Should There be a Consensus Statement about Managing Inguinal Hernia In females? A Case of Delayed Diagnosis in Complete Androgen Insensitivity Syndrome (CAIS)

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Introduction

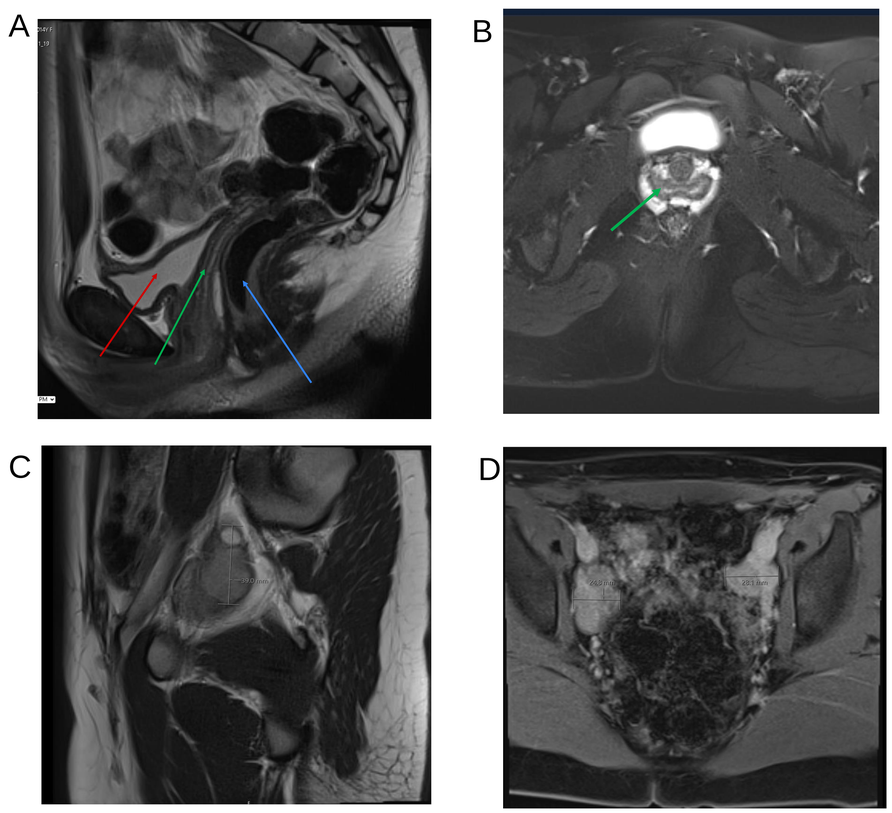
Complete Androgen Insensitivity Syndrome (CIAS) is due to mutations in the androgen receptor gene located in Xq11-12 region. CIAS is diagnosed at various stages in development including prenatal, childhood and post pubertal phases. During the childhood stage, more than 50% of females with CAIS present with inguinal hernias. The incidence of CAIS is estimated to be 0.8% to 2.4% in girls with inguinal hernias [1], with 90% of the girls with CAIS undergo inguinal hernia repair during childhood [2]. The risk of germ cell neoplasm is estimated as 0.8% [3] and carcinoma in situ lesions to be 1.4% [4]. Currently post-pubertal gonadectomy is the recommended therapy for individuals with CIAS due to aforementioned risks[5], however some patients choose to retain gonads with regular surveillance. If gonadectomy is chosen, hormone replacement therapy is necessary to avoid complications caused by hypogonadism, including osteoporosis, cardiovascular diseases, and a shortened life expectancy [6]. Unfortunately, there is currently no consensus on the management of females with inguinal hernias in the available literature. Through this case presentation, we aim to express the necessity for a consensus statement among healthcare providers in the management of patients CAIS.

