An unusual case of genital bleed in a preschool girl

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- Under the guidance of-
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A 5 year old female child was brought to the hospital with the following complaints

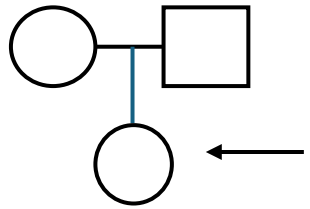
- Staining of undergarments with blood – 1st episode
- Not associated with abdominal pain ,fever, loose stools, burning micturition ,seizure ,headache
- No h/o abuse
- No h/o injury
- No h/o itching or rash.
- No h/o intake of any hormone based tablets .

Past History-

3 months ago the patient was operated for Balloon valvuloplasty i/v/o pulmonary stenosis with pericardial fluid drainage and started on Tab Lasilactone.

No h/o similar complaints in the past.

Family History-



Only child born from non consanguineous marriage .

Menarche in mother –at 14 years of age

Birth History-

FT/LSCS i/v/o meconium stained liquor /Cried Immediately after birth/2.5kg/No NICU stay

Immunisation History-

Child Immunised upto 1.5 years of age (As per national immunisation schedule)

Developmental history- Appropriate for age.

Differential Diagnosis ?

- **Local causes** –
  - Foreign body
  - Local injury
  - Rectal prolapse
- **Urinary tract infection**
- **Precocious puberty** – central or peripheral

GENERAL EXAMINATION

- Vitals –
- PR -70/min
- RR-20/min
- BP-100/68
- Sp02-98%
- PP-well felt

- No pallor, icterus, clubbing, cyanosis, lymphadenopathy
- No neck swellings

ANTHROPOMETRY

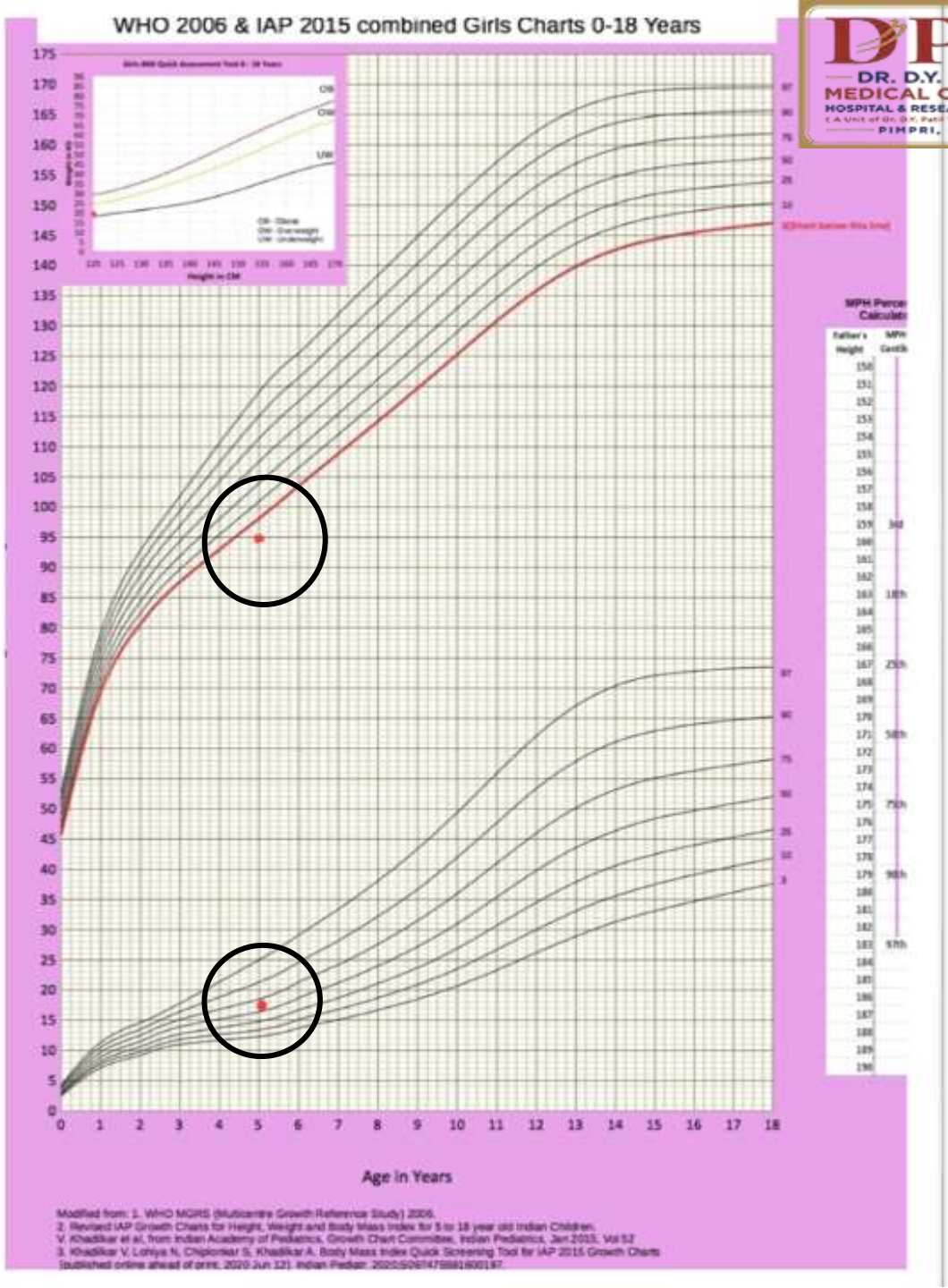
PARAMETER	VALUE	
WEIGHT	16.9KG	25th centile
HEIGHT	95CM	<3rd centile
HEAD CIRCUMFERENCE	46CM	
BMI	17.6Kg/m2	

