

## Research Article

Zong-Yu Miao<sup>#</sup>, Shi-Feng Chen<sup>#</sup>, Hong Wu, Xiao-Yan Liu, Hui-Yuan Shao\*

# Analysis of genetic characteristics of 436 children with dysplasia and detailed analysis of rare karyotype

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**Abstract:** Chromosomal abnormality is one of the important causes of dysplasia in children. However, due to regional and ethnic differences, the reported rates of chromosomal abnormalities in patients with dysplasia vary greatly. Moreover, the clinical manifestations in children with rare chromosomal diseases were heterogeneous. So, we retrospectively analyzed the karyotype results of 436 children with dysplasia and conducted a detailed analysis of rare chromosomal diseases. The results showed that chromosomal abnormalities were present in 181 of 436 cases. Intellectual disability, dysmorphology, congenital malformations, the disorder of sexual development, and short stature were the main five clinical symptoms in children with chromosomal abnormalities. Moreover, 136 cases of Trisomy 21 (Tri21) were detected, of which 130 were standard Tri21, 5 were robertsonian Tri21, and 1 was chimera type. In addition, 16 cases of rare abnormal karyotype, including complex Tri21, complex Turner syndrome, 4p-syndrome, 18q-syndrome, and 5p-syndrome, were also detected. In summary, chromosome abnormality is one of the important causes of dysplasia in children. Furthermore, prenatal screening and diagnosis could play a great significance in preventing dysplasia in children. In addition, the retrospective analysis of rare cases is valuable for clinical diagnosis and risk assessment of recurrence.

# These authors contributed equally to this work.

\* **Corresponding author: Hui-Yuan Shao**, Medical Laboratory, Yantai Yu Huang Ding Hospital, 20#, The East Road of Yu Huang Ding, Zhifu District, Yantai, 264000, Shandong, China, tel: +86 0535-6691999-83189, e-mail: shaohuiyuan313@163.com

**Zong-Yu Miao, Shi-Feng Chen, Hong Wu, Xiao-Yan Liu:** Medical Laboratory, Yantai Yu Huang Ding Hospital, 20#, The East Road of Yu Huang Ding, Zhifu District, Yantai, 264000, Shandong, China

**Keywords:** dysplasia, trisomy 21, 4q-syndrome, monomer 9p, 18q-syndrome

## 1 Introduction

Dysplasia in children is increasingly becoming a prominent public health and social problem. Dysplasia in children affects children's health and quality of life and the healthy and sustainable development of society. So, reducing congenital disabilities has great social significance. Therefore, it is necessary to delve into the causes of dysplasia in children.

Congenital heart disease (CHD) is one of the most common dysplasias in children. The incidence of CHD in neonates is 8–9/1,000, and nearly 1.35 million CHD neonates are born every year in the world [1]. Chromosomal causes of CHD include chromosome aneuploidies, such as Trisomy 21 (Tri21). Chromosomal aneuploidies represent 12.5% of CHD causes [2]. In addition, Tri21 syndrome, a common chromosomal disorder, is the most common cause of severe mental retardation, special facial features, and abnormal bone development in children.

Disorder of sexual development (DSD) and short stature are also the most common dysplasia symptoms in children. Sex chromosome abnormality is one of the most common causes of DSD and short stature. Common sex chromosomal disorders include Klinefelter syndrome (1/1,000–1/2,000 in male newborns), Turner syndrome (TS, approximately 1/5,000 in newborn girls), XYY syndrome (1/900 in males), and XXX syndrome (1/1,000 in newborn girls). Patients with sex chromosome diseases are often accompanied by gonadal dysplasia, secondary sexual signs dysplasia, fertility disorders, mild mental abnormalities, mental deficiencies, and other symptoms. In addition, children with TS often have short stature. Children with severe short stature are vulnerable to diverse developmental, social, and educational problems [3].

Therefore, the abnormality of the sex chromosome is one of the important causes of dysplasia in children.

There is a significant evidence in the literature that the chromosome partial monomer or trisomy can lead to severe dysplasia in children. The clinical examination of the patients with structurally abnormal chromosome 15 revealed a series of clinical symptoms, such as intellectual disability, CHD, severe growth retardation, hypertelorism, microcephalus, dysmorphology, and multiple sclerosis hyperpigmented or café-au-lait spots, short stature, and clinodactyly [4–7]. The common clinical features of the patients with partial trisomy of chromosome 8 included developmental delay, intellectual disability, mental retardation, severe hypotonia, hypospadias, skeletal anomalies, renal dysplasia, attention-deficit hyperactivity disorder, atypical facial appearance, and congenital hypoplasia of the tongue [8–13]. The short arm monosomy of chromosome 9 may present developmental delay, hypotonia, trigonocephaly, psychomotor developmental delay, learning difficulties, trigonocephaly, facial dysmorphism, and genital abnormalities [14,15].

