From Retained Gonads to Seminoma: Timing of Gonadectomy and Cancer Risk in Complete Androgen Insensitivity Syndrome

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Introduction

Androgen insensitivity syndrome (AIS) is a **rare X-linked genetic condition** caused by mutations in **the androgen receptor**, which impair the body's ability to respond to androgens in individuals with a **46,XY karyotype**.

In **complete AIS (CAIS),** affected individuals typically present with **female external genitalia** despite having XY chromosomes, but they do not develop internal female reproductive organs such **as the uterus or fallopian tubes**. The **testes remain undescended**, often located in the abdomen or inguinal canal.

Retained gonads carry an age-dependent risk of germ cell malignancy, estimated at **1–2% before puberty and 5–6% in adulthood.**

This increased risk is due **to arrested germ cell development** caused by androgen receptor dysfunction, as well as the **ectopic location of the testes**, which exposes them to elevated body temperatures and disrupts normal development, increasing the likelihood of malignant transformation.

Case Presentation

- 34-year-old phenotypic female with primary amenorrhea, evaluated for infertility
- Pelvic exam: absent cervix and uterus, shortened vaginal canal
- Karyotype: 46,XY; Imaging: bilateral normal-appearing gonads, absent Müllerian structures
- Diagnosed with CAIS, advised to undergo risk-reducing gonadectomy
  Seven years later, the patient presented with abdominal pain and worsening distension
- Imaging: 12 cm complex pelvic mass in right adnexa and retroperitoneal lymphadenopathy
- Underwent bilateral orchiectomy and radical pelvic lymph node dissection
  Pathology: pure seminoma; tumor markers (β-hCG, AFP) were negative
- 13 lymph nodes removed; all negative, but imaging suggested persistent disease
- Pathologically Stage Ib, but treated as clinical Stage III due to imaging findings

Imaging

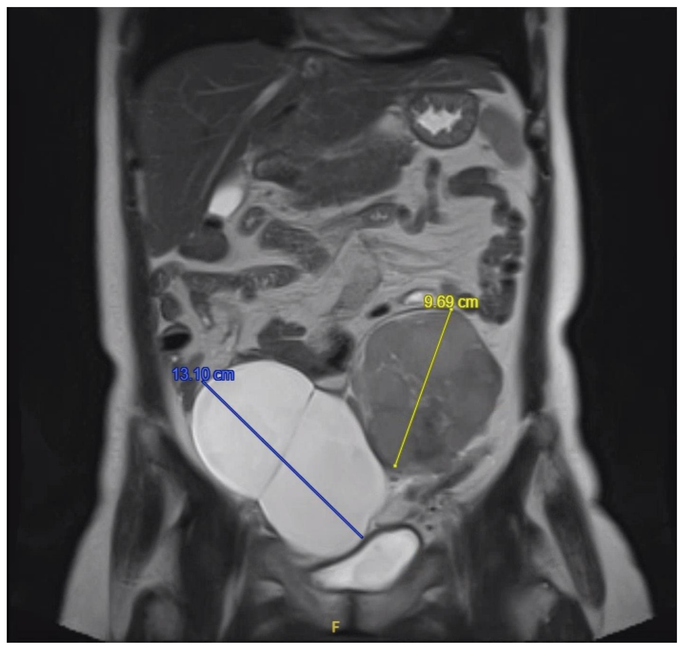

Figure 1: Pelvic MRI illustrating Complex Right Adnexal Mass

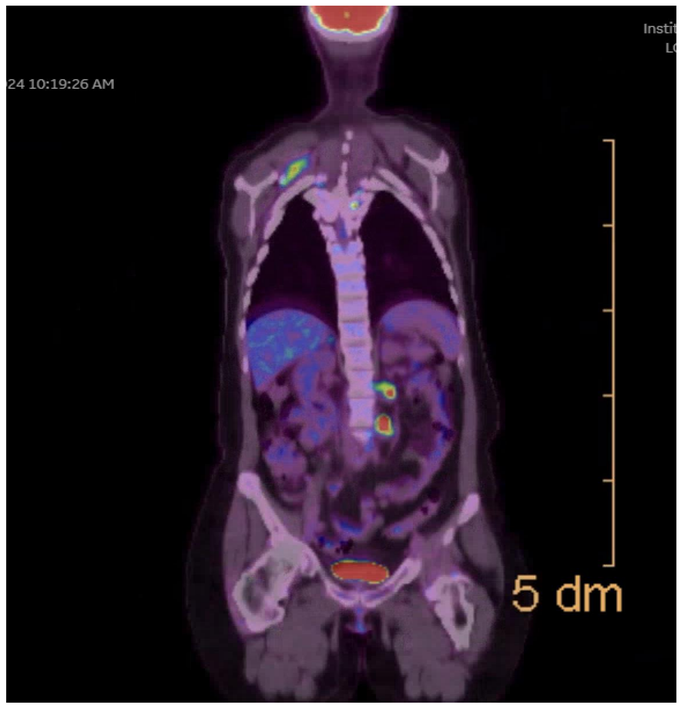

Figure 2: PET highlighting RP Nodes

Management

- Treated with 4 cycles of BEP chemotherapy (Bleomycin, Etoposide, Cisplatin)
- Complications: neutropenia and RSV infection
- Post-treatment PET CT: no evidence of active retroperitoneal or periaortic disease
- Biopsy of cervical node: no malignancy
- Patient transitioned to surveillance with stable imaging findings

Discussion

Management of **complete androgen insensitivity syndrome (CAIS)** requires balancing the **risk of gonadal malignancy** with the benefits of **natural hormone exposure**. While **early gonadectomy** reduces cancer risk, delaying removal until after puberty allows for **feminization** and **optimal bone development**.

Germ cell tumors in CAIS are most commonly **seminomas**, which generally have an **excellent prognosis** and respond well to standard treatments such as **BEP chemotherapy**. **Staging and surgical planning** can be challenging due to **atypical anatomy** and **ectopic gonads**, making a **multidisciplinary approach essential**.

Beyond oncologic management, CAIS carries significant **psychosocial implications,** including concerns about **identity, fertility, and body image,** highlighting the importance of **integrated psychological support**.

This case emphasizes the need for **personalized monitoring** and timely intervention to optimize both oncologic and quality-of-life outcomes.

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