Case Report

Severe growth retardation and distinctive phenotype in a child with 1q24 deletion syndrome

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ABSTRACT

Microdeletions on the long arm of chromosome 1 are relatively uncommon. In recent years, a consistent phenotype has emerged in association with 1q24q25 deletions. These patients have mild to moderate intellectual disability and characteristic skeletal features including small hands and feet with brachydactyly, prenatal onset growth retardation and persisting significant postnatal short stature of up to -5SD with microcephaly up to -4SD. The reported dysmorphic facial features include micrognathia, small, low set ears, a short nose with a broad bridge and bulbous tip, full eye lids, a tented upper lip and a small chin. Other features less frequently described include renal, cardiac and genital malformations, craniosynostosis, hypotonia and seizures.

We report a rare, microarray-confirmed case of 1q24 deletion syndrome presenting with classic phenotypic features. The patient, a three-year-old female, presented with failure to thrive, developmental delay including intellectual disability and motor delay. She has characteristic facial and skeletal features, as well as multiple congenital anomalies. The diagnosis was confirmed by genetic analysis during the evaluation process. Supportive management was initiated, and available informations were shared with the parents about course and probable prognosis.

Key words: *1q24q25 deletions, growth retardation, intellectual disability.*

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INTRODUCTION

1q24 deletion syndrome is an extremely rare chromosomal disorder (prevalence <1 in 1,000,000), caused by mostly a de novo interstitial deletion in the 1q24 region of chromosome 1, which plays key roles in skeletal and neurodevelopment.[1-3] Clinically, as there is variable phenotypic expression, it manifests with severe pre- and persistent post-natal growth retardation (up to -5SD), microcephaly (up to -4SD), brachydactyly, clinodactyly and distinctive craniofacial dysmorphism, including low-set ears, broad nasal bridge with a bulbous tip, full eyelids, tented upper lip and micrognathia. Growth hormone therapy offers limited benefit. Additional features may include renal, cardiac, genital and anorectal anomalies, as well as seizures and hypotonia.[1-6]

First described by Kutay Taysi in 1982,[6] over 30 microarray-confirmed cases have since been reported globally,[1] though none from Bangladesh. We report this microarray-confirmed rare case of 1q24 deletion syndrome, presenting with classic features along with cardiac, renal and anorectal malformations and early-onset seizures.

CASE REPORT

A three-year-old female child. born of a non-consanguineous marriage, presented with failure to thrive, intellectual disability, motor delay and characteristic facial as well as skeletal features. She was delivered by lower uterine Cesarean section at 36

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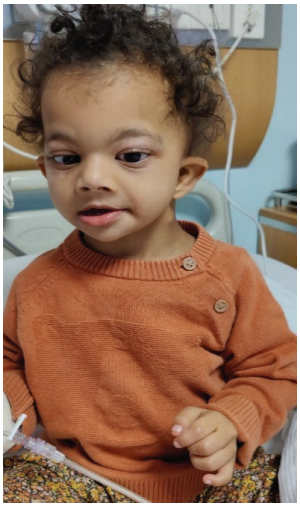