Thus, the chromosomal abnormality is one of the important causes of dysplasia in children, which seriously endangers children's physical and mental health and brings heavy spiritual and economic burdens to families and society. However, due to regional and ethnic differences, the reported rates of chromosomal abnormalities in patients with dysplasia vary greatly. So, we retrospectively analyzed the karyotype results of 436 children with dysplasia and conducted a detailed analysis of rare cases to clarify the chromosomal abnormality rate and distribution of abnormal chromosomes in local children with dysplasia and provide a theoretical basis for clinical diagnosis and prenatal diagnosis, and assess the risk of recurrence.

## 2 Patients and methods

### 2.1 Patients

Four hundred and thirty-six cases (359 male and 77 female) in children with clinically diagnosed dysplasia in the affiliated Yantai Yu Huang Ding Hospital of Qingdao University Medical College from January 1, 2012 to October 31, 2019, were recruited. The age group of the participants ranged from 1 day to 16 years. Patients with dysplasia caused by autoimmune, chemo- or radio-therapy, infectious, and iatrogenic injury were excluded. The clinical

data of confirmed cases were retrospectively collected and analyzed.

**Informed consent:** Informed consent has been obtained from all individuals included in this study.

**Ethical approval:** The research related to human use has been complied with all the relevant national regulations, institutional policies, and in accordance with the tenets of the Helsinki Declaration and has been approved by the Ethical Committee of Yantai Yu Huang Ding Hospital.

### 2.2 G banding

Standard chromosomal analyses with G banding were performed on routinely cultured peripheral blood lymphocytes [16]. Thirty metaphases per patient were counted, and a minimum of five metaphases were analyzed. For the chimeric case, at least 100 metaphases were counted. Chromosome polymorphisms, such as pericentric inversion of chromosome 9, centromeric heterochromatin variants, and satellite variants, were classified as normal. The karyotypic reports were based on the International System for Human Cytogenetic Nomenclature.

## 3 Results

Chromosomal abnormalities were detected in 181 of 436 cases. The abnormal rate was 41.51%. Among them were 153 cases of autosomal abnormality (84.53%, 153/181, Table 1) and 28 cases of a sex chromosome abnormality (15.47%, 28/181, Table 2). The main clinical symptoms of 181 children with chromosomal abnormalities were intellectual disability (80.66%, 146/181), dysmorphology (71.82%, 130/181), congenital malformations (22.10%, 40/181), DSD (12.15%, 22/181), and short stature (8.29%, 15/181).

One hundred and thirty-six cases of Tri21 were detected (31.19%, 136/436), including 89 male and 47 female, with a ratio of 1.89:1. Among them, 130 cases were standard Tri21 (95.59%, 130/136), 5 cases were Robertsonian Tri21 (3.79%, 5/132) and 1 case was a chimeric type (0.74%, 1/136).

Twenty-eight cases of sex chromosome abnormalities were detected, among which 20 cases were TS (7 cases were 45,X, 13 cases were 45,X mosaic), 5 cases were 46,X,i(X)(q10), 2 cases were sexual reversal, and 1 case was 46,X, idic(X;X)(q21.3;q11.1).

**Table 1:** Distribution of autosomal abnormalities in children with dysplasia

| Classification                | Chromosome karyotypes  | Number of cases | Constituent ratio (%) | Abnormality rate (%) |
|-------------------------------|--|-----------------|-----------------------|----------------------|
| <b>Numerical abnormality</b>  |  | <b>132</b>      | <b>86.27</b>          | <b>30.27</b>         |
|                               | 47,XX,+21  | 40              | 26.14                 | 9.17                 |
|                               | 47,XY,+21  | 86              | 56.21                 | 19.72                |
|                               | 47,XX,+21[12]/46,XX[177]   | 1               | 0.65                  | 0.23                 |
|                               | 47,XY,+21,inv(9)(p11q12)   | 1               | 0.65                  | 0.23                 |
|                               | 47,XY,+21,13pstkst   | 1               | 0.65                  | 0.23                 |
|                               | 47,XX,+21,inv(9)(p11q13)   | 1               | 0.65                  | 0.23                 |
|                               | 47,X,Yqs,+21   | 1               | 0.65                  | 0.23                 |
|                               | 47,XX,+mar[74]/46,XX[26]   | 1               | 0.65                  | 0.23                 |
| <b>Structural abnormality</b> |  | <b>21</b>       | <b>13.73</b>          | <b>4.82</b>          |
|                               | 46,XX,der(13;14)(q10;q10),+21                                    | 1               | 0.65                  | 0.23                 |
|                               | 46,XY,der(14;21)(q10;q10),+21                                    | 2               | 1.31                  | 0.46                 |
|                               | 46,XX,der(21;21)(q10;q10),<br>t(1;12)(q43;p12.1),inv(15)(q13q24) | 1               | 0.65                  | 0.23                 |
|                               | 46,XX,der(21;21)(q10;q10)  | 1               | 0.65                  | 0.23                 |
|                               | 46,XY,del(4)(q33)  | 1               | 0.65                  | 0.23                 |
|                               | 46,XY,del(5)(p14)  | 1               | 0.65                  | 0.23                 |
|                               | 46,XY,del(5)(p14.3)  | 1               | 0.65                  | 0.23                 |
|                               | 46,XX,del(13)(q31)   | 1               | 0.65                  | 0.23                 |
|                               | 46,XX,del(8)(p23.1)  | 1               | 0.65                  | 0.23                 |
|                               | 46,XX,add(16)(q24)   | 1               | 0.65                  | 0.23                 |
|                               | 46,XY,r(9)(p24q34)   | 1               | 0.65                  | 0.23                 |
|                               | 46,XY,der(9)t(2;9)(p25;p22)mat                                   | 1               | 0.65                  | 0.23                 |
|                               | 46,XY,der(9)t(7;9)(p15;p22)pat                                   | 1               | 0.65                  | 0.23                 |
|                               | 45,XX,der(15;21)(q10;q10)mat,del(18)(q21)                        | 1               | 0.65                  | 0.23                 |
|                               | 46,XX,der(3)del(3)(p21.3p23)t(2;3)<br>(q11.2;p23)                | 1               | 0.65                  | 0.23                 |
|                               | 46,XX,t(9;15)(p24;q13)   | 1               | 0.65                  | 0.23                 |
|                               | 46,XX,t(9;16)(q13;q22)   | 1               | 0.65                  | 0.23                 |
|                               | 46,XX,t(2;8)(q13;q23)  | 1               | 0.65                  | 0.23                 |
|                               | 46,XX,t(1;3)(p22.1;q27)  | 1               | 0.65                  | 0.23                 |
|                               | 46,XX,inv(12)(p12.2q15)  | 1               | 0.65                  | 0.23                 |
| <b>Combination</b>            |  | <b>153</b>      | <b>100</b>            | <b>35.09</b>         |

