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

Introduction: Androgen insensitivity syndrome (AIS) is a rare X-linked condition caused by mutations in the androgen receptor gene, impairing androgen response in individuals with a 46, XY karyotype. In complete AIS (CAIS), patients present with female external genitalia, absent internal female organs, and undescended testes. The risk of germ cell malignancy rises with age, from 1–2% prepuberty to 5–6% in adulthood, due to arrested germ cell development and ectopic testes exposed to elevated body temperature. Prophylactic gonadectomy reduces this risk, though timing is debated, as delaying surgery allows natural feminization and bone development through endogenous hormone exposure.

Case Report: A 34-year-old phenotypic female with primary amenorrhea presented for infertility evaluation. Exam revealed absent uterus and cervix with a shortened vaginal canal. Karyotype confirmed 46, XY. Imaging showed bilateral gonads with absent Müllerian structures. CAIS was diagnosed, and risk-reducing gonadectomy was recommended, but she deferred surgery and was lost to follow-up. Seven years later, she reported persistent abdominal pain and distension. Imaging revealed a 12 cm right adnexal mass with retroperitoneal lymphadenopathy. She underwent bilateral orchiectomy with radical pelvic lymph node dissection. Pathology confirmed pure seminoma. Thirteen lymph nodes were removed with no malignancy, though imaging suggested persistent retroperitoneal involvement. She was staged clinically as Stage III and treated with four cycles of BEP chemotherapy. Treatment was complicated by RSV infection and neutropenia requiring delays. Post-treatment PET CT showed no refractory disease; a persistent cervical node biopsy was benign, and she transitioned to surveillance.

Discussion: Management of CAIS requires balancing gonadectomy timing, malignancy risk, and psychosocial care. Delaying gonadectomy until after puberty allows natural feminization and bone development while mitigating cancer risk, with many clinicians recommending surgery shortly after puberty. Germ cell tumors are predominantly seminomas, which generally have an excellent prognosis and respond well to therapy. TNM staging can be challenging due to ectopic gonads and altered anatomy, making multidisciplinary surgical planning essential. Imaging aids in gonad localization and tumor assessment, though early neoplastic changes may be missed. BEP chemotherapy is standard for advanced disease, achieving cure rates above 95% but carries significant toxicity including pulmonary, renal, and neuropathic risks. Beyond medical management, CAIS carries profound psychosocial implications affecting identity, fertility, and body image. Multidisciplinary care including psychological support is crucial. This case underscores the importance of personalized monitoring strategies that balance cancer prevention with the benefits of endogenous hormone exposure.