Case presentation

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A 20 days old patient with genital asymmetry

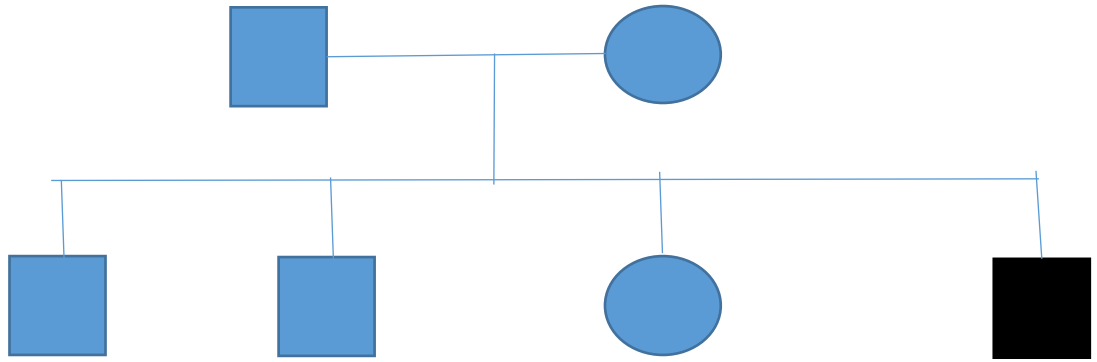
- A 20 days old patient reared as male was brought by his parents to DEMPU clinic at Cairo University for atypical genitalia and bilateral undescended testes

- There was no history suggestive of salt wasting crisis, gastroenteritis, dehydration or NICU admission

- There is history of infertility on the mother's side (2nd degree relative)

- There was no history of similar conditions, abortions or deaths in the family

- The patient is the 4th child of non consanguineous marriage. He was the product of uneventful pregnancy, born at full term by cesarean section. His birth weight was 3.5 kg which was appropriate for his gestational age.



- On examination of the patient, he was fully conscious, and of normal facies.

- The patient did not have any signs of dehydration. His vital signs were of normal values for age.

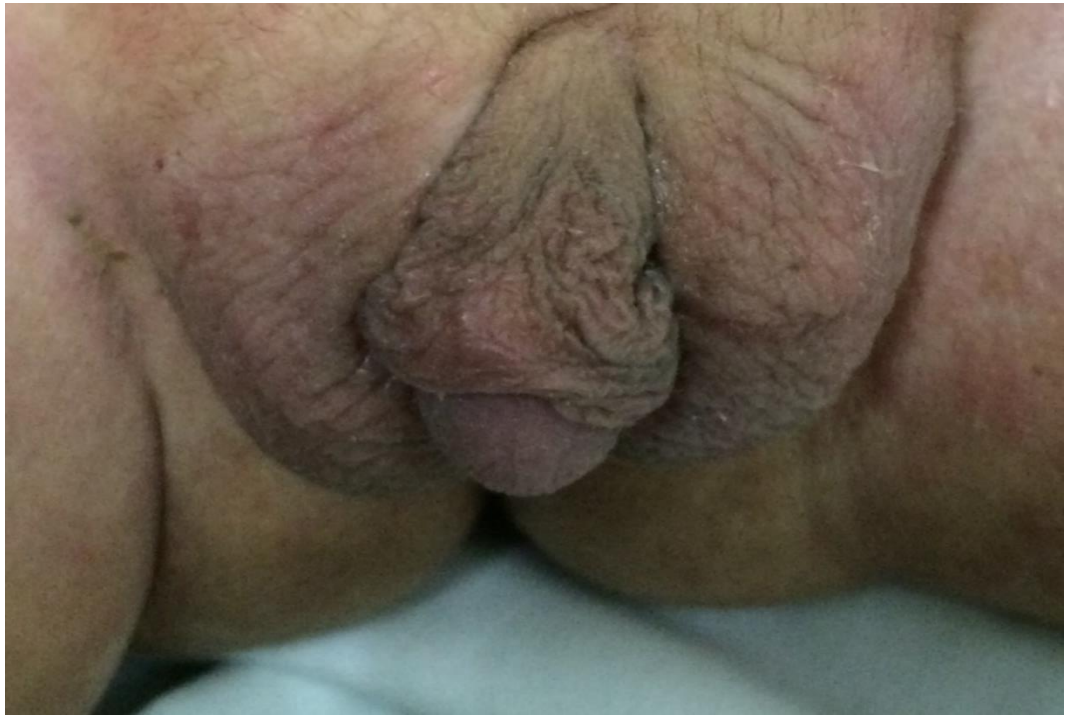
- No other congenital anomalies could be detected.

