Long-Term Followup of a Large Cohort of Patients with Ovotesticular Disorder of Sex Development

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Abbreviations and Acronyms

DSD = disorder of sex development

OTDSD = ovotesticular DSD

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Study received approval from the ethics committee of the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo.

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Purpose: We present the followup of a large cohort of patients with ovotesticular disorder of sex development treated at a single tertiary center.

Materials and Methods: We reviewed the records of 20 patients with ovotesticular disorder of sex development. We retrospectively evaluated clinical and surgical characteristics. A prospective study was also performed, including evaluation of surgical results, gonadal function, sexual activity and voiding symptoms of these patients during adulthood.

Results: All patients had ambiguous genitalia, including 18 with a 46,XX karyotype and 2 with a 46,XX/46,XY karyotype. Gender assignment at birth was male in 13 patients and female in 7. Three females were later reassigned to the male gender. Bilateral gonadectomy was performed in 10 patients. Testicular tissue was preserved in 8 males and ovarian tissue was preserved in 2 females. Average followup was 25 years (range 4 to 46). Puberty started spontaneously in 14 patients between ages 11 and 14 years. Seven patients showed spontaneous puberty after conservative gonadal surgery and 4 required hormonal replacement during adulthood. The most frequent complications in males were urethral fistula in 6 and late urethral stenosis in 3. Two patients with urethral stenosis had symptoms 10 years postoperatively. One female presented with temporary dyspareunia. In adulthood 8 males and 2 females reported sexual activity. All male patients reported orgasm and 2 reported ejaculation.

Conclusions: Male gender assignment was more prevalent. Long-term followup revealed adequate pubertal development and sexual activity. Complications involving the urethra developed frequently in male patients.

Key Words: testis, ovary, disorders of sex development, sex reassignment procedures, follow-up studies

OVOTESTICULAR DSD is characterized by the coexistence of testicular and ovarian tissue in the same individual. It is a rare form of DSD, representing 3% to 10% of DSD cases.[1] These individuals present with a wide range of genital phenotypes from genital ambiguity to normal female or male genitalia.[2,3] Sexual ambiguity is frequently observed in patients with OTDSD. It can have a major impact on quality of life and result in multiple psychological, gynecological and urological problems. Long-term followup of patients with OTDSD is necessary to evaluate gender identity

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and quality of life as well as voiding and sexual functions.[4]

Larger, mainly retrospective series of patients with OTDSD have been published in the literature but long-term outcome data on these patients have been rarely reported.[5] We present information collected retrospectively on the clinical and surgical features of a large cohort of patients with OTDSD. We also performed a prospective study of surgical results, gonadal function, sexual activity and voiding symptoms in these patients during adulthood.

PATIENTS AND METHODS

A total of 20 patients were evaluated, treated surgically and followed under our care from 1963 to 2013. We retrospectively assessed clinical, anatomical, histological and cytogenetic characteristics, gender assignment and treatment. Under our care 12 patients underwent surgery and 8 were referred from elsewhere to complete surgical procedures and hormonal treatment.

A multidisciplinary team including endocrinologists, urologists, biologists and psychologists was involved in the diagnosis and treatment of all patients and specifically involved in proposing the most appropriate gender of each newborn. Parents were informed of all factors involved in the condition of each patient. They were ultimately asked to make the decision regarding the gender assignment of the child.

All patients who sought treatment after gender assignment at birth underwent psychological tests done by the same mental health professional to confirm the gender identity of the patient before surgical treatment.

Anatomical evaluation included the degree of virilization of the external genitalia, gonadal position, existence of the urogenital sinus and breast development. Older patients were questioned on menstruation or cyclic hematuria. The internal genitalia were evaluated by pelvic ultrasound, genitography and laparotomy or laparoscopy. Gonadal tissue and ductal structures that were discordant with the patient gender identity were removed. Patients were distributed by age at genital surgery into 3 groups, including before age 2 years, before puberty (between ages 2 and 12 years) and after puberty (after age 12 years).

Surgical exploration of the gonadal tissue and ductal structures was followed by genital reconstruction (feminizing/masculinizing genitoplasty). Histological analysis of gonadal tissue confirmed the presence of testicular and ovarian tissue in all patients. Partial resection of the ovotestis was performed, guided by frozen sections to define the margins between the 2 components, with preservation of gonadal tissue that was concordant with the gender identity.

Feminizing genitoplasty consisted of clitoroplasty, urogenital sinus opening and vulvoplasty. Clitoroplasty was performed by resecting the corporeal bodies with preservation of the dorsal neurovascular bundle while the urogenital sinus was opened using a Y-V flap.[6] Masculinizing genitoplasty consisted of orthophalloplasty, urethroplasty and scrotoplasty. Urethroplasty was performed using a modified 2-stage Denis-Browne technique.[7] Colpectomy was included in this procedure as needed.

Early and late surgical complications were evaluated by physical examination and patient records.

The prospective part of our study consisted of physical examination of the external genitalia, which were performed by the same investigator (MHPS). Voiding symptoms were assessed using an adapted questionnaire based on the International Prostate Symptom Score and direct observation of the urinary stream by the same physician. Functional results of feminizing genitoplasty were evaluated by assessing the menstrual flow and vaginal introitus.[6]

In male patients sexual activity was evaluated using previously described questionnaires[7] adapted from the International Index of Erectile Function.[8] Preservation of hormonal gonadal function was estimated by considering spontaneous pubertal development and the presence of pubertal levels of gonadotropins and sexual steroids.

Gonadal surveillance for tumor development was done annually using ultrasound in adulthood.

This study was approved by the ethics committee of the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo. Written informed consent was obtained from all patients or their legal guardians.

RESULTS

Mean age at diagnosis was 11 years (range 0.1 to 38). All patients were born with ambiguous genitalia. Gender assignment at birth was male in 13 patients and female in 7. Three patients assigned to the female gender at birth presented with a male gender identity, which was confirmed by psychological tests. They were reassigned to the male gender at ages 5, 10 and 20 years, respectively. Breast development was present in 7 male patients and cyclic hematuria was noted in 3 patients. No patient presented with associated somatic malformations. A 46,XX karyotype was observed in 18 patients (90%) and 2 (10%) had a 46,XX/46,XY karyotype (see table).

Median age at genital surgery was 9.7 years (range 1 to 30). Genitoplasty was performed before age 2 years in 3 patients, at age 2 to 12 years in 10 and after age 12 years in 7. Gonadal exploration was part of the initial surgical procedure in 19 patients. The table shows the position and characteristics of gonadal tissue. Complete bilateral gonadectomy was performed in 2 females and 8 males. One female underwent complete gonadectomy at age 1 year and in another this was done after puberty at age 23 years. Three males underwent complete gonadectomy before puberty at ages 1, 4 and 5 years, and 5 underwent complete gonadectomy after puberty at ages 14, 16, 18, 30 and 36 years, respectively (supplementary table, http://jurology.com/).