Sixteen cases of rare abnormal karyotype were detected, including complex Tri21 (Figure 1), complex TS (Figures 2–4), partial monomer and partial trisomy (Figures 5), 4p-syndrome (Figure 6), 18q-syndrome (Figure 7), and 5p-syndrome.

## 4 Discussion

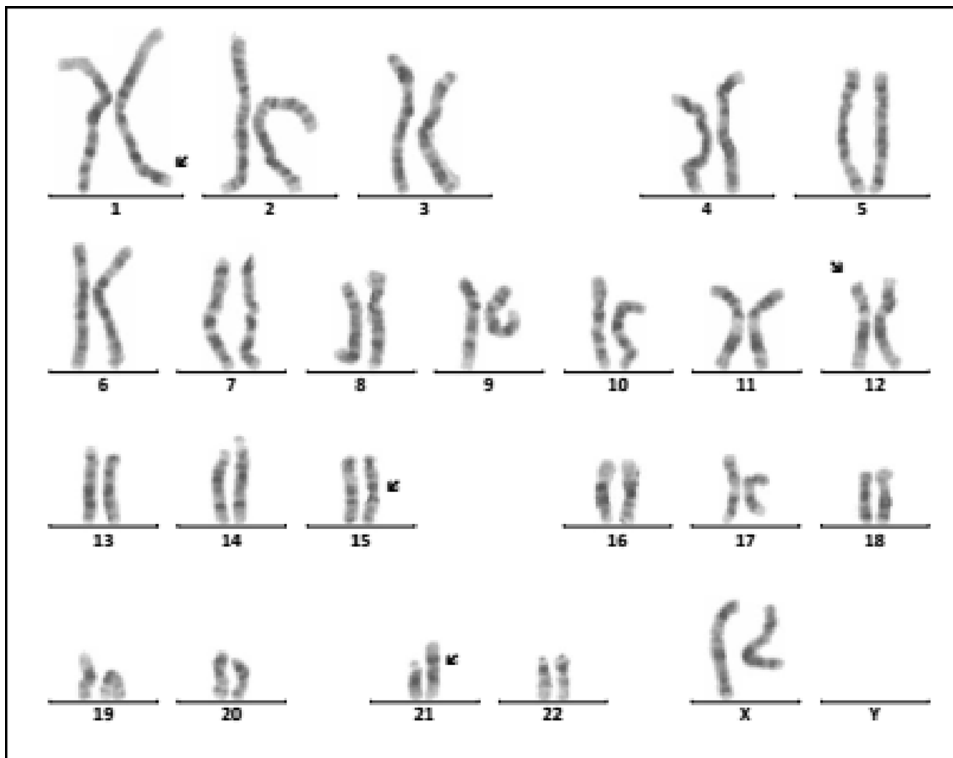
Chromosomal diseases are often associated with growth retardation, mental retardation, and multiple malformations of organs, which are congenital diseases caused by chromosome number or structural abnormalities. In our study, 181 cases with abnormal karyotype were detected, and the abnormal rate was 41.51% (181/436), which

indicated that chromosomal abnormalities were one of the important causes in children with dysplasia.

