Endocrine Society of Thailand's
Interhospital conference

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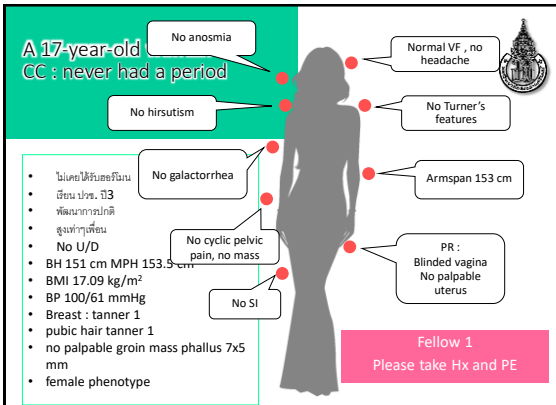
A 17-year-old
CC : never had a period



- ไม่เคยได้รับฮอร์โมน
- เรียน ปวช. ปี3
- พัฒนาการปกติ
- สูงเท่ๆเพื่อน
- No U/D
- BH 151 cm MPH 153.5 cm
- BMI 17.09 kg/m²
- BP 100/61 mmHg
- Breast : tanner 1
- pubic hair tanner 1
- no palpable groin mass phallus 7x5 mm
- female phenotype

Fellow 1
Please take Hx and PE

Tanner staging

Pertinent data

- Primary amenorrhea with tanner stage1
- Normal growth and developments
- Female phenotype with blinded vagina
- No palpable testes

Investigations

Fellow 1
Please make requests

E2 <5 pg/ml LH 25.81 (1-18 mIU/ml) FSH 72.84 (2-12 mIU/ml)	Cortisol 16.72 mcg/dl 17OHP 0.35 ng/ml	Testosterone 75 ng/dl	11-DOC corticosteron

CT whole abdomen
No normal uterus
ovaries or suspected gonad can be identified Vagina is seen

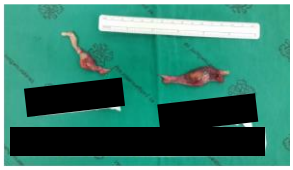
Chromosome : 46, X?

Chromosome : 46,XY

Fellow 2
Please give DDx

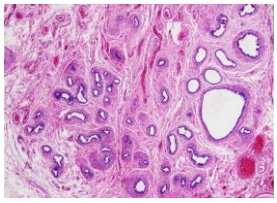
- Complete gonadal dysgenesis
- Vanishing Testis
- Leydig cell hypoplasia
  LH receptor mutation
- 17-hydroxylase def./ 3β-HSD def CAH

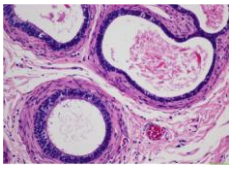
Gross pathology



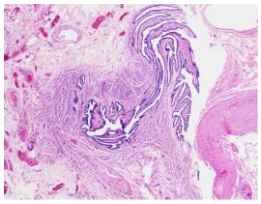
Gonad, Lt ; presence of uterine tube and atrophic testicular tissue
Gonad, Rt ; presence of uterine tube and atrophic testicular tissue

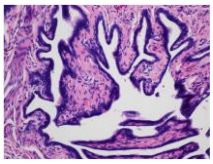
Histology : Atrophic testicular tissue





Histology: uterine tube





What is the most likely diagnosis? Please give an explanation

Testicular regression syndrome *or*
Vanishing testes

No Sertoli cells → no AMH → Mullerian duct
No Leydig cells → no Testosterone → female genitalia with no breasts & pubic hair
Pathology : testicular remnants

Primary amenorrhea and 46,XY DSD

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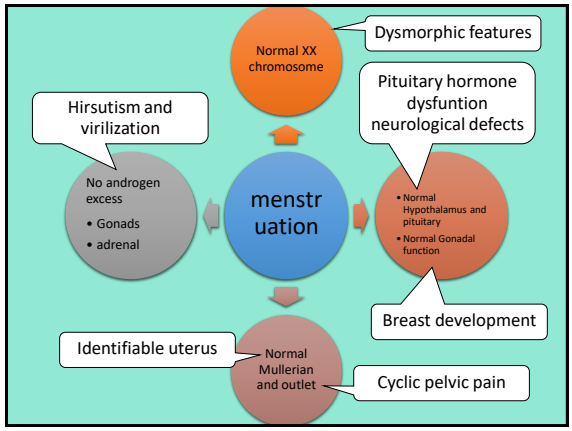
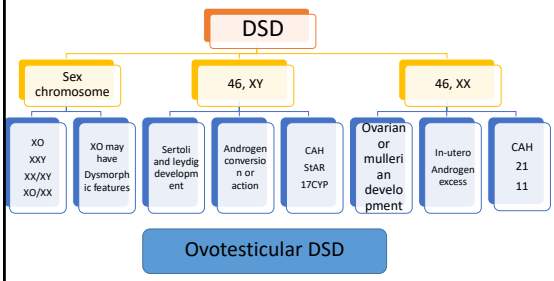
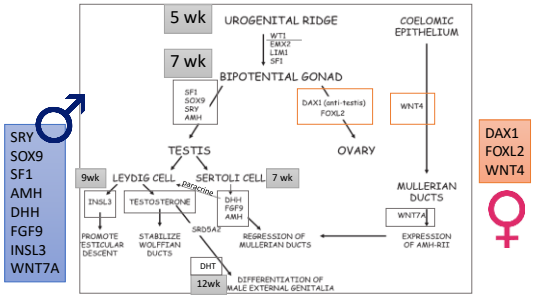