IAP GROWTH CHART

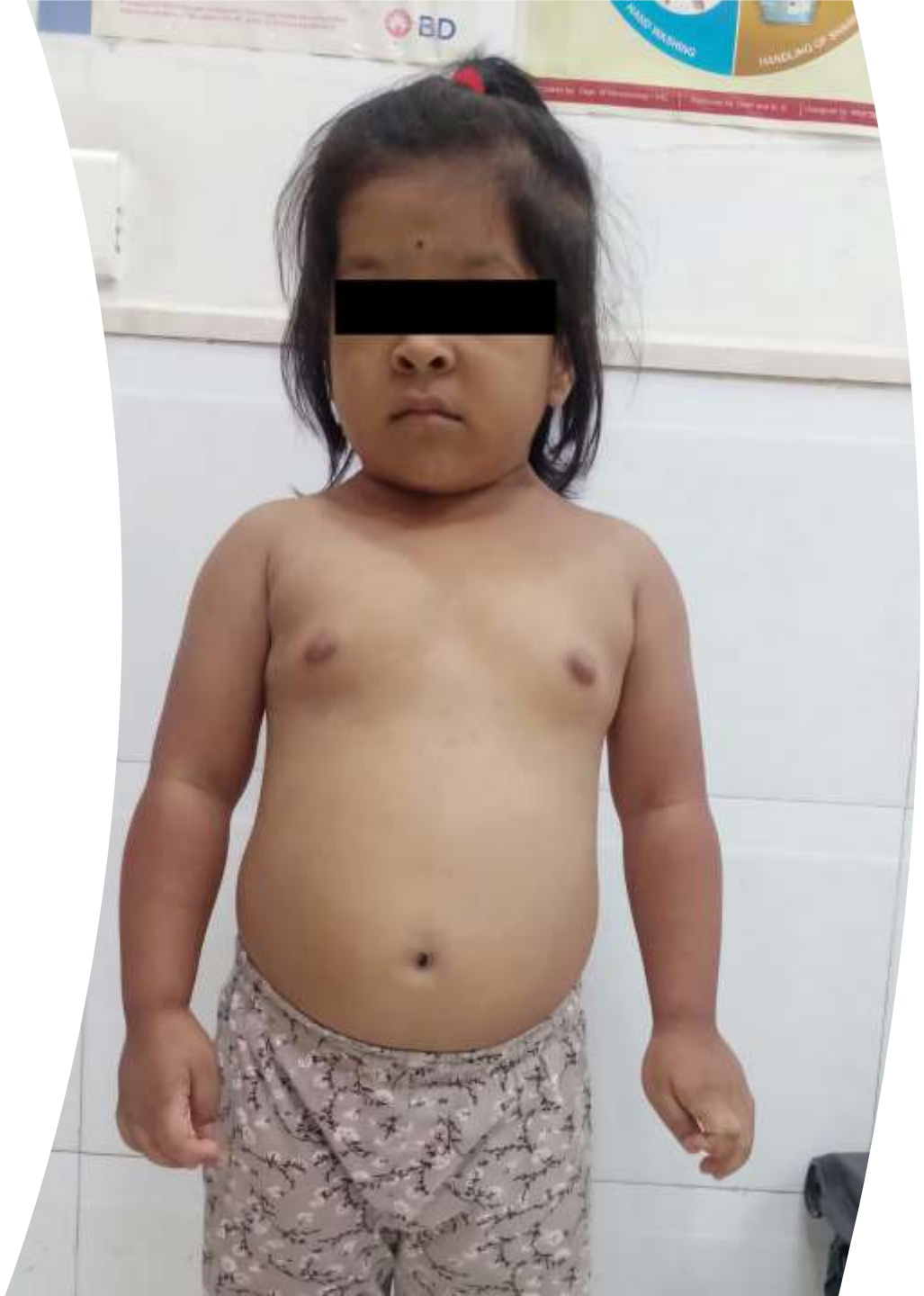
WEIGHT - NORMAL FOR AGE

HEIGHT – DISPROPORTIONATE SHORT STATURE (US:LS = 1.5: 1)

MID PARENTAL HEIGHT= 162 CM



Head to Toe Examination



- Coarse facies
- Flat nasal bridge
- Epicanthal folds
- Periorbital puffiness present
- Slightly upturned nose
- Short neck
- Clinodactly present
- Abdominal distension
- Non pitting edema over the legs
