no other associated clinical signs. The prevalence of any change in carbohydrate metabolism in patients with pheochromocytoma is highly variable, according to different studies. In a series of 60 patients, 24% had DM and a clear relationship was seen between urinary catecholamine and blood glucose levels.[6] In another series of 191 patients, its prevalence was a little higher than 35%.[7] By contrast, in a study conducted on 1093 diabetic patients with abdominal ultrasound and glucagon tests, pheochromocytoma was diagnosed in 0.96/1000 patients,[8] a prevalence similar to that found in the hypertensive population (1/1000).[2] Although hypoglycemia secondary to pheochromocytoma is not an uncommon finding, its onset with cardinal clinical signs is rare, and only four patients with ketoacidosis have been reported in the literature.[9] Although our patient had no acidosis, hyperglycemia and ketosis were very significant and, because of the patient's age, suggested the onset of classical type 1 diabetes. The absence of the characteristic clinical signs of pheochromocytoma, except for hypertension, delayed final diagnosis.

In pheochromocytoma, carbohydrate changes are due to multiple factors. There is, on the one hand, decreased insulin secretion, increased glucagon levels, and stimulation of glucogenolysis secondary to increased norepinephrine levels, and on the other hand, decreased peripheral glucose uptake and increased hepatic gluconeogenesis secondary to excess epinephrine. After tumor resection, a majority of patients do not require hypoglycemic treatment.[10]

In conclusion, the variable presentation of these tumors should be emphasized. In this case, the only sign was gradual weight loss until the onset of the cardinal symptoms of diabetes mellitus. Pheochromocytoma should therefore be considered in young patients with arterial hypertension and non-autoimmune diabetes mellitus.[7,8]

Conflict of interest

The authors state that they have no conflicts of interest.

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46 XX Male syndrome☆

Síndrome del varón 46 XX

46 XX male syndrome is a rare condition, described by De la Chapelle et al. in 1964.[1] It occurs in one out of every 20,000–25,000 newborn males. Three groups have traditionally been described, based on phenotype: males with normal male phenotype, males with ambiguous genitalia, and true hermaphrodites.[2] Male phenotype, small testes, and azoospermia are found in most cases. Gynecomastia may be associated with one-third of all patients, while low height, cryptorchism, and hypospadias are less frequently seen.[3] Diagnosis is based on karyotype, which identifies any inconsistency between chromosomal sex and phenotypic and gonadal sex. The case of a 46 XX 48-year-old male who was diagnosed on the basis of a two-year infertility study, after the female factor had been ruled out as a cause, is reported below.

No personal or family history of interest was initially reported. The patient had spontaneous testicular descent to scrotum since birth, and a normal pubertal development. He denied decreased libido and abnormal erection or ejaculation. Physical examination revealed a weight of 69.5 kg, a height of 173 cm, normal development of secondary sexual characteristics, including distribution and density of normal body hair, and the absence of gynecomastia. No cardiopulmonary, abdominal or lower limb changes were found.

☆ Please cite this article as: Sánchez Fuentes S, et al. Síndrome del varón 46 XX. Endocrinol Nutr. 2012;59:276–8.

Scrotum palpation revealed a 6-mL right testis and an 8-mL left testis, as measured with a Prader orchidometer (normal adult range, more than 15 mL), in which deferent ducts were identified. No varicocele or hypospadias were found.

A general evaluation was performed, consisting of a complete blood count and chemistry tests including total protein, glucose, uric acid, renal function, and lipid and liver profile. All test results were normal. A hormonal study detected primary hypogonadism with an elevated FSH level (37.5 mIU/mL, normal 1.5–12.4 mIU/mL), as well as increased LH (23.1 mIU/mL, normal 1.14–11.1 mIU/mL), and decreased free testosterone level (4.15 pg/mL, normal 9–47 pg/mL), while total testosterone was normal (3.27 ng/mL, normal 2.41–10.5 ng/mL). 17-β-Estradiol and prolactin were normal, and PSA level was 0.40 ng/mL. A spermiogram showed azoospermia, with a sperm volume of 3 mL. A pelvic ultrasound examination showed normal seminal vesicles and an 8.3 mL prostate gland of homogeneous echo structure. Testes were ovoid in shape and small, the right testis 20 mm × 9 mm × 8 mm and the left testis 18 mm × 9 mm × 9 mm. Calcifications were seen in both parenchymas.

