

Original Article

Congenital absence of the testis in human fetuses and in cryptorchid patients

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Abstract

Background: The aim of the present study is to make a comparative study in human fetuses and in patients with cryptorchidism, analyzing the incidence of a number anomalies of the testes for both populations.

Methods: We studied 326 testes from 163 human fetuses ranging in age from 10 to 35 weeks postconception (WPC) and 133 testes from 101 cryptorchid patients aged from 1 to 15 years old (mean, 6.4 years). The Fisher's exact test was used for comparison.

Results: Among 326 fetal testes, 224 (68.7%) were abdominal, 45 (13.8%) were inguinal and 55 (16.8%) were scrotal. In one fetus at 23 WPC, both testes (0.6%) were absent. Of the 133 cryptorchid testes, 17 (12.78%) were abdominal, 92 (69.1%) were inguinal and 24 (18%) were high scrotal. Of the 17 abdominal testes, three (17.6%) were atrophic and two were vanished (11.7%). Of the 92 inguinal testes, one (1.08%) was vanished. Twenty-eight (21%) of the cryptorchid testes were impalpable and among these, 17 were located in the abdomen (60.7%) and 11 (38.2%) in the inguinal region (internal ring).

Conclusions: Testicular agenesis is a very rare anomaly, both in fetuses and patients with cryptorchidism.

Key words congenital defect, cryptorchidism, development, fetus, testis.

Introduction

Human testes originate from an inspissation in coelomic epithelium in the mid region of the mesonephric duct, among the 4th and 6th week after conception. During the fetal period, the testis migrates from the abdomen to the scrotum, crossing the abdominal wall through the inguinal canal. The most accepted theories for explaining testicular migration are: (i) the elevation of intra-abdominal pressure;^{1,2} (ii) the development of gubernaculum testis and of paratesticular structures;^{3,4} (iii) remodeling of gubernaculum testis;⁵ (iv) hormonal stimuli (chorionic gonadotrophin, testosterone, Müllerian duct inhibiting substance);^{6–9} and (v) stimuli from genitofemoral nerve.⁸

Testes anomalies can be divided in two groups: (i) anomalies in number, divided in agenesis (uni- or bilateral), and supernumerary testes; and (ii) anomalies of position, divided into cryptorchidism and ectopia. All these anomalies are important, because infertility is most common in patients with testicular anomalies.^{10,11}

Cryptorchidism affects between 3.4% and 5.5% of full-term boys, whereas the incidence is between 9.2% and 30.0% in premature boys.^{11–13} Approximately 20% of cryptorchid testes are impalpable.^{14,15} Among unilateral impalpable testes, approximately 50% are atrophic or absent.¹⁶ Some authors report that the incidence of congenital absent testis form approximately 3%^{10,17} to 10%¹⁴ of cryptorchidism cases. The absent testis is also called a vanished (or vanishing testis). Bilateral absence (anorchia) is a very rare condition, occurring in approximately 1 of every 2000 births.¹⁸

Cryptorchidism is a multifactorial condition, associated with several congenital anomalies (hypospadias, inguinal hernia, epididymal anomalies and renal anomalies) and genetic syndromes (trisomy 13, trisomy 18,

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Fraser's, Carpenter's, Prader-Willi's and Prune-belly syndromes).^{11,17}

Epididymal anomalies and hernias are among the most frequent anomalies associated with cryptorchidism.^{11,19} In undescended testes, there was an increased incidence of paratesticular structure malformations accompanied by gubernacular attachment anomalies compared to the testes in normal fetuses.²⁰ Absent testis have an incidence of 3–5% in cases of cryptorchidism and it is important to differentiate it from impalpable testes. Several studies have shown the incidence of absent testis associated with cryptorchidism,^{10,11,14,17,18} however, there are no studies in the published literature comparing the incidence of congenital absent testis in human fetuses with cryptorchid patients.