- Calf hypertrophy

Genital Examination

- No injuries around the genital area / no blood clots seen
- Non tender
- No redness , rashes
- No erythema
- No inguinal lymph nodes palpable

SYSTEMIC EXAMINATION

CNS EXAMINATION

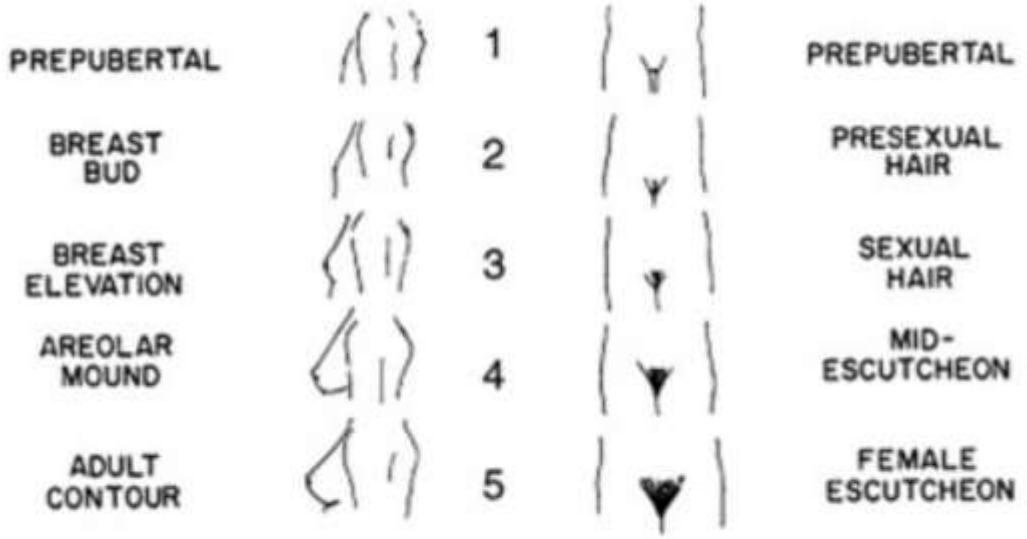
- Child conscious , alert
- Cranial nerves-all cranial nerve functions intact
- Tone –normal
- Power -5/5
- Reflexes-2+ .
- Sensory system normal

