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SHORT SYNDROME - A BIZARRE GENETIC ODDITY

Oral Medicine

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ABSTRACT

SHORT syndrome is a rare genetic anomaly with multiple birth defects affecting different organ systems. The terminology SHORT is an abridgment of its emblematic manifestations such as short stature, hyper extensibility of joints / hernia (inguinal), ocular depression, Rieger anomaly and teething delay.

KEYWORDS

Genetic disease, short stature, inguinal hernia, Rieger anomaly, delayed teething.

INTRODUCTION

SHORT syndrome is a rare genetic disorder showing an autosomal recessive pattern of inheritance[1] which is registered in Orphan diseases database as ORPHA:3163, Phenotype MIM number 269880, Gene/Locus MIM number 171833[2]. The acronym SHORT can be expanded as Short stature, Hyperextensibility of joints and/or inguinal hernia, Ocular depression, Rieger anomaly, and Teething delay[1]. SHORT syndrome was first described in two separate studies conducted by Gorlin et al and Sensenbrenner et al in the year 1975[3]. Fewer than 50 cases were reported so far in literature.

Babies with this syndrome are often born with low weight and length. The patients usually have a triangular-shaped face, prominent forehead, deeply-set eyes, thin or underdeveloped nostrils, thin lips and mouth downturned, a small chin with a dimple, low-set ears, wrinkles.[1]

This multisystem disease is characterized by intrauterine growth restriction (IUGR), urinary tract diseases and nephrocalsinosis. Rieger anomaly is characterized by the dysgenesis of the iris and cornea with marked hypoplasia of the iris stroma, displacement of the pupil (corectopia) and full-thickness colobomas of the iris (pseudopolycoria) which lead to higher ocular pressure and glaucoma development impairing vision. The patients might require hearing aid implementation because of sensorineural hearing loss. The syndrome also comprises of delayed tooth eruption, microdontia, hypodontia and absence of the protective layer on the teeth. Delayed bone age, hyperextensibility of the joints, epiphyseal plate thickening as well as clinodactyly are some other features.

The patients might also suffer from carbohydrate metabolism disorder and insulin resistance during their second decade of life[4]. SHORT syndrome is caused by mutations of PIK3R1 (phosphoinositide-3-kinase regulatory subunit 1) located on the long arm of chromosome 5 with the position 5q13.1. The PIK3R1 gene comprises of 86102 bp of DNA and 16 exons which is involved in many functions such as growth, proliferation, migration, metabolism, survival and apoptosis.[5]

This case report focuses on a sixteen-year adolescent with the features of SHORT syndrome.

CASE REPORT

A 16-year-old male presented with the chief complaint of painful decayed teeth in the lower right and left back region since one week. History of presenting illness revealed that he developed tooth ache one week back. Pain was sudden in onset, severe in intensity, continuous in nature, lancinating type and radiating to the ear. It aggravated on chewing food and also at night. The pain relieved on taking analgesics. The patient did not give any history of swelling or pus discharge.

Medical history showed that the patient had a low birth weight, delayed achievement of milestones like walking and speech and impaired hearing. He is currently undergoing speech therapy.

Dental history revealed that primary teeth erupted when the patient was 3 years old.

On general physical examination, the patient was poorly built and nourished with a height of 100cm and weight of 14kg. [Figure 1] He had a moderate IQ level.

On extra-oral examination, clinodactyly was seen in both hands. [Figure 2] Patient also showed microcephaly (head circumference: 50cm), microthelia [Figure 3] and phymosis [Figure 4]. He had a triangular face with incompetent lips, lack of subcutaneous fat, prominent nasal bridge and deep set eyes associated with Rieger anomaly and hypertelorism. [Figure 5]

Intra-oral examination revealed a high lingual frenal attachment with tongue tie. The deciduous teeth present were the lateral incisor on the second quadrant, the canines and second molars on all quadrants and first molars in the first, second and fourth quadrants. The permanent teeth present were upper and lower central incisors on all quadrants, the lateral incisors in the first, third and fourth quadrants, the first premolar in the third quadrant and the first molars on all four quadrants. Deep dental caries with pulpal involvement was seen in relation to 36 and46 which was tender to vertical percussion. [Figure 6]

On investigation, an orthopantomograph of the patient revealed multiple impacted teeth in the upper arch and missing tooth buds in the lower arch. Deep dental caries with pulpal involvement was seen in relation to left and right lower first molars with periapical radiolucency. [Figure 7] Delayed bone age was evident in the hand wrist radiograph and ultrasonography revealed lack of subcutaneous fat. [Figure 8] Routine blood investigations were within normal limits and peripheral blood smear showed normocytic normochromic red blood cells. Mantoux test was negative and thyroid profile was normal.