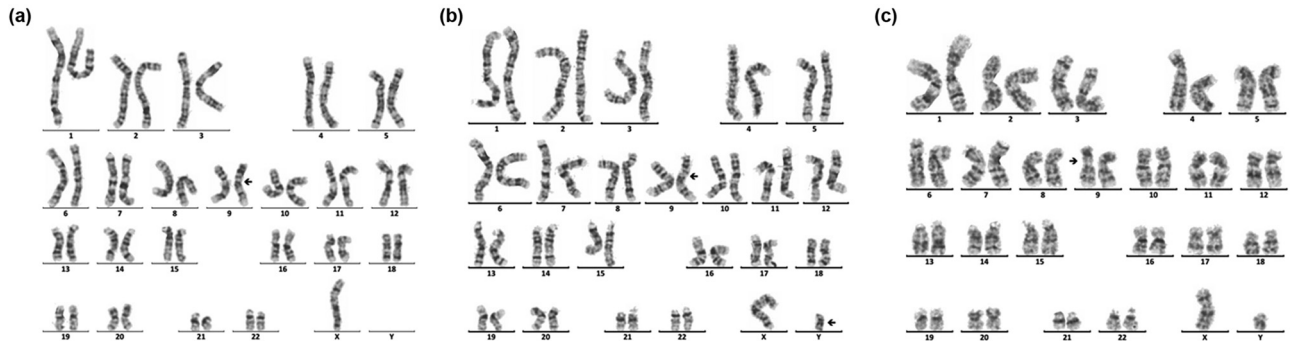
Intellectual disability (80.66%, 146/181) and dysmorphology (71.82%, 130/181) are the main clinical symptoms of 181 children with chromosomal abnormalities. As known, Tri21 is the most common chromosomal disorder, which implicated with intellectual disability and dysmorphology. The prevalence of Tri21 ranges from 1/700 to 1/2,000 in different ethnic populations investigated [17]. The cause of Tri21 is related to a variety of factors, such as increased reproductive age in women (>35 years old), degeneration of ovarian function, and genetic susceptibility [18,19]. In our study, 136 cases of Tri21 were detected (31.19%, 136/436), including 89 male and 47 female (1.89:1, 89/47). Among them, 130 cases were standard Tri21 (95.59%, 130/136), 5 cases were

**Table 2:** Distribution of sexual chromosomal abnormalities in children with dysplasia

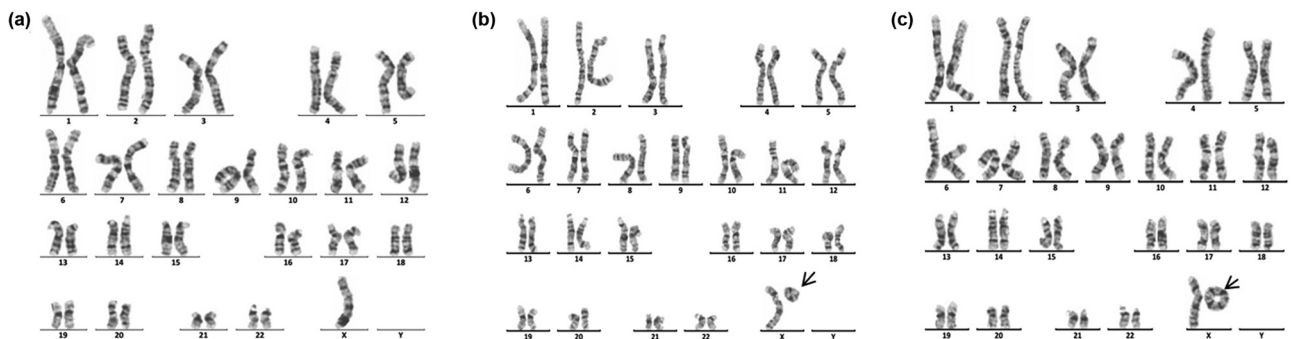
| Classification                  | Chromosome karyotypes  | Number of cases | Constituent ratio (%) | Abnormality rate (%) |
|---------------------------------|--|-----------------|-----------------------|----------------------|
| <b>Numerical abnormality</b>    |  | <b>10</b>       | <b>35.71</b>          | <b>2.29</b>          |
|                                 | 45,X   | 7               | 25.00                 | 1.61                 |
|                                 | 45,X[73]/47,XXX[27]  | 1               | 3.57                  | 0.23                 |
|                                 | 45,X[78]/47,XXX[22]  | 1               | 3.57                  | 0.23                 |
|                                 | 45,X[90]/46,XX[6]  | 1               | 3.57                  | 0.23                 |
| <b>Structural abnormality</b>   |  | <b>16</b>       | <b>57.15</b>          | <b>3.67</b>          |
|                                 | 46,X,i(X)(q10)   | 5               | 17.87                 | 1.15                 |
|                                 | 45,X[91]/46,X,i(X)(q10)[9]   | 1               | 3.57                  | 0.23                 |
|                                 | 46,X,i(X)(q10)[89]/45,X[11]  | 1               | 3.57                  | 0.23                 |
|                                 | 45,X[61]/46,X,i(X)(p11.3)[39]  | 1               | 3.57                  | 0.23                 |
|                                 | 46,X, idic(Y)(q11.22)[94]/45,X[6]  | 1               | 3.57                  | 0.23                 |
|                                 | 45,X, inv(9)(p11q13)[72]/46,X, dic(Y)(q11.23), inv(9)(p11q13)[10]/46,XY, inv(9)(p11q13)[4] | 1               | 3.57                  | 0.23                 |
|                                 | 46,X, idic(Y)(q11.23)[44]/45,X[56]   | 1               | 3.57                  | 0.23                 |
|                                 | 45,X[120]/46,X,r(X)(p22.2q22.2)[12]/46,X,r dup(X)(p22.2q22.2)[4]                           | 1               | 3.57                  | 0.23                 |
|                                 | 45,X[80]/46,X, idic(X)(p11.3)[20]  | 1               | 3.57                  | 0.23                 |
|                                 | 46,X, idic(X)(p11.2)[92]/45,X[9]/47,X, idic(X)(p11.2), idic(X)(p11.2)[5]                   | 1               | 3.57                  | 0.23                 |
|                                 | 46,X, idic(X)(p11.2)[90]/45,X[10]  | 1               | 3.57                  | 0.23                 |
|                                 | 46,X, idic(X;X)(q21.3;q11.1)   | 1               | 3.57                  | 0.23                 |
|                                 | 46,XX (male)   | 2               | 7.14                  | 0.46                 |
| <b>Sex reversal combination</b> |  | <b>28</b>       | <b>100</b>            | <b>6.42</b>          |