- The patient's weight was 4 kg (between 50^{th} and 75^{th} percentiles), length:54 cm (between the 25^{th} and 50^{th} percentiles) and skull circumference: 38 cm (on the 50^{th} percentile)

• Genital examination revealed the presence of:

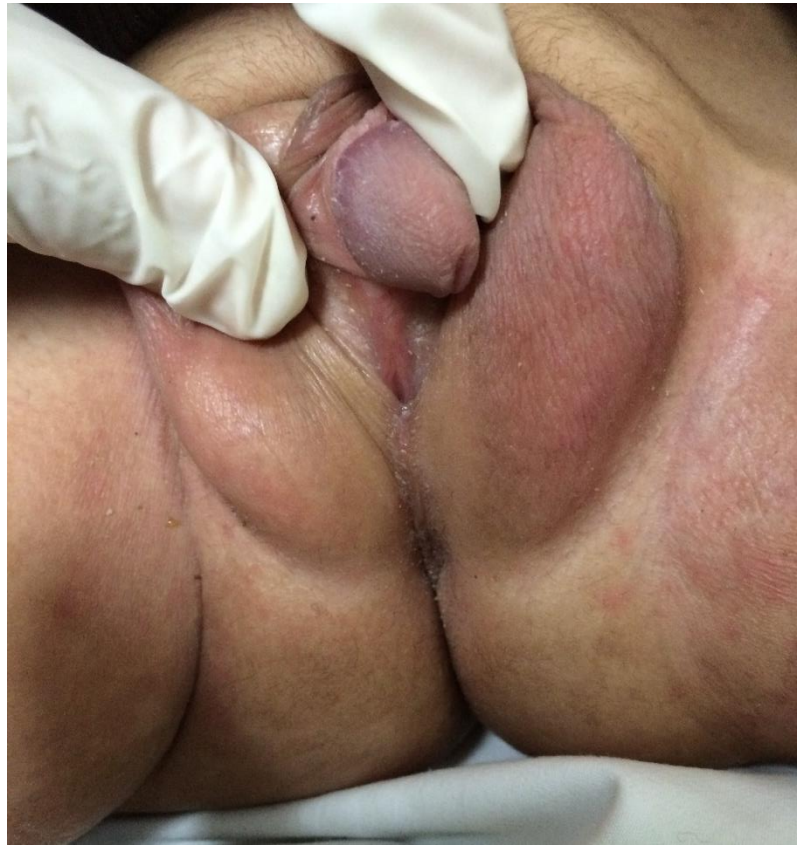
- Underdeveloped right scrotal compartment

