

## Case Report

# Down-Klinefelter Syndrome with Multiple Dysmorphic Features: Case Report and Literature Review

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### Abstract

**Objective:** The Down-Klinefelter syndrome (48,XXY,+21) is a rare chromosome abnormality. The aim is to describe the clinical features and diagnosis of rare event. **Method:** Case report and literature review. **Case presentation:** A newborn boy was presented to our unit because of cyanosis for 13 hours after birth. He was born at 38 weeks' gestation without asphyxia via caesarean section due to oligohydramnios. He presented cyanosis about 30 minutes after birth and relieved after oxygen supplied. The boy was 50 cm in length, 2.7 kg in weight with head circumference of 33.5 cm. His respiratory rate was about 60 times every minute without rales in the lung. He had the characteristic features, including flat facial profile, flat nasal bridge, short thick neck, low-set ears, high palate, low hair line, simian crease, and slanted palpebral fissures. Hypotonia was noted as well. Chest X-ray showed exudative lesions in the lung. The Doppler echocardiography showed atrial septal defect with bidirectional shunt, enlarged right heart, and mild tricuspid regurgitation. Cytogenetic analysis confirmed a karyotype of 48,XXY,+21. **Conclusion:** Down-Klinefelter syndrome is a rare disease. Karyotyping should be performed for all patients with suspected Down syndrome anyway, even born from young parents.

### Key words

48,XXY,+21; Chromosomal abnormality; Congenital heart disease; Down-Klinefelter syndrome

### Introduction

Chromosomal abnormality is an important cause of congenital anomalies, psychiatric disorders, and mental retardation.<sup>1,2</sup> Abnormal number of the chromosomes, usually caused by parental nondisjunction during gametogenesis, may affect the autosomal chromosome and sex chromosome. Down syndrome (trisomy 21, DS) is the most common chromosomal disorder in human with an incidence of one in 770 live births. Among sex chromosomal disorders, Klinefelter syndrome (KS) is the

most common in males with a prevalence of one in 1000 males, while Turner syndrome is one of the most common chromosomal disorders in females. The occurrence of double aneuploidy in the same individual is very rare, with 3% to 7% of fetuses with cytogenetic abnormalities having double aneuploidy.<sup>3,4</sup> Double trisomy leading to trisomy and/or monosomy of two different chromosomes arises because of two meiotic non-disjunctional events. These aneuploidies could have the same or different parental origin. The incidence of both DS and KS in the same individual, named Down-Klinefelter syndrome with a karyotype of 48,XXY,+21, is about 0.4 to 0.9 per 10,000 male births in the general population,<sup>5,6</sup> and about 0.098% in live born individuals with DS.<sup>7</sup> Since the first case reported in 1959 by Ford et al,<sup>8</sup> only 65 cases have been reported in the literature.<sup>9-12</sup>

Herein, we reported a case of Down-Klinefelter syndrome with multiple dysmorphic features and reviewed associated literatures to emphasize the clinical features and diagnosis of this rare event.

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## Case Report

A 13-hour-old boy presented to our unit because of cyanosis for 13 hours. The boy was the gravida 3 and para 1 of 21-year-old mother and 23-year-old father. He was born at 38 weeks' gestation via caesarean section due to oligohydramnios. The Apgar score was 10 at the first minute, and his birth weight was 2.75 kg. He presented cyanosis in lips and face about 30 minutes after birth. It relieved after oxygen supplied and referred to our unit. His mother had 2 times abortion, and denied a history of alcohol, drugs, or any medications use during this pregnancy.

On physical examination, the boy was 50 cm in length, 2.7 kg in weight with head circumference of 33.5 cm. His respiratory rate was 60 times per minute without rales in the lung. No cyanosis was noted. He had the characteristic features, including flat facial profile, flat nasal bridge, short thick neck, low-set ears, high palate, low hair line, simian crease, and slanted palpebral fissures. Generalised hypotonia was noted. Anterior fontanelle was 2×2 cm. The external genitalia were immature male with palpable testis in the scrotum. The dermal, aural, ocular, nasal, thoracic, and cardiac exam were unremarkable.