Left and right lower first molars were diagnosed with apical periodontitis and root canal treatment was suggested. In view of the history, clinical and radiographic findings, the case was diagnosed as SHORT syndrome.

Differential diagnosis of SHORT syndrome includes Russell-Silver syndrome, achondroplastic dwarfism, Albright's hereditary osteodystrophy, Down's syndrome and progeria. Table 1 shows the similarities and dissimilarities of the above mentioned conditions with SHORT syndrome The treatment given was symptomatic and supportive. Genetic counseling was also given to patients and their families.[6] It is advised to avoid growth hormone treatments since there is increased risk for insulin resistance in such patients.[7] Root canal treatment was compeleted with respect to left and right lower first molars and subsequently prosthetically rehabilitated. Retained deciduous maxillary right first molar was extracted.

DISCUSSION.

SHORT syndrome is an autosomal recessive pattern of inheritance.

Heterozygous mutations in exon 14 of PIK3R1 gene is currently believed to be the cause of this disorder. So far 9 mutations had been described evidently to be associated with SHORT syndrome.[5]

Other clinical finding include Rieger anomaly, intra-uterine growth retardation, delayed speech with normal intellect, hearing impairment, bilateral clinodactyly, triangular facies, broad forehead, lack of subcutaneous fat, prominent ears, hypoplastic nasal alae with overhanging columella, insulinopenic diabetes, nephrocalcinosis and ventricular septal defect[1,6]. The radiographic features include large cone-shaped epiphysis and thin gracile diaphysis[6].

The diagnosis is based on clinical and radiographic findings. The final diagnosis of the syndrome can only be confirmed using molecular genetic testing (sequence analysis of PIK3R1).

The clinical and radiographic features described in our case report when compared to other SHORT syndrome cases reported in literature were found to have almost similar findings[1,8,9]. The features like microthelia and phymosis were unique in this case.

Tables

Table 1: Similarities and dissimilarities of SHORT syndrome with the differential diagnosis conditions

CONDITION	SHORT STATURE	HYPEREXTENSIBLE JOINTS AND/OR INGUINAL HERNIA	OCULAR DEPRESSION	RIEGER ANOMALY	TEETHING DELAY	OTHER COMMON FEATURES
RUSSELL-SILVER SYNDROME	YES	NO	NO	NO	YES	TRIANGULAR FACE CLINODACTYLY HYPOGLYCEMIA LIPODYSTROPHY DELAYED BONE AGE
ACHONDROPLASTIC DWARFISM	YES	NO	NO	NO	NO	PROMINENT FOREHEAD
ALBRIGHT'S HEREDITARY OSTEODYSTROPHY	YES	NO	NO	NO	YES	ENAMEL HYPOPLASIA
DOWN'S SYNDROME	YES	YES	NO	NO	NO	MICRODONTIA HEARING IMPAIRMENT CLINODACTYLY GLAUCOMA
PROGERIA	YES	NO	NO	NO	YES	LIPODYSTROPHY LARGE EARS

Figure

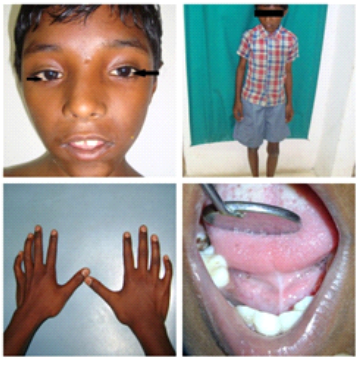

Figure 1: Dysmorphic feature showing short stature, clinodactyly in both hands, Rieger anomaly, hypertelorism and intra oral features

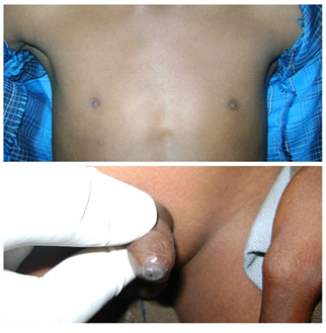

Figure 2: Dymorphic feature showing microthelia and phymosis

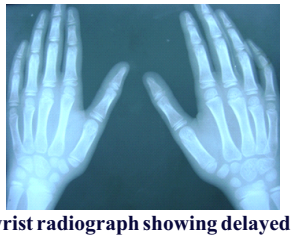

Figure 3: Hand wrist radiograph showing delayed bone age

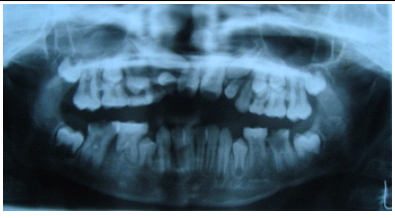

Figure 4: Orthopantomograph showing multiple impacted teeth in the upper arch, missing tooth buds in the lower arch and deep dental caries with pulpal involvement in relation to left and right lower first molars.

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