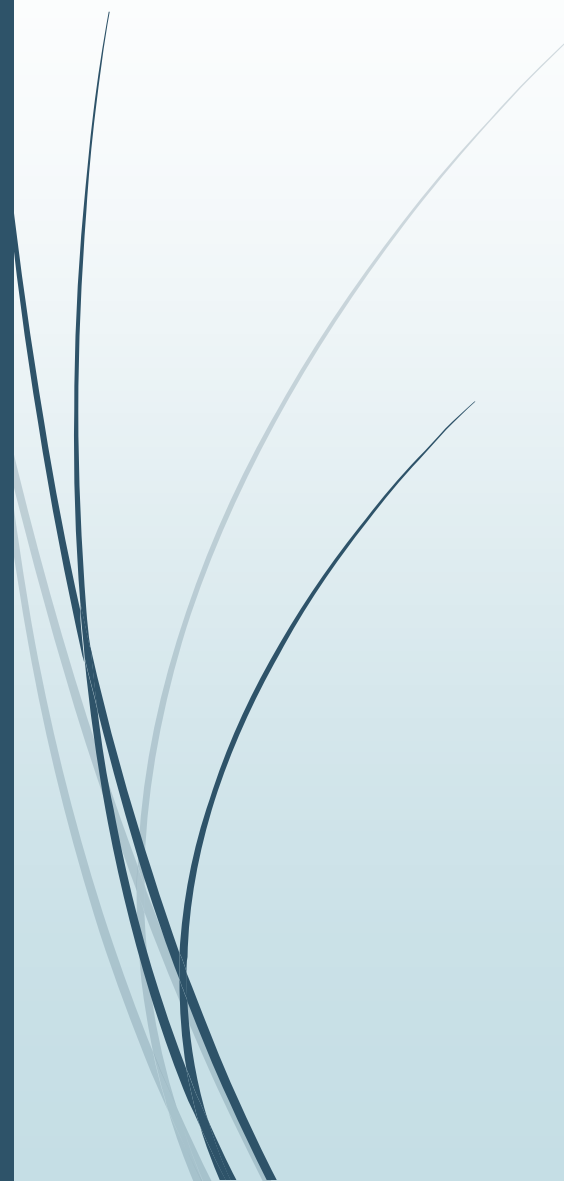
CONCLUSIONS

- ▶ 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



REFERENCES

- ▶ Nelson's textbook of paediatrics
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- ▶ Bhadada S, Rastogi A, Bhansal A. An unusual presentation of a usual disorder: Van Wyk Grumbach syndrome. Indian journal of endocrinology and metabolism 2011; 15(6):141
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THANK YOU