- Per Abdominal examination - soft ,non tender , no organomegaly present

- CVS- Heart sounds normal , no murmur

- RS- Air entry bilaterally equal, no added sounds

Tanners Staging(Sexual Maturity Rating)



- Tanner staging-
- B2 -Bilaterally(breast bud development)
- P1- No pubic hair(prepubertal)
- A1- No axillary hair(prepubertal)
- ?Menarche

Child had multiple episodes of frank bleeding per vaginum during the hospital stay.

LAB INVESTIGATIONS

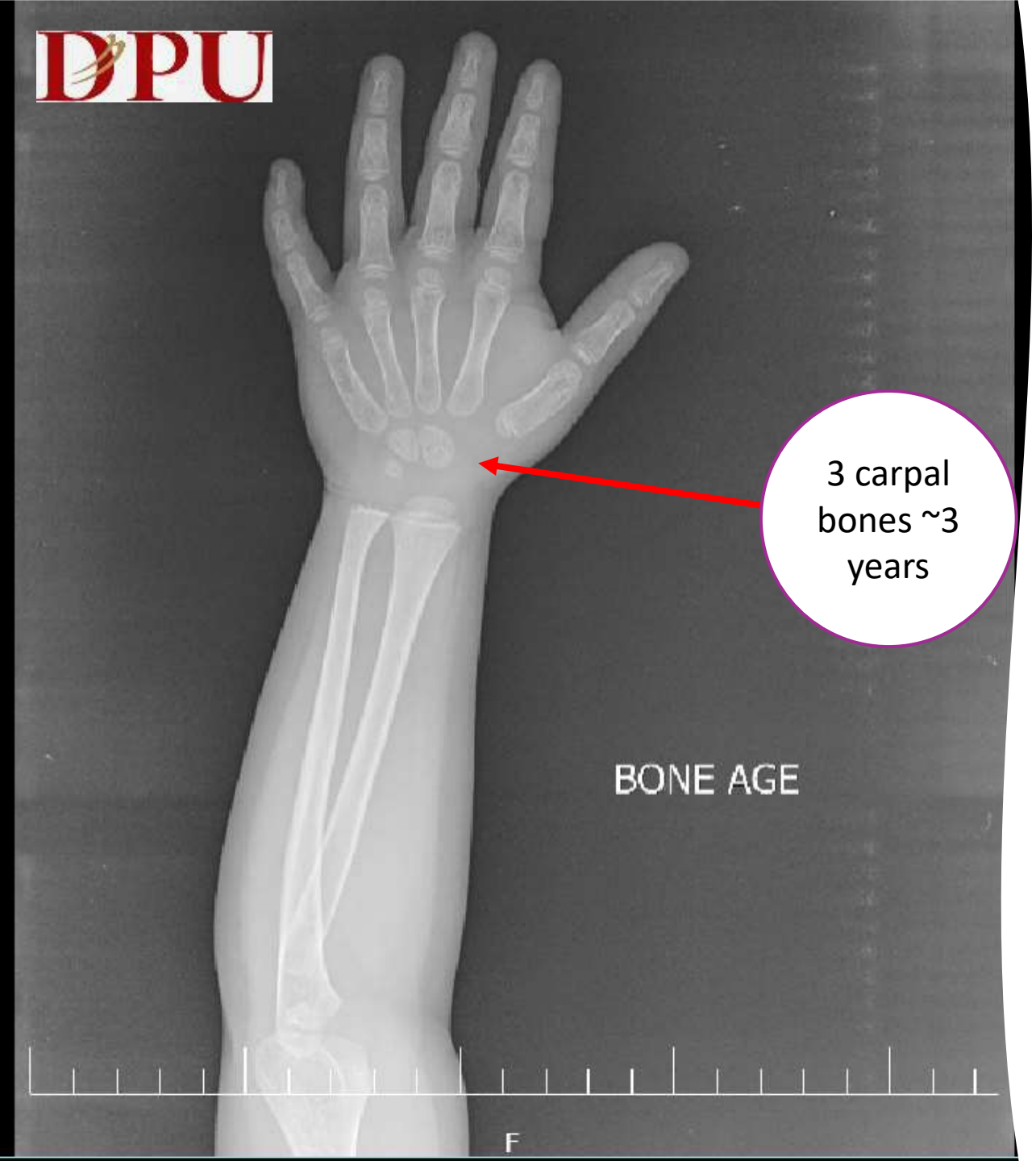
- TSH
- FSH
- PROLACTIN
- LH- suppressed