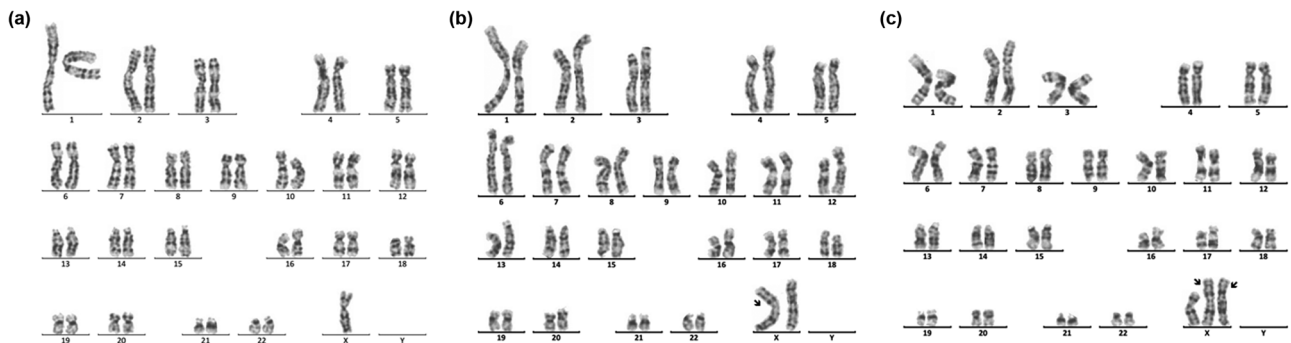
**Figure 1:** Karyotype of 46,XX, der(21;21)(q10;q10),t(1;12)(q43;p12.1),inv(15)(q13q24). The arrows show abnormal chromosomes.



**Figure 2:** Karyotype of 45,X,inv(9)(p11q13)[72]/46,X,dic(Y)(q11.23),inv(9)(p11q13)[10]/46,XY,inv(9)(p11q13)[4]. The arrows show abnormal chromosomes. (a) 45,X,inv(9)(p11q13). (b) 46,X,dic(Y)(q11.23), inv(9)(p11q13). (c) 46,XY,inv(9)(p11q13).



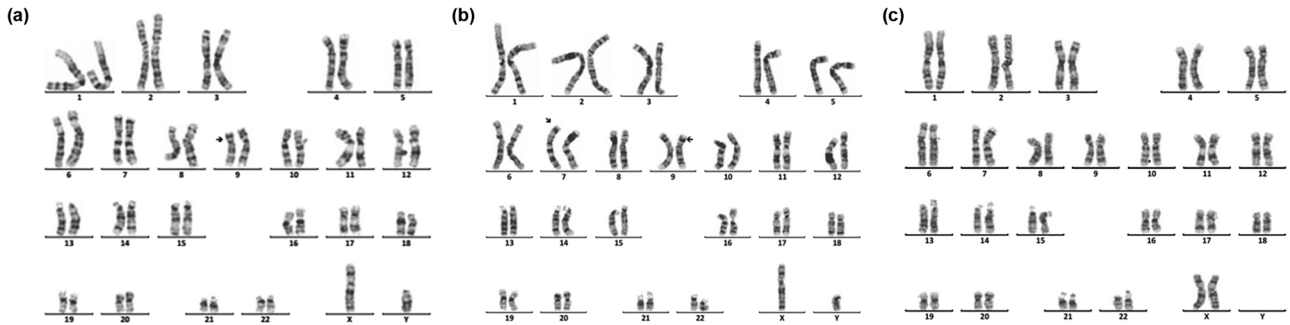
**Figure 3:** Karyotype of 45,X[120]/46,X,r(X)(p22.2q22.2)[12]/46,X,rdup(X)(p22.2q22.2)[4]. The arrows show abnormal chromosomes. (a) 45,X. (b) 46,X,r(X)(p22.2q22.2). (c) 46,X,rdup(X)(p22.2q22.2).



