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RESEARCH ARTICLE

PURE GONADAL DYSGENESIS: CLINICAL CASE AND REVIEW OF THE LITERATURE

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Abstract

XX or XY pure gonadal dysgenesis (PGD) is defined by premature destruction of the fetal gonads which reduce to an undifferentiated stroma with absence of germ line and endocrine secretion. The phenotype is unambiguously female with a clinical picture associating primary amenorrhea and impuberty. We present in this article a clinical case illustrating this pathology in a young patient who presents a primary amenorrhea. The diagnosis of pure XX gonadal dysgenesis was retained based on the clinical and para-clinical examinations. The patient was treated with hormone replacement therapy. The chances of fertility are almost absent in our context, and the only way out is egg donation.

Introduction:-

XX pure gonadal dysgenesis (PGD) is related to a developmental abnormality of the ovaries that occurs early in intrauterine life. It is a premature destruction of the fetal gonads which are reduced to an undifferentiated stroma with absence of germ line and endocrine secretion. The result is a sexually unambiguous infertile girl; the case of our patient.

Observation:-

The patient was Miss E.I, 18 years old, from a non-consanguineous marriage, and the reason for consultation was primary amenorrhea.

The detailed clinical examination carried out found a patient with an androgynous profile, slender, with a poorly developed pelvis, with a height of 172 cm.

Examination of her external genitalia did not reveal the presence of sexual ambiguity.

Her breasts were poorly developed with minimal axillary and pubic hair, classified as S 2-P 2 by TANNER.

Her hormonal workup showed: FSH: 48.53mIU/ml, LH: 19.5mIU/ml and estradiol<5pg/mL.

Pelvic ultrasound did not visualize the ovaries and showed a hypoplastic uterus of 50x10x10mm.
Finally, the genetic study showed a karyotype with a chromosomal formula 46 XX.

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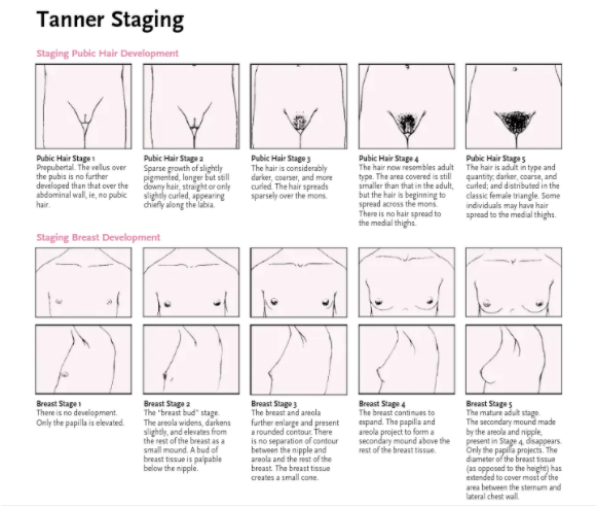

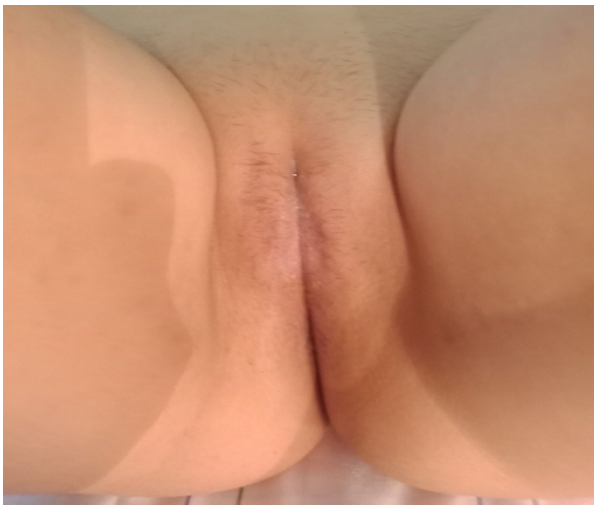

Figure 1and 2:- Female Tanner Staging: Stage II in our patient's case.