raised

	Patient values	Normal range
Hb	11g/dl	12-14.5g/dl
PCV	34.5%	35.7-43%
TLC	6200/microlitre	4000-10800/micro litre
N/L	43/51	
Platelets	2,40,000	1.5-4Lakh

PT	11.2 sec	10.2-14.7 secs
INR	0.94	0.85-1.1
APTT	40.6 sec	23.7-34.2sec

	Patient values	Normal range
TSH	>100 microIU/ml	0.70-6
LH	<0.007 mIU/mL	<0.02-0.3
FSH	9.61 mIU/mL	0.40-5.50
Prolactin	64.6 ng/mL	4.23
Estradiol	35 pg/mL	
T4	<0.91ng/dl	6-14.7
Anti TPO Antibodies	POSITIVE	
Cortisol(early morning)	9.30 microgram/dL	



- Chronological age (CA) –5 years 1 month
- Bone age (BA)– 2 years 9 months (using the Digital Atlas of Skeletal Maturity)
- Height age (HA)-3 years

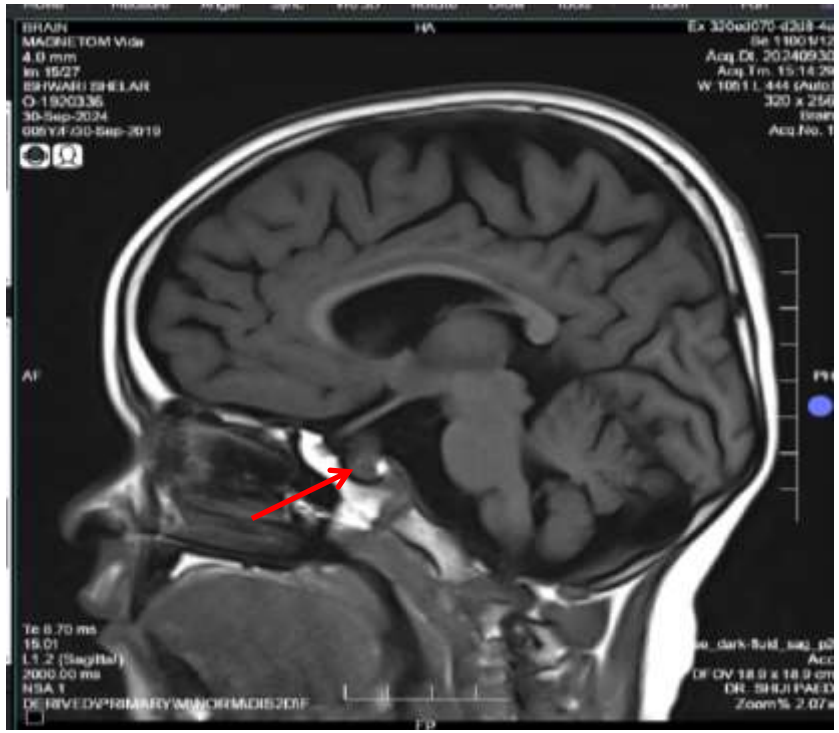
- Thus, CA>HA>BA…. Suggesting Endocrinological etiology

