18p Deletion Syndrome: Case Report with Clinical Consideration and Management

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Abstract

18p deletion syndrome is characterized by the deletion of short arm of chromosome 18. Presentation of this syndrome is quite variable with dysmorphic features, growth deficiencies, and mental retardation with poor verbal performance. Few patients even fail to thrive when malformations involving the heart and brain are severe. In the present article, we report an isolated case of 18p deletion in a 23-year-old female who for the first time reported to the hospital for dental problems. The patient was short statured with mental retardation and craniofacial, skeletal, dental, and endocrinal abnormalities. Such presentation warrants prompt diagnosis for effective management. Furthermore, genetic counseling for such patients and their families should be considered as a part of treatment itself.

Keywords: *18p deletion, craniofacial abnormalities, dental caries, dysmorphic features, hypothyroidism, mental retardation*

Introduction

18p deletion refers to a chromosomal disorder resulting from the deletion or absence of all or part of the short arm of chromosome 18. It was first reported in 1963 by the French geneticist Jean de Grouchy, and hence, it is also known as de Grouchy syndrome.[1] 18p deletion syndrome is a genetic condition caused by a deletion of all or part of the short arm (the P arm) of chromosome 18. More than 150 patients have been reported worldwide, and most cases are no longer subject to publication. The incidence of the disorder could be estimated at about 1:50,000 live-born infants. The female-to-male ratio is 3:2.[2] Clinical features vary considerably within patients. Most common features include moderate-to-severe mental retardation, postnatal growth retardation, a round face, drooped corners of mouth, and dysplastic ears. However, microcephaly, epicanthic folds, ptosis, hypertelorism, micrognathia, dental anomalies, short neck, and pterygium colli are found less frequently.[3] Malformations such as congenital heart defects or brain malformations mostly of the holoprosencephaly spectrum have also been reported.[4] The fact that partial deletions are essentially secondary to unbalanced translocations so that the phenotype is influenced by the concomitant trisomy may explain the phenotypic variability reported in the 18p deletion syndrome. Other factors influencing this variability may include age differences of the patients, inhomogeneous clinical classification, incomplete penetrance of the trait, undetected mosaicism, and the uncovering of a recessive trait by the deletion.[3] Most cases of 18p deletion are supposed to originate from *de novo* deletions, which accounts for 85% of cases.[5] The remainder is suspected to come from imbalanced familial transmission of structural rearrangements. Here, we report an unusual case of 18p deletion ascertained by molecular cytogenetic studies, together with clinical findings.

Case Report

A 23-year-old female patient attended our outpatient department for the first time with the chief complaint of missing upper front teeth. Dental history revealed exfoliation of the upper front teeth 4 months back due to compromised periodontal condition. Medical history was significant for moderate mental retardation since childhood. The patient achieved normal milestones except for delayed speech, however, hearing being normal. Menarche was attained at the age

How to cite this article: Goyal M, Jain M, Singhal S, Nandimath K. 18p deletion syndrome: Case report with clinical consideration and management. Contemp Clin Dent 2017;8:632-6.

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Access this article online

Website: www.contempclindent.org

DOI: 10.4103/ccd.ccd_129_17

Quick Response Code:

of 16 years. There was no family history of consanguineous marriage, and other siblings were normal. The prenatal history was unremarkable.

General physical examination revealed that the patient was short statured with mild microcephaly, flat, and expressionless face with short neck. Slowness in motion and action was noted. Arachnodactyly of hands and spacing between the 1st and 2nd left toe was observed [Figure 1].

Extraoral examination revealed flat and broad nasal bridge, horizontal palpebral fissures with hypertelorism. The mouth was wide with short philtrum (carp mouth) and deficient midface [Figure 2]. Clinically, palpable nodular swelling was observed in the neck on the left side [Figure 3] which on further investigations was found to be goiter of the left lobe of thyroid with high thyroid-stimulating hormone levels (0.57 IU/mL).

Intraoral examination showed poor oral hygiene, generalized enamel hypoplasia with high caries index, multiple root stumps, high palatal arch, geographic tongue, and generalized gingival enlargement [Figure 3].