- Phallus length: 3 cm and of normal girth



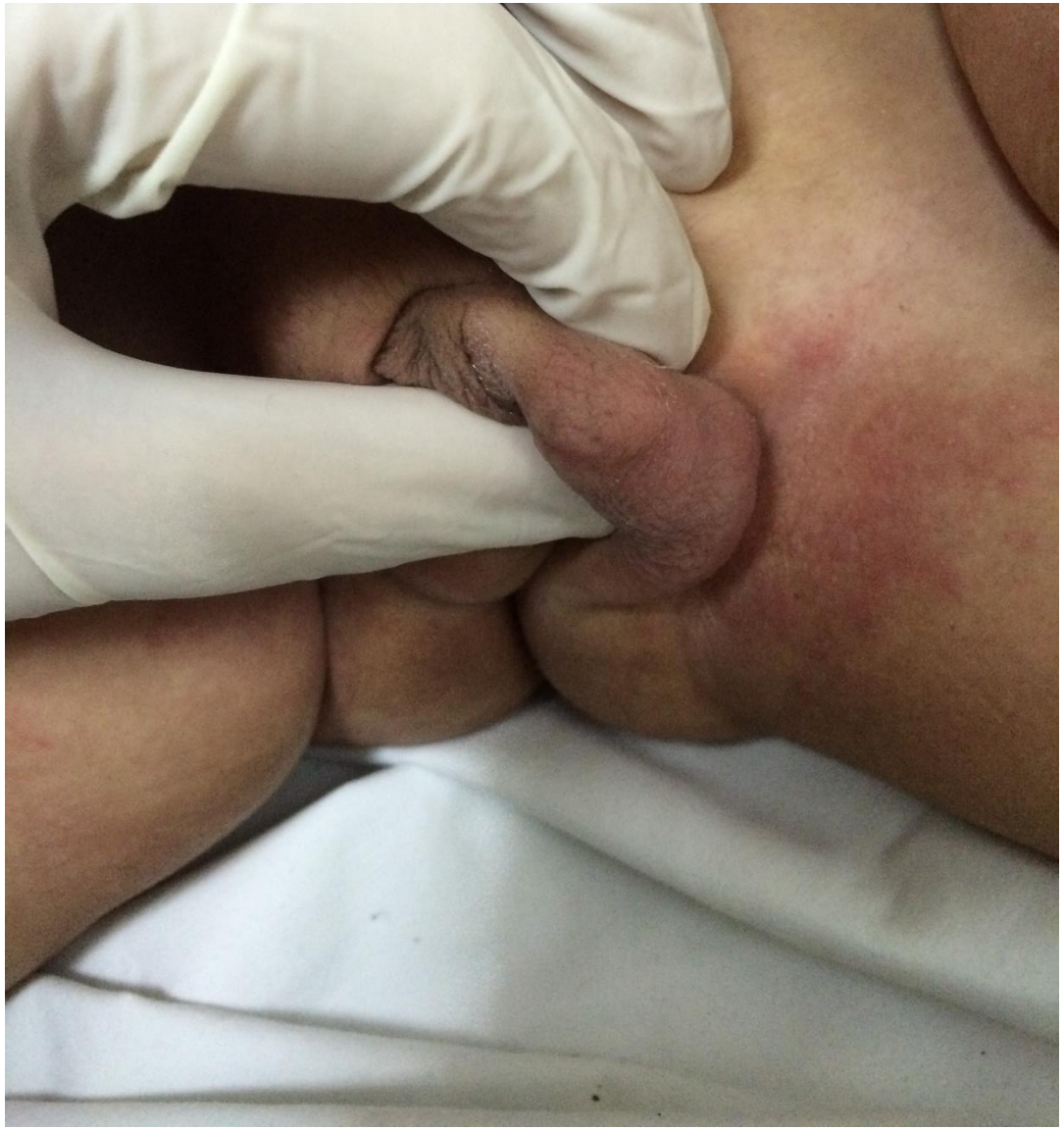
- Bifid scrotum

- Penoscrotal hypospadias



- Left gonad could be felt at the medial end of the inguinal canal and it could also be brought down to the scrotal compartment.
Its size was T3 using the Prader Orchidometer

