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Dubowitz Syndrome- A Review

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ABSTRACT

Dubowitz syndrome is a genetic and chromosomal instability disorder characterized by growth hormone deficiency or defects in the cholesterol biosynthetic pathway. It is characterized by retarded growth, several craniofacial manifestations, skin eruption, soft-tissue syndactyly, central nervous system and oral manifestations. There are reports of even malignant tumors associated with this syndrome. This manuscript reviews the manifestations and management of the dubowitz syndrome.

Keywords: Dubowitz, Growth deficiency, Malignant

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INTRODUCTION

The Dubowitz syndrome was first described in 1965 by Victor Dubowitz and this nomenclature was proposed in 1973 by Grosse and Opitz.[1] The disorder was first discovered in a female child in 1965 by Victor Dubowitz. The cause of Dubowitz syndrome remains unknown, however, literature points to genetics and chromosomal instability. Sporadic cases suggest growth hormone deficiency or defects in the cholesterol biosynthetic pathway as the source of the disorder.[2]

Clinical features (Figure 1):

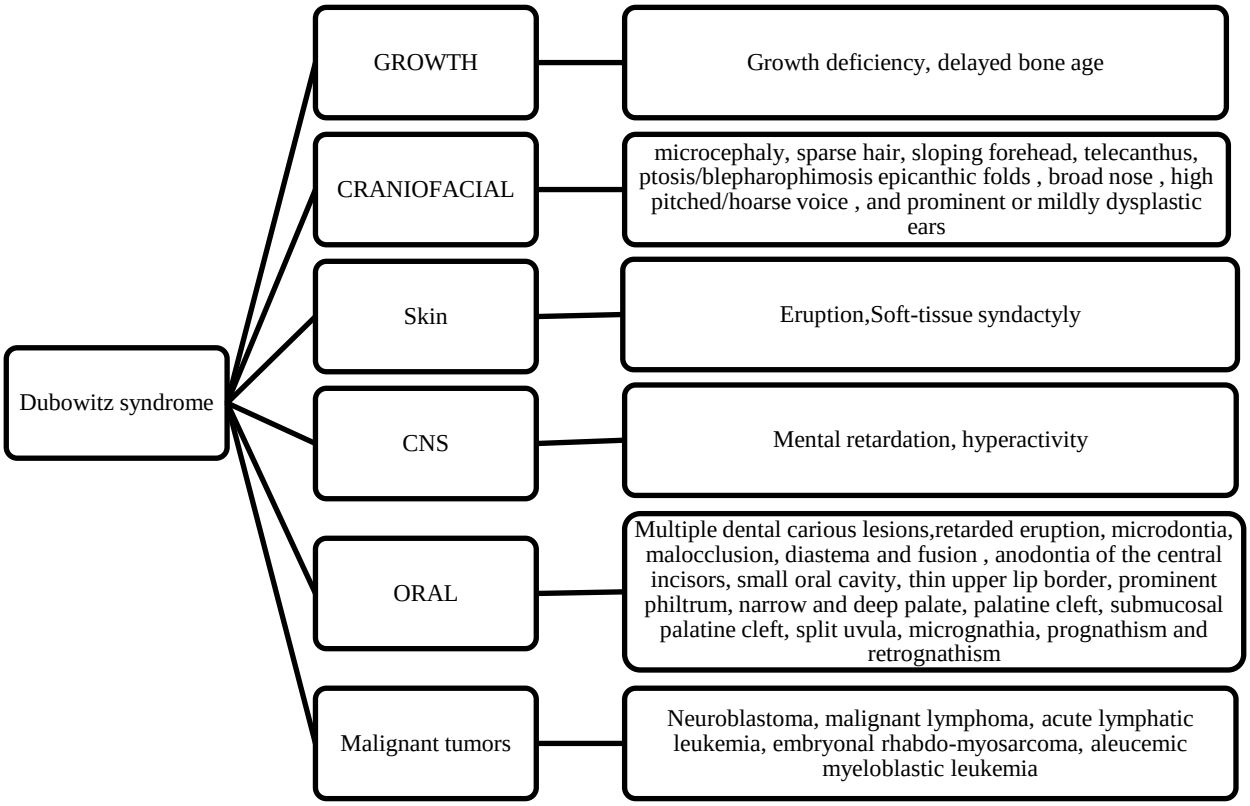

Figure 1: Clinical manifestation flow chart

Growth

As reported at birth the average weight is 2-3 kg, the average length is 45 cm, and the average head circumference is 30 cm. postnatal growth deficiency is usual, but not severe. Delayed bone age has been reported in approximately 50% of cases.[3]