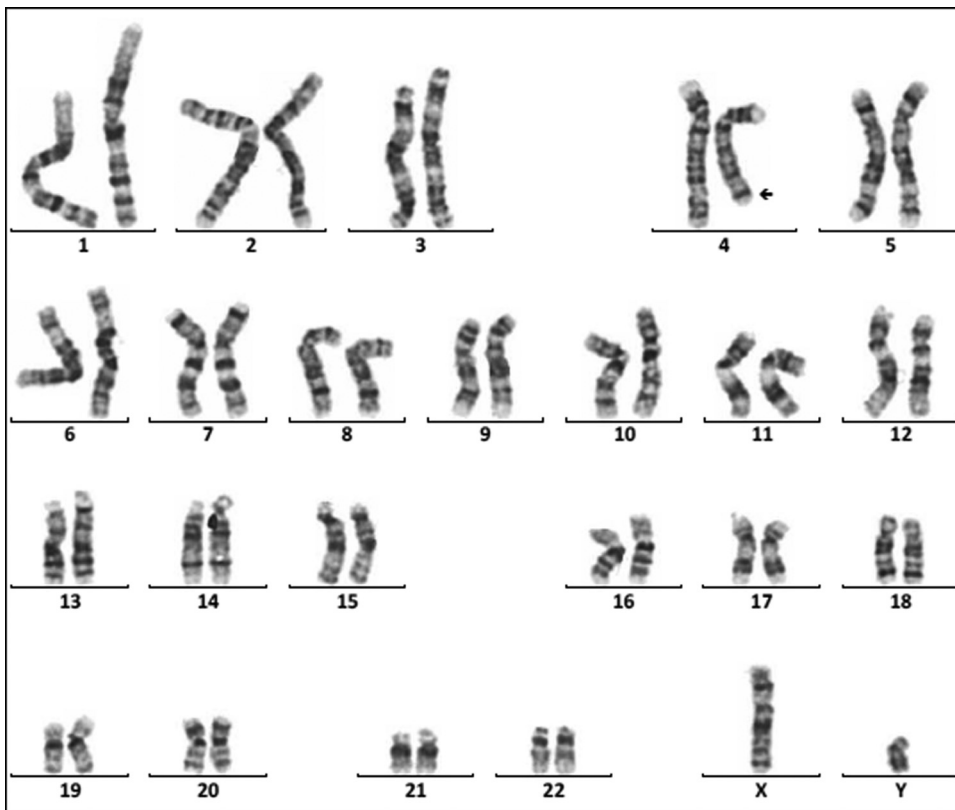
**Figure 4:** Karyotype of 46,X,idic(X)(p11.2)[92]/45,X[9]/47,X,idic(X)(p11.2),idic(X)(p11.2)[5]. The arrows show abnormal chromosomes. (a) 45,X. (b) 46,X,idic(X)(p11.2). (c) 47,X,idic(X)(p11.2),idic(X)(p11.2).

Robertson translocation Tri21 (3.79%, 5/132), and 1 case was a chimerical type (0.74%, 1/136), which is consistent with previous studies [20–22]. In 136 cases of Tri21, about two-thirds of pregnant women did not receive maternal serum screening for DS, and 16 pregnant women's results of maternal serum screening for DS were high risk, but they did not receive a prenatal diagnosis. Therefore, enhancing people's awareness of

the importance of prenatal screening and genetic counseling in eugenics may be an important means of reducing birth in children with Tri21. In addition, one case with 46,XX,der(21;21)(q10;q10),t(1;12)(q43;p12.1), inv(15)(q13q24) (Figure 1), which is a rare complex Tri21 karyotype, was detected. So, this case is especially helpful to supplement the karyotype diversity of patients with Tri21.



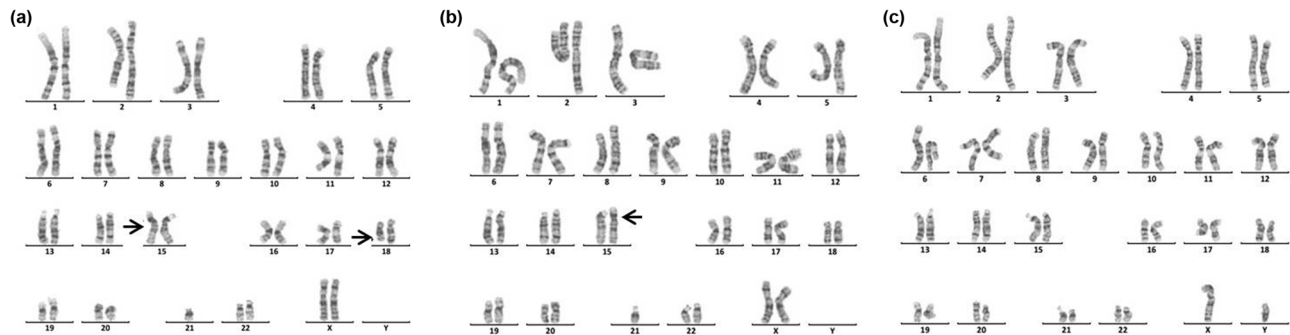
**Figure 5:** Karyotype of 46,XY,der(9)t(7;9)(p15;p22)pat. The arrows show abnormal chromosomes. (a) The karyotype of the patient. (b) The karyotype of the patient’s father. (c) The karyotype of the patient’s mother.