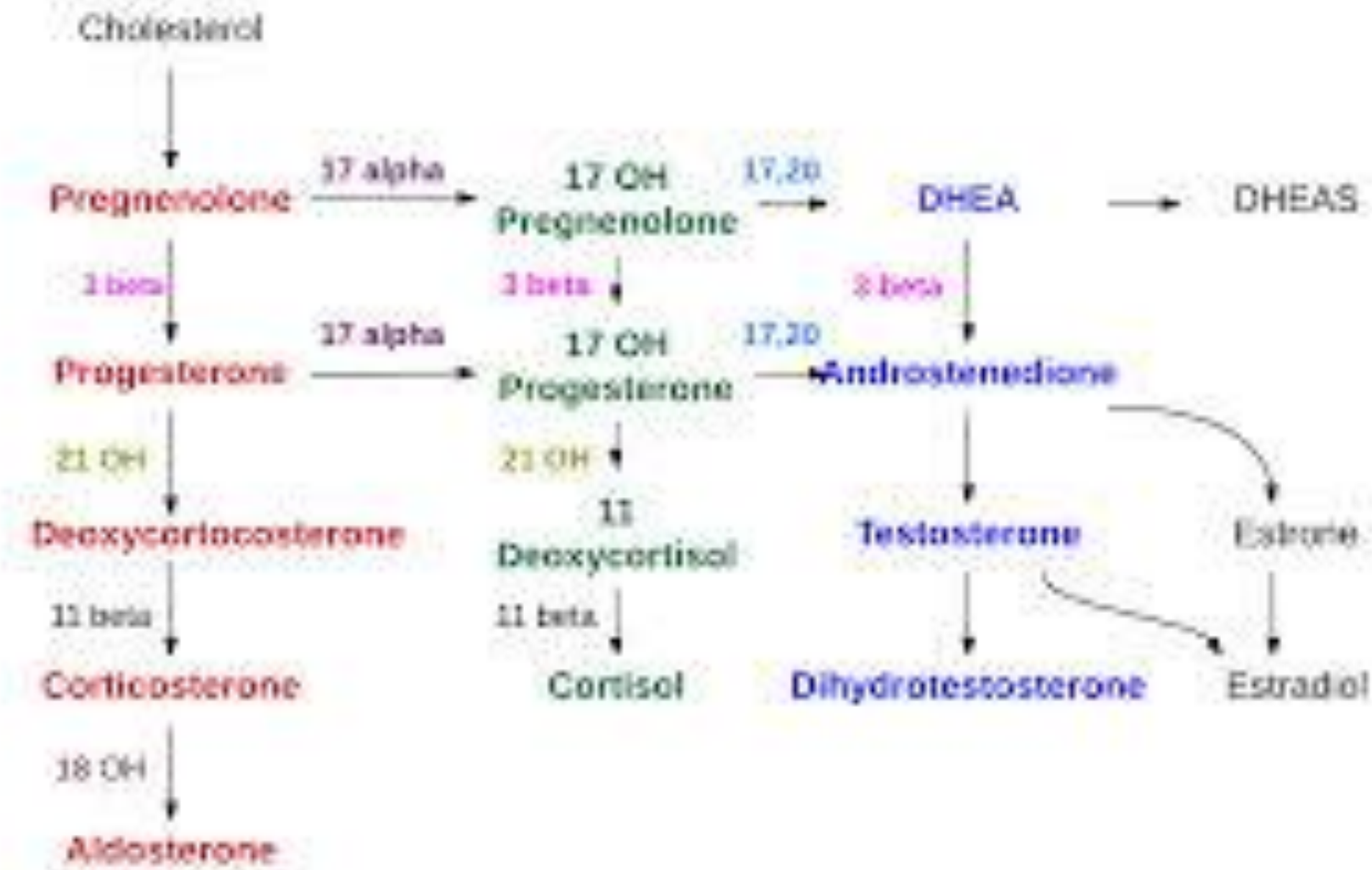
- Right gonad could not be felt along its course



‘What are the possibilities?’

Differential diagnosis

- <u>D.D. of genital asymmetry:</u>
- Mixed gonadal dysgenesis
- Ovotesticular DSD
- <u>Other differential diagnoses that should be considered in any undervirilized male</u>:
- CAH (non salt loser) (3 beta steroid dehydrogenase deficiency, POR, 17 alpha hydroxylse deficiency or 17, 20 lyase deficency)
- Testosterone biosynthetic defects

