# Ophthalmological abnormalities in Dubowitz Syndrome

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## ABSTRACT

**Introduction:** Dubowitz syndrome is a rare autosomal recessive disorder characterized by several congenital abnormalities, which include a wide range of both external and intraocular ophthalmologic deformities. We present a case report of a patient with Dubowitz Syndrome.

**Case Report:** A 3-year-old boy with Dubowitz syndrome was referred for ophthalmology consultation. The external ophthalmological examination showed bilateral blepharophimosis/ptosis, telecanthus and epicanthic folds. Cycloplegic retinoscopy revealed high hyperopia (+ 8.00 diopters) and the patient had convergent strabismus. Biomicroscopy and fundus examination were normal.

**Discussion/Conclusion:** Dubowitz syndrome should be considered in the differential diagnosis of syndromes that present with the described external ophthalmological malformations. The ophthalmologist has an important role in the referral of these patients for a multidisciplinar and specialized group to integrate these anomalies with other systemic deformities, allowing a correct diagnosis and proper treatment.

**Keywords:** Dubowitz syndrome; ophthalmological abnormalities; facial dysmorphy; blepharophimosis; ptosis

## RESUMO

**Introdução:** O síndrome de Dubowitz é um síndrome autossómico recessivo, caraterizado por anomalias congénitas severas, incluindo um conjunto de deformidades oftalmológicas externas e internas. Descreve-se o caso clínico de um paciente com síndrome de Dubowitz.

**Caso Clínico:** Paciente sexo masculino, 3 anos de idade, diagnosticado com síndrome de Dubowitz, foi referenciado à consulta de Oftalmologia. O exame oftalmológico externo evidenciou presença de blefarofimose/fimose bilateral, telecanto e pregas epicanto. A retinoscopia ciclopégica evidenciou alta hipermetropia (+ 8.00 dioptrias) e apresentava estrabismo convergente. A biomicroscopia e fundo ocular não revelaram alterações.

**Discussão/Conclusão:** O síndrome de Dubowitz deve ser considerado no diagnóstico diferencial de outros síndromes que apresentam as malformações oftalmológicas externas descritas. O oftalmologista tem um papel importante na referenciação destes pacientes para uma equipa multidisciplinar para integração destas deformidades oftalmológicas com outras deformidades sistémicas, para um diagnóstico e tratamento adequado.

**Palavras-chave:** Síndrome Dubowitz; deformidades oftalmológicas; dismorfia facial; blefarofimose; ptose

## INTRODUCTION

Dubowitz syndrome (DS) is a rare autosomal recessive disorder considered as an association of multiple congenital abnormalities, intellectual disability, growth failure, an immune defect predisposing to eczema and allergies and increased risk of blood dyscrasias and malignancy[2,3,4,6,8,9,10]. Facial appearance is characteristic with high or sloping forehead, flat supraorbital ridge, scanty lateral eyebrows, short palpebral fissures, ptosis, abnormally modeled ears, broad and flat nasal bridge, and unusual configuration of the mouth. Ocular problems occur in about 20%: strabismus, blepharophimosis, ptosis, telecanthus and epicanthal folds being the most frequent ones. Hyperopia, cataracts and degeneration of the retina can also be found[2,3,4,6,8,9,10]. Genital abnormalities include hypospadias and cryptorchidism. Affected individuals may also have a sacral dimple, clinodactyly of the 5th fingers, and cutaneous syndactyly of the 2nd and 3rd toes. The objective of this case report was to clarify the particular ocular findings of a patient with DS, and highlight the importance of early recognition of this condition, to prevent amblyopia in the future.

## CASE REPORT

A 3-year-old Caucasian boy with DS presented to our institution for ophthalmological examination. The boy was born at term, with weight of 2000 g, length of 43 cm and head circumference of 34 cm. He was the second child of unrelated parents. His 5-year-old sister is healthy. Pregnancy proceeded without any complications and the mother denies use of drugs or tobacco and alcohol consumption. Family history was unremarkable.

The clinical records of the multidisciplinary team described a child with postnatal growth retardation, mild psychomotor delay, hyperactive behavior, atopic dermatitis, and asthma. Craniofacial anomalies included microcephaly, broad nasal bridge, anteverted nostrils, ocular anomalies, low-set dysmorphic ears, unusual configuration of mouth, and micrognathia. Skeletal manifestations such as clinodactyly and sacrococcygeal dimple were present. Genital abnormalities included hypospadia, micropenis and impalpable right testis. Gastrointestinal problems during the neonatal period were characterized by feeding dificulties and vomiting. A congenital heart defect described as an atrial septal defect closed spontaneously. Cytogenetic analysis and biochemical/metabolic screening were apparently normal. The external ophthalmological examination showed bilateral blepharophimosis/ptosis, telecanthus and epicanthic folds (Figure 1). The pupils were equal, round and reactive to light. Eye movements were large and symmetric. Cycloplegic retinoscopy revealed high hyperopia (+ 8.00 diopters) and the patient had convergent strabismus. Biomicroscopy and fundus examination were normal.

