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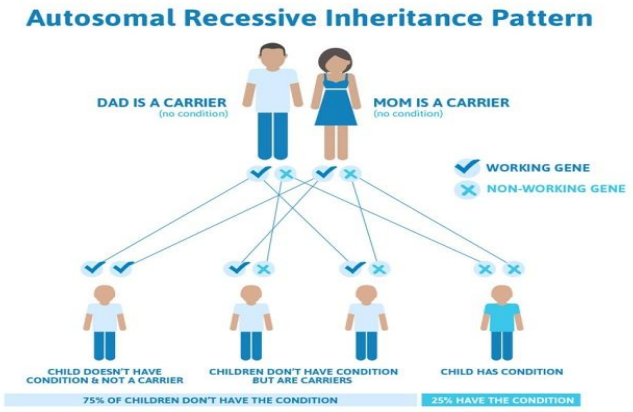
A Rare Case of Dubowitz Syndrome with Polyendocrinopathy

Authors
Gaurav Gupta[1], Dr Ila Pahwa[2], Dr Hemant Kumar Sharma[3]
[1]Junior Resident, Department of Medicine, Muzaffarnagar Medical College Muzaffarnagar, Uttar Pradesh, India
[2]Professor & Head, Department of Medicine, Muzaffarnagar Medical College Muzaffarnagar, Uttar Pradesh India
[3]Professor, Department of medicine, Muzaffarnagar Medical College Muzaffarnagar, Uttar Pradesh India

Abstract
Dubowitz Syndrome – A very rare genetic and developmental disorder, characterized by Microcephaly, Stunted Growth, Small Jaw (Micrognathia), Sparse Hair, Mental Retardation. Symptoms may vary among patients, facial appearance is the key to the diagnosis. H/O Consanguineous Marriage in parents. Thus far only about 200 cases have been reported worldwide since 2002. Here, we report a case of a male, 30 years, presented with Non Healing Ulcer over left foot, with characteristics features of Short Stature, Microcephaly, Microganathia, and High Arched Palate with Polyendocrine involvement like Diabetes Mellitus, Hypothyroidism, and Hypoparathyroidism. H/O Consanguineous Marriage in Parents is present. Prompt diagnosis with regular follow up and supportive care remains the key to the management of this disorder.

Introduction

A very rare genetic and developmental disorder, characterized by microcephaly, stunted growth, small jaw (micrognathia), sparse hair, mental retardation.[1] Symptoms may vary among patients; facial appearance is the key to the diagnosis. History of consanguineous marriage in parents is present. Thus far only about 200 cases have been reported worldwide since 2002.[2] The pathogenesis of this syndrome is unknown and is presumed to represent the inherited by autosomal recessive manner.[3]



Case History

Here, we report a case of a male, 30 years born of a consanguineous marriage presented with non healing ulcer over left foot. A general physical examination found with characteristics features of – short stature/ growth failure**,** small head (microcephaly), small face**,** small lower jaw

(micrognathia)**,** high arched palate, prominent ears, hook nose, delayed eruption of teeth with missing teeth, sparse hair, scanty lateral eyebrows, micropthalmia, high pitched voice, genu valgum (knock-knee)**.**

Developmental assessment revealed shy nature with normal intelligence. Ophthalmological and audiological assessment was normal. Endocrinal gland involvement-diabetes mellitus (HbA1c 9.5%)**;** hypothyroidism (TSH 75.04 Uiu/ml,T3 total 0.58 ng/ml,T4 total 2-10 ug/ml, anti TPOab positive 100 IU/ml)**;** hypoparathyroidism (intact PTH 12.8 pg/ml; calcium 7.6 ; phosphorus 6.64).

