

OLGU SUNUMU

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**A KLİNEFELTER SYNDROME CASE WITH IRIS COLOBOMATA AND GLAUCOMA**

**İRİS KOLOBOMU VE GLOKOMUN EŞLİK ETTİĞİ BİR KLİNEFELTER SENDROMU OLGUSU**

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**ABSTRACT**

In this study A Klinefelter syndrome case with iris colobomata and glaucoma A 40 year old man was referred for bilateral open angle glaucoma and colobomata of the iris. His IOP's were regulated by bilateral trabeculectomy. The clinical findings of azoospermia, abdominal testes, mild mental retardation and high levels of FSH.

**Key words:** Klinefelter syndrome, iris colobomata, glaucoma.

**ÖZET**

Bu çalışmada iris kolobomu and glokomun eşlik ettiği 40 yaşında bir Klinefelter sendromlu olgu sunulmaktadır. Hasta bilateral açık açılı glokom ve iris kolobomlarıyla sevk edilmişti. Göz içi basıncı bilateral trabekülektomiyle regüle edildi. Klinik bulgular; azoospermi, abdominal testis, hafif mental gerilik, ve FSH yüksekliği idi.

**Anahtar kelimeler:** Klinefelter sendromu, iris kolobomu, glokom.

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## INTRODUCTION

Iris colobomas are caused by defective closure of the fetal fissure. Many genetic alterations may be associated with coloboma, however; associated abnormalities of the sex chromosomes are rare in the literature(1). We report a case of Klinefelter syndrome presenting with colobomas of the iris and primary open angle glaucoma.

## CASE REPORT

A 40 year old man was referred for bilateral open angle glaucoma and colobomata of the iris. On examination; corrected visual acuity with +1.0D lenses was 20/20 in both eyes. Intraocular pressures measured with Goldmann applanation tonometry were 24mmHg in the right eye and 28mmHg in the left eye with a prostoglandin analogue and a dorzolamide-timolol fixed combination. Slit lamp examination revealed an infero nasal iris coloboma and pulverulent cataract in both eyes. An open angle with debris of mesenchymal tissue was observed on gonioscopy. The optic nerve heads had cup/disc ratio of 0,7 (OD) and 0,8 (OS). Humphrey computed perimetry showed an inferior arcuate scotoma at the right eye. Superior and inferior arcuate scotomas were detected at the left eye. Trabeculectomy was performed on both eyes and postoperative IOP's remained well under 20mmHg.

Examination of his mother and his aunt revealed primary open angle glaucoma. His (13 year-old) nephew had bilateral mesenchymal debris on gonioscopy with no sign of glaucoma. Eyes of the other members of the family were normal.

### Systemic findings

A cutaneous angioma was present on the left side of his face. He had a mild mental retardation and his speech was slow. He couldn't continue further on his education after elementary school. He had an operation for bilateral nephrolithiasis when he was nine years old. On puberty; he had treatment for gynecomastia; however endocrine and genetic evaluation hadn't been performed.

On consultation with Urology azoospermia and abdominal testes were found. Thyroid and parathyroid functions as



Figure 1 Colobomata of the iris

well as total testosterone levels were normal. Blood FSH level was high. Genetic counseling disclosed a 47,XXY karyotype. Although he had a positive family history of glaucoma, genetic examination of glaucoma was unavailable.

## DISCUSSION

Klinefelter syndrome represents the most common human sex chromosomal abnormality. It is characterized by small firm testes, elevated gonadotropins and azoospermia. The classic form is together with the karyotype of 47,XXY. It is seen with a prevalence of one in 500 males. 47XXY males may present with a variety of subtle clinical signs that are age related. In infancy; hypospadias, small phallus, cryptorchidism and developmental delay may be seen. The school age child may present with language delay, and learning disabilities. The older child on adolescence may be discovered during on endocrine evaluation for delayed or incomplete pubertal development, gynecomastia and small testes. Adults are often evaluated for infertility or breast malignancy due to higher estradiol or testosterone levels. The incidence of diabetes mellitus, hypoparathyroidism and hypothyroidism systemic lupus erythematosus, Sjogren syndrome and rheumatoid arthritis is high. Osteoporosis occurs in %25 of the cases possibly due to the increased bone

resorption or hypogonadism. Diagnostic tests: Karyotype analysis of peripheral blood, elevated FSH, LH and estradiol and low to low-normal testosterone level and increased urinary gonadotrophins due to abnormal Leydig cell function(2). Most of the colobomas arise from inherited genetic, sporadic (mutational) genetic or chromosomal abnormalities during spermatogenesis and oogenesis and very few of them have their primary origin during embryogenesis.

The association of uveal coloboma and Klinefelter syndrome is rare and it has been reported previously in 1970 by Francois, Matten-Van Leuven and Gombault. After reviewing the incidence of uveal coloboma and Klinefelter syndrome as separate entities, they have concluded that the probability of the chance of association was in the region of one in six million and coloboma might occasionally be part of the phenotypic expression of Klinefelter syndrome(1).

The possible theories which might explain this association are:

1. The mother may be a carrier of the X linked gene for uveal coloboma and the patient may be homozygous for this gene.
2. The extra X chromosome may occasionally influence the genetic mechanism involved in the closure of the optic cleft.
3. The environmental influence on gametogenetic non-dysjunction may exert a mutagenetic effect on the genetic mechanism of the closure of the optic cup.

Another case of 17 year-old boy with bilateral iris and choroidal coloboma and Klinefelter syndrome was reported in 1976 by Hashmi and Karseras(3). They emphasized that the patient had suffered emotional trauma from the defective development of his gonads, and earlier diagnosis would remove much of the patient's concern.

Boettger et al described a case of Klinefelter syndrome with ocular and brain anomalies in 2004(4). The 5 year old patient had microphthalmos, colobomata of the iris, choroid and optic nerve head as well as brain anomalies. They noted that the child showed psychomotoric delay with a marked delay of speech development and magnetic resonance imaging of the brain showed multipl bilateral asimetric high

signal intensity foci in the subcortical and periventricular white matter.

Our case is 40 year old man referred for open angle glaucoma and iris colobomata. His IOP's were regulated by bilateral trabeculectomy. The clinical findings of azoospermia, abdominal testes, mild mental retardation and high levels of FSH made us think about genetic defect. Cytogenetic studies revealed a 47,XXY type. He was unaware of his genotype. The endocrine complications (diabetes mellitus, hypopara-thyroidism and hypothyroidism), and autoimmune diseases (Systemic lupus erythematosus, Sjogren syndrome and rheumatoid arthritis) associated with Klinefelter syndrome were investigated and no acquiring diseases were found. Brain MR and breast ultrasonography was normal. The patient was referred to endocrinology department for the treatment of osteoporosis. Genetic counseling was not available for glaucoma. The patient's mother and aunt had primary open angle glaucoma. It is possible that the extra X chromosome may also be a carrier of glaucoma as well as iris coloboma; however, we couldn't answer the question where the extra chromosome has been derived from: mother or father. This case report presenting Klinefelter syndrome with colobomata of the iris and open angle glaucoma is unique in the literature to our knowledge. The purpose of the paper is to provide ophthalmologists information about Klinefelter syndrome and its rare association with uveal coloboma. Being aware of the rare occurrence of these two entities may help early diagnosis and treatment of Klinefelter syndrome and improve the quality of life and the health of the patients with this disorder.

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