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RESEARCH ARTICLE

COMPLETE ANDROGEN INSENSITIVITY SYNDROME : A CASE REPPORT AND REVIEW OF LITERATURE

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Abstract

Complete androgen insensitivity syndrome or testicular feminization syndrome is the most common form of male pseudohermaphrodism, caused by a failure of androgen receptor binding. Patient with male genotype 46 XY, has a female morphotype with well developed external sexual organs. We report the case of two young patients aged 23 and 21 with a TF syndrome discovered during the exploration of primary amenorrhea. A bilateral orchiectomy was performed with institution of estrogen-progestogen hormone treatment.

Introduction:-

Male pseudohermaphroditism is a pathological condition characterized by the coexistence in the same subject of a male karyotype (46 XY), with male gonads, and a normal female morphology.

Complete androgen insensitivity syndrome, formerly known as feminizing testis, is the most complete and common form of male pseudohermaphroditism. It results from a disorder of peripheral receptivity to androgens. It is a rare condition, often revealed by primary infertility or amenorrhea. This condition poses two problems :
- the legitimacy of hiding the genetic diagnosis ;
- the experience of the announcement of the definitive sterility of these young girls

We report the case of two related patients (sisters)

1st Case repport :
23 year old patient consulting for primary amenorrhea. She is from a 1st degree consanguineous marriage. The patient reports that her puberty started at the age of 14 with normal breast development, contrasting with poorly developed axillary and pubic hair. On physical examination, the patient is 1.69 m tall with a weight of 52 kg; her voice is feminine. On inspection, a feminine morphology is noted with normally implanted hair; the breasts are well developed; on the other hand, the sexual pilosity is insufficiently developed.

The gynecological examination showed female external genitalia with an enlarged clitoris, normal labia majora with agenesis of the labia minora, the vagina was impermeable. We also noted the presence of a right inguinal mass of 3cm. The rest of the somatic examination was unremarkable.

The hormonal assessment showed: FSH at 6.9 m IU/ml, LH at 21.8 m IU/ml, estradiol at 44 pg/ml and a very high testosterone level at 7 ng/ml (normal value between 0.1 to 0.9 ng/ml) and delta 4 androstenedione at 2 ng/ml.

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Pelvic ultrasound confirmed the absence of uterus and ovaries and localized the left testicle within the external iliac vessels and the right testicle at inguinal level

Genetic examination showed a chromosomal formula of type 46 XY

This patient underwent a laparotomy with removal of the gonads followed by estrogen replacement therapy and psychological care.

2nde case repport :

Patient is 21 years old, from a first degree consanguineous marriage. In her family history, one sister was for a newly discovered feminizing testis syndrome. . The patient consulted for primary amenorrhea. Around the age of 12-13 years, the development of the breasts started but the sexual pilosity did not appear.

On clinical examination, breast development was normal, pubo-axillary hair was almost absent, external genitalia were female without ambiguity, The clitoris was not enlarged and the vagina was permeable. On vaginal touch, a 2 cm deep cul-de-sac was noted with absence of the cervix. There were no palpable inguinal masses.

The hormonal assessment revealed a very high plasma testosterone concentration of 6 ng/ml. The karyotype was male 46 XY.

Pelvic ultrasound showed the presence of two intraperitoneal testes located medial to the iliac axes, but the ovaries and uterus were absent.

Surgical castration was performed in this patient and estrogen replacement therapy was hormone replacement therapy was initiated.

Discussion:-

Complete androgen insensitivity syndrome is a recessive hereditary disease linked to the X chromosome.[1] Its incidence is in fact very variable, ranging, according to the authors, from 1 to 62.4 per 2000 individuals[2]. It is characterized by an insensitivity of peripheral tissues to androgens, linked to an absence or a qualitative defect for the corresponding cellular receptor or possibly to a defect affecting either the transcription of the gene or the nuclear binding of the steroid receptor complex [3]. Prenatal diagnosis can be made by ultrasound, karyotype and testosterone levels [5]. In the In newborns, the diagnosis is strongly suspected in the presence of a 46 XY karyotype of a baby with a female morphotype [2].

The diagnosis is rarely made before puberty, in case of surgical extraction and histological study of the testicles after inguinal hernia repair [5]. At puberty, attention should be drawn to the absence or scarcity of pubic and axillary hair (inconstant sign) [1, 6].

After puberty, the diagnosis is made on the occasion of primary amenorrhea or in a context of infertility.

The physical examination often reveals a harmonious and feminine morphological development; The fat distribution is gynoid; the breasts are well developed and the hair is normally implanted. On the other hand, the ambosexual hair is insufficiently developed, or even replaced by a fine downy hair [1]. On gynecological examination, the external genitalia are female: the clitoris is small but may be slightly enlarged, the labia majora and minora are well developed, the vagina is small and permeable ending in a cul-de-sac, but the internal genitalia (cervix, uterus, ovaries) are absent. The gonads are usually in an intraperitoneal position and rarely found in the inguinal canals [7].

Hormonal investigations classically reveal testosterone levels in the normal male range and elevated serum LH levels due to hypothalamic-pituitary insensitivity to testosterone. The HCG stimulation test is useful for diagnosis; the testosterone response should be significant. At the same time, plasma levels of delta 4 androstenedione and testosterone binding globulin are increased [1, 4, 6, 7]. Pelvic ultrasound, MRI and possibly laparoscopy confirmed the absence of uterus and ovaries. The karyotype is male 46 XY.

Currently, the diagnosis of complete androgen insensitivity syndrome is based on the search for the mutation; however, it can be strongly suggested by the clinic and the karyotype. Recently, an antenatal diagnosis has become possible by searching for the causative mutation or using polymorphisms of the androgen receptor gene; on analysis of amniotic fluid or by trophoblastic biopsy [8-11]. Our two patients had a complete clinical picture including well-developed breasts, scarce pubic and axillary hair and a very high plasma testosterone level. Pelvic ultrasound confirmed the absence of uterus, ovaries and the presence of male gonads in intra-abdominal position. For reasons of accessibility, none of our patients benefited from the search for of the gene mutation.

From an evolutionary point of view, the feminizing testis, like any ectopic testis, exposes the risk of malignant transformation [12, 13]. This risk is assessed differently by the authors [3, 4]. it is estimated to be 5 to 10% according to some authors and 22% according to others. Moreover, it has been established that the risk of malignant degeneration increases with age, justifying castration as soon as the diagnosis is confirmed

The management of complete androgen insensitivity syndrome requires close collaboration between gynecologist, endocrinologist and psychologist. Castration should be performed as a matter of principle because of the risk of gonadal degeneration [6, 12]. Estrogen replacement therapy should be initiated to prevent regression of secondary sexual characteristics, maintain normal sexual activity, and prevent the consequences of estrogen deficiency.

It can be a low-dose pill or a sequential treatment combining estradiol and a progestin without metabolic effects, according to the scheme proposed for the replacement therapy of menopause

At the same time, psychological support in collaboration between the psychologist and the family is necessary; it aims to inform the patient about the nature of her disease and to reduce the psychological impact of the announcement of sterility to these patients who want to have children while hiding their genetic identity .

Our two patients underwent surgical castration followed by estrogen replacement therapy.

Conclusion:-

Complete androgen insensitivity syndrome is an X-linked recessive inherited disorder. It is a rare condition. The diagnosis is often made after puberty, during primary amenorrhea. The attention is drawn by the scarcity of ambosexual pilosity contrasting with a good breast development and a feminine and harmonious morphotype. Castration should be performed as a matter of principle, followed by estrogen replacement therapy to prevent involution of secondary sexual characteristics.

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