BRIEF COMMUNICATION

A 46,XX Male Adolescent Presenting with a Chief Complaint of Gynecomastia

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1. Introduction

Gynecomastia is a common condition characterized by the benign excessive development of breast tissue in boys and men. The condition is caused by excessive estrogen production that induces an increase in the estrogen-to-androgen ratio. 1

46,XX male syndrome is a rare disease characterized by male phenotype expression in an individual with XX sex chromosomes and no Y chromosome. The presence, absence, or mutation of the SRY gene can result in a diverse set of phenotypic expressions. The condition is typically diagnosed in late adolescence or adulthood, as it manifests in infertility and/or small testicular size. It is particularly difficult to differentiate pathological from physiological gynecomastia in adolescents. Here, we report the case of a 17-year-old boy with the 46,XX male syndrome who presented to our hospital with gynecomastia.

2. Case report

A pediatric patient aged 17 years and 6 months was admitted to our hospital with the chief complaint of gynecomastia that had been worsening for 1 year. The patient reported no other symptoms besides bilateral nipple pain. He reported no family history of gynecomastia, had not received any pharmacological treatment, and did not have testicular trauma. Physical examination revealed Tanner Stage IV symmetrical breast development and pubic hair. The patient experienced tenderness in the breasts, and bilateral palpable concentric firm masses were noted (Figure 1 (A), (B)). His external genitalia were symmetrical, and the volume of both testes was 6 mL.

We examined the patient’s hormone levels to elucidate the reason for the gynecomastia. We observed increased luteinizing hormone (LH; 22.6 mIU/mL; normal range: 0.4–7.0 mIU/mL), follicle-stimulating hormone (FSH; 40.8 mIU/mL; normal range: 2.6–11.0 mIU/mL), and estradiol (8.34 pg/mL; normal range: 1.0–3.6 pg/mL) levels. By contrast, the patient’s testosterone levels were lower than normal (2.87 ng/mL; normal range: 3.5–9.7 ng/mL). A gonadotropin-releasing hormone stimulation test revealed that the maximum serum LH and FSH levels were 74.8 mIU/mL and 59.3 mIU/mL, respectively. The serum levels of alpha-fetoprotein, beta-human chorionic gonadotropin, prolactin, cortisol, dehydroepiandrosterone, growth hormone, and adrenocorticotropic hormone and thyroid function test were all within the reference range. Hence, the patient was diagnosed with hypergonadotropic hypogonadism.

We then performed a blood chromosome analysis that revealed a 46,XX karyotype. Because of the relatively normal male genitalia with small testis in men with the 46,XX genotype, we conducted a multiplex polymerase
chain reaction and detected the SRY gene in a blood sample obtained from the patient (Figure 1 (C), (D)). Pelvic magnetic resonance imaging revealed that both scrotums contained testicles, although the testicles were small. No female reproductive organs were seen on imaging. The size of the patient’s penis was found to be normal.

After the final diagnosis of 46.XX SRY-positive male syndrome was made, the patient consistently received monthly testosterone treatments and underwent liposuction surgery for gynecomastia.

3. Discussion

Gynecomastia, which affects about 60% of all boys during adolescence between the ages of 13 years and 14 years, induces an increase in estradiol over testosterone production. By late adolescence, testosterone production begins to increase more significantly, allowing the adolescent to recover normal conditions. Consequently, gynecomastia is typically asymptomatic during late adolescence and spontaneously regresses.
In the present case, the patient presented with gynecomastia accompanied by hypergonadotropic hypogonadism. The patient’s hypogonadism was primarily caused by testicular failure that likely caused decreased testosterone synthesis and an increase in the testosterone-to-estradiol conversion, which ultimately caused gynecomastia.2

The 46,XX male syndrome was first reported by de la Chapelle et al4 in 1964. It is a rare condition only affecting one in 20,000–25,000 male newborns. The incidence rates do, however, differ by region.5 In general, cases of 46,XX male syndrome are categorized according to the presence of the SRY gene. In a previous study, 80% of 46,XX cases were SRY-positive.6 The morphology of the external genitalia and masculinization are often normal in 46,XX SRY-positive men. Before puberty, these individuals typically do not show any clinical symptoms; however, during late adolescence or adulthood, 46,XX SRY-positive men often present with infertility or small testicular size. A diagnosis of 46,XX male syndrome is then typically made by chromosomal analysis.7 The patient in the present case was also SRY-positive. His external genitalia were normal, although his testes were small. 46,XX SRY-negative males can be diagnosed based on abnormal virilization of their external genitalia after birth.

46,XX male syndrome can be treated with testosterone replacement that will induce normal adolescent development and promote psychological stability. Future counseling and treatment regarding any residual psychological issues and infertility are also deemed necessary. Furthermore, surgical corrections to correct any morphological abnormalities of the external genitalia should be performed.

In conclusion, a male adolescent who exhibits symptoms of gynecomastia and hypogonadism should not only undergo routine biochemical tests for thyroid, liver, and kidney function, but also evaluations of LH, FSH, testosterone, estradiol, and prolactin levels. When the patient is diagnosed with hypergonadotropic hypogonadism, chromosomal and SRY gene testing should also be performed to aid in the differential diagnosis.

Conflicts of interest

The authors declare no conflicts of interest.

References