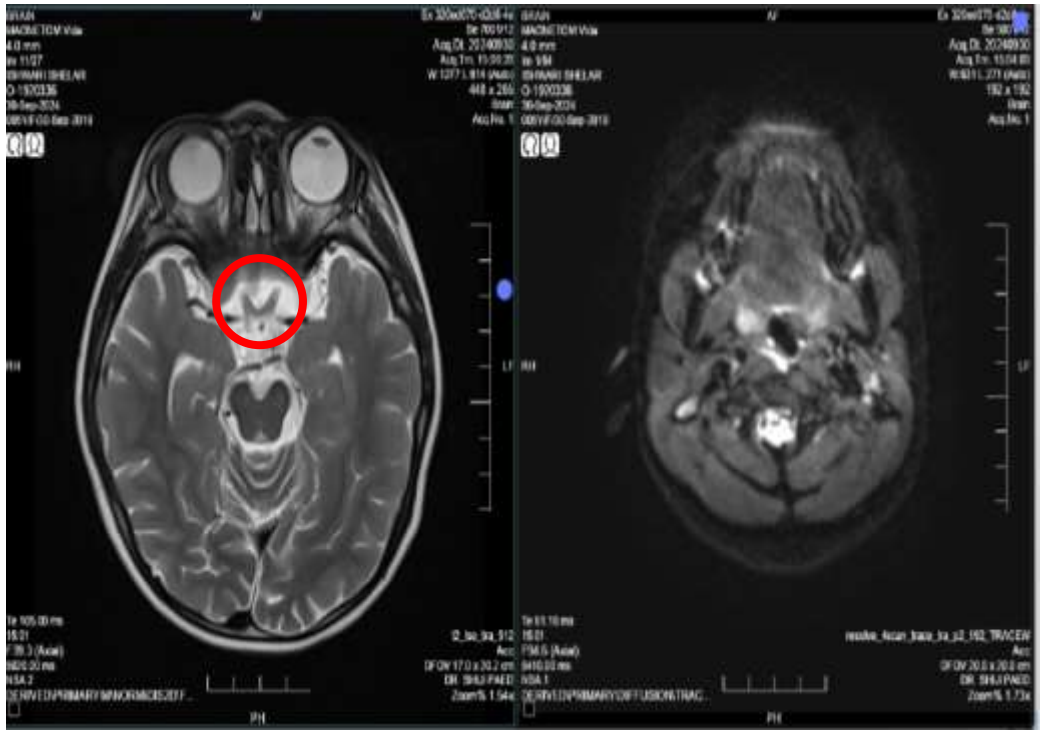
S. Vitamin D-18 ng/mL (Vit D insufficiency)
S. Calcium- 8.6 mg/dL (normal)

Radiological Investigations

- **Ultrasound abdomen and pelvis-**
  - Bilateral bulky ovaries (right ovarian cyst-30*14mm and left ovarian cyst-25*24mm)
  - Increased endometrial thickness s/o pubertal changes discordant with clinical staging.
- **Ultrasound Neck –**
  - Heterogenous echotexture of thyroid with 2 anechoic cysts with subcentimetric enlarged lymph nodes s/o thyroiditis
- **MRI brain –**
  - Pituitary gland enlarged with lobulated margins mostly due to pituitary macroadenoma.