Provisional diagnosis included a wide number of syndromes presenting with short stature and mild-to-moderate mental retardation. The following syndromes such as Down syndrome, Turner syndrome, partial trisomy 14, trisomy 13 (Patau syndrome), chromosome 18p monosomy, monosomy 18q, and trisomy 18 (Edwards' syndrome) can be considered as differential diagnoses.

Chest radiograph revealed kyphoscoliosis and barrel-shaped chest (emphysematous) [Figure 4]. Anterior-posterior spine revealed spina bifida with generalized decrease in bone density [Figure 5]. Chromosomal analysis from peripheral blood lymphocytes was carried out which uncovered deletion of short arm of chromosome 18 [Figure 6].

Management

The patient was put on thyroxine supplements for hypothyroidism. Oral prophylaxis was done. Decayed teeth were restored and root stumps were extracted under general anesthesia followed by fixed prosthesis; the patient was also advised desensitizing paste and composite restoration for enamel hypoplasia and recalled after every 6 months to evaluate the immunological and endocrinal status.

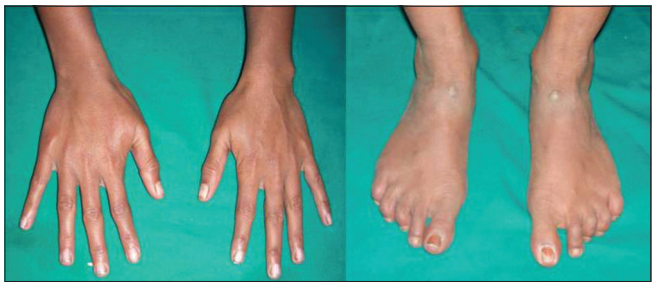

Figure 1: Photograph showing arachnodactyly of hands and abnormal spacing between the 1st and 2nd left toe

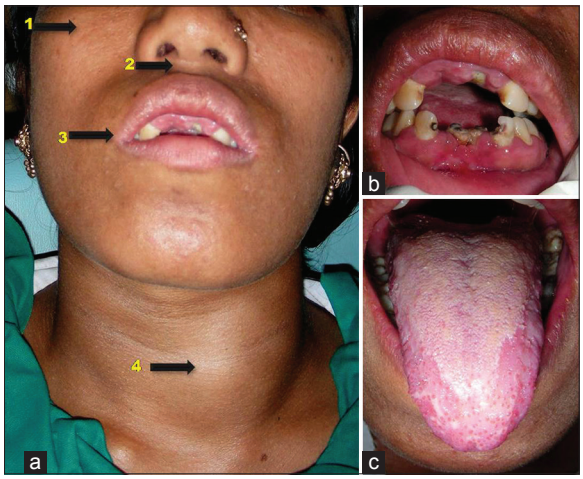

Figure 3: Photograph of the patient showing (a) 1. Flattened malar prominence 2. Short philtrum. 3. Carp-shaped mouth. 4. Swelling in the left side of neck. (b) Multiple decayed teeth, enamel hypoplasia, gingival enlargement. (c) Geographic tongue

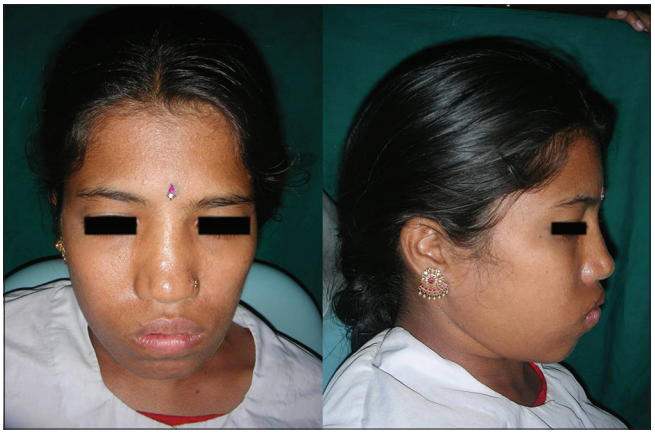

Figure 2: Front and profile photograph of patient depicting flat face, broad and flat nasal bridge, hypertelorism, deficient midface, and short neck

