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Case Report

A 13-year-old girl with 18p deletion syndrome presenting Turner syndrome-like clinical features of short stature, short webbed neck, low posterior hair line, puffy eyelids and increased carrying angle of the elbows

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ABSTRACT

Objective: We report a 13-year-old girl with 18p deletion syndrome presenting Turner syndrome-like clinical features.

Case report: A 13-year-old girl was referred for genetic counseling of Turner syndrome-like clinical features of short stature, short webbed neck, low posterior hair line, puffy eyelids and increased carrying angle of the elbows. The girl also had mild intellectual disability, psychomotor developmental delay, speech disorder, high-arched palate, hypertelorism and mid-face hypoplasia. Cytogenetic analysis of the girl revealed a karyotype of 46,XX,del(18) (p11.2). The parental karyotypes were normal. Array comparative genomic hybridization analysis on the DNA extracted from the peripheral blood revealed a 13.93-Mb deletion of 18p11.32-p11.21 or arr 18p11.32p11.21 (148,993–14,081,858) × 1.0 [GRCh37 (hg19)] encompassing 52 Online Mendelian Inheritance in Man (OMIM) genes including *USP14*, *TYMS*, *SMCHD1*, *TGIF1*, *LAMA1*, *TWSG1*, *GNAL* and *PTPN2*. Polymorphic DNA marker analysis revealed a maternal origin of the deletion.

Conclusion: Females with Turner syndrome-like clinical features in association with intellectual disability, facial dysmorphism and psychomotor developmental delay should be suspected of having chromosome deletion syndromes.

Introduction

Chromosome 18p deletion syndrome [Online Mendelian Inheritance in Man (OMIM) 146390] is a contiguous gene deletion syndrome characterized by mental retardation, short stature, growth retardation, craniofacial dysmorphisms of depressed nasal bridge, round face, short protruding philtrum, palpebral ptosis, strabismus, large dysplastic ears, wide mouth and dental abnormalities, short webbed neck, cognitive impairment, speech delay,

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hearing loss, holoprosencephaly (10% of the cases), pectus excavatum, kyphoscoliosis, pituitary hormone deficiencies, seizures, dystonia, autoimmune disorders, congenital heart defects of ventricular hypertrophy, patent ductus arteriosus tetralogy of Fallot (~10% of the patients), cryptorchidism, IgA, IgG, or IgM deficiency, optic nerve hypoplasia, congenital cataracts, sacral agenesis, myelomeningocele and keratosis pilaris [1–6].

Here, we report a 13-year-old girl with 18p deletion syndrome presenting Turner syndrome-like clinical features of short stature, short webbed neck, low posterior hair line, puffy eyelids and increased carrying angle of the elbows.

Case report

A 13-year-old female was referred for genetic counseling of Turner syndrome-like phenotype of short stature, short webbed neck, low posterior hair line, puffy eyelids and increased carrying angle of the elbows. The girl was the second child of a 33-year-old father and a 27-year-old mother at her birth at 37 weeks of gestation with a birth weight of 2850 g. At referral, she had a body weight of 45 Kg (50th–75th centile) and body height of 149 cm (25th–50th centile). She had additional manifestations of mild intellectual disability, psychomotor developmental delay, speech disorder, high-arched palate, hypertelorism, large ears and midface hypoplasia. The intelligence quotient (IQ) test at age 8 years revealed the result of mild intellectual disability with a full IQ of 56. She had regular menstrual cycle. Her menarche occurred at age 11 years. She had normal female external genitalia. Cytogenetic analysis of the patient's peripheral blood revealed a karyotype of 46,XX,del(18)(p11.2) (Fig. 1). The parental karyotypes were normal. Array comparative genomic hybridization (aCGH) analysis on the DNA extracted from the peripheral blood using CytoChip ISCA Oligonucleotide Array (Illumina, San Diego, CA, USA) revealed a 13.93-Mb 18p11.32-p11.21 deletion or arr 18p11.32p11.21 (148,993–14,081,858) × 1.0 [GRCh37 (hg19)] encompassing 52 OMIM genes including *USP14*, *TYMS*, *SMCHD1*, *TGIF1*, *LAMA1*, *TWSG1*, *GNAL* and *PTPN2* (Fig. 2). Polymorphic DNA marker analysis on the DNAs extracted from the bloods of the patient and her parents revealed a maternal origin of the deletion (Fig. 3).