The aim of this paper is to perform a comparative study in human fetuses and cryptorchid patients, analyzing the incidence of a number of anomalies of testes in both populations.

Materials and methods

A total of 326 testes from 163 human fetuses and 133 testes from 101 cryptorchid patients submitted to orchiopexy were studied.

The committee on human research at the State University of Rio de Janeiro, Brazil, approved the investigation. Informed consent was obtained from the parents of each fetus and cryptorchid patient.

The fetuses had died of causes not related to the urogenital tract, were macroscopically well preserved and no signs of congenital malformation were detected. The gestational age of the fetuses ranged from 15 to 29 weeks postconception (WPC), which corresponds to 17 and 31 menstrual weeks, respectively, and was estimated according to the foot length criteria.^{21–24}

After fetal classification, the abdomen, the inguinal canal and the scrotum were opened in order to identify the testes, epididymides and gubernacula. The fetuses under 20 WPC were dissected with the aid of a stereoscopic magnifier, with 2.5× magnification.

One hundred and one cryptorchid patients were analyzed between December 1999 and August 2002. Patients' age ranged from 1 to 15 years old (mean, 6.4 years).

The testes of cryptorchid patients were divided, following previous classification,¹¹ into 3 groups: abdominal, inguinal and high scrotal. Patients were submitted to conventional or laparoscopic orchiopexy. Testes were considered vanished when, during surgery, we observed blind-ended vas deferens and spermatic vessels. The cases of testicular atrophy and vanished testes were

removed and the material sent for histopathological analysis.

To compare these populations we used Fisher's exact test.²⁵

Results

Of the 326 fetal testes, 224 (68.7%) were abdominal, 45 (13.8%) were inguinal and 55 (16.8%) were scrotal. In one (0.6%) 23-WPC fetus, both testes were absent (anorchia). In this same fetus, epididymis and vas deferens were not found, as well as the gubernaculum; however, the penis and scrotum were well individualized. The positions of the fetal testes is shown in Table 1.

Of the 133 cryptorchid testes, 17 (12.78%) were abdominal, 92 (69.1%) were inguinal and 24 (18%) were high scrotal. From the 17 abdominal testes, three (17.6%) were atrophic and two were vanished (11.7%). From the 92 inguinal testes, one (1.08%) was vanished. The positions of the cryptorchid testes are shown in Table 2. In total, from the 133 cryptorchid testes, three testes (2.25%) were vanished.

Of the 133 cryptorchid testes, 28 were impalpable (21%). Of these, 17 were in the abdomen (60.7%) and 11 (39.2%) were in the inguinal region (internal ring). Of the 11 inguinal testes, one was vanished. Laparoscopic surgery was performed on six of the 28 non-palpable testes. In three cases, the testes were bilaterally non-palpable and in one of them, both testes were in the abdomen.

Table 1 Position of fetal testes

Region	Number of testis (%)
Abdominal	224 (68.7%)
Inguinal canal	45 (13.8%)
Scrotum	55 (16.8%)
Absence	2 (0.6%)
Total	326 (100%)

Table 2 Location of cryptorchid testis. Among the 17 abdominal testis, three (17.6%) were atrophic and two were vanished (11.7%). Of the 92 inguinal testes, one was vanished (1.08%)

Region	Number of testis (%)
Abdominal	17 (12.78%)
Inguinal canal	92 (69.1%)
High scrotal	24 (18%)
Total	133 (100%)

The histopathological analysis of the three vanished testes did not show seminiferous tubules in any case, however, epididymal tubules and atrophic vessels were found in all three cases. Also, no signs of calcium and hemosiderin deposition were observed in any of the cases.

There was no statistically significant difference ($P = 0.150$) in the incidence of absent testis in fetuses (two cases, 0.6%) or in cryptorchid patients (three cases, 2.25%).