MRI BRAIN





Pediatric Endocrinologist consultation

- ✓ Bleeding PV with short stature
- ✓ Thyroid workup s/o severe hypothyroidism
- ✓ Ovarian cyst and enlarged ovary
- ✓ Pituitary macroadenoma

✓ Diagnosis of Van Wyk Grumbach syndrome

✓ Tab Thyroxin 12.5 mcg once a day. Gradually dose of thyroxin was increased to 25 mcg once a day.

OBGY consultation

In view of ovarian cyst - tumor markers were advised and tranexamic acid was started(Parents were unaffording).

Neurosurgery Consultation

Surgical management was advised

ON FOLLOW UP AFTER 3 MONTHS

- Bleeding PV stopped
- Height was 97 cm (increased by 2 cm after starting treatment)
- Weight was 15.5 kg (decreased by 1.4 kg)
- TSH decreased to 72.5

DISCUSSION

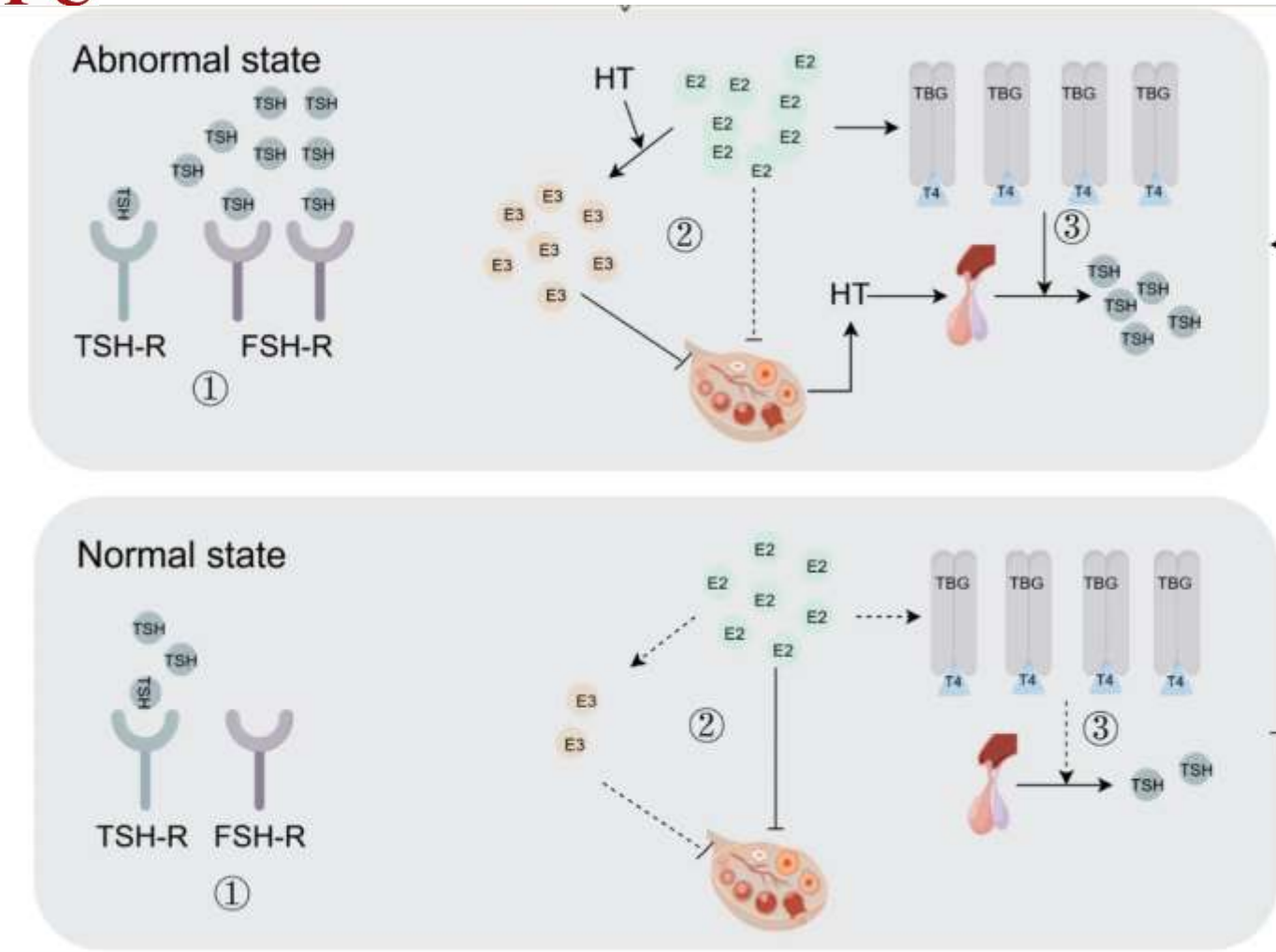
- Van Wyk and Grumbach described a syndrome characterized by-