Discussion

The present case had a *de novo* pure isolated deletion of maternal origin. Schaub et al. [7] found that about half of the cases with 18p deletion had breakpoints in the centromeric region, and about half of the deletions, regardless of breakpoint location, occurred on the maternal chromosome. Hasi-Zogaj et al. [5] in a cohort study of individuals with 18p deletion found that 89% had *de novo* isolated deletions, and among 56% *de novo* cases, 25 cases had the deletion occurring on the paternal chromosome, whereas the other 31 cases had the deletion occurring on the maternal chromosome. Women with chromosome 18p deletion syndrome may be fertile, and familial 18p deletion syndrome of direct parent-to-child transmission of the deletion have been reported [5,8–13]. To our knowledge, in all of the reports of familial transmission, the deletion was inherited from the mother. In this regard, genetic counseling of possible familial transmission is important in females with 18p deletion syndrome, especially when they are pregnant, and prenatal diagnosis is mandatory.

The present case manifested Turner syndrome-like clinical features of short stature, short webbed neck, edema of face and increased carrying angle of the elbows. Turner syndrome is characterized by short stature, webbed neck, characteristic facies, short metacarpals, broad chest with widely spaced nipples, hyperconvex fingers and toenails, decreased growth velocity and delayed puberty [14]. Barstow and Rerucha [14] suggested that differential diagnosis of short stature in children should include (1) normal variants of constitutional delay of growth and puberty, familial short stature and idiopathic short stature; (2) chronic diseases of anemia, celiac disease, chronic renal insufficiency and inflammatory bowel disease; (3) endocrine disorders of achondroplasia, acquired growth hormone deficiency, congenital growth hormone

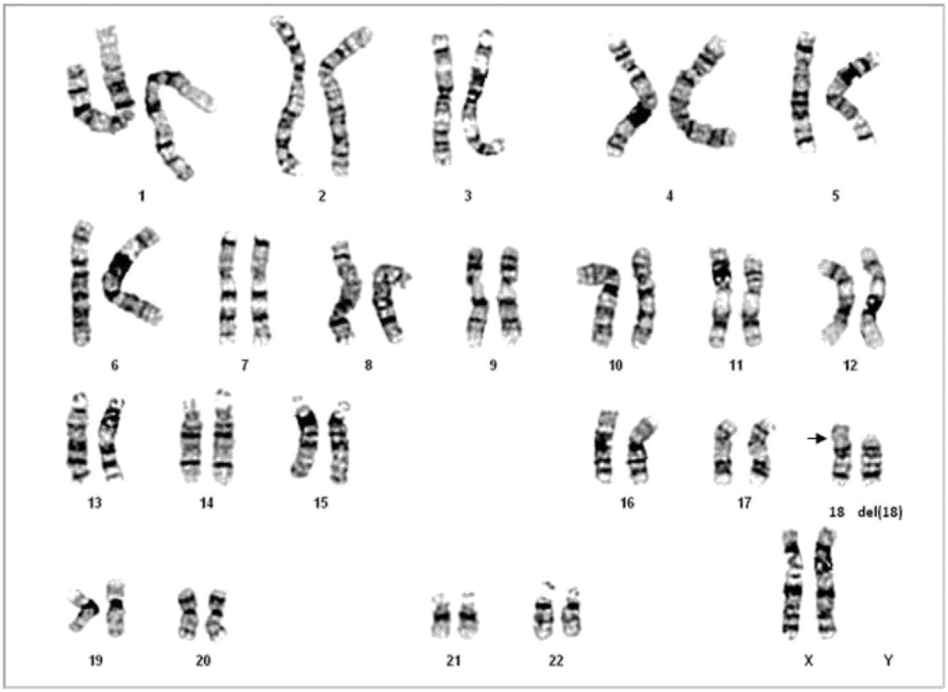

Fig. 1. A karyotype of 46,XX,del(18) (p11.2). The arrow indicates the breakpoint.