

Craniofacial and Dental Manifestations in Dubowitz Syndrome – Case report

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Abstract

Dubowitz is a rare genetic disorder involving dental and craniofacial abnormalities, growth and mental retardation. This includes a variable phenotype with many manifestations as well as craniofacial, ocular, dental, cutaneous, gastro-intestinal, skeletal, cardiovascular, urogenital, neurological and behavior problems. The craniofacial and dental characteristics have been diagnosed; however, there has been no publication of this description. The objective of this report was to show the importance of recognition, and clarify the peculiar characteristics of a patient with Dubowitz syndrome.

Introduction

The Dubowitz syndrome was first described in 1965 by Victor Dubowitz and this nomenclature was proposed in 1973 by Grosse and Opitz. It includes variable phenotypes and is a very complex syndrome with multiple congenital anomalies, mental retardation, and growth failure condition with immune defects predisposing to allergies and eczema, predisposition to blood dyscrasias, hematologic malignancies, and neuroblastoma. Among congenital anomalies, craniofacial manifestations are observed in the mouth (large or small mouth), lips (flat

philtrum, thin vermilion border of the upper lip, long upper lip with prominent philtrum), palate (hard, narrow palate, submucous cleft palate, cleft palate, bifid uvula, large adenoids and tonsils), chin (microgenion and progenion, narrow chin), and neck (short webbed and long) are present.^{1,2}

The dental manifestations that were noted included delayed eruption; caries; crowded teeth; microdontia; malocclusion; malalignment; diastema; conical crowns; macrodontia; missing upper central incisors; doubled, bifid incisors; rotated lower incisors and incomplete true fusion of the primary right mandibular canine and first molar.²

Since there is no laboratory test to confirm this diagnosis, it is primarily diagnosed through the distinctive facial features of affected individuals, subsequent to the exclusion of other genetic syndromes. The gene localization is unknown, however it is passed on through an autosomal pattern of inheritance.

Case Report

A 9-year-old child, female, white, with Dubowitz syndrome presented to Estomatologic Diagnosis Clinical of Federal University of Rio Grande do Norte for a dental examination in April 2006. The diagnosis was previously made in the Onofre Lopes University Hospital, where the patient is being monitored by a multidisciplinary group. During the odontological evaluation, she was subjected to anamnesis, as well as clinical and special examinations. The radiological examination included panoramic, periapical and occlusal radiographs.

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Figure 1: Small head, frontal bossing, triangular face and characteristic facial features with palpebrae ptosis, micrognathia, low-set ears and saddle nose.



Figure 2: Diastema upper interincisors, incipient cavities, bilateral posterior cross bite.

The clinical anomalies observed consisted of a small head, frontal bossing, bilateral low-set ears, saddle nose, triangular face and characteristic facial features with palpebral ptosis and micrognathia (Figure 1). Her mother reported that although she had undergone a surgical procedure for a clinical correction, her principal complaint was difficulty in opening her mouth, which remained unchanged. She suffered constant fever from the age of five years. Her voice was high pitched and the skin examination revealed eczema, which responded to topical medication with hydrocortisone cream. The examinations of Thyroid hormone levels (TSH: 4,1 UI/ml and T_4 : 11,8 mcg/ml) were normal.

Bone age was compatible with the girl's chronological age and was verified by radiographic analysis of the x-rays of the hand and wrist.

The oral clinical examination revealed the absence of two lower and the upper right canines, delayed eruption and rotation of the lower incisors, upper interincisor diastema, incipient cavities, bilateral posterior cross bite (Figure 2), high, narrow palate (Figure 3), mandibular atresia (Figure 4).

Panoramic radiography showed the absence of upper right premolars, upper left second premolar, lower left lateral incisor and second premolar, lower right lateral incisor and second premolar. Based on the panoramic radiograph, this patient presented chronologic delayed eruption (Figure 5).

Behavioral patterns were obtained through medical analysis and were reported as "aggression and agitation".

The condition had been treated with Phenobarbital for the previous 3 years. A nutritional assessment was performed due to her refusal to accept certain foods. The nutritional diagnostician reported the nutritional condition as Grade I malnutrition.

Her mother disclosed her susceptibility to a high number of infections during her younger years.

Lumbar column radiography indicated a right convex scoliosis.

The results of routine biochemical and metabolic screening were normal, including erythrocyte sedimentation rate, blood counts, renal and liver function tests, serum electrolytes, serum lipids, blood gases, urinalysis, urinary steroids, blood and urine, amino acid chromatography, serum creatine phosphokinase, and aldolase and transaminase levels. Results of endocrine surveys were also normal, including pituitary, thyroid function tests, adrenal cortical function test, and growth hormone levels.