Figure 1a. Characteristic facial features and low set ears

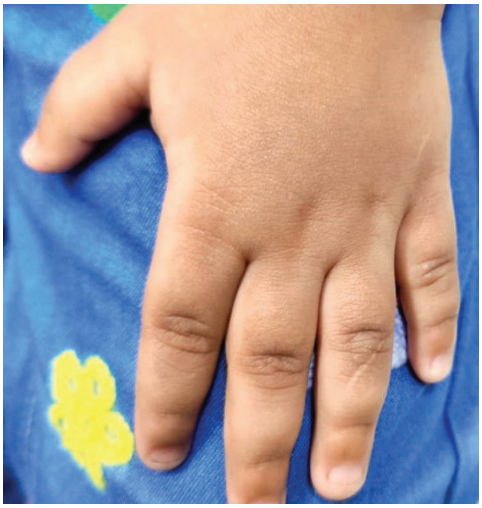

Figure 1b. Small hand with brachydactyly

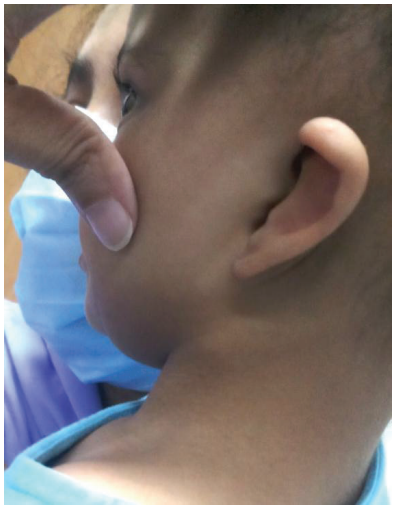

Figure 1c. Low set ear with hypoplastic lobe

weeks of gestation with intrauterine growth retardation (IUGR) of weight 1700 gm (< 10th percentile), length 40 cm (< 10th percentile) and occipitofrontal circumference (OFC) 29 cm (< 10th percentile). She had anorectal malformation (rectovaginal fistula) and underwent reconstructive surgery at the age of 7 months. Ultrasonogram of abdomen showed smaller kidneys with mildly increased cortical echogenicity. The child has characteristic facial features like micrognathia, small, low set ears with hypoplastic lobes, a short nose with bulbous tip, full eye lids (Figure 1a) and small hands (Figure 1b). At the age of 3 years, her height was 70.5 cm (-6.30 SDs), weight was 7.03 kg (-5.97 SDs) and her head circumference was 41 cm (-8.70 SDs). She had normal thyroid, growth hormone and inborn error of metabolism (IMD) panel and normal female Karyotype 46 XX. Skeletal survey was also normal. Echocardiogram showed small secundum atrial septal defect (ASD) shunting left to right with patent ductus arteriosus (PDA), severe pulmonary hypertension and mild septal hypertrophy. At the age of 2 year due to repeated seizure evaluation revealed left temporoparietal seizure in electro-encephalogram (EEG). Magnetic resonance imaging (MRI) of brain reported apparent cortical thickening in the left frontal opercula, slightly delayed myelination and slightly thinned corpus callosum.

She has been evaluated for pathogenic variations. Clinical exome sequencing revealed heterozygous deletion in chromosome 1 (chr1:g {_164562836)_(179576128_)}del (Table I).

Table I. Results of exome sequence

LIKELY PATHOGENIC COPY NUMBER VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS IDENTIFIED

Gene (Transcript) #	Location	Variant	Zygosity	Disease	Inheritance	Classification
Chromosome 1	chr1:g.(?_164562836)_(179576128_?)del	-	Heterozygous	1q24 deletion syndrome	-	Likely Pathogenic

DISCUSSION

1q24 deletion syndrome is a rare genetic disorder caused by heterozygous interstitial deletions in the long arm of chromosome 1, typically presenting with multisystem involvement including profound growth failure, neurodevelopmental delay, craniofacial dysmorphism and in some cases, congenital organ malformations. The phenotypic spectrum observed in our patient corresponds closely to previously reported cases, underscoring the characteristic clinical presentation of this microdeletion syndrome.

The patient, a 3-year-old female, exhibited hallmark features such as severe IUGR, postnatal failure to thrive and microcephaly (head circumference -8.70 SD), consistent with the findings described in a cohort study of 9 patients with deletion of chromosome 1q24-q25, where patients presented with growth parameters up to -5 SD and profound microcephaly.[2] Her dysmorphic craniofacial features—micrognathia, small low-set ears with hypoplastic lobes, short nose with a bulbous tip and full eyelids—align with the phenotype commonly described in the literature.[1,2,4]

Notably, described patient presented with additional anomalies, including an anorectal malformation requiring surgical intervention, renal hypoplasia with increased cortical echogenicity and congenital heart defects (secundum ASD, PDA and pulmonary hypertension). While renal and cardiac anomalies have been variably reported, these are not uniformly present in all patients, suggesting phenotypic variability depending on the size and gene content of the deletion.[7] In the series by Chen et al. patients with overlapping deletions in the 1q24 region also demonstrated renal malformations and congenital heart defects, corroborating the findings in our case.[2,8]

Neurologically, the patient exhibited global developmental delay, motor delay and early-onset seizures. EEG findings were consistent with epileptogenic activity and MRI revealed cortical thickening, delayed myelination and a thinned corpus callosum—neuroimaging features that have been reported in previous cases and reflect structural brain involvement secondary to gene dosage effects.[1,9] The severity of neurodevelopmental delay is likely attributable to haploinsufficiency of one or more genes within the 1q24 locus, which may include genes involved in centrosomal function and cortical development.

Genetically, the diagnosis was confirmed by clinical exome sequencing, identifying a heterozygous deletion spanning chr1:g.164,562,836–179,576,128, which encompasses the critical region implicated in 1q24 deletion syndrome. Standard cytogenetic analysis (karyotype 46, XX) failed to detect the microdeletion, highlighting the necessity of high-resolution techniques such as chromosomal microarray or next-generation sequencing in diagnosing submicroscopic deletions.

No specific survival statistics are found for 1q24 deletions. Prognosis and management depend on the specific genes and regions deleted, as well as the severity of symptoms. Management is multidisciplinary, involving various specialists to address individual needs and supportive care to improve the quality of life of child as well for the family. With appropriate interventions, some individuals show improvement in their cognitive and communication skills.[2]

If the deletion is de novo (new in the child), recurrence risk for future pregnancies is generally low (<1%). If one parent carries a balanced chromosomal rearrangement, the recurrence risk can be substantially higher.[2] So, accurate diagnosis is crucial for providing appropriate supportive care and genetic counseling.

To our knowledge, this is the first genetically confirmed case of 1q24 deletion syndrome reported from Bangladesh, contributing to the expanding clinical and geographic spectrum of the disorder. The case underscores the importance of considering chromosomal microdeletion syndromes in children presenting with severe growth retardation, intellectual disability, seizures and dysmorphic features, even in the context of a normal karyotype and standard metabolic workup.

Authors' contribution: FZ: Conceptualization, literature search and writing manuscript. NN: Review and editing. NB: Review and editing.

Consent: Informed consent of parents was taken for publication of this case report and accompanying images.

Conflicts of interest: Nothing to declare.

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