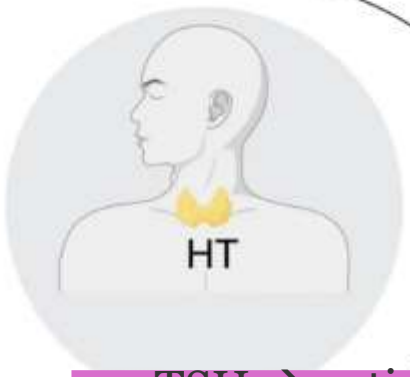
✓ Long standing primary hypothyroidism

✓Advanced breast development

✓Multicystic ovary and uterine bleeding

- Specific incidence rates in India are not readily available but a study from southern India reviewed cases from 2005- 2020 and identified 30 patients.





- TSH → activate the FSH-R → stimulation of ovaries→ excessive release of gonadotropins(estrogen)
- Elevated serum E_2 levels → increase serum TBG levels→ ↑levels of TBG bind more FT4) → ↓ serum FT4 and ↑ serum TSH levels
- Elevated estrogen levels→precocious puberty

- **Precocious puberty** –
- **Definition**-

➢ Premature pubertal development due to elevated sex steroids – estrogen in girls and testosterone in boys leading to the appearance of physical changes of pubertal maturation **before 8 years in girls and 9 years in boys.**

➢ Menarche before the age of 9.5 years is also considered precocious menarche.

- **Types**-

➢ Central → Early maturation of hypothalamic-pituitary-gonadal axis
→Idiopathic, CNS lesions(hypothalamic hamartomas , pituitary gland tumour)

➢ Peripheral →Ovarian cyst , ovarian tumour , exogenous sex steroids , primary hypothyroidism , McCune Albright syndrome.

DIAGNOSIS AND MANAGEMENT OF VAN WYK GRUMBACH SYNDROME

- Lab investigations –

➢Very high level of thyroid stimulating hormone and follicle stimulating hormone , prolactin and beta estradiol with suppressed luteinising hormone.

- Most common cause of hypothyroidism is auto immune thyroiditis.

- Management-

➢Thyroid replacement therapy

- Delayed bone age with precocious puberty is important to diagnose Van Wyk Grumbach syndrome.

- In this case precocious puberty , multicyctic ovaries with bleeding per vaginum and long standing hypothyroidism has led us to the diagnosis of Van Wyk Grumbach syndrome.

KEY POINTS

- Van Wyk Grumbach is the only form of precocious puberty with delayed bone age .

- A high index of suspicion and early identification and initiation of thyroid hormone replacement in a female child with Van Wyk Grumbach syndrome can avoid unnecessary investigations and surgical interventions.

- In any female child presenting with periodic per vaginal bleeding along with bilateral enlargement of ovary , primary hypothyroidism must be excluded.

TAKE HOME MESSAGE

- Common disorders can have uncommon consequences.

- A stitch in time saves nine : Treatment of hypothyroidism can reverse all the symptoms and signs

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THANK YOU