International Journal of Pediatric Surgery

ISSN: 2766-5577

Research Article

Ovotesticular Disorders of Sexual Development: Epidemiological, Clinical, and Genetic Profile

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Abstract

Our study aims to describe the epidemiological, clinical, and genetic aspects of ovotesticular disorders of sexual development (DSD-OT). We conducted a prospective descriptive study on the medical records of DSD-OT cases in the Pediatric surgery department of the Albert Royer National Children's Hospital in Dakar, from January 2019 to December 2023. Various epidemiological, anatomo-clinical, and genetic parameters were analyzed. We recorded 16 cases of DSD-OT, accounting for 18.39% of all DSD cases over the 5 years of the study. Half of the patients were infants at the time of the first consultation, with an average age of 3 years. Two patients presented with signs of puberty. The raised sex was female in ten patients, representing 62% of cases, and male in five patients, or 32%. Nine patients (56%) had an "ambiguous" phenotype. In eight patients (50%), the genital tubercle was well-developed. Nine patients (56%) had a single urogenital orifice. In half of the children, at least one gonad was palpable. According to the degree of virilization, six patients (37%) were classified as Prader type 3, and five patients (32%) as type 2 in the same classification. The presence of Müllerian remnants was consistent, and all of our patients had a 46XX karyotype. DSD-OT is a common cause of DSD. The karyotype is 46XX with varying degrees of virilization.

Keywords: Disorders of sexual development; Ovotestis; Epidemiology; Pediatric surgery

Introduction

Ovotesticular Disorders of sexual Development (DSD-OT), formerly known as "true hermaphroditism," are characterized by the simultaneous presence of both ovarian and testicular tissues in the same individual. DSD-OT is a rare form of DSD, with an estimated incidence of less than 1 in 100,000 births, representing between 3% and 10% of all DSD cases [1,2]. However, it appears to be more common in certain African countries [3,4]. Despite its rarity, DSD-OT is among the most frequent causes of sexual differentiation disorders. The karyotype is often 46XX, although all genetic forms are possible [5]. Ovotesticular origin of a DSD can be suspected based on certain clinical signs depending on the patient's genetic sex. At puberty, the production of sex steroids leads to the development of secondary sexual characteristics of both sexes, or in the sex opposite to the one assigned to the child until that point. The objective of this study is to describe the epidemiological, genetic, and anatomo-clinical profile of children with ovotesticular DSD.

Citation: Ndoye NA, Elfeki H, Zeng FTA, Diouf C, Sy F, Seck NF. Ovotesticular Disorders of Sexual Development: Epidemiological, Clinical, and Genetic Profile. Int J Pediatr Surg. 2024;5(1):1045.

Publisher Name: Medtext Publications LLC

Manuscript compiled: Nov 12th, 2024

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Patients and Methods

We conducted a prospective descriptive study from January 2019 to December 2023 in the Pediatric surgery department at Albert Royer Children's Hospital in Dakar. During the five years of the study, 87 children were seen for DSD, 20 of which were suspected to have ovotesticular DSD. We included all children in whom the diagnosis of ovotesticular disorders of sexual development was confirmed. The parameters studied were frequency, age at first consultation, raised sex, phenotype, number of urogenital orifices, presence or absence of palpable gonads, Prader clinical classification, type of puberty, presence or absence of Müllerian remnants, and karyotype.

Results

During the five years of the study, 16 children were followed for ovotesticular DSD, representing 3.2 cases per year, and 18.39% of all sexual differentiation disorders. The average age at the first consultation was 3 years, with a range from 3 days old to 16 years, and a median age of 2 years. Half of the patients were infants. The raised sex was female in ten patients (62% of cases) and male in five patients (32% of cases). In one patient (6%), the raised sex was mixed.

The phenotype was "ambiguous" in nine children, representing 56% of the sample. Table 1 shows the different phenotypes. In eight patients (50%) from our cohort, the genital tubercle was considered developed, measuring over 2.5 cm. Figure 1 shows the appearance of the external genitalia in one of our patients. Nine patients had a single urogenital orifice, accounting for 56% of cases, while seven patients (44%) had two distinct orifices, urethral and vaginal (Figure 1).

A gonad was palpable in seven patients, representing 44% of the population. Additionally, in one patient, both gonads were palpable,

accounting for 6% of cases. According to the Prader classification, six patients were classified as Prader III (Figure 2). In Table 2, the different Prader types are illustrated. Two patients had a gynoid type puberty, representing 13% of the cases. Figure 3 shows gynecomastia associated with a developed genital tubercle in a 16-year-old patient with a 46XX karyotype, diagnosed with ovotesticular DSD and raised as a boy.

Table 3 summarizes the epidemiological and clinical aspects of the patients. Müllerian remnants were present on ultrasound in all patients and confirmed during surgical exploration. The genetic sex was female in all patients.

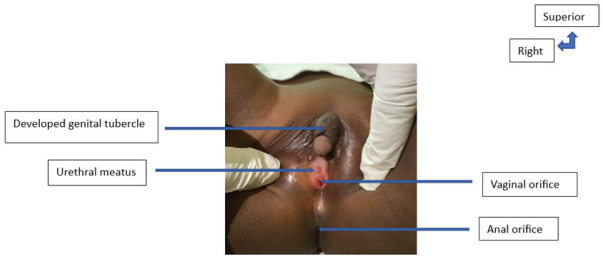

Figure 1: Appearance of external genitalia in a patient with a lateral ovotestis.

