CASE REPORT

Anterior transperitoneal laparoscopic gonadectomy in a patient with complete androgen insensitivity syndrome (CAIS): case report and surgical technique

Gonadectomia transperitoneal anterior via laparoscópica em paciente com síndrome de insensibilidade aos andrógenos completa: relato de caso e descrição cirúrgica

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ABSTRACT

Introduction: complete androgen insensitivity syndrome is an X-linked mutation that causes a female phenotype, despite normal serum androgen levels. Patients have a 46,XY karyotype, female external genitalia, ectopic testes and absent Müllerian duct remnants. **Case report:** we present the case and surgical procedure of a 28-year-old patient who underwent laparoscopic gonadectomy in order to prevent gonadal malignancy. **Conclusion:** laparoscopy allows for the removal of gonads with the advantages of minimally invasive procedures.

Keywords: Laparoscopy. Androgens. Urogenital system.

RESUMO

Introdução: a síndrome de insensibilidade aos andrógenos completa resulta de uma mutação ligada ao X que causa fenótipo feminino, mesmo com a vigência de níveis de andrógenos séricos anormais. Pacientes tem um cariótipo 46,XY, genitália externa feminina, testículos ectópicos e ausência de vestígios do ducto de Müller. **Relato de Caso:** apresentamos aqui o caso clínico e procedimento cirúrgico de uma paciente de 28 anos que se submeteu à gonadectomia laparoscópica para evitar o desenvolvimento de neoplasias testiculares malignas. **Conclusão:** a laparoscopia permite a remoção gonadal com as vantagens relacionadas aos procedimentos minimamente invasivos.

Palavras-chave: Laparoscopia. Androgênios. Sistema urogenital.

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INTRODUCTION

Androgen insensitivity syndrome (AIS), was first described by Morris in 1953 to characterize individuals with a 46,XY kariotype who are phenotypically female due to a resistance to androgen activity. Mutations in the X-linked androgen receptor gene that codes for the ligand-activated androgen receptor are responsible for the lack of androgen activity, despite normal hormone concentrations.[1]

The degree of androgen insensitivity determines patient phenotype and may be classified as either partial (PAIS) or complete (CAIS).[2] Presentation ranges from males with infertility or undervirilization to a completely female phenotype with estrogen-dependent secondary sexual characteristics but no menses.[2] Androgens are essential for male sexual differentiation to occur during fetal life, while female fetal characteristics are independent of estrogen activity. For this reason, the lack of androgen response elements in target tissues result in an essentially female phenotype. The normally functioning testis produce adequate amounts of Müllerian-inhibiting factor (MIF), thus inhibiting the development of Müllerian-derived structures such as the Fallopian tubes, uterus, cervix and the upper one-third of the vagina. The classic presentation, therefore, is an individual of female appearance with female external genitalia, a short vagina, ectopic or palpable testes, no uterus and primary amenorrhea. Since the peripheral conversion of androgens to estrogens is not impaired, secondary sexual characteristics such as breast development may also be present.

Clinical management of the syndrome involves functional, sexual and psychological issues, with a multidisciplinary approach. The incidental finding of a palpable gonad, a gonad during a hernia repair, or an intra-abdominal mass suggestive of testicular composition encourages further investigation. Although there is still controversy as to the ideal time for gonadectomy when such mass is found in childhood, a biopsy should be performed for diagnostic purposes. In adults, gonadectomy is recommended due to the increased risk of gonadal tumors.[1]

In the majority of patients with CAIS, surgical vaginal elongation is generally not recommended. Many surgical options are available for the correction of underdeveloped vaginal pouches in Morris syndrome,[3] vaginal size is usually sufficient for intercourse; when not, vaginal dilators are considered first-line treatment. Unfortunately, infertility remains an issue for these patients; options are to adopt or to use donor oocytes and a surrogate mother.

In this article, we present the case and surgical technique of a patient diagnosed with CAIS at age 28 who underwent bilateral gonadectomy.

CASE REPORT

A 28-year-old woman presented to our outpatient clinic with primary amenorrhea. She had a history of thelarche at age 12-13, and physical examination revealed female facies, small breasts, periareolar hair growth and female external genitalia consisting of a normal clitoris and a narrowed, blind-ended and low-set vagina with 4 centimeters in length. Further investigation revealed a 46,XY karyotype. She was submitted to a pelvic Magnetic resonance imaging (MRI), which showed non-specific, multiloculated, cystic-appearing images that were symmetric and bilateral. The uterus, ovaries and other adnexes were absent. A diagnosis of Morris syndrome was thus established.

We then proceeded to perform a laparoscopic bilateral gonadectomy. With the patient in a modified lithotomy position and under balanced general anesthesia, we placed a urinary catheter, performed antisepsis and affixed surgical draped. Laparoscopic trocars were then placed through incisions in the umbilicus (11mm trochar), the right hemiclavicular line (5mm), left hemiclavicular line (10mm) and median infraumbilical line (5mm). Upon inspection of the abdominal cavity, we found no uterus, ovaries or other uterine appendages. The left testicular mass was seen near the ureter; and the right testicle, near the inguinal canal. We then dissected the retroperitoneal space and proceeded to electrocoagulation and section of the spermatic cords after proper identification of both ureters. Surgical specimens were extracted with retrieval bags and sent for histopathologic studies, which showed that they represented male gonads with no signs of malignancy. The post-operative period was uneventful.