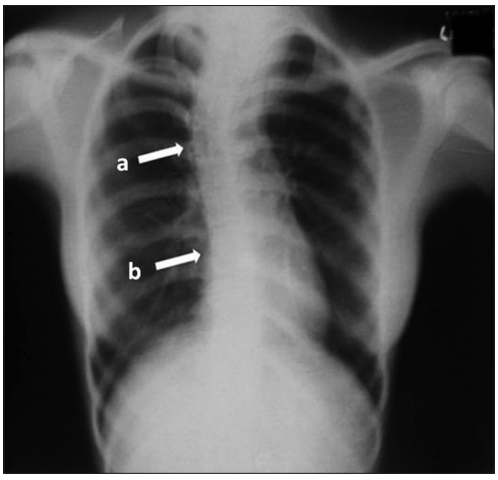

Figure 4: Posteroanterior chest radiograph showing kyphoscoliosis and barrel-shaped chest. Arrow a and b – showing curvature of spine

Discussion

The 18p deletion syndrome was the only autosomal deletion syndrome whose survival is variable depending on the severity ranging from few months to several decades.[6,7] Fitzgerald reported a case with gross dysmorphic features along with low survival rate. However, in our case, the survival rate was good.[6] Several clinical features were reported including mental retardation ranging from severe mental retardation to borderline normal intelligence.[1,8-12] In our case, moderate mental retardation was seen. Brenk *et al*. reported four cases with similar features reported in our case. They also established the phenotypic correlation with genotype.[3] Harmesh *et al*. reported nine children with 18p deletion syndrome with high caries index which was also observed in our case.[13] Thompson *et al*. reported three cases of girl child with mild-to-severe mental retardation and dysmorphic features and high caries risk with various intellectual, behavioral, and linguistic problems. Similar features were observed in the present case.[12] The various clinical features reported by various authors are summarized in Table 1 and compared with the features seen in the present case.

Genotype-phenotype correlation

In spite of the syndrome's frequency, no reliable phenotype map has been established. The fact that most of the 18p pure deletions involve the entire short arm is the main reason for this. In 2007, Brenk *et al*. proposed a phenotypic map for 18p deletions [Figure 7] based on the findings in their patients and analysis of published cases.[3] Even based on this phenotypic map, clinical features were quite variable among patients. This could be attributed to the fact that partial deletions are essentially secondary to unbalanced translocations so that the phenotype is influenced by the concomitant trisomy may explain the phenotypic variability reported in the 18p deletion syndrome. Other factors influencing this variability may include age differences of the patients, inhomogeneous clinical classification, incomplete penetrance of the trait, undetected mosaicism, and the uncovering of a recessive trait by the deletion.[3]