Case Presentation

We present a case of a 15-year-old, self-identified female, with primary amenorrhea referred to our pediatric endocrinologist clinic for a second opinion. Her clinical exam revealed Tanner 5 breast, Tanner 2 pubic hair, no axillary hair, no clitoromegaly or labial fusion. History revealed the patient underwent bilateral inguinal hernia repair at the age of 5 weeks. Her pediatrician ordered Initial ultrasound and subsequent MRI at 14 years old, which revealed an absent uterus and complex hemorrhagic cysts of the “ovaries”. The patient was referred to a local pediatric endocrinologist who ordered laboratory studies including karyotype which revealed 46 XY, confirming the diagnosis of CAIS. Review of past medical records and post operative note from the outside hospital stated that her gonads appeared “more like testes” and had been relocated inside the abdomen without undergoing biopsy. After the procedure, there was no subsequent follow-up or consultation with a pediatric endocrinologist. Per mothers’ recollection, she was not informed of the findings.

The patient experienced significant emotional distress when presented with her final diagnosis and had concerns about her reproductive options. We offered psychological and genetic counseling for both the patient and her mother, especially since mother may have transmitted the mutation to her prepubertal child who is 7 years old. Currently genetic counseling is still pending.

The patient was also referred to the pediatric urologist to further assess the need for vaginal dilation and/or desire for gonadectomy in view of concerning imaging findings. We also presented the patient and her family with the option to delay orchiectomy with appropriate annual surveillance of gonads. Ultimately, the patient and family decided to pursue orchiectomy and initiate lifelong estrogen supplementation. The patient underwent vaginoscopy and bilateral orchiectomy via laparoscopic approach. The Operative note reported the patient’s vaginal opening was sufficient to pass Hagar uterine dilator with length 5cm. Pathology report for testes shows benign testicular parenchyma and stromal tissue with focal atrophic features of seminiferous tubules and focal stromal fibrosis. Negative for dysplasia or neoplasia



MRI images of patient with CAIS; A. Sagittal view :Red arrow-Bladder, Green arrow- Vagina, Blue arrow rectum. B. Axial view showing patient’s vagina. C. Sagittal view Showing patient’s left testes. D. Axial view showing B/L testes

Patient’s initial labs

TSH	3.05 mU/L (<4.5)
T4	6.1 ug/mL (4-12)
fT4	2.4 ng/mL (1.2-4.9)
FSH	6.0 mIU/mL (1.0 to 18.6)
prolactin	15.6 ng/mL (<25)
17OHProgesterone	49 ng/dL (<265)
LH	17 mIU/mL (0.4 -11.7)
AFP	1.25 ng/mL (<11)
AMH	368 ng/mL (<13)
Testosterone	629 ng/dL (<55)
E2	30 pg/mL (<47)

Conclusion

After extensive review of the literature, it seems evident that consensus statement needs to be created between pediatricians, urologist, obstetrician-gynecologist, and endocrinologists to perform systematic genetic testing in all females with inguinal hernia. We feel that genetic testing should be offered before hernia repair in all girls. It could be as simple as a buccal mucosal smear, fluorescence in situ hybridization for Y chromosome, or skin biopsy in all females and would result in early identification of this condition. This would be beneficial to avoid delays in diagnosis, to prevent morbidity and improve the quality of life [7]. It would allow for early discussions and age-appropriate education regarding post-pubertal expectations; such as reproduction, optimizing hormonal replacement and necessity for psychological routine assessments. In regard to hormonal replacement, it is noted that many patient’s may feel “unwell” after gonadectomy, and their care should be individually customized [8].

Another option currently being studied at the NIH, is to delay orchiectomy with health surveillance to include monitoring gonads annually and reviewing metabolic and bone health issues. It is recommended that during inguinal hernia repair, the gonads should be repositioned in a location that allows easy monitoring using annual transabdominal ultrasound [8]. Although there is evidence concerning bone mineral density in CIAS patients, one recent study demonstrated no relationship between age of gonadectomy with bone density [9].

Utilizing these strategies, we advocate for a consensus statement to minimize the consequences of late diagnosis of CAIS in adolescent girls. It would be advantageous to increase awareness and have conversations about its clinical ramifications and appropriate management options among healthcare providers.

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