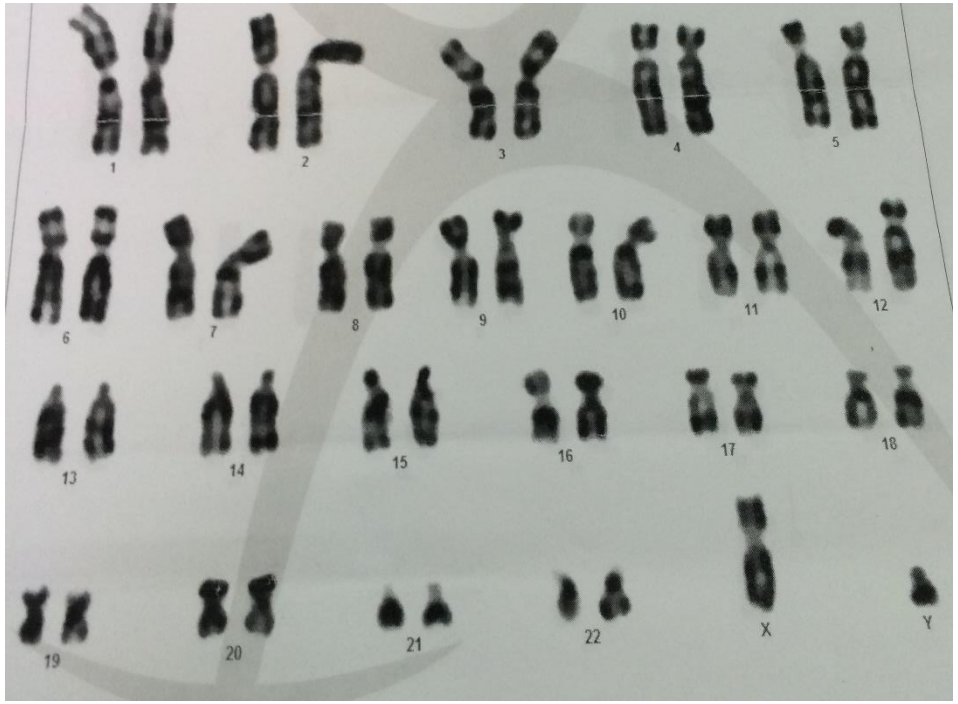

Cholesterol
Pregnenolone
17 alpha
17 OH Pregnenolone
17,20
DHEA
DHEAS
3 beta
3 beta
3 beta
Progesterone
17 alpha
17 OH Progesterone
17,20
Androstenedione
21 OH
21 OH
11 Deoxycortisol
Deoxycorticosterone
Testosterone
Estrone
11 beta
11 beta
Corticosterone
Cortisol
Dihydrotestosterone
Estradiol
18 OH
Aldosterone

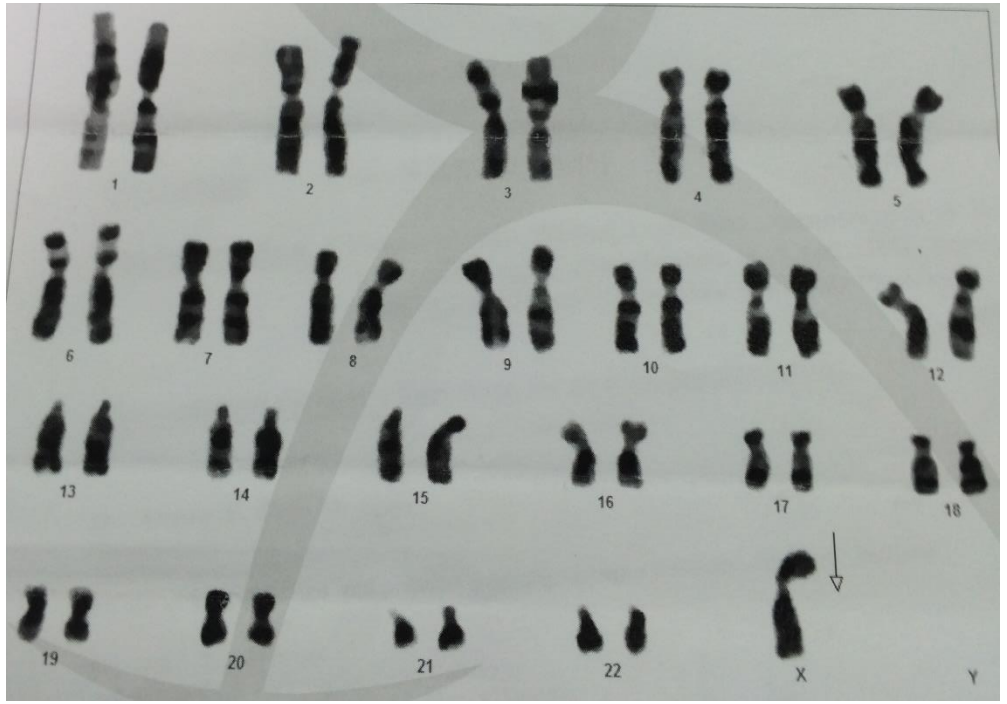
“What are the investigations needed to diagnose the case?"