Discussion

Congenital unilateral absence of the testis occurs with an estimated frequency of 4% in the cryptorchid male population, which is much more common than bilateral absence or anorchidism.²⁶

There are three theories that attempt to explain congenital absence of the testis: (i) absence of testicular development during the fetal period; (ii) discontinuation of vascular supply to the testes during the fetal period; and (iii) atrophy caused by intrauterine testicular torsion.¹¹ Discontinuation of testicular vascularization during the fetal period would occur by extravaginal torsion (spermatic chord torsion) and would be the most frequent mechanism involved in testicular agenesis.¹¹ That is, most cases of testicular absence result from the degeneration of a previously formed testis rather than primary agenesis.²⁷

Testicular absence may be separated into four groups:¹¹ (i) scrotal: vas deferens and epididymis generally present in high scrotal region; (ii) inguinal: vas deferens and epididymis in the canal; (iii) abdominal: inguinal canal present with atrophic gubernaculum and obliterated processus vaginalis, vas deferens and epididymis in the abdomen; and (iv) total absence: absence of testis, epididymis and vas deferens, the inguinal canal would be rudimentary, with the presence of ilio inguinal nerve. In the current sample, the case of bilateral absence of the testes (anorchia) in a fetus was in group (iv), as we did not visualize the epididymis and vas deferens. In three cases of absent testes in cryptorchid patients, two pertained to group (iii) and one to group (ii).

We observed bilateral absence (anorchia) in one fetus in the current sample (0.6%). This fetus presented male phenotype (penis and scrotum formed). Bilateral anorchia with male phenotype preserved is explained due to the period in which the fetal testes vanish (probably because of twisting). In the cases where vanishing testes occurs after the 16th week of development, the penis and the scrotum are normally formed.^{10,18} Therefore,

anorchia with male phenotype indicates that the testes were present until 16th week of development and then vanished. We did not find any case of anorchia among the patients with cryptorchidism.

Diagnosis of anorchia must be suggested in cases of bilaterally impalpable testis.²⁸ Several imaging methods may be used to study non-palpable testis, however, none are reliable enough to differentiate anorchia from an abdominal testis.²⁹ The most accurate method to confirm localization and identification of non-palpable testes is laparoscopy.³⁰ In the present sample, 28 of the 133 cryptorchid testes were impalpable (21%). Among these, 17 were abdominal (60.7%) and 11 (39.2%) were in the inguinal region. We performed laparoscopic surgery in six of the 28 cases with impalpable testes (21.4%).

Some authors claim that laparoscopy is a costly procedure and that it could be avoided in most cases of impalpable testes, since approximately 50–60% are found in the inguinal region or at the external ring and actually constitute difficult palpable testis.^{15,29} Almost 40% of the cases of non-palpable testes in the present sample were located at the inguinal canal, where standard orchiopexy is the best management. Nevertheless, in cases of a true abdominal testis, laparoscopy is a very useful method to identify, locate and differentiate it from absent testis and to evaluate its viability and its treatment: laparoscopic orchiopexy or orchiectomy.

Management of the remnants of vanished testis is controversial. Previous studies of these remnants showed that in 6% of the cases of vanished testis there are testicular remnants, in 36% of case there are epididymal remnants, and in 24% of cases there are remnant vessels with calcium and there are hemosiderin depositions that would indicate previous testicular torsion in 35% of cases.¹⁴ In all three cases of testicular absence in cryptorchid patients we did not find testicular remnants.

In 6% of cases with vanished testes, there is a risk of the presence of testicular tissue¹⁴ which would be associated with a greater risk of developing neoplasm.³¹ Consequently, in the case of abdominal location of the vanished testis with blind end vessels, we must always remove the vessel and the surrounding tissue.¹⁴

In fetuses, we observed only two cases (in the same fetus) of absent testis, which constitutes an incidence of less than 1% (0.6%). In cryptorchid patients, we found three cases of absent testis, also a low incidence (2.25%). Therefore, after studying an important fetal sample, we conclude that testicular agenesis is a very rare anomaly, both in fetuses and in cryptorchid patients.

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