**Figure 6:** Karyotype of 46,XY,del(4)(q33). The arrows show abnormal chromosomes.

SDS and short stature are the two other major clinical symptoms of 181 children with chromosomal abnormalities. As known, chromosomal abnormalities are one of the important causes of gonadal dysgenesis and physical retardation. In this study, 28 cases of sex chromosome abnormalities were detected, among which 20 cases were TS, and 5 cases were 46,X,i(X)(q10). The main manifestations of TS patients were immature uterus or no uterus, streak ovary or no ovary, primary amenorrhea, breast dysplasia, and short stature, and the main clinical symptoms

of the patients with 46,X,i(X)(q10) were short stature and primary amenorrhea. These results suggested the necessity of two intact X chromosomes in the normal growth and development of a female. A single X chromosome in females randomly becomes inactive, but not all genes on which are transcriptionally silenced. Still, 15–20% of genes on inactive X chromosome remain operative and escape from X inactivation [23]. Moreover, normal female development is supported by a double dose of several specific genes on the X chromosome, such as the short stature



**Figure 7:** Karyotype of 45,XX,der(15;21)(q10;q10)mat,del(18)(q21). The arrows show abnormal chromosomes. (a) The karyotype of the patient. (b) The karyotype of the patient's mother. (c) The karyotype of the patient's father.

homeobox (SHOX) gene, which is located at the Xp22, determines the height [24]. So, the haploinsufficiency of SHOX may be the main cause of short stature in patients. Dymorphology and short stature caused by an X chromosome abnormality are more sensitive to estrogen before 12 years old. So, these kinds of patients need to receive treatment in the early stage. However, in this study, the average age of the patient with TS was 11.94, greater than 6.6, which was reported by Massa et al. [25]. Consequently, the growth and development of children should be highly concerned during the preschool period. In addition, another three rare complex karyotypes were detected. One karyotype was 45,X,inv(9)(p11q13)[72]/46,X,dic(Y)(q11.23),inv(9)(p11q13)[10]/46,XY,inv(9)(p11q13)[4] (Figure 2), the other was 45,X[120]/46,X,r(X)(p22.2q22.2)[12]/46,X,rdup(X)(p22.2q22.2)[4] (Figure 3), and the third was 46,X,idic(X)(p11.2)[92]/45,X[9]/47,X,idic(X)(p11.2),idic(X)(p11.2)[5] (Figure 4).

Chromosome monomer or trisomy is one of the important causes of congenital malformation in children. Monomer 9p is a rare condition accompanied by trigonocephaly, facial dysmorphism, and developmental delay [26,27]. In this study, two cases with monosomy 9p were described. The karyotype of one patient was 46,XY,der(9)t(2;9)(p25;p22)mat, which presented with small ears, low ear position, small jaw, wide breast distance, short chest, long fingers and toes, inability to extend the second joint of the middle finger of both hands, special clenched fist posture (index finger pressed on the middle finger, little finger pressed on the ring finger) [28]. The karyotype of another patient was 46,XX,der(9)t(7;9)(p15;p22)pat (Figure 5). Studies have shown that patients with der(9)t(7;9) are mostly characterized by developmentally delayed psychomotor retardation and generalized developmental deficits (Table 3). In this study, the patient presents as developmentally delayed and psychomotor retardation, according to the previous report.

Chromosome 4q deletion syndrome (4q-syndrome) is a rare condition, with an estimated incidence of 1 in 100,000 and the death rate was about 28% [36,37]. Although the clinical symptoms of patients with 4q-syndrome are complex and diverse (Table 4), through statistical analysis of the clinical symptoms of 101 patients, Strehle et al. found that craniofacial (99%), digital (88%), skeletal (54%), and cardiac (50%) were the most common anomalies [37]. Keeling et al. have reported that the critical region involved in the 4q terminal deletion syndrome may be 4q33 [43]. In this study, we reported a 16-month-old boy with 4q33-qter deletion (Figure 6). The patient presents with cleft palate, micrognathia, Sydney line of the left hand, and developmental delay. Our results further support the idea that cleft palate-related genes might be located at 4q33 [43]. In addition, although most patients with 4q-syndrome have de novo deletions, familial cases have been reported, suggesting a high risk of recurrence of 4q-syndrome [47,48]. So, for these patients, prenatal diagnosis is necessary.

