Masked Klinefelter Syndrome

Dear Sir,

I recently encountered a patient who presented with gynecomastia. He was a 17-year-old male and was obese. He had consulted a couple of other doctors before presenting to our institute. The patient had consulted a general practitioner first, who attributed the "girlishness" of his chest to lack of male hormone and suggested that he will be better off with "male hormone" supplementation. Testosterone was given, and the patient presented to an endocrinologist 2 months later, ostensibly, due to worsening of gynecomastia. Hormonal evaluation was done which showed normal luteinizing hormone (LH) (6.1 IU/L), follicle-stimulating hormone (FSH) (8.1 IU/L), and testosterone (425 ng/dl). The doctor had attributed his intake of chicken to be the reason for his gynecomastia. The patient was asked to avoid chicken, was advised to work out, and was given lifestyle advice by the doctor. His testicular volume was 4 ml bilaterally, and he had a stretched penile length of 10 cm.

As the patient was not satisfied, he went to another doctor after 20 days who evaluated him again – by which time, the testosterone was still normal. He reassured the patient and

advised lifestyle modifications and referred the patient to a nutritionist. He also broached the option of surgical treatment. Over the course of a month, the patient lost 2 kg of weight. The patient's mother, meanwhile, had Googled his symptoms and suspected that if he could have more than just obesity and did a karyotype on her own. The results showed that he had 46 XXY and was diagnosed as Klinefelter syndrome (classic) by the patient's mother! Repeat hormonal testing showed increased LH (25.1 IU/L) and FSH (42.6 IU/L) levels.

This case illustrates an underrecognized pitfall in the diagnosis of hypergonadotropic hypogonadism. The reduction of gonadotropin levels after exogenous testosterone therapy is well known – both in hypergonadotropic hypogonadism and hypogonadotropic hypogonadism. In a study by Shimon *et al.*,[1] FSH level decreased from 43.1 ± 31.0 to 25.4 ± 30.8 IU/L and the LH level decreased from 22.2 ± 20.2 to 13.9 ± 21.5 IU/L after testosterone therapy in 11 patients with primary hypogonadism. Thus, treatment with exogenous testosterone can potentially reduce gonadotropin levels to near-normal range and obscure the diagnosis. Other reasons exist for normal or low gonadal hormones in patients with hypergonadotropic hypogonadism (both Klinefelter syndrome and Turner's syndrome) as follows:

- Coexisting organic pituitary disease[2]
- Functional hypopituitarism such as anorexia nervosa[3]
- Exhaustion of gonadotrophs in long-standing primary hypogonadism
- Coexisting uncontrolled diabetes – leading to pituitary microvasculature abnormalities.[4]

Prior treatment with testosterone is not a problem in health-care systems where the referral link points in one way from general practitioner to specialist – where a patient is less likely to receive testosterone supplementation before diagnosis. However, in the Indian setup, such safety valves are absent.

Hence, it is important for endocrinologists to ensure that the patient has not received testosterone elsewhere (or wait for an appropriate washout period) before hormonal evaluation to avoid missing the diagnosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to b`e reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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