Craniofacial

The main features are microcephaly (100%), sparse hair (70%), sloping forehead (80%), telecanthus (60%), ptosis/blepharophimosis (often asymmetrical) (65%), epicanthic folds (50%), broad nose (55%), high pitched/hoarse voice (55%), and prominent or mildly dysplastic ears (75%). The facial appearance changes with age. However, the contour of the face elongates with

age and the nasal bridge becomes more prominent; in older patients it is high and almost continuous with the forehead. The base of the nose is broad. The supraorbital ridges are hypoplastic with arched eyebrows, sparse laterally.[3]

Skin

An eczematous skin eruption, especially of the face and extremities, has been noted in approximately 60%, usually from birth. The site of involvement has varied from a limited area to the entire body. It often clears by age 2 to 4 years, but it may last until adulthood. Variable minor soft-tissue syndactyly of the second and third toes has been documented in 25%.[4]

Central nervous system

Motor milestones are reached at normal times. Moderate or severe mental retardation has been evident in 15% and 10%, respectively. Most children have been estimated to be in the dull normal range. However, normal intelligence has been noted. Hyperactivity has been manifested by approximately 70%. Speech is delayed in 60%.[4]

Oral manifestations

Multiple dental carious lesions are found in the majority of cases. Other dental features include retarded eruption, microdontia, malocclusion, diastema and fusion of dental elements, anodontia of the central incisors is generally present, small oral cavity, thin upper lip border, prominent philtrum, narrow and deep palate, palatine cleft, submucosal palatine cleft, split uvula, micrognathia, prognathism and retrognathism. In 1990, velopharyngeal insufficiency was described for the first time.[5]

A case report described radiological manifestations of this syndrome includes chronologically delayed eruption and radicular abnormalities of the second molars. Ponderal growth was delayed. Anteroposterior radiological sinonasal findings showed hypoplastic frontal sinuses and mild nasal septum deviation. Lateral radiography showed skeletal class II, ethmoid cell hypoplasia, frontal bone thickness and mild hyperostosis frontalis. Radiographs of the lumbar column indicated a right convex scoliosis.[5]

Others

Thuret et al. reported the cases of 2 caucasian sisters who, in addition to other features, had repeated infections and recurrent ulcerative stomatitis. They suffered from recurrent neutropenia. One had complete IgA deficiency with elevated IgM levels; the other had low values of both IgA and IgG with an increased level of IgM. An increased rate of chromosomal breakage was demonstrated in both.[6]

Frequency of malignant tumors are increased in this syndrome reported cases are neuroblastoma, malignant lymphoma, acute lymphatic leukemia, embryonal rhabdomyosarcoma, aleucemic myeloblastic leukemia.[6] An association between Dubowitz syndrome, hyper-IgE syndrome, and nasal polyposis (due to allergic fungal sinusitis) has been reported.[7]

Diagnosis

Since the mutant gene is not yet identified, genetic testing cannot be used for diagnosis. Usual diagnostic approach for Dubowitz syndrome is the history, growth characteristics and other craniofacial manifestations.

Treatment

Like most genetic disorders, Dubowitz syndrome management is mainly targeted towards the symptomatic features. Counseling the patients and their family forms the essential management section for this genetic disorders.[8] Regular, long term follow up of the patients is recommended. Regular study of[9]

1. Growth: plot carefully; consideration of treatment with growth hormone or anabolic steroids may be discussed with Pediatric Endocrinology consultant.
2. Regular physical examination, urinalysis and complete blood count
3. Dermatological management is treated with creams containing corticosteroid[8]
4. Speech and dental development and hearing especially in those who had multiple middle ear infection
5. Behavior/ neurologic problem
6. Developmental and intellectual quotients
7. Surgical needs: repair of craniofacial, limb, or urogenital anomalies
8. Surveillance for hematological and malignant disorders
9. Educational programs appropriate for each individual.

Prognosis

The prognosis is maintained well as long as the symptomatic features are treated properly. They can survive to adulthood and lead fairly normal lives, although some of them have mild mental retardation.[8]

CONCLUSION:

Role of Pedodontist, Orthodontist and Oral surgeon play a significant role to treat the oral manifestations with this syndrome. Even reports of even malignant tumors are found to be associated with this syndrome. So this syndrome requires early diagnosis and multidisciplinary

approach.

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