CSK SCIENTIFIC PRESS
Volume 1 | issue 2
Case Report
JOURNAL OF CLINICAL CASE STUDIES, REVIEWS AND REPORTS

# Klinefelter's syndrome with type 1 diabetes mellitus: A case report

**Riham Shoushan[1], Leys Ahmet[2], Nada Darwish[3], Mohammed Kamel Alhaj Saleh[4] and Maher Al-Hajjaj[5*]**

[1]*Pediatric specialist, Doha Health Care Group, Doha, Qatar.*

[2]*Medical student, Harran University, Sanliurfa, Turkey*

[3]*Medical graduate, Alexandria University, Faculty of Medicine, Alexandria, Egypt.*

[4]*Medical student, Al Andalus University for Medical Sciences, Tartous, Syria.*

[5]*Department of Surgery, University of Aleppo, Aleppo, Syria*

[*]**Corresponding author:** Maher Al-Hajjaj, Department of Surgery, University of Aleppo, Aleppo, Syria.

**Submitted:** 27 July 2023 **Accepted:** 31 July 2023 **Published:** 05 Aug 2023

***Citation:*** *Riham Shoushan, Leys Ahmet, Nada Darwish, Mohammed Kamel Alhaj Saleh & Maher Al-Hajjaj (2023). Klinefelter's syndrome with type 1 diabetes mellitus: A case report. J of Clin Case Stu, Reviews & Reports 2(1), 01-02.*

***Abstract***

*Type 1 diabetes mellitus (T1DM), once known as juvenile diabetes or insulin-dependent diabetes, is an autoimmune and chronic condition. T1DM patients may have some associated genetic disorders such as Down's syndrome, Turner's syndrome, or Klinefelter's syndrome (KS). We had a 13-year-old boy who was diagnosed with T1DM, who had been confirmed by absolute insulin deficiency and positive glutamic acid decarboxylase antibody (GAD). Full examination and laboratories showed Klinefelter's syndrome. We confirmed the diagnosis by a chromosomal analysis, which was 47 XXY. We started treatment with insulin injections. On the follow-up, our patient underwent testosterone replacement therapy.*

## Introduction

Klinefelter syndrome (KS) is the most frequent sex chromosome disorder of the male population, and the estimated prevalence of KS ranges from 1 in 500 to 1 in 1000 in males [1].

The defining feature of the syndrome, the supernumerary X chromosome, is the result of meiotic non-disjunction, which can occur in either parent during gametogenesis. More than one extra copy of the X chromosome may be present, although these variants are rarer, and mosaicism is also possible.

The concurrence of KS and autoimmune diseases such as type 1 diabetes mellitus (T1DM) is known [2].

Over the past 50 years, multiple studies have examined the prevalence of diabetes in men with KS. Most of the literature involves T2DM, which is significantly more common than type 1 diabetes (T1DM) in this patient population, as in the general population [3].

Here, we report a rare case of a patient with type 1 diabetes mellitus and Klinefelter syndrome.

## Case Presentation

A 13-year-old boy presented to our center complaining of polyuria, polydipsia, and weight loss two weeks ago. He has no brothers because his mother died in a car accident before. His parents are nonconsanguineous. There was no family history for diabetes mellitus or other chronic diseases. On admission, his vital signs were as follow: blood pressure 97/65 mmHg; heart rate 102 beats per minute; respiratory rate 31/ minute and revealing kussmaul breathing (deep and rapid breathing). He had acetone odor breathing.

On physical examination, his weight was 45 kg, height 169 cm and body mass index 15.75 kg/m2. His penile length was 8.3 cm. The volume of his right testis was 7 ml and the left was 9 ml.

Abdominal examination showed mild tenderness without rebound or guarding.
Other systems were normal.

Laboratory tests are shown in Table 1.
His blood glucose was 387 mg/dl, his blood cell count was 16000 /ml, hemoglobin was 10.3 mg/dl, hemoglobin A1c was 9.9 %.

A further test for glutamic acid decarboxylase antibody (GAD) was positive. His HLA genotypes were DRB1*03, DRB3, and DQB1*02. We reached the diagnosis of Diabetes mellitus type 1.

Furthermore, the total testosterone was 600 ng/dl (normal: 140-920 ng/dl) and the follicle-stimulating hormone level was 21.8 mlU/ml (0.8 -12 mlU/ml). According to clinical and laboratory findings, we performed chromosome analysis. The karyotype was 47 XXY and the diagnosis was Klinefelter's syndrome.

We started with insulin glargine therapy with 14 U and 4-6 U of insulin aspart per meal. This resulted in a good response in levels of glucose. In addition, testosterone therapy was planned for this patient at the follow-up.

## Discussion

An association between KS and diabetes has been reported in a number of studies. In 1969 Nielsen described an increased prevalence (39%) of a diabetic oral glucose tolerance test in 31 KS patients [4].

Some studies have reported that the positive detection of diabetes-related autoantibodies is much higher in KS patients than in healthy males (8.2% vs. 0.01%, respectively; p=0.016) [5].

Epidemiological studies have found that the morbidity and mortality of DM in KS are greater than threefold increased [6,7].

Other mechanisms, such as changes in body composition, inflammation status, socioeconomic factors, high triglyceride levels, fatty liver and acute pancreatitis, might also play important roles in the development of DM in KS patients [6-9].

The coexistence of insulin deficiency and insulin resistance in this KS patient made it difficult to obtain glycemic control. Some groups reported that testosterone replacement therapy (TRT) was beneficial for treating insulin resistance and dyslipidemia in T2DM [10].

KS is frequently believed to be associated with insulin resistance. Yesilova et al found a high prevalence (38.5%) of insulin resistance in Klinefelter's syndrome patients using hyperinsulinemic euglycemic clamp. Insulin resistance plays an important role in the onset of diabetes in KS. Plasma testosterone concentration was inversely related to insulin resistance in patients with Klinefelter syndrome. Hypogonadism in Klinefelter's syndrome may cause an unfavorable change in body composition, primarily through increased truncal fat and decreased muscle mass, leading to insulin resistance. Hyperinsulinemic euglycemic clamp test is the golden standard for evaluating insulin sensitivity [4].

We had a patient with no previous important medical history to have type 1 diabetes accompanied with KF syndrome. According to the literature, there are a few cases of these two diseases accompanied. Our patient underwent a strict program for monitoring his blood glucose levels. In his first follow-up visit, his blood glucose was 112 mg/dl. Then, we started with testosterone replacement therapy for his delay of puberty.

## Conclusion

We had a rare case of T1DM in a boy who had Klinefelter's syndrome. There are some cases reported by this company. Full examination and laboratory tests will be direct toward the diagnosis. Chromosomal analysis is confirmative.

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