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Primary Hypogonadism, Aazoospermia and Sertoli Cell Only Syndrome in a 46, XY Male with Yq Satellite Chromosome (Yqs) and Seronegative Primary Hypothyroidism

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ABSTRACT

Hypothyroidism and primary hypogonadism are prevalent endocrine disorders with diverse etiologies. Spermatogenesis is regulated by many Y chromosome specific genes. Most of these genes are located in a specific region known as the azoospermia factor (AZF) region in the long arm of the human Y chromosome. Satellited Y chromosome (Yqs) has been regarded as a benign familial variant of no clinical significance; however, considering patient's infertility, if the patient presents with oligospermia/azoospermia, Y chromosome microdeletion analysis for the AZF region should be performed. Patients with these prevalent endocrine disorders are often misdiagnosed resulting in long term treatment. Here we present a case with hypothyroidism and hypogonadism with Sertoli cell only and 46, XY Male with Yq Satellite Chromosome (Yqs).

Keywords

Hypothyroidism, Chromosomes, Sertoli Cell Only Syndrome.

Introduction

Hypothyroidism and primary hypogonadism are prevalent endocrine disorders with diverse etiologies [1,2]. Diagnoses are often obscured by long-term hormone replacement therapy and incomplete historical data. A satellite chromosome is an abnormality where extra material (heterochromatic blocks or satellites) is present, often in the Y chromosome long arm (Yq). The Y chromosome's long arm (Yq) harbors the azoospermia factor (AZF) regions which are critical for spermatogenesis. Structural abnormalities or microdeletions in Yq can be associated with Sertoli cell only syndrome and disrupt spermatogenesis.

This case describes a 48-year-old male with presumed chronic hypothyroidism and testosterone deficiency who underwent comprehensive re-evaluation after cessation of hormone therapies. Although the patient has both conditions of hypothyroidism and primary hypogonadism, the patient had no features of Addison's disease, type 1 diabetes, or other autoimmune disorders suspected of polyglandular autoimmune syndrome [3]. The case illustrates diagnostic pitfalls and the relevance of revisiting presumptive endocrine diagnoses with updated evaluations. It also illustrates

the potential association of Y-chromosomal anomalies with male primary hypogonadism, and azoospermia [4].

Methods

The patient discontinued long-standing levothyroxine (50 mcg daily) and testosterone injections (100 mg weekly) to assess baseline thyroid and gonadal function. Laboratory testing included serial thyroid function tests (TSH, free T4, free T3), thyroid antibodies (TPO-Ab, TRAb), pituitary hormones (LH, FSH), serum testosterone (total and free via equilibrium dialysis), inhibin B, prolactin, and metabolic panels. Imaging included thyroid ultrasound and testicular ultrasound [1,2,5]. Semen analysis was done. Cytogenetic analysis was performed to evaluate chromosomal abnormalities [4].

Results

Six weeks post-discontinuation of thyroid hormone, the patient demonstrated a markedly elevated TSH (17.05 U/L), normal free T4 (1.0 ng/dL), and persistently negative thyroid antibodies. Ultrasound revealed a relatively small homogeneous thyroid, supporting a diagnosis of antibody-negative thyroiditis, and primary hypothyroidism [6,7]. Levothyroxine was resumed at 100 mcg daily, with normalization of TSH thereafter.

Following testosterone cessation, progressive hypogonadism was documented with total testosterone (immunoassay) of 178 ng/dL (250-827), LH of 12.4 U/mL (1.5-9.3), FSH of 22.7 U/mL (1.4-12.8), and inhibin B of 38 pg/mL (47-308), confirming primary testicular failure and clinical picture of Sertoli cell only syndrome. A previous semen analysis showed azoospermia. Chromosome analysis revealed a 46, XY male with a Yq satellite chromosome (Yqs) (Figure 1). Scrotal ultrasound showed normal testicular morphology with a right epididymal cyst and otherwise unremarkable. The Yqs variant was interpreted as a benign structural anomaly [8,9]. Additional Y chromosome microdeletion analysis was unremarkable. Genetic counseling was recommended given the patient's azoospermia and clinical diagnosis of Sertoli cell-only syndrome (SCOS) [10,11]. The patient refused testicular biopsy.

Conclusion

This case underscores the importance of diagnostic reassessment in long-term hormone-treated patients and highlights two distinct but converging endocrinopathies: seronegative primary hypothyroidism, and primary hypogonadism with azoospermia and Sertoli cell only syndrome. Though a Yqs chromosomal variant was detected, microdeletion analysis was unremarkable in this case but has been associated with some patients with SCOS. The findings reinforce the utility of withholding hormone therapy to unmask underlying pathology, the diagnostic value of semen analysis, gonadotropin levels and inhibin B in male infertility, and the importance of follow-up genetic testing in suspected Y-linked spermatogenic failure. Seronegative primary hypothyroidism is often associated with longstanding or end stage Hashimoto's thyroiditis and can be a feature along with primary hypogonadism in some patients with polyglandular endocrinopathy. As stated previously, the patient had no characteristcs of Addison's disease, type 1 diabetes, or any other autoimmune disorders suspected of polyglandular autoimmune syndrome.

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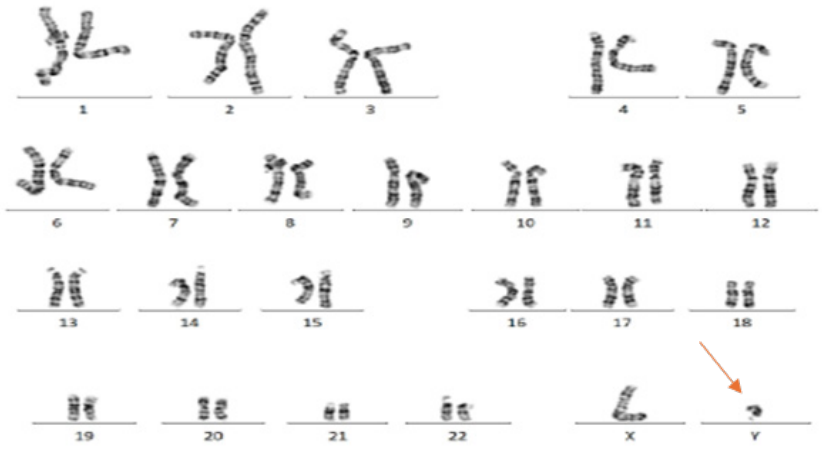

Figure 1: All examined cells in metaphase showed a Y chromosome with an extra satellited region at the end of its long arm (Yqs). Satellited Y chromosome (Yqs) has been regarded as a benign familial variant.

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