- The following investigations were ordered:

- Karyotyping
- Basal hormones (17 (OH) progesterone, progesterone, DHEA, androstendione, testosterone, DHT, cortisol and ACTH) & Anti- Mullerian hormone
- Abdominopelvic Ultrasonography

Karyotyping:45 XO / 46 XY





- Samples for basal hormones were collected during the 1st month of life showing the following results

17 OH progesterone (0.36-7.6ng/ml)	Progesterone (0.07-0.52 ng/ml)	DHEA (0.5-7.6 ng/ml)	Androstendione (0.06-0.68 ng/ml)	Testosterone (0.75-4 ng/ml)	DHT (5-60 ng/dl)	Cortisol (am: 6-16 ug/dl)	ACTH Up to 56 pg/ml
0.5	0.35	0.4	0.6	0.8	1.5	9	34

- Anti mullerian hormone was also measured showing a value of 14.8ng/ml which was normal for the age and sex (Reference range for boys : 3.8-159.8)

- Testicular function was assessed by giving the patient HCG injections on alternate days at a dose of 1500 IU/dose for seven doses (long course stimulation regimen).

- Clinically, the phallus size increased from 3 cm to 4cm.

- Samples were collected to measure testosterone levels post-stimulation which showed a significant increase (2.2 ng/ml)

Abdominopelvic Ultrasonography

- Abdominopelvic sonar done revealed:

- The presence of normal infantile uterus seen behind the urinary bladder by longitudinal and transverse sections
- The vaginal canal was mildly dilated with fluid contents
- A gonad mostly testis was seen on the left side measuring 12x7.2 mm
- No gonad could be detected on the right side along its path of descent
- No renal abnormalities could be detected

What next?

1. Karyotype: 45XO/46XY
2. Good testosterone response to HCG stimulation
3. Abdominal sonar: mullerian structures, a left gonad most probably testis but no right gonad

- The patient was prepared for laparoscopic exploration at the department of Pediatric Surgery, Cairo University.
- An Echocardiography was performed before the procedure revealing no cardiac abnormality
- A tubo-ovarian structure together with a right very thin gonad most probably streak were detected.
- Specimens were obtained from the right gonad and sent for histopathological examination.

Histopathology

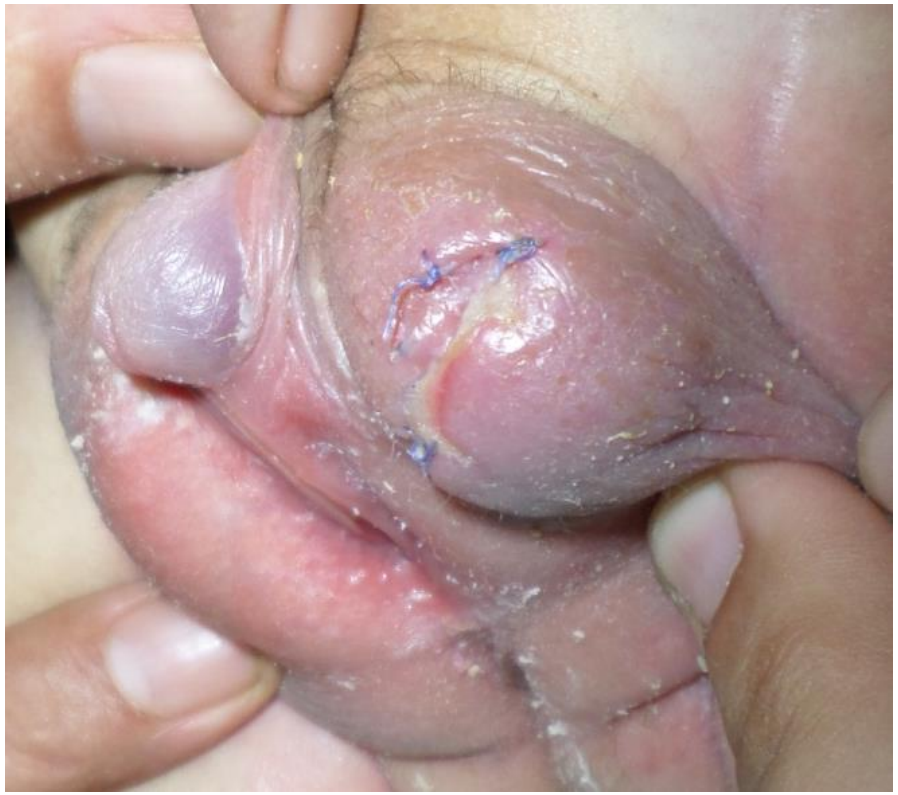
- The results of the histopathological examination came back revealing the presence of ductal structures with patent lumen and intact epithelial lining resembling the seminal vesicle, the vas deferens and primitive epididymal ducts; a tiny fibrotic nodule (streak testis) was seen at one end of dense compact closely packed spindle cells; however no seminiferous tubules were seen