Hemoglobin and mean corpuscular hemoglobin concentration (MCHC) were in the lower limit of normal, which was attributed to a tendency to anemia due to androgen deficiency. Transaminase (GOT and GPT) levels in the lower limit of normal have also been related to testosterone deficiency, and are common in other chromosomal changes associated with hypergonadotrophic hypogonadism, such as Klinefelter syndrome.[4]

Based on the above findings, primary hypogonadism clinically manifested as azoospermia and testosterone deficiency, with no apparent external cause, was diagnosed. G-band karyotyping was therefore performed in peripheral blood, and a 46 XX chromosome formula was obtained. No chromosome abnormalities were noted.

Based on the available data, the patient was diagnosed with the 46 XX male syndrome, also called XX sex reversal or 46 XX testicular disorder of sexual development, after the review of syndrome nomenclature proposed in 2006.[5] Replacement therapy was started with testosterone undecanoate, currently at doses of 1 g every 12 weeks, with which the patient maintains normal levels of FSH, LH, and total and free testosterone, and has no symptoms of hypogonadism. As regards infertility, secondary to the hyalinization of the seminiferous tubules, the reported patients have fulfilled their desire to father children through adoption or sperm donation.

The 46 XX male syndrome is a sexual differentiation disorder where a mismatch exists between chromosomal sex (female) and gonadal phenotype and type, which are male. 46 XX males may be divided into two groups, those who have variable amounts of Y chromosome sequences and those who do not, who only account for 10% of cases.[6] Carriers of Y chromosome sequences have the SRY gene (sex-determining region of the Y chromosome) in one of their X chromosomes. This gene encodes for the so-called testis-determining factor (TDF) and is normally located in the distal portion of the short arm of the Y chromosome,[7,8] adjacent to its pseudoautosomal region. This region is usually paired to the homonymous region in the X chromosome during meiosis of the male germ cells (spermatocytes) to exchange genetic material. If this exchange extends beyond normal, it will result in an X chromosome that carries the SRY gene. If the sperm carrying the X chromosome with the SRY gene causes fertilization, a 46 XX embryo with the SRY gene will be formed, which will activate male differentiation of the indifferent gonad from the sixth week of embryonic development, and from the fourth month of development, the fetal gonad will produce anti-müllerian hormone, which will induce male differentiation of the external genitalia. Since the genes involved in spermatogenesis are normally located in the long arm of the Y chromosome, they will be absent in most cases, and the restoration of fertility will not be possible.

The SRY gene is thought to encode the so-called testis-determining factor, whose presence and expression are needed to inactivate signals of female sexual differentiation and activate male sexual differentiation. Although the presence of the SRY gene (+) was initially associated with normal male genitalia and gene absence with ambiguous genitalia, there have been a growing number of reports of 46 XX, SRY (−) males with a male phenotype, which would suggest the involvement of autosomal genes or other X-linked genes.[9,10] These genetic changes include duplication in the long arm of chromosome 22[10] or the presence of the SOX9 gene,[10] located in the distal region of the SRY gene. If the autosomal gene is altered, male phenotype development will depend on the extent of the loss of or the function of the mutated gene. In the event of heterozygous mutations of an X-linked gene, male phenotype development will depend on the level of activity or inactivity of gene copies.[11]

This is, therefore, an uncommon sexual differentiation disorder in which, in addition to the management of hypogonadism and infertility, it is essential that specialists involved in diagnosis and patient counseling employ a consistent approach, do not attempt to question the sexual identity of the patient and try to explain the condition as clearly as possible.

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