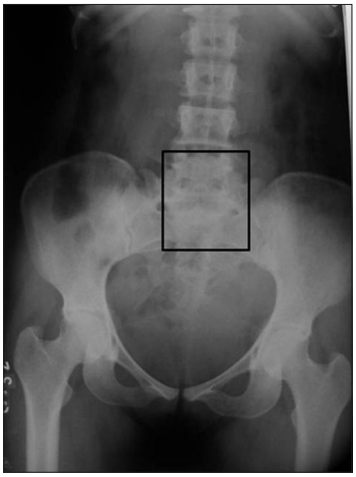

Figure 5: Anteroposterior radiograph for the spine showing spina bifida

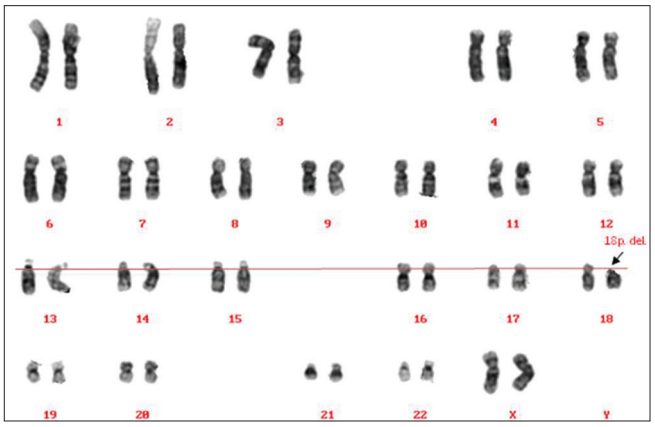

Figure 6: Karyotyping from the peripheral lymphocytes showing deletion of short arm of chromosome 18

Table 1: Clinical features

Clinical features as reported in various cases	Frequency in 18p deletion (%)	Present case
Postnatal growth retardation[14]	85	Present
Microcephaly and holoprosencephaly[4,15]	29	Microcephaly present
Congenital malformations[14,15]	3-18	Skeletal abnormalities such as kyphoscoliosis, spina bifida, and emphysematous chest
Mental retardation/developmental delay[14]	100	Present
Dental anomalies[13,15]	29	Present - enamel hypoplasia, multiple dental caries, high-arched palate, and geographic tongue
Craniofacial anomalies[15-17]	14-57	Present - flat face, broad nose, hypertelorism, deficient midface, carp mouth
Anomalies of neck and trunk[14]	42	Short neck present
Anomalies of extremities (toes)[14,16]	Present	Present
Endocrinal thyroid abnormalities and growth hormone abnormalities[8,18]	Present	Hypothyroidism present
Immunological[19]	Present	Not assessed as no history of frequent infection
Congenital heart anomalies	Present	Not present

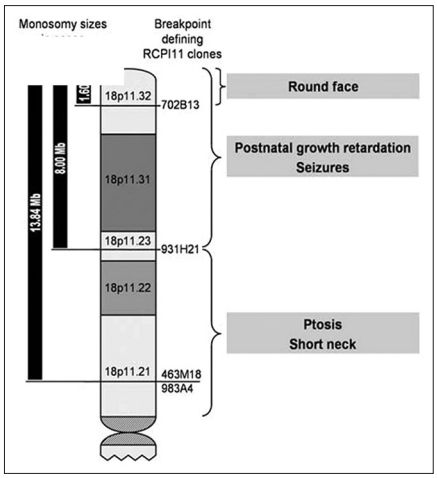

Figure 7: Phenotypic map for deletions of 18p

Diagnostic methods

It is not possible to base the diagnosis of 18p deletion syndrome merely on the phenotype, and cytogenetic analysis is necessary to make a definite diagnosis. Diagnosis is usually done by karyotype analysis from peripheral blood. It is also possible in prenatal period from amniocytes or trophoblast cells.[2]

Differential diagnosis

Differential diagnosis may include a wide number of syndromes presenting with short stature and mild mental retardation. In young children, 18p deletion may be vaguely evocative of either Turner syndrome or trisomy 21. In all cases, cytogenetic analysis allows the right diagnosis.

Management including treatment

The treatment is directed toward the specific symptoms that are apparent in each individual. Such treatment may require the coordinated efforts of pediatricians, surgeons, physicians, orthopedician, neurologists, speech-language pathologists, and/or other health-care professionals. The specific surgical procedures performed will depend on the severity and location of the anatomical abnormalities, their associated symptoms, and other factors. Endocrinopathies should be taken care, and the patient should be evaluated for immunological deficiencies at timely intervals. The prognosis is poor for those patients with severe brain malformations otherwise survival up to the 6th decade was reported.[7] Genetic counseling will also be of benefit for affected individuals and their families. Other treatment for this disorder is symptomatic and supportive.

Conclusion

It is important to report such cases in the literature as phenotypes of these cases are quite variable. It is imperative to do karyotyping in such individuals to delineate 18p deletions from other syndromes with similar clinical presentation and to detect the extent of deletion as management may vary with the amount of chromosomal loss. Furthermore, it is essential to detect partial deletions for proper genetic counseling of such individuals and their families.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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