Conclusion: streak testis with male type ductal system

Diagnosis

Mixed Gonadal Dysgenesis

- After analysis of the clinical data, the results of laboratory investigations & laparoscopic examination in addition to the histopathology of the biopsies obtained, the diagnosis was consistent with Mixed Gonadal Dysgenesis
- After explanation of the condition to the parents and taking their consent, the patient was prepared for laparoscopic removal of the mullerian duct remnant and the right streak gonad
- A left orchidopexy and biopsy were also performed and now the patient is waiting for correction of penoscrotal hypospadias



Plan

- He has been followed up in the growth clinic at DEMPU.
- Now, he is 1 year and 3 months old and his growth parameters are as follows

- Height is 77cm (SDS:-1)
- Weight: 11kg (SDS:-0.5)
- Target height: 173.3 cm(SDS:-0.2)

- The patient is being followed up by performing yearly ultrasound of the left gonad especially at the onset of puberty.

McCann Crosby B et al., State of art review in gonadal dysgenesis : challenges in diagnosis and management, int j of Ped endo, 20

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State of the art review in gonadal dysgenesis: challenges in diagnosis and management.

McCann-Crosby B[1], Mansouri R[2], Dietrich JE[2], McCullough LB[3], Sutton VR[4], Austin EG[4], Schlomer B[5], Roth DR[5], Karaviti L[1], Gunn S[1], Hicks MJ[6], Macias CG[7].

Author information

Abstract

Gonadal dysgenesis, a condition in which gonadal development is interrupted leading to gonadal dysfunction, is a unique subset of disorders of sexual development (DSD) that encompasses a wide spectrum of phenotypes ranging from normally virilized males to slightly undervirilized males, ambiguous phenotype, and normal phenotypic females. It presents specific challenges in diagnostic work-up and management. In XY gonadal dysgenesis, the presence of a Y chromosome or Y-chromosome material renders the patient at increased risk for developing gonadal malignancy. No universally accepted guidelines exist for identifying the risk of developing a malignancy or for determining either the timing or necessity of performing a gonadectomy in patients with XY gonadal dysgenesis. Our goal was to evaluate the literature and develop evidence-based medicine guidelines with respect to the diagnostic work-up and management of patients with XY gonadal dysgenesis. We reviewed the published literature and used the Grading of Recommendation, Assessment, Development, and Evaluation (GRADE) system when appropriate to grade the evidence and to provide recommendations for the diagnostic work-up, malignancy risk stratification, timing or necessity of gonadectomy, role of gonadal biopsy, and ethical considerations for performing a gonadectomy. Individualized health care is needed for patients with XY gonadal dysgenesis, and the decisions regarding gonadectomy should be tailored to each patient based on the underlying diagnosis and risk of malignancy. Our recommendations, based on the evidence available, add an important component to the diagnostic and management armament of physicians who treat patients with these conditions.

KEYWORDS: Carcinoma in situ; Complete gonadal dysgenesis; Dysgerminoma; Ethics; Gonadal biopsy; Gonadectomy; Gonadoblastoma; Malignancy risk; Partial gonadal dysgenesis; XY gonadal dysgenesis

