46,XY ovotesticular disorders of sex development: A therapeutic challenge

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Abstract

46,XY ovotesticular disorder of sex development is extremely rare and indicates the presence of both testis and ovary in the same patient. Gender assignment in newborns represents a therapeutic challenge. We describe and comment on our multidisciplinary approach, ten years after the Chicago consensus meeting on disorder of sex development.

Introduction

Ovotesticular disorder of sex development (OT-DSD) means the simultaneous presence in the same individual of both, histologically proven, testis and ovary. OT-DSD is very rare: it occurs between 3% and 10% of the total DSD. In Europe, 46,XY has the less common karyotype in OT-DSD. Matsui reports that the most frequent gonadal combination is ovotestis-ovary (33.9%). The gonadal combination of ovotestis-streak gonad occurs in only 1.2% of the cases.1 Gonadal tumours occur between 2.6 and 4.6% of OT-DSD, more frequently in 46,XY cases. The chance of degeneration in Müllerian remnants is exceptional, although some authors describe it.2

Gender assignment in newborns with OT-DSD represents a therapeutic challenge. In 2005 the Chicago Consensus Statement on Management of Intersex Disorders established that the factors that influence gender assignment include: i) diagnosis; ii) genital appearance; iii) surgical options; iv) need for lifelong replacement therapy; v) potential for fertility; vi) views of the family; vii) circumstances relating to cultural practises.3 According to recent trends, it is better to postpone surgery, leaving a neutral gender until patients are able to participate to the decision. There is, however, little evidence provided regarding the impact of non-treated DSD during childhood on individual development, parents, society and risk of stigmatization.4

The opinion of the parents about the sex of rearing is crucial especially when diagnosis is made in neonatal age. A constant psychological support is essential for supporting the family. The child well-being in the family and in the society is the final goal of the treatment and should be considered.

We describe and comment on our multidisciplinary approach in a case of 46,XY OT-DSD.

Case Report

A newborn was transferred to our Institute for genital ambiguity. At birth the patient presented: i) hypospadias without microphallus; ii) penile curvature; iii) not palpable gonads

No familiar, gestational or perinatal problems were reported. The socio-cultural level of the family was low.

Investigations

Fetal sonogram assessed a male phenotype. Postnatal karyotype was 46,XY. A cytogenetic analysis of 200 metaphases on peripheral blood excluded a X0/XY mosaicism and the SNPs-array was negative for pathological deletions and duplications. A deletion of 1.89 Mb in the region 8p23.3 was found, being of maternal origin. As we know, the gene is not directly correlated to sexual development.

The attempt to investigate mutation of SRY failed and wasn’t repeated.

When the patient was nine days old, he daily received an intramuscular injections of 1000 U of human chorionic gonadotropin (hCG) during 17 months. The injection of 1000 U of hCG resulted in the presence of both testis and ovary. The family was satisfied with the good response of the patient.

Outcome and follow-up

At the age of 17 months the laparoscopic exploration showed us to make a diagnosis of 46,XY OT-DSD. A macroscopically streak gonad (Figure 2) was found and removed on the left side. A small primitive ovary containing follicles was confirmed histologically. On the right side we were able to perform an extraperitoneal orchiopexy and the first correction stage of hypospadias were performed; we left the definitive correction with repair of a urethral dehiscence.

Treatment

Preoperatively, parents expressed a strong desire for a male child. At the age of 17 months the laparoscopic exploration allowed us to make a diagnosis of 46,XY OT-DSD. A macroscopically streak gonad (Figure 2) was found and removed on the left side. A small primitive ovary containing follicles was confirmed histologically. On the right side we were able to perform an extraperitoneal orchiopexy and the first correction stage of hypospadias were performed; we left the asymptomatic Müllerian tissue (uterus and vagina) in situ. At the age of 24 months we performed the second phase of hypospadias correction and eight months later the definitive correction with repair of a urethral dehiscence.

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annually visit, testicular ultrasound scan and blood dosage of beta hCG and alfa fetoprotein for the risk of development of germ cell tumors. The family was informed that the risk of cancer is higher for a dysgenetic gonad than a simple cryptorchidism, especially in the puberal age. If signs of degeneration will become evident, an orchietomy will be the therapy together with a substitutive hormonal treatment. The parents understood and accepted the yearly follow-up and its implications.

Discussion

According to potential fertility, the medical and surgical decisions could be difficult in 46 XY OT-DSD. It seems that males report greater satisfaction with their gender and sexual lives.5

The ovarian tissue is usually normal and demonstrates follicular growth. The testicular tissue is often dysgenetic with hyalinization of the seminiferous tubules and poor germ cell development almost always resulting in infertility in patients assigned to the male gender.

Conservative treatment is the goal of the multidisciplinary treatment of DSD, especially when the sex assignment is required during neonatal period.

The aims of surgery are: i) to restore functional genital anatomy; ii) to facilitate future reproduction; iii) to reduce urological hazards related to abnormal genitourinary anatomy; iv) to avoid fluid or blood retention in vaginal or uterine cavities; v) to avoid late virilization at puberty in individuals raised as girls or breast development in individuals raised as boys; vi) to reduce risk of gonadal cancers; vii) to foster development of individual and social identities; viii) to avoid stigmatization related to atypical anatomy; ix) to respond to the parents’ desire to bring up a child in the best possible conditions.4

The timing of surgery remains controversial.3

Our surgical interventions will not preclude the future possibility of a male-to-female genitoplasty.

At birth, a no gender registration is allowed in many countries because of the impossibility of consulting the patient about his or her gender assignment. However, families often ask for an early surgical reconstruction: our opinion is to respect families’ will. The child well-being in the family, in the school and in any social interaction is the most important goal. The treatment requires a multidisciplinary approach and excellent medical, surgical and psychological expertise. After adequate psychological counseling, family pressure about male sex assignment was strong in our case and we took into account the familiar desires and the fact that the social visibility or gender is recommended by most to make the child socially visible.4 The female intra-abdominal gonad macroscopically looked like a streak gonad, despite the histological presence of follicles. No evidence exists about prophylactic removal of asymptomatic discordant structures, such as Müllian remnant. A clinical surveillance is mandatory. Annual ultrasound surveillance is recommended for gonadal cancer risk even when the gonad is in the scrotum. If precancerous lesions are suspected, more invasive procedures (MRI, serum tumor markers, biopsy) are mandatory.

Conclusions

OT-DSD is a very rare anomaly: its sexual assignment is a challenge and the treatment debated. To date, only few studies have been conducted on gender dysphoria in this group of patients and no specific well-coded guidelines exist. It is important to accommodate the requests of the patient, if he or she can express the preference about the sex of rearing. However, after the Consensus Conference of Chicago, most authors suggest not to proceed with a surgical treatment if it is not considered life-saving. The question is: what should be done in front of an insistent request of operation by the parents? If the diagnosis is made in the neonatal period, the role of the psychologist becomes essential. A constant psychological support to the family and a multidisciplinary follow-up are the keys for an optimal outcome. The surgery must be more conservative as possible: in our opinion, the

Figure 1. Martial image of pre-operative magnetic resonance imaging.

Figure 2. Laparoscopic image of streak gonad.
fact of keeping *in situ* the asymptomatic Müllerian remnants, provides the possibility of a future sex reassignment surgery, on patient’s request. What about cryptorchidism and hypospadias? We think that the surgeon and the multidisciplinary team should consult the psychologist.

References