Chest X-ray showed exudative lesions in the lung. The Doppler echocardiography showed atrial septal defect (ASD, secundum 0.6 cm) with bidirectional shunt, enlarged right heart, and mild tricuspid regurgitation. Laboratory tests of liver and kidney function were all normal. Cytogenetic study from two peripheral blood cultures revealed a complement of 48 chromosomes with two extra chromosomes in the G and C groups, respectively. Two X chromosomes were readily recognised on morphological criteria, and the other extra G group chromosome was confirmed to be a 21. The karyotype was 48,XXY,+21 (Figure 1). All metaphases were found to have the same pattern in 200 cells and no mosaicism was detected.

Neonatal wet lung, Down-Klinefelter syndrome, and congenital heart disease (CHD) were diagnosed. Unfortunately, further investigation for the parent-of-origin of the extra chromosomes was not performed. His parents refused further management on the third day of hospitalisation.

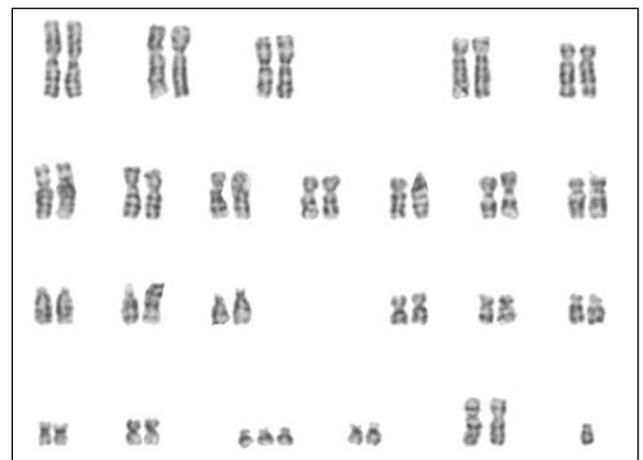
## Discussion

The abnormal number of chromosomes, aneuploidy, was caused by an error in meiosis. Although the origin of extra X and 21 chromosomes of our case was not analysed,

molecular analysis in previous studies showed that extra X chromosome may arise from an error in paternal meiosis I and the remaining in maternal meiosis I or II<sup>13</sup> while trisomy 21 were regarded a predominantly maternal origin although it can originate in either of the divisions in both parents.<sup>14</sup> This comparison of molecular analysis of double aneuploidy shows that these are similar to single aneuploidy and predominantly of maternal origin. However, because the involvement of a sex chromosome non-disjunction, which is frequently of paternal origin, it is possible that other mechanisms such as independent non-disjunctions may play a role in the aetiology of these types of double aneuploidy.

Abnormal separation of chromosomes may occur in older individuals because of dysfunction of structures related to chromosome separation, such as the spindle apparatus and kinetochore.<sup>7,13,15</sup> However, we noted that the parents of the case were both very young. It has also reported that infants with Down-Klinefelter syndrome were born to teenage mother.<sup>10</sup> Hence, it is also required to pay attention to this rare event in young parents. Prenatal triple screen and sonographic examination may be helpful for early diagnosis.<sup>9,16,17</sup>

It was reported that the DS phenotype often predominates in early life period of patients with Down-Klinefelter syndrome. The typical clinical features of DS included clinical facial anomalies (e.g. flat facial profile, flat nasal bridge, large protruding tongue, and low-set ears), brachycephaly, short thick neck, high palate, low hair line, simian crease, slanted palpebral fissures, omphalocele, and clinodactyly. Also, congenital cardiac disease is common



**Figure 1** Cytogenetic investigation shows double aneuploidy of 48,XXY,+21.

in patients with DS, occurring in 40% to 50% of patients while KS may occasionally suffer from mitral valve prolapse. Moreover, Freeman et al<sup>18</sup> reported that the incidence of CHD was 44% in 227 patients with DS, of which 45% were atrioventricular, 35% ventricular and 8% with an isolated atrial septal defect. According to the literatures, the incidence of congenital heart disease in Down-Klinefelter syndrome was relatively lower than that of DS patients. Our patient presented characteristic DS features with atrial septal defect. It is notable that our patient had caesarean section due to amniotic fluid reduction. Whether amniotic fluid reduction is associated with this chromosome abnormality is still unclear.

Moreover, our patient showed no tall height, genital hypoplasia or other abnormalities associated with KS till now. It was reported that the characteristics of KS may develop as the child ages, most not apparent until the post-pubertal stage.<sup>19,20</sup>

In conclusion, Down-Klinefelter syndrome is a rare disease. Karyotyping should be performed for all patients with suspected Down syndrome anyway, even born from young parents.

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## Conflict of Interest

The authors declare that they have no conflict of interest.

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