Discussion

Heredity of Dubowitz syndrome was previously hypothesized to be autosomal recessive,³ but current data suggests an autosomal dominant pattern. The phenotype is quite variable, suggesting incomplete penetrance and a strong possibility of modifying genetic and epigenetic factors.²

The specific gene mutation responsible for this syndrome had not yet been identified and the exact molecular and biochemical pathogenesis is unknown. However, a



Figure 3: High, narrow palate, incipient cavity.



Figure 4: Mandibular atresia, incipient cavities.

metabolic and/or DNA repair must be ruled out 2. The diagnosis of Dubowitz syndrome therefore remains based on the characteristic phenotypes found during clinical examination 3.

Victor Dubowitz described a group of congenital anomalies in a 13-year-old female patient in 1965, which had been established with various phenotypes. Patients with Dubowitz syndrome also have a predisposition for hematological malignancy, like lymphoblastic leukemia,^{4,5} non Hodgkin lymphoma,^{5,6,7} malignant lymphoma, neuroblastoma,^{7,8} embryonic rhabdomyosarcoma.^{5,9}

Other blood dyscrasias that could be apparent are aplastic anemia, thrombocytopenia, leucopenia and granulocytopenia.^{5,10,11} Patients with this syndrome are susceptible to infections, mainly involving the respiratory tract, as well as light or moderate mental deficiencies. Severe deficiency is rare.⁵ In this case the patient had suffered a high number of infections during her younger years.

In childhood, patients may experience difficulty in physical motor and speech development. Certain characteristics such as lack of attention, aggression, hyperactivity, depression, only appear in adulthood.^{12,13,14,15,16} All these characteristics were identified in this case.

Chronic episodes of diarrhea and vomiting can appear in the beginning of the syndrome, and if not treated, can become more serious, particularly in patients with an altered immunological system.

Ocular manifestations occur in 20% of patients with Dubowitz.¹⁷ In some patients, their small size can be related

to a growth hormone deficiency.¹⁸ Vertebral alterations such as scoliosis have been described in this syndrome.^{19,20} In ocular manifestations we observed ptosis, vertical strabismus, hypertelorism and the use of spectacles for myopia. This patient has small stature, and a right convex scoliosis.

Regarding the oral manifestations,² a wide array of characteristics could be present. Multiple dental carious lesions are to be found in the majority of cases. Other potential features are a small oral cavity, thin border of the upper lip, prominent labial philtrum, narrow and deep palate, palatine cleft, submucosa palatine cleft, split uvula, micrognathia, prognathism, and retrognathism can be seen. In the dental elements, retarded eruption, caries, microdontia, malocclusion, diastema, fusion of dental elements and anodontia of the central incisors are generally present.

In this case, the patient presented with typical oral alterations like microstomia, thin border of the upper lip, prominent labial philtrum, narrow and deep palate, retrognathism, retarded eruption, diastema, malocclusion (overclosure and cross bite posterior bilateral), and anodontia of some dental elements.

The diagnostic phenotypic manifestations of Dubowitz Syndrome in this patient include the following system alterations: small sized and bilateral low-set ears, saddle nose, triangular face, mental retardation, abnormal voice, hypertelorism and other ophthalmologic alterations, hyperactivity with periods of aggressiveness, infections and scoliosis.

This syndrome involves various systems, including the

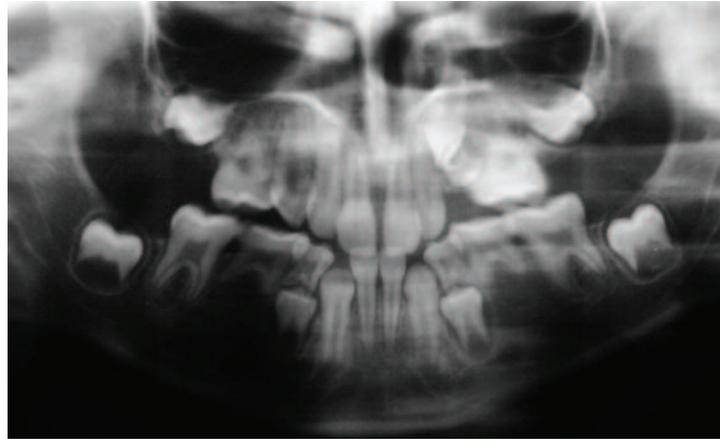


Figure 5: Radiographic observation demonstrated two missing lower canines and impacted upper right canine.

stomatognathic system, emphasizing one of the reasons why it is important for health professional to recognize the characteristics.

Conclusion

As there are few reports of Dubowitz syndrome in the literature, the authors have endeavored to enable health professionals to recognize the phenotypic alterations of this syndrome, and consequently refer such patients for the necessary multidisciplinary treatments.

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