



## Case Report

## Combination of Klinefelter syndrome and celiac disease: A case report



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## ABSTRACT

Klinefelter syndrome (KS) is a chromosomal abnormality characterised by a 47, XXY karyotype associated with hypogonadism and infertility. We present a case of a 20-year-old patient who applied to our clinic because of growth deficiency and was concurrently diagnosed with Klinefelter syndrome and celiac disease.

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## 1. Introduction

Klinefelter syndrome is the most common chromosomal aneuploidy affecting males, and its most common karyotype is 47, XXY. It results from the formation of a sperm or ovum with a supernumerary X chromosome and the regular number of autosomes during gametogenesis and its subsequent combination with a gamete containing a single sex chromosome at fertilisation [1]. This disease is characterised by hypogonadism, gynecomastia and azoospermia. Klinefelter syndrome has been reported in combination with alport syndrome, schizophrenia and similar psychotic disorders and acromegaly cases [2–5]. Some studies have also indicated that the occurrence rate of autoimmune disorders is increased in Klinefelter syndrome [6,7]. Celiac disease is a chronic disorder caused by a serious intolerance to the gluten in some foods. It is characterised by inflammation in the small intestine and possible malabsorption as a result of serious gluten intolerance. The most common symptoms are chronic diarrhea, abdominal bloating, pain and growth deficiency [8]. Patients are diagnosed with the presence of specific antibodies in the blood and concordant symptoms of the small intestinal mucosa. Some autoimmune diseases, such as type 1 diabetes mellitus, and a number of disorders, such as dermatitis herpetiformis, infertility, ataxia and epilepsy, often accompany celiac disease [9–11]. Additionally, celiac disease is more common in diseases such as Down syndrome and Turner syndrome [12–14].

## 2. Case presentation

A 20-year-old male patient applied to Erzurum Regional Training and Research Hospital because of growth deficiency. The patient had no additional complaints. System examination indicated a large amount

of bloodless mucus in the stool 4–5 times per day, 2–3 times per month. His family history neither included chronic diseases nor consanguineous marriages. The patient stated that he had been diagnosed with undescended testes in childhood.

The patient, who was examined because of growth deficiency, was 162 cm tall and weighed 43 kg. BMI was calculated as 16.3 kg/m<sup>2</sup>. Physical examination indicated that the patient had micropenis and microtestis and a slight amount of pilosity on the genital region, armpits and face. Other system examinations revealed no pathologies.

Laboratory analyses indicated mild anaemia (haemoglobin [Hb]: 12.4 g/dL, Ferritin: 12.12 ng/mL). Folate, Vitamin B12, thyroid peroxidase antibody (anti-TPO), TSH and FT4 levels were measured in the normal range. High levels of the hormones FSH and LH were determined FSH: 55.35 mIU/ml (Male N: 0.95–11.95), LH: 32.22 mIU/ml (Male N: 0.57–12.07). IgA level: 162 mg/dL, anti-transglutaminase IgA level: >200 RU/mL (N: <20) was reported high, indicative of celiac disease (Table 1).

Scrotal ultrasonography examination indicated that the right and left testicles measured 8 ml and 9 ml, respectively (N: 15–30 ml). Age determination by wrist graph was concordant with the age of 19. The patient had endoscopy and a biopsy of his duodenal mucosa was sent for pathologic examination in which eroded areas on the surface epithelium, villous atrophy on areas where the surface epithelium was protected, increased intraepithelial lymphocytes and a lamina propria infiltrate of mixed inflammatory cells were observed. These findings were reported as concordant with 'celiac disease Marsh IIIB'.

Genetic disease evaluation determined that secondary sex characteristics were undeveloped and hypergonadotropic hypogonadism was present. Chromosome analysis indicated 47, XXY chromosome structure.

The patient's clinical data, laboratory examinations and chromosome analysis and the pathological results of the duodenum biopsy were evaluated, and the patient was concurrently diagnosed with

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**Table 1**  
Results of laboratory examinations.

HGB	12.4 g/dl (N: 12.9–18.1)
HCT	40.84 (%) (N: 36–53.7)
MCV	81.39 fL (N: 78–100)
Ferritin	12.12 ng/mL (N: 21.8–274.6)
Folate	4.6 ng/mL (N: 3.1–20.5)
Vitamin B12	462 pg/mL (N: 187–883)
TSH	1.071 mu/mL (N: 0.35–4.94)
FT4	1.12 ng/dl (N: 0.7–1.48)
FSH	55.35 mU/ml (N: 0.95–11.95)
LH	32.22 mU/ml (N: 0.57–12.07)
Anti-TPO	0.11 U/ml (N: 0–5.61)
Total testosterone	16.38 nmol/mL (N: 4.94–32)
IgA (nephelometric)	162 mg/dL
Anti- Transglutaminase IgA	>200 RU/mL (N: <20)

Klinefelter syndrome and celiac disease. A gluten-free diet was recommended to the patient, and he was again referred to the medical genetics department for genetic counselling.

### 3. Discussion

Several publications suggest that the rate of occurrence of autoimmune diseases is increased in the presence of Klinefelter syndrome. However, this is still controversial. Patients with Klinefelter syndrome are considered at particular risk of developing diseases such as Addison's disease, type1 diabetes mellitus, multiple sclerosis, rheumatoid arthritis, Sjogren's syndrome and systemic lupus erythematosus (SLE) [6]. Certain genetic diseases, such as Turner syndrome and Down syndrome, are likely to accompany celiac disease. The frequency of combined Klinefelter syndrome and celiac disease seems uncertain. In addition, there are no studies in the literature that show the presence of these two diseases together.

SLE is an autoimmune disease that preferentially affects females. The reason for this is not yet known. It has been determined that the frequency of SLE in males with Klinefelter syndrome is in a similar range to that in females. Gene demethylation on the inactive X chromosome can possibly lead to this result [15]. Celiac disease has a greater impact on females, although it is not as notable as that of SLE. Consequently,

the risk of celiac disease is increased when Klinefelter syndrome is present.

In conclusion, a 20-year-old patient who applied to our clinic because of growth deficiency was concurrently diagnosed with Klinefelter syndrome and celiac disease after several examinations. There have been no studies on the presence of Klinefelter syndrome combined with celiac disease so far. This study recommends that celiac disease should be kept in mind with patients who have malabsorption, diarrhea and abdominal pain symptoms accompanying genetic disorders.

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