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Two cases of gonad retention in adolescent patients with complete androgen insensitivity syndrome (CAIS)

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Abstract

Bilateral gonadectomy was the historical recommendation for patients diagnosed with complete androgen insensitivity syndrome (CAIS) due to the perceived risk of malignancy in the gonads. However, new shared-decision making approaches are allowing patients to explore the option to defer surgery. Here we report two patients who presented with primary amenorrhea to their primary care provider (PCP). After imaging and karyotyping, these patients were diagnosed with CAIS. They underwent exams under anesthesia and diagnostic laparoscopies in which the gonads did not present any immediate concerns or indications for removal. After discussing their options using the shared-decision making approach with the differences in sex development (DSD) team, they opted to defer gonadectomy and follow up annually with imaging to monitor the gonads.

Keywords

Complete androgen insensitivity syndrome; Gonadectomy; Shared-decision making

1. Introduction

Complete androgen insensitivity syndrome (CAIS) is caused by a mutation in androgen receptors (AR), that results in resistance to androgen in XY individuals [1]. The prevalence of CAIS is estimated to be about 1 in 20,000 to 1 in 99,000 [2,3]. Historically, recommendations for persons affected by CAIS included gonadectomy, usually performed during the first few years of life or in the late teens after spontaneous puberty occurred. Recommendations then included lifelong hormone replacement therapy. Care is shifting to

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Patient consent

The Phoenix Children's Hospital Institutional Review Board acknowledged this case series as not meeting the criteria for human subject research and as such, patient consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.epsc.2019.101332.

defer early surgery in these individuals which includes a shared decision-making checklist and careful monitoring of the gonads [4–6]. The following cases describe the shared decision-making process used to care for two patients who chose to defer gonadectomy.

2. Case reports

2.1. Case 1

A 15-year-old female presented to her primary care provider (PCP) with primary amenorrhea. The patient was documented to have Tanner stage 1 pubic hair and absent axillary hair, and Tanner stage 5 breast development. Ultrasound (US) imaging described the absence of a uterus with the presence of a vagina. Magnetic resonance imaging (MRI) was ordered and showed soft tissue structures along the pelvic sidewalls as well as the agenesis of a uterus and the absence of follicles in what was described as ovarian tissue. The patient was referred to endocrinology in multidisciplinary differences of sex development (DSD) clinic where she underwent genetic testing that confirmed 46, XY karyotype, suggesting a diagnosis of androgen insensitivity syndrome (AIS). At this point, the patient was informed by an outside gynecologist of the risk of malignancy in gonads in patients with CAIS, and that gonadectomy was the standard treatment with estrogen supplementation to follow. The patient underwent a pelvic exam under anesthesia (EUA) and diagnostic laparoscopy that documented a normal appearing urethra, a normal appearing introitus and vaginal opening, and the absence of a cervix. The diagnostic laparoscopy revealed bilateral healthy-appearing gonads consistent with testes, and no other abnormalities, adhesions, or evidence of hernias. After multiple discussions with the Phoenix Children's Hospital DSD team, the patient and family opted to defer gonadectomy as long as the gonads appear healthy. The patient has followed up yearly for US imaging, and has not complained of any abdominal pain or discomfort. The testes are normal in size and echogenicity, though small cysts have been described in the left gonad.

2.2. Case 2

Similar to Case 1, a 17-year-old female presented to her PCP with primary amenorrhea, and the physical exam showed an absence of pubic and axillary hair with Tanner stage 5-breast development. This patient was referred to an outside gynecologist where labs showed a high testosterone level of 255 ng/dL, and US imaging showed the absence of a uterus with presence of gonads. Genetic testing revealed 46, XY karyotype. MRI was recommended and showed the absence of the uterus and cervix with small probable uterine remnant on the right, and the gonads appeared to be either ovarian tissue or testicular tissue with cystic Mullerian remnants. The patient was told that the diagnosis was likely AIS or Swyer syndrome. A gonadectomy was recommended as standard course of treatment by the outside gynecologist who also wanted a genetics evaluation before any action was taken. However, the patient was referred to Phoenix Children's Hospital and she underwent a EUA and a diagnostic laparoscopy that showed a normal appearing urethra and vaginal opening, as well as uterine agenesis and presence of two gonads that were unfixed to any surrounding structures, with the left gonad having a cyst that was not decompressed. There was no evidence of torsion or masses, and the surface of the gonads was glistening and smooth. AR receptor gene testing was done and was consistent with AIS. The patient and the DSD team

used a shared decision making approach to discuss the risks and benefits of leaving the gonads in place. The patient was informed that there is a small but unknown risk of cancer in the gonads. The patient is to follow up with yearly imaging to ensure the gonads have remained healthy.

3. Discussion

We described two patients with CAIS who opted to defer surgery rather than undergo a gonadectomy. Individuals with CAIS have XY chromosomes and testes located anywhere in the path of fetal descent from pelvis to labia. Secretion of Mullerian inhibiting substance suppresses development of the uterus, oviducts, and upper one-third of the vagina in utero. Although the testes produce male-typical levels of androgens, aromatase activity in the face of androgen resistance allows estrogen-mediated development with typical female external genitalia and absent or scant pubic and axillary hair during puberty [7].

Traditional treatment recommendations for patients with CAIS included gonadectomy due to the perceived risk of malignancy. A recent review of the literature shows that testicular germ cell tumors are rare and rates can be as low as 0% in AR confirmed individuals with AIS [8]. It should be noted that individuals with PAIS may have a higher risk for malignancy than those with CAIS. However, this is hard to determine based on historical literature where AR testing was not common and PAIS is often a clinical diagnosis. In addition, literature may have grouped other diagnosis in with AIS further muddying the waters [9]. Recent studies have shown that invasive germ cell tumor growth is rare in adults with CAIS and PAIS [8]. Individuals with CAIS who decide to retain their gonads and defer surgery do so for a variety of reasons, including the inconvenience of surgery, lack of a desire to take hormone replacements throughout their life, and fears of the risks of having surgery [9]. Recommendations for those wishing to defer surgery have included regular MRI or US imaging to monitor for signs of malignant change [4,5,10]. For those individuals diagnosed prenatally, parents should be counseled regarding the gonads and their role in puberty and allowing the individual to participate in the shared decision-making process regarding lifelong implications for treatment.

Deferring surgery is an option not widely discussed with patients with CAIS; however, care models are emerging that include consistent imaging and careful monitoring with the possibility of avoiding gonadectomy over the course of a patient’s lifetime [4,5].

4. Conclusion

Though gonadectomy has typically been recommended for patients with CAIS, the risk of malignancy in the gonads is low, and deferment of the surgery is an option. A shared decision-making approach can be used to educate patients on the issues involved with long-term surveillance and a thorough discussion of all options. As long as the patients have regular imaging and routine monitoring to ensure the gonads are healthy, it may be possible to avoid gonadectomy throughout the patient’s life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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