DISCUSSION

Androgen insensitivity syndrome (AIS) is the most common single cause of male undermasculinization. Complete insensitivity is present in one case to every 64,000 newborn male, and is usually diagnosed in childhood or early puberty, with the median age at diagnosis being 1 year.[4] Individuals with PAIS are especially in need of early diagnosis for proper sex assignment and genetic counseling.

Gender assignment is usually made based on genitalia appearance at birth, and thus complete androgen insensitivity syndrome patients are generally raised as females. In previous studies, women with CAIS have reported high degrees of femininity throughout their development. In a scale of 1 (not feminine) to 5 (highly feminine), the average rating of the 14 women studied by Wisniewski et al. was 4.4 in childhood, 4.2 in adolescence and 4.6 in adulthood. These women also reported a 93% female heterosexual orientation and heterosexual experiences in adulthood. All of the participants reported satisfaction with being a woman, and none reported desire to undergo sex change.[5] Slijper et al. also studied 12 girls with CAIS, none of which underwent sex reassignment.[6] In fact, even the classic work of Money et al, which included patients with all types of disorders of sexual differentiation, found that only 4.7% of the 105 patients studied had a gender orientation that was ambiguous or differed from the gender of assignment and rearing, highlighting the importance of the assigned sex over chromosomal sex.[7] Psychological support is needed to reinforce their gender identity after diagnosis and to prepare them during treatment, as well as to detect, at an early stage, mental disorders that may arise during this process.[6]

The timing of gonad removal is one of the issues that should be well discussed with the patient and, if applicable, their families. The optimal time for orchiectomy in a patient with CAIS is not well defined, and neither is the real risk of testicular malignancy in these patients. When the diagnosis is made in infancy, gonadectomy may be delayed until late adolescence to allow for spontaneous puberty and growth spurt. Endogenous hormones generally produce more steady puberal development than hormone replacement therapy. Development of malignancies is rare in the pediatric population;[8] adults, however, have higher chances of developing testicular malignancies if gonadectomy is not performed.

Kravarusic et al.[9] evaluated the risk of testicular malignancy in 11 children and adolescents, and noted that none of the 6 patients with CAIS showed tumors, either benign nor malignant. Liu et al. showed that approximately 30% of untreated patients develop germ cell malignancies by the age of 50.[10,11] A review of the literature by Deans et al[10] estimated that malignant testicular tumors occur in approximately 16% of adult patients with CAIS. This is much higher than the frequency seen in pediatric CAIS patients, where malignancy rates range from 0.8 to 2% of patients. Therefore, although there is no precise recommendation as to the time of gonadectomy in CAIS patients when diagnosis is made before puberty, orchiectomy is mandatory in adult patients, such as the one presented in this case, due to increased risk of malignancy.

Testes in CAIS may be located anywhere along the path of testicular descent.[10] In patients with impalpable gonads, their precise location must be determined in order to perform their removal. In 1976, Cortesi et al. first performed the diagnosis of a patient with impalpable testis through laparoscopy, and the use of this procedure in the management of patients with criptorchidy has been continuously studied since then.[12] Laparoscopic access allows for a complete inventory of the abdominal cavity, facilitating gonadal identification and the search for Müllerian duct remnants, being a procedure useful in both diagnosis and treatment of sex differentiation disorders. The use of a retrieval bag may prevent the dissemination of potentially malignant cells in normal-appearing gonads, and is especially useful in patients who present for gonadectomy at an age when malignancy risk is increased.[13]

In the experience of Chertin et al.[14] with laparoscopy in 5 patients with AIS, they were able to visualize all internal genitalia using only a 5mm umbilical port, but needed an extra 5mm port in order to manipulate them surgically. The study showed that gonadal biopsy through laparoscopy was the only way to reach a definite diagnosis in doubtful cases and to define gonadal morphology.

Our patient did not present with any complications in the post-operative period. Estrogen replacement therapy was initiated in order to maintain feminization and prevent bone loss.

Additional minimally invasive procedures for gonadectomy in Morris syndrome patients are currently being developed. Single-port surgery succeeded in providing excellent aesthetic results in these patients while maintaining the advantages of minimally invasive surgery such as decreased length of hospital stay, low bleeding and low incidence of postoperative complications.[15]

CONCLUSION

Timing for gonadectomy in infants presenting with Morris syndrome is controversial. In adults, however, the increased risk of malignancy justifies surgery, which may also serve as a diagnostic tool. Since testis in CAIS may be impalpable and present anywhere along the path of testicular descent, laparoscopy has the advantage of allowing for complete inspection of the abdominal cavity. Furthermore, use of retrieval pouches facilitates gonadal removal without spreading malignant cells. Minimally invasive surgery provides rapid patient recovery, decreased risk of wound infections, better aesthetic appearance and improved psychological outcomes.

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