Deletion of the long arm of chromosome 18 (18q-) is relatively common among cytogenetic abnormality, which occurs incidentally in approximately 1 in 40,000 live births [49]. 18q-syndrome is characterized by a wide range of phenotypic abnormalities related to the size of the deletion and the position of breakpoints. The common clinical features of the 18q-syndrome are growth retardation, mental retardation, microcephaly, facial dysmorphisms, ear atresia, abnormal bone development, CHD, cerebral white matter abnormalities, and immature myelin formation [50–52]. In this study, the patient with a rare karyotype of 45,XX,der(15;21)(q10;q10)mat,del(18)(q21) (Figure 7) presented with mental retardation, unclear diction, facial dysmorphisms, abnormal bone development, the little finger end bending, poor balance ability, and unsteady walking. In addition, the patient also suffered from type I diabetes and Hashimoto's

**Table 3:** Clinical symptoms of the patient with der(9)t(7;9)

| Karyotype                              | Abnormal phenotype   | Authors                    |
|--|--|----------------------------|
| 46, XY, der(9) t(7;9)<br>(p15;p22) pat | Seizure, developmentally delayed, delayed myelination, and widened brain extracellular space   | Zhong et al. [29]          |
| 46, XY,t(7;9)(p22;q22)mat              | Hypotrophic, full and wavy hair; a prominent forehead (middle facial part); microcephaly; low-set abnormal ears; hypertelorism; narrow, short eye slits; antimongoloid eye slant; broad, flat nasal bridge; bulbous nasal tip; microretrognathia; high palate; macrostomia; short neck; hollow stomach; short upper and lower extremities; bilateral clinodactyly of second and fifth fingers; thumbs and first toes are positioned far from other fingers (sandal gap); hypoplasia of toes nails; single transverse palmar crease; hypoplastic aortic arch; and hypoplastic lungs | Manvelyan et al. [30]      |
| 46, XY,der(9)t(7;9)<br>(p21.2;p23.5)   | Bilateral choanal atresia, growth delay, marked psychomotor retardation, hydronephrosis, muscular hypotonia  | Back et al. [31]           |
| 46,XY, der(9),t(7;9)<br>(q31.1;p23)pat | Generalized mild dysmorphic, heart failure, and hydrocephalus, sex reversal  | Crocker et al. [32]        |
| 46,XX,der(9)t(7;9)<br>(p15.3;p24)      | Psychomotor retardation, upward slant of palpebral fissures, and dolichomesophalangy   | Teebi et al. [33]          |
| 46,XX,der(9)t(7;9)<br>(q35;q22.2)      | Hypoplasia of the cerebellar vermis, dilated foramen Magendii, and dilatation of the cisterna magna  | von Kaisenberg et al. [34] |
| 46, XX, der(9)t(7;9)<br>(p15; p24)     | Generalized developmental deficits, a high and large forehead, hypertelorism, and broad nasal bridge, hypothyroidism, obesity, cerebral palsy, severe mental retardation   | Kozma et al. [35]          |
| 46,XX,der(9)t(7;9)<br>(p15;p22)pat     | Developmental retardation and mental retardation   | Present case               |

**Table 4:** Clinical symptoms of the patient with 4q-syndrome

| Karyotype                             | Abnormal phenotype   | Authors               |
|---------------------------------------|--|-----------------------|
| Deletion of the segment<br>4q22.1-q23 | Slight developmental delay, mild dysmorphic features   | Strehle et al. [38]   |
| Deletion of segment<br>4q28.3-q31.23  | Growth failure, developmental delay, ventricular septum defect in the subaortic region, patent foramen ovale and patent ductus arteriosus, vascular malformation of the lung, dysgenesis of the corpus callosum and craniofacial dysmorphism | Duga et al. [39]      |
| Deletion of segment<br>4q31-qter      | Craniofacial dysmorphism, skeletal anomalies, ocular findings, and cardiac defect  | Sandal et al. [40]    |
| Deletion of segment<br>q31.2-q35.2    | Craniofacial hypoplasia of left side of face, ipsilateral ptosis, erythroderma, and bilateral thumb anomalies  | Kuldeep et al. [41]   |
| Deletion of segment<br>4q31.21-q31.23 | Pseudohypoaldosteronism  | Pritchard et al. [42] |
| Deletion of segment<br>4q31.3-qter    | Complex CHD  | Strehle et al. [38]   |
| Deletion of segment<br>4q32-q34       | Mild developmental delay; a left ulnar ray defect with absent ulna and associated metacarpals, carpals, and phalanges; and a right ulnar nerve hypoplasia  | Keeling et al. [43]   |
| Deletion of segment<br>4q32.3-q34.3   | Congenital heart defects   | Xu et al. [44]        |
| Deletion of segment<br>4q33-qter      | Mildly dysmorphic, heart failure, and hypercalcaemia   | Strehle et al. [45]   |
| Deletion of segment<br>4q33-qter      | Cleft palate, micrognathia, sydney palm of left hand, and developmental delay  | Present case          |
| Deletion of segment<br>4q34.2-qter    | CHD, submucosal cleft palate, hypernasal speech, learning difficulties, and right fifth finger anomaly manifestations  | Tsai et al. [46]      |
| Deletion of segment<br>4q34.3-qter    | Asymptomatic cor triatriatum sinister  | Marcì et al. [47]     |



thyroiditis, which were rarely reported. Therefore, this case is especially helpful in supplementing the phenotypic diversity of patients with 18q.

## 5 Conclusion

Chromosome abnormality is one of the important causes of dysplasia in children, and prenatal screening and diagnosis could play a great significance in preventing dysplasia in children. In addition, the retrospective analysis of the rare case is valuable for clinical diagnosis and risk assessment of recurrence.

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**Data availability statement:** The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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