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Orofacial manifestations of Robinow syndrome: A rare case report

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Abstract

Robinow syndrome (Online Mendelian Inheritance in Man, OMIM - 268310) is an extremely rare genetic disorder with characteristic skeletal deformities and orofacial dysmorphism (fetal facies). The purpose of the present case report is to highlight the orofacial manifestations in a pediatric patient which can facilitate the general practitioners in the early diagnosis and multidisciplinary dental and medical management of the syndrome.

Keywords: Fetal facies, Brachymelia, Genetic disorder, Multidisciplinary management.

Introduction

First described by Meinhard Robinow in 1969, Robinow syndrome, also known as Robinow-Silverman-Smith syndrome and Fetal-facies syndrome is an extremely rare genetic disorder. This syndrome is characterized by short-limbed dwarfism, abnormalities in the head, face, external genitalia and vertebral segmentation.(1) A few more than 100 cases of Robinow syndrome have been reported in the literature so far. Both autosomal dominant and recessive modes of inheritance have been recorded, with the recessive form having more severe symptomology.(2) Multiple medical anomalies like frequent ear infections, renal problems and congenital heart defects have been reported with variable frequencies in these patients.(3)

Despite of the extremely rare occurrence of Robinow syndrome, diagnosis can be made confidently if the typical clinical and radiological features are known. The present case report highlights the characteristic orofacial manifestations in a pediatric patient which can facilitate the general practitioners in the early diagnosis and multidisciplinary dental and medical management of the syndrome.

Case Report

An eight year old Indian female patient, born to non-consanguineous parents, reported to the dental department with complaint of decayed upper front teeth for last four months. There was no significant peri-natal history and family history was negative for birth defects and hereditary disorders.

Extraoral examination revealed dysmorphic facial features including macrocephaly, frontal bossing, mid facial hypoplasia, hypertelorism, down-slanting palpebral fissures, flat nasal bridge, prominent philtrum, down turned angles of the mouth and posteriorly rotated ears. (Fig. 1) Intraoral examination revealed ankyloglossia, crowded maxillary anterior teeth, decayed 52, 62, 81 and missing 72, 82. (Fig. 2)

Anthropometry (at age 8) revealed a height of 110 cms (25^{th}-50^{th} percentile), weight of 20.4kg (75^{th}-90^{th} percentile), mesomelic dwarfism with upper limb to lower limb ratio of 1.7 and forearm brachymelia with arm to forearm ratio of1.5:1 in comparison to an average child of the same age group. (Fig. 3) The patient had genital anomalies in the form of hypoplastic labia majora. No obvious neurological delay was observed with a functioning intelligence quotient at an 8-year-old level. Cardiac and renal assessment did not reveal any associated anomalies. Endocrine evaluation (growth hormone, LH, FSH, oestrogen, progesterone, T3, T4, and, TSH) as well as immunological evaluation (T-cell and B-cell functions) were within the normal range. The postero-anterior cephalogram revealed open skull sutures and brachycephaly resulting in a light bulb like shape to the silhouette of the skull and mandible. (Fig. 4)

Based on the history, clinical examination, laboratory and radiological investigations, a final diagnosis of Robinow syndrome was arrived at. The patient's parents were psychologically counseled for the generally good prognosis of the syndrome. The decayed teeth were restored and oral prophylaxis was performed. The ankyloglossia was surgically corrected. The patient was referred to the department of pediatrics and orthopedics for the management of skeletal and genital anomalies.

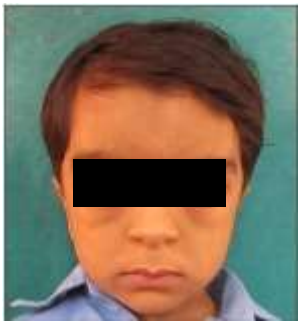

Fig. 1: Extraoral photograph revealing dysmorphic facial features

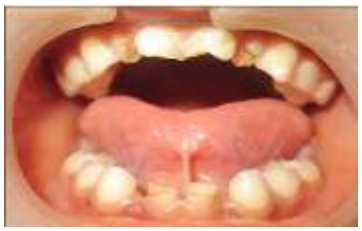

Fig. 2: Intraoral photograph revealing ankyloglossia and crowded maxillary anterior teeth

Fig. 3: Short stature & mesomelic dwarfism in comparison to an average child of the same age group

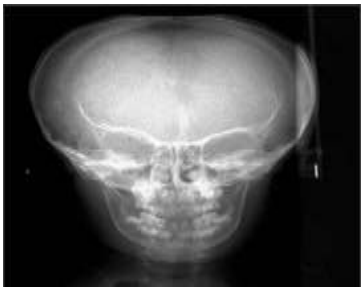

Fig. 4: Postero-anterior cephalogram revealing open skull sutures and brachycephaly

Discussion

First described in 1969 by human geneticist Meinhard Robinow, along with physicians Frederic N. Silverman and Hugo D. Smith, Robinow syndrome is an extremely rare genetic disorder.[(1)] The incidence of Robinow syndrome is about 1:500000 but the prevalence is still lesser since 5-10 % of patients die in infancy or early childhood. The male to female ratio of Robinow syndrome is 1:1.[(4)] Till date, a little more than 100 cases have been reported in the literature.

