Late diagnosis of mixed gonadal dysgenesis - clinical and psychological implications

CASE REPORT

Mixed gonadal dysgenesis (MGD) is a disorder of sex development associated with a numerical sex chromosome abnormality (45,X/46,XY; 45,X/46,XY/47,XYY); Reported genital phenotypes range from female external genitalia or mild clitoromegaly through all stages of ambiguous genitalia to hypospadias or a normal penis, depending on the proportion of monosomic cells.

*Male genitalia*
- bilateral testicle
- 46 XY cell line may predominate
- spontaneous puberty
- the delay in development of pubertal development due to testicular failure
- short stature

*Ambiguous sex organs*
- the most common clinically
- early diagnosis
- testicles disgenetic / a testicle and a bands gonads disgenetic
- difficult decision for parents in choosing the sex

*Female genitalia*
- associate bilateral gonadal bands
- may stigma of Turner syndrome (probably predominanta 45 cell line , X)
- 2-5% of patients with Turner syndrome have mixed gonadal dysgenesis

**Introduction**

**Case Report**

**Patient:**
- female patient
- 18 years old
- was send to Endocrinology Department for primary amenorrhea
- absence of secondary sexual characteristics
- obesity

**Medical history:**
- Hypertension (maximum Sistolic Blood Pressure 180 mmHg)
- Ventricular Septal Defects
- Childhood obesity

**Treatment:**
- Beta blockers
- Sartans

**May be stigma of Turner syndrome but with high stature?**
- Short 4th and 5th metacarpals
- Epicanthic fold
- Hiperconvex nails
- Height 172 cm, Weight 102 kg (BMI =32,9 kg/m²)

**Clinical examination**
- Pubertal stage (Tanner):PIVBI
- Moon facies
- Facial erythema
- Achantosis nigricans in the posterior cervical and axillary region
- Female External Genital Organs (vagina ~ 8 cm)

**Treatment**
- Oestradiol 0.75 mg/d
- Metformin 1000 mg/d
- Vitamin D 300 000 UI/3 m
- Beta blockers
- Sartans

**Laboratory findings**
- Hypogonadism hipergonadotrop
  - Estradiol < 5 pg/ml
- FSH = 49.5 mIU/mL
- LH = 17.7 mIU/mL
- Dyslipidaemic syndrome
  - Cholesterol >233 mg/dl (N:120-200)
  - LDL =191 mg/dl (N:0-130)
  - HDL =33 mg/dl (N: 45-65)
- Vitamin D deficiency 10.47 ng/ml (>30)

**Investigations**
- Abdominal and Pelvic Ultrasound:
  - hepatic steatosis
  - small uterus (41/11/9 mm)
  - two small hypoechochogenic formations (possible ovarian residue)
- Breast ultrasound - absence of breast tissue
- Karyotype - 45,X/46,XY
- Bilateral gonadectomy - histological examination revealed gonadoblastoma and dysgerminoma on both gonads, without capsular penetration or vascular invasion
- Immunohistochemistry:
  - CD117, PLAP, inhibin and calretinin – positive
  - AFP, EMA, cK7, CD 30 - negative
- Psychological consultation - generalized anxiety disorder and female gender identity
- Other data - Delayed bone age ~ 16 years
  - BMD/DXA: osteopenia
  - Z-score spine= - 1,6 DS

**Discussions**

- Early diagnosis of mixed gonadal dysgenesis is very important because its high potential for malignant transformation, prophylactic gonadectomy is strongly recommended soon after diagnosis.
- And because a timely hormonal therapy can avoid complications induced by hormonal imbalance: lack of secondary sexual characters and because.
- Delayed diagnosis favoured several complications like: obesity, hypertension, dyslipidemia, hepatic steatosis, insulin resistance and last but not least, generalized anxiety disorder.

**References**

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