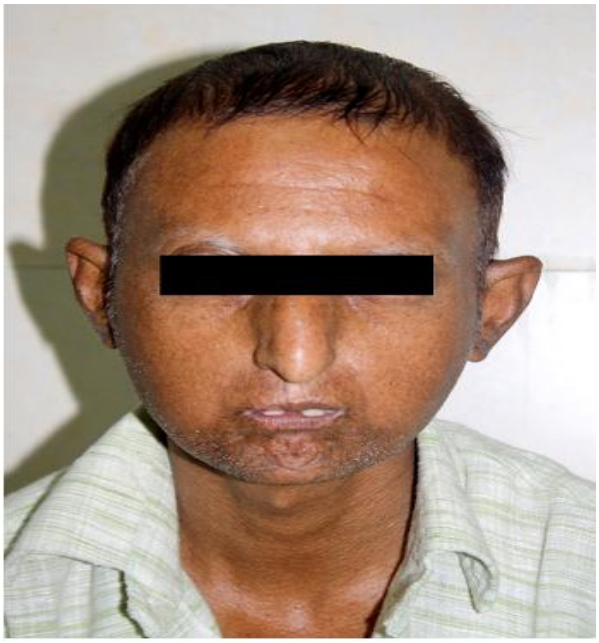


Figure 1- Dubowitz Syndrome patient frontal view

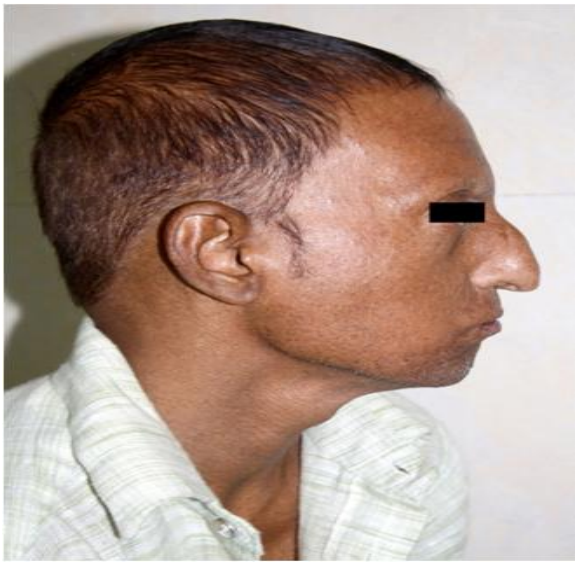


Figure 2- Dubowitz Syndrome patient lateral view

Investigation

S.no	Test name	Result	Units	Bio.ref.interval
1.	Haemoglobin	8.4 ↓	g/dl	14-18
2.	Mcv	58 ↓	fl	75-95
3.	Mch	18 ↓	pg	27-32
4.	Mchc	29 ↓	%	30-32
5.	Iron	20 ↓	ug/dl	50-170
6.	Tibc	543 ↑	ug/dl	250-425
7.	Transferrin saturation	3.68 ↓	%	15-50
8.	Ferritn	4.60 ↓	ng/ml	10-291
9.	Hba1c	9.5 ↑	%	<6.5
10.	Tsh	75.04↑	uIU/ml	0.35-5.60
11.	T3 total	.58 ↓	Ng/ml	.60-1.81
12	T4 total	2.10 ↓	ug/ml	5.01-12.45
13.	Anti tpo antibody	100 ↑	IU/ml	<35 IU/ml
14.	Intact parathyroid hormone	12.80 ↓	pg/ml	14-72
15.	Calcium	7.6 ↓	mg/dl	8.8-10.60
16.	Phosphorus	6.64 ↑	Mg/dl	2.40-4.40
17.	Provocative growth hormone	0.45 ↓	Ng/ml	>5
18.	Serum cortisol	15.16 N	ug/dl	4.30-22.40
19.	Serum insulin fasting	29.40 ↑	uU/ml	2.00-25.00
20.	Serum ttg antibody	6.64 N	units	<20
21.	Serum iga	237 N	Mg/dl	70-400
22.	Serum testosterone total	270.79 N	ng/dl	175-781

Echocardiography- normal left ventricle systolic function (lvef-60%), x-ray skull suggestive of micrognathia of mandible.