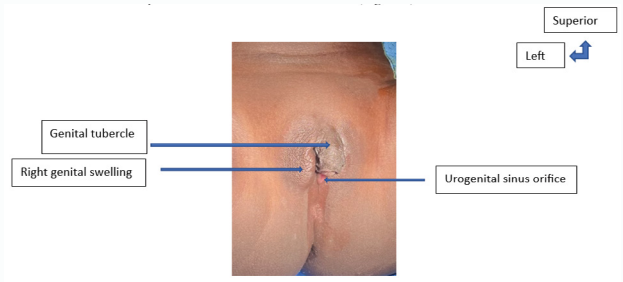

Figure 2: Appearance of external genitalia, Prader type 3.

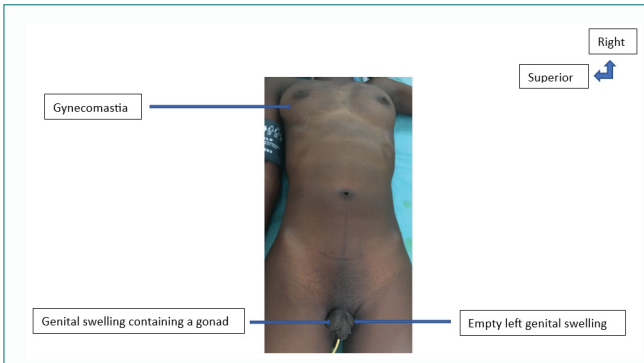

Figure 3: Gynoid Puberty on Right Unilateral Ovotestis.

Discussion

Ovotesticular disorders of sexual development (DSD-OT) are rare, with an incidence of 1 in 100,000 births [1,2], representing between 3% and 10% of all DSD cases [6,7]. Our study reveals a notable incidence of DSD-OT, representing 18% of DSD cases. These results align with frequencies reported in Europe and North America [3,5]. Significant incidences have also been observed in certain African countries [3,8-11]. In our study, the average age at first consultation

Table 1: Distribution of Patients Based on Their Phenotype.

Phenotype	Number	Percentage (%)
Ambiguous	9	56
Female	5	31
Male	2	13
Total	16	100

Table 2: Distribution of Patients According to the Prader Classification.

Prader Classification	Number	Percentage (%)
Type I	2	13
Type II	5	31
Type III	6	37
Type IV	1	6
Type V	2	13
Total	16	100

was 3 years, with extremes ranging from 3 days of life to 14 years. This average is below the global average, which is 9 years according to data compiled by Krob and colleagues [8]. Indeed, after the age of 3 years, considered the psychological age, any DSD is assumed to be diagnosed late, potentially leading to psychosocial issues [12]. While in developed countries this delay is intentional to consider the child's opinion [13], in our practice it is due to unfavourable social conditions, limited access to qualified healthcare professionals, and advanced investigations [4,14,15]. Additionally, issues related to sex are taboo in our regions, and paraclinical assessments are often very costly for families. DSD-OT is characterized by varied clinical presentations, although the most common manifestation occurs during the neonatal period or early childhood, often marked by atypical external genitalia [8,16].

Our study shows that 62% of patients were initially raised as girls and 32% as boys. Indeed, all our patients were genetically female, and their phenotype was more aligned with this sex. These results differ from some previous studies where, when a decision is made regarding the assigned sex for DSD-OT patients by the family and/or the Gynecologist, it tends to favour a male in 55% to 75% of cases [17,18].

In our study, the genital tubercle was well-developed in half of the patients. According to the Prader classification, type III was the most common, representing 37%, followed by type II at 31%. In several studies, DSD-OT were primarily classified as types IV and III according to the Prader classification [17,19].

In our study, 56% of patients had a single urogenital orifice, while 44% had a vagina. The number of urogenital orifices can vary in patients with DSD-OT. In those with a female phenotype, labial fusion or vaginal atresia may be observed [8].

In our study, all our patients had a 46XX karyotype, which is consistent with results observed in South Africa and West Africa [10], where very high rates of 46XX DSD-OT are found. However, other patients may present with chimerism (46XX/46XY) or different mosaic combinations as observed in Europe [8]. Less frequently, a 46XY karyotype may be observed [18], as is the case in Japan [20].

Conclusion

Ovotestis is a frequent cause of sexual differentiation variation. Their karyotype is 46XX, and the degree of virilization in patients is highly variable, which can lead to a late diagnosis.

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Table 3: Summary of Epidemiological and Clinical Aspects of Patients.

Patient #	Age at First Consultation	Raised Sex	Gonad Position		Number of Urogenital Orifices	Prader Classification
			Right	Left		
1	1 year 3 months	Female	Abdominal	Abdominal	1	III
2	New Born	Female	Abdominal	Genital Swelling	2	II
3	New Born	Female	Abdominal	Abdominal	2	II
4	2 months	Female	Abdominal	Abdominal	2	II
5	1 month	Mixed	Genital Swelling	Genital Swelling	2	III
6	1 year et 11 months	Female	Abdominal	Genital Swelling	1	III
7	2 years et 6 months	Male	Abdominal	Genital Swelling	1	I
8	2 years	Male	Abdominal	Abdominal	1	III
9	4 months	Female	Inguinal	Abdominal	2	IV
10	1 year et 8 months	Female	Genital Swelling	Abdominal	1	II
11	3 months	Female	Abdominal	Abdominal	1	III
12	New Born	Female	Abdominal	Abdominal	1	I
13	4 years et 6 months	Male	Abdominal	Abdominal	1	III
14	2 months	Female	Abdominal	Abdominal	2	II
15	13 years	Male	Abdominal	Inguinal	1	V
16	14 years	Female	Abdominal	Genital Swelling	2	V

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