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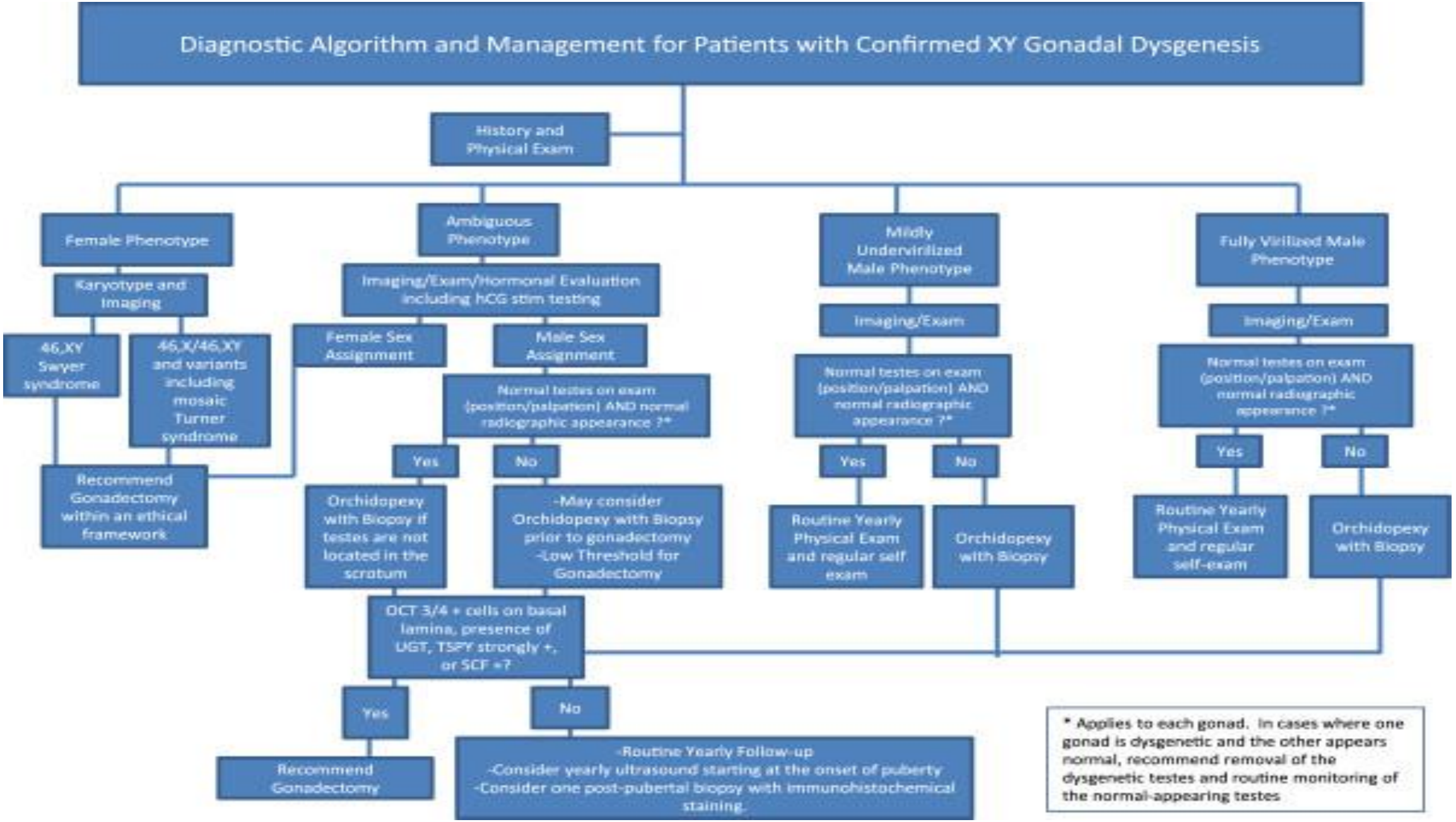

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Take home message

- In any case of undervirilized male with genital asymmetry, the diagnosis of mixed gonadal dysgenesis should be considered
- Karyotyping, abdominopelvic ultrasonography and laparoscopic exploration help to confirm the diagnosis
- The streak gonads should be removed because they are at high risk of malignant transformation

Take home message (cont.)

- Screening of the patient for cardiac and renal anomalies is mandatory as MGD is considered to be a variant of Turner syndrome (Turner syndrome with Y cell line)
- Follow up of those patients should include monitoring their growth and performing yearly ultrasonography of the normal testis.
- Psychological, social and religious issues should be considered and respected in these patients and their parents

وحدة السكر والغدد الصماء والميتابوليزم ٢٠١٢

أ.د/منى حافظ – أ.د/ثرمين صلاح-أ.د/ايزيس غالى - أ.د/ منهامراد - أ.د/ منى عطية
أ.د/ فايزة عبد الحميد -أ.د/فاطمة النوجى -أ.د/منى ممدوح -أ.د/ مها امين -
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أ.د/غادة النور -د/ نهى عرفة – د/نها موسى – د/ امانى ابراهيم – د/ محمد اسماعيل

Thank You