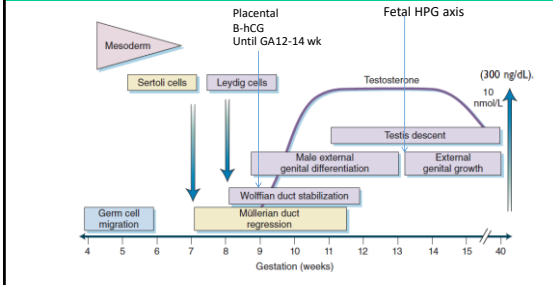
Classification of DSD



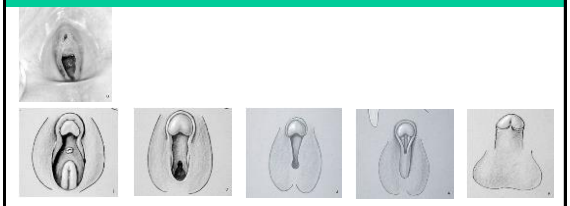
Genetic control of the sex development



Genetic control of the sex development



Prader Classification



0, normal female genitalia
1, female external genitalia with clitoromegaly;
2, clitoromegaly with partial labial fusion forming a funnel-shaped urogenital sinus;
3, increased phallic size with complete labioscrotal fusion forming a urogenital sinus with a single opening;
4, complete scrotal fusion with the opening of the urogenital sinus at the base of the phallus;
5, normal male external genitalia

46,XY DSD: Female phenotype

Dx	Testis	Int. genitalia	breast	Pubic hair	testosterone	Clues
46,XY complete gonadal dysgenesis	Streak (cancer risk↑)	Mullerian	No	Yes	Low	mutation SRY, *MAP3K1 NR5A1, DHH*
Leydig cell hypoplasia	Yes	Wolffian (Sertoli – AMH)	No	Yes	Low	
Vanishing testes <8wk	Testicular remnant	Mullerian	No	Yes	Low	
Complete androgen insensitivity	Yes	Wolffian (Normal AMH)	Yes (T → E)	No	High	Breasts development Hairless lady
StAR protein deficiency	Yes	Wolffian	No	No	Low	Salt wasting Hyperpigmentation
17-OH deficiency	Yes	Wolffian	No	No	Low	Hypertension with hypoKalemia
5α-reductase deficiency	yes	Wolffian	No	yes	High	T : DHT > 5:1 Puberty onset male

Testicular regression syndrome (TRS) or 'vanishing testis'

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Introduction

www.omim.org/entry/273250

- The absence of gonads in an XY person
  Sarto GE, Opitz JM.J Med Genet. 1973 Sep;10(3):288-93
- Uterus and fallopian tubes are absent mullerian rudiments are present.
- breast development is absent postpubertal eunuchoid habitus is the rule.

Clinical presentation

De Marchi M, et al.Hum Genet. 1981;56(3):417-9
Pirgon O, Dundar BN. J Clin Res Pediatr En docrinol 2012;4(3):116-120

Females	Females	Males	Normal males
+ hypoplastic normal external genitalia	+ well-formed hypoplastic uterus, and well-formed tubes	+ anorchia, micropenis	+ unilateral nonpalpable testis

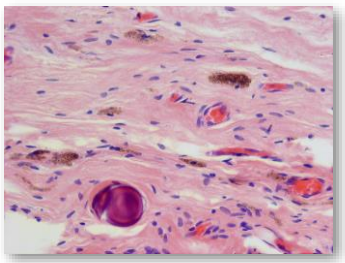
Pathogenesis: The current concept

Hegarty PK. et alJournal of Pediatric Urology (2007) 3, 206-208

- Normal embryological development
- Followed by a catastrophic event such as torsion
- Microdeletion of the Y chromosome may be associated

Histology

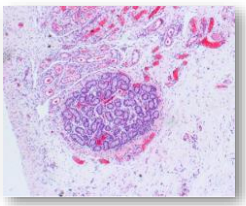
Hegarty PK. et alJournal of Pediatric Urology (2007) 3, 206-208



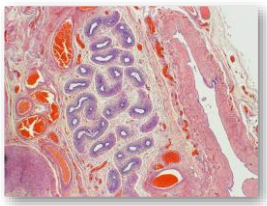
Fibrous tissue with scattered foci of dystrophic calcification and numerous haemosiderin-laden macrophages

Histology

Hegarty PK. et alJournal of Pediatric Urology (2007) 3, 206-208



fibrous tissue with a small residual cluster of seminiferous tubules. No germ cells are identified



No identifiable testis but epididymal and spermatic cord structures

Risk of malignancy

Pirgon O, Dundar BN. J Clin Res Pediatr En docrinol 2012;4(3):116-120

- Uncertain but considering low risk
- Infrequent finding of seminiferous tubules or other germinal tissue