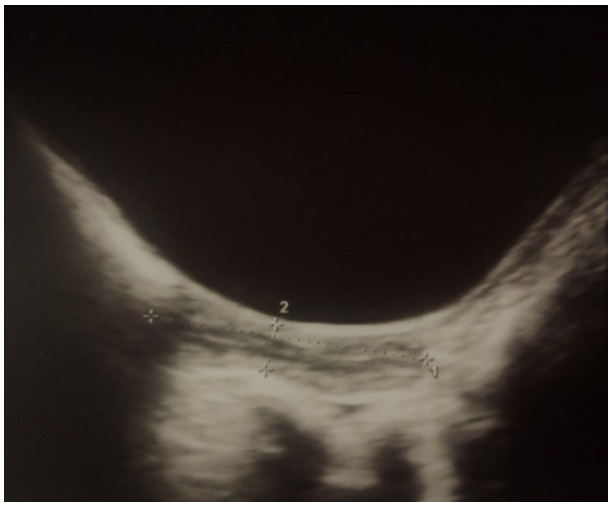

Figure 3:- Hypoplasic uterus on untrasound

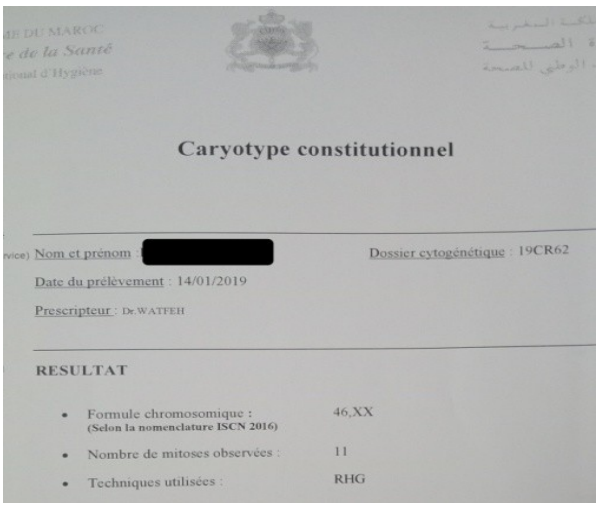

Figure 4:- Patient's Karyotype.

Given the impuberty and the hypogonadal hypergonadotropic hormonal profile, associated with the absence of gonadal visualization on imaging, we were able to retain the diagnosis of pure XX gonadal dysgenesis.

A laparoscopic investigation was discussed to explore the pelvis in order to confirm the absence of gonads and the hypoplasic caracter of the uterus, but the patient refused.

Therefore, the patient received hormone replacement therapy and calcium and vitamin D supplementation, to preserve secondary sexual characteristics and especially to prevent and slow down possible complications due to hormone deficiency.

Discussion:-

Pure gonadal dysgenesis at 46XX is an anatomical and clinical entity. Women with this syndrome have a female morphotype without somatic anomalies.

Epidemiologically:

The age of discovery of PGD is usually between 18 and 23 years in the face of primary amenorrhea. However, observations in younger patients have been reported.

The prevalence is unknown but is thought to be < 1/10000. The genetic transmission is autosomal dominant, recessive or X-linked.

Clinically:
This syndrome is most often revealed by primary amenorrhea with impuberty due to early ovarian failure and normal statural growth, even large size. There is no sexual ambiguity at birth. The external and internal genitalia are normal or poorly developed. Associated signs are rare: deafness with or without cerebellar ataxia (Perrault syndrome) or association with pulmonary fibrosis-immune deficiency.

On the paraclinical level :
Pure gonadal dysgenesis at 46XX manifests as hyper gonadotropic hypogonadism: high FSH and LH with low estradiol.

Pelvic ultrasound shows uterine hypoplasia associated with ovaries reduced in size or not visualized at all.

The karyotype is 46 XX. Laparoscopy shows gonads mostly reduced to fibrous bands.

Thus, the absence of turnerian dysmorphia, a vagina of normal depth, the presence of uterus on digital rectal examination and/or ultrasound, an elevated FSH and LH level, a low estradiol level and a 46 XX karyotype define PGD.

Etiology:
PGD corresponds to genetic abnormalities of ovarian development. Although the etiology remains unknown in most cases, several genes have been implicated: homozygous or heterozygous composite inactivating mutations of the follicle stimulating hormone receptor (FSHR; 2p21-p16) gene, mutations of the BMP15 gene (Xp11.2) and mutations of the NR5A1 gene (9q33).

Differential diagnoses:
Other causes of premature ovarian failure as well as complete PGD at 46 XY which manifests with the same picture but whose complications may be more severe because of the risk of cancerisation of the dysgenic gonads, requiring prophylactic gonadectomy.

Management and support :
From puberty onwards, these patients are put on hormone replacement therapy allowing a satisfactory development of secondary sexual characteristics, a fight against the deleterious effects of prolonged hypoestrogenism and the occurrence of a withdrawal hemorrhage, psychologically reassuring.

Monitoring must be regular to ensure that it is properly followed and adapted in order to guarantee normal feminization, uterine and vaginal trophicity for a satisfactory sexual life. Associated with hygienic and dietary rules (vitamin and calcium intake, physical activity, etc.).

This treatment also aims to prevent osteoporosis, by building up adult bone mass, as well as the cardiovascular risk associated with osteogenic deficiency.

Finally, in our context, infertility is definitive, although pregnancy is still possible through oocyte donation, in the case of medically assisted procreation.

A psychological follow-up is therefore recommended for these patients who generally do not suspect the diagnosis before it is established, and allows them to benefit from an adequate accompaniment ensuring a good therapeutic compliance.

Conclusion:-

Pure gonadal dysgenesis 46XX is a rare pathology due to an accelerated apoptosis of the gonad at an early stage of embryogenesis whose diagnosis is easily retained in front of a 46 XX girl, impubescent of great size, without sexual ambiguity, who presents a hypergonadotropic hypogonadism, and in whom the ovaries could not be visualized by

ultrasound and possibly by laparoscopy. Hormone replacement therapy is necessary. Screening of female siblings is necessary because of the genetic nature of the disease.

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