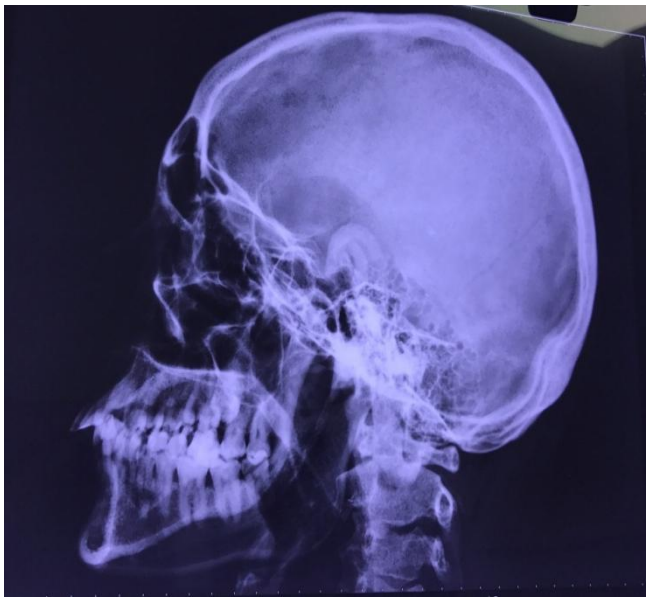
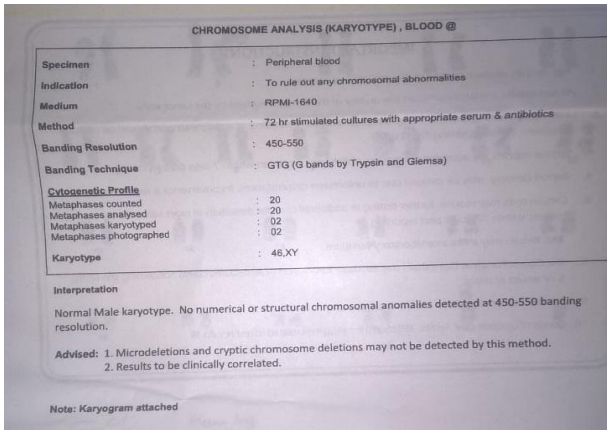


Figure 3- x-ray skull lateral view



CHROMOSOME ANALYSIS (KARYOTYPE) , BLOOD @

Specimen	:	Peripheral blood
Indication	:	To rule out any chromosomal abnormalities
Medium	:	RPMI-1640
Method	:	72 hr stimulated cultures with appropriate serum & antibiotics
Banding Resolution	:	450-550
Banding Technique	:	GTG (G bands by Trypsin and Giemsa)
Cytogenetic Profile		
Metaphases counted	:	20
Metaphases analysed	:	20
Metaphases karyotyped	:	02
Metaphases photographed	:	02
Karyotype	:	46,XY

Interpretation

Normal Male karyotype. No numerical or structural chromosomal anomalies detected at 450-550 banding resolution.

Advised: 1. Microdeletions and cryptic chromosome deletions may not be detected by this method.
2. Results to be clinically correlated.

Note: Karyogram attached

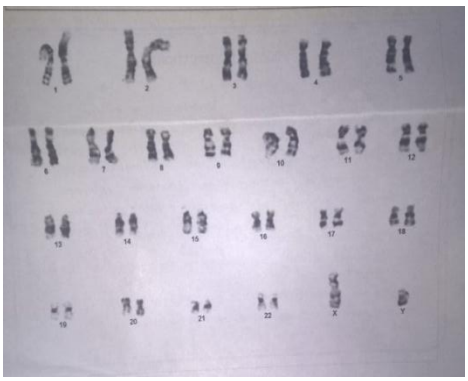


Figure-4 chromosomal analysis (karyotype), blood

Discussion

The constellation of features in this patient was consistent with the diagnosis of dubowitz syndrome. This syndrome was first described in 1965 by English physian Victor Dubowitz.[4] There is no precise medical test that will conclusively consign the diagnosis of this syndrome since genetic reason is unknown.[5] Apart from the characteristic facies, a variety of ocular, dental, cutaneous, skeletal, cardiovascular, gastrointestinal, neurological, immunological and hematological difficulties have been described. Other features are- partial webbing of finger, eczema 50 %, sacro coccygeal anomaly undescended / ectopic testes, persistent low cholesterol level.[6]

Polyendocrinal involvement occur likes diabetes mellitus, autoimmune hypothyroidism, hypoparathyroidism. Patient also found iron deficiency anemia with growth hormone deficiency.

Conclusion

Prompt diagnosis with regular follow up and supportive care remains the key to the management of this disorder. For involvement of endocrine gland treatment is replacement of hormone and according to investigation.

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