Both dominant and recessive forms of the syndrome exist, with the dominant form being more common. Patients with the recessive version (previously known as Covesdem syndrome) are usually more physically marked and may exhibit more skeletal abnormalities. The recessive form is particularly frequent in Turkey.[(5)] Mutation of the gene encoding the ROR 2 tyrosine kinase on position 9 of the long arm of chromosome 9 has now been implicated in Robinow syndrome. No specific metabolic abnormalities have been identified as the causal factors.[(6)]

Robinow syndrome is characterized by short stature and abnormalities in the head, face, and external genitalia associated with vertebral segmentation defects. Robinow noted the resemblance of affected patients' faces to that of a fetus, using the term "fetal facies" to describe the appearance of a small face and widely spaced eyes.[1]The various dysmorphic orofacial features of the syndrome include macrocephaly, frontal bossing (broad and prominent forehead), midfacial hypoplasia, hypertelorism, down-slanting palpebral fissures (abnormalities in the lower eyelid may give that impression), flat nasal bridge, prominent philtrum, down turned angles of the mouth, posteriorly rotated ears and a deformed pinna as seen in our patient. The upper lip may have an inverted "V" appearance, thus exposing the incisors and maxillary gingiva. Usually gum hypertrophy is present from birth and teeth show crowding. Ankyloglossia, a shortened tongue devoid of tongue tip and a geographic tongue can be observed in the syndrome.[(7)]

Patients with Robinow syndrome can present with various skeletal deformities such as Short stature, mesomelic shortening of the extremities, dislocation of the radial head and limitation of forearm rotations. There are abnormalities in the hands and fingers also with shortening of the distal phalanges. The thumb may be displaced and some patients, notably in Turkey, experience ectrodactyly.[(1)]

All patients in the recessive form suffer from vertebral segmentation abnormalities, resulting in kyphoscoliosis and chest deformities. Thoracic vertebrae are commonly fused with frequent hemivertebrae; hence, this anomaly was previously known as COVESDEM (costovertebral segmentation defect with mesomelia) syndrome. Ribs are also commonly deformed. Hemivertebrae and scoliosis may be present in more than 75% of patients with the recessive form, but in less than 25% of patients with the dominant form.[(8)]

Genital defects characteristically seen in males include a micropenis with a normally developed scrotum and testes. Sometimes, testicles may be undescended. Female genital defects may include a reduced size clitoris and underdeveloped labia minora. Infrequently, the labia majora may also be underdeveloped.[(5)]

Multiple medical conditions are associated to the syndrome which include frequent ear infections, respiratory problems, eating difficulties, light sensitivity, and esophageal reflux. Data on fertility and the development of secondary sex characteristics is relatively sparse. It has been reported that both male and female patients have had children. Males who have

reproduced have all had the autosomal dominant form of the disorder; the fertility of those with the recessive variant is unknown.[1]

A number of other conditions are often associated with Robinow syndrome. About 15% of reported patients suffer from congenital heart defects. Though there is no clear pattern, the most common conditions include pulmonary stenosis and atresia. Abnormalities in the renal tract of affected patients have also been reported.[3] In addition, though intelligence is generally normal, around 15% of patients show developmental delays.[1]

The causative gene is ROR2 on position 9 of the long arm of chromosome 9. This gene is responsible for bone and cartilage growth. Prenatal diagnosis is possible from the 19th week of pregnancy by fetal ultrasonography. Assessment of the length of the long bones and the ulna/humerus ratio has been used in prenatal diagnosis.[9]

This syndrome has to be differentiated from other causes of vertebral malsegmentation, rib hypoplasia, and forearm dysplasias like Aarskog-Scott syndrome, Opitz G syndrome and autosomal recessive spondylocostal dysostosis. These syndromes are differentiated by the characteristic facial changes and the genital hypoplasia of Robinow syndrome.

Prognosis of Robinow syndrome is generally good, with more than 80% patients having normal intelligence. Management of the orofacial deformities should include a multidisciplinary approach. The syndrome should be diagnosed as early as possible based on clinical features and radiological findings. Oral surgical procedures may be required for correction of gingival hyperplasia and ankyloglossia. Orthodontic correction of crowded and malpositioned teeth should be considered. Orofacial dysmorphism should be corrected with plastic reconstruction surgeries. Management of skeletal deformities includes bracing or surgical correction of scoliosis. The forearm deformities are correctable to a certain extent by callotaxis with a ring fixator. There are also reports of treatment with human chorionic gonadotrophin to increase the penile length and testicular volume. Recombinant human growth hormone is known to increase the growth rate of children with the coexisting growth hormone deficiency.[10]

Conclusion

Despite the extreme rarity, diagnosis and management of Robinow syndrome depend upon a detailed history, thorough clinical examination and imaging requiring a multidisciplinary approach and co-ordination between different fields of dentistry, medicine and surgery which can be life saving for the affected patients. The importance of newborn diagnosis, multicentre clinical research and continuing genetic research is very essential in Robinow syndrome, which will lead to an increase in understanding of the syndrome and wider treatment options for the clinicians.

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