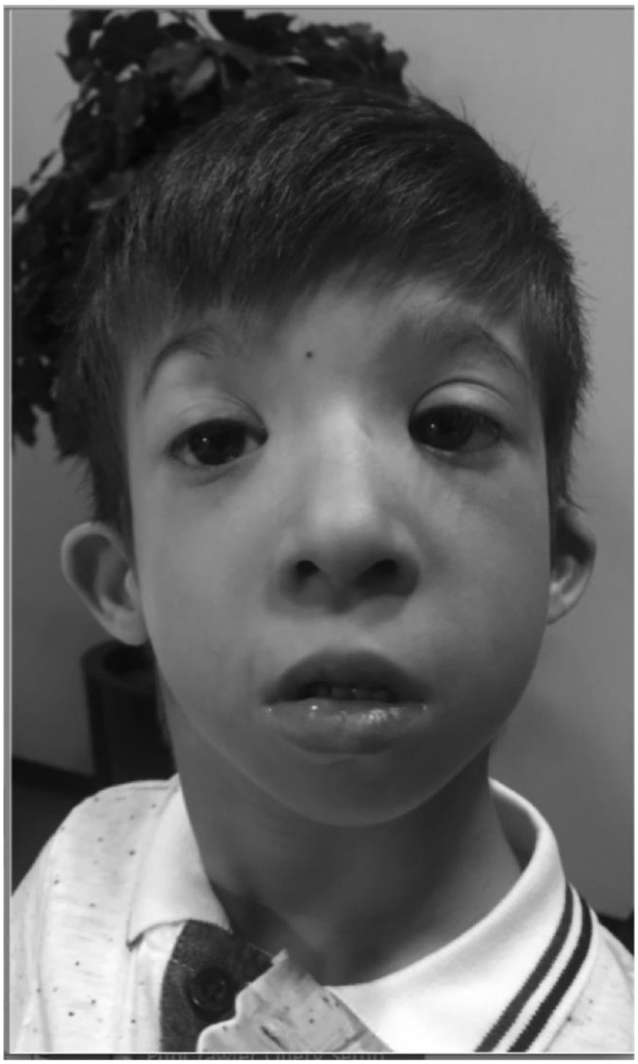

**Figure 1** - Caniofacial malformations of a 3-year-old boy with Dubowitz syndrome. Note the ophthalmologic anomalies: bilateral telecanthus, blepharophimosis/ptosis, epicanthic folds and convergent strabismus.

## DISCUSSION / CONCLUSIONS

Dubowitz syndrome, first described in 1965, is a rare disorder defined as a condition with multiple congenital abnormalities[2]. To date, over 150 patients with this condition have been reported. DS seems to affect equally both sexes [2,3,4,9,10] and all ethnicities [3,4,8]. This syndrome is consistently described as an autosomal recessive inherited disorder [2,3,4,6,8,9,10]. However, the precise etiology of DS remains unknown. It has been recently suggested that DS is a microdeletion/microduplication syndrome involving 13q, 14q32.3 and 17q24.2 [1,5,7]. Some causative genes, such as NSUN2, LIG4 and DNA ligase IV[7], have been referred to single case descriptions.

Diagnosis is commonly made in early childhood and is based on clinical observation of behavioral patterns and multiple clinical manifestations. The results of laboratory examinations were normal in most cases [3,4,8]. The phenotypic spectrum of DS is extraordinarily variable. The clinical features include varying degrees of developmental and growth retardation, microcephaly, hyperactivity, characteristic facies, immune defect predisposing to allergies and eczema, and genital anomalies [2,3,4,6,8,9,10]. Facial anomalies are perhaps the most diagnostic of all physical signs[8], including high or sloping forehead, flat supraorbital ridge, eye and ocular adnexa malformations, abnormally modeled ears, broad and flat nasal bridge, and unusual configuration of the mouth and lips. A variety of ophthalmologic problems have been reported (Table 1). The most common findings are blepharophimosis, ptosis and Telecanthus [2,3,4,6,8,9,10]. Ocular impairment was present in about 22% of patients[8]. Strabismus was the most frequent pathology. Other less common problems included esotropia, microphthalmia, myopia, hyperopia, nystagmus, anisocoria, iris coloboma, iris hypoplasia, megalocornea, cataracts, paresis, poor vision, astigmatism, blue sclerae, deep optic nerve cupping, and immature retinal vessels [3,6,8].

**Table 1** - Ophthalmological Abnormalities in Dubowitz Syndrome

| | Wilroy, 1978 n = 21 | Kuster, 1986 n = 33 (previous cases) | Kuster, 1986 n = 5 (own cases) | Tsukahara, 1996 n = 105 | Dentici, 2011 n = 141 | Huber, 2011 n = 148 |
|---|---|---|---|---|---|---|
| **EXTERNAL ANOMALIES** | | | | | | |
| **Blepharophimosis** | - | - | - | 57% | 43% | - |
| **Ptosis** | - | - | - | 50% | 38% | - |
| **Blepharophimosis/ ptosis** | 52% | 83% | 40% | - | - | 25% |
| **Telecanthus** | 62% | 86% | 80% | - | 25% | - |
| **Hypertelorism** | - | - | - | - | 19% | - |
| **Telecanthus/ Hypertelorism** | - | - | - | - | - | 15% |
| **Upward palpebral fissures** | - | - | - | - | 11% | - |
| **Epicantic folds** | 48% | 61% | 100% | - | - | - |
| **OCULAR IMPAIRMENT** | - | - | | 30% | 22% | - |

We believe that this case report improves the knowledge about DS and points out the importance of the ophthalmologist in the referral of patients with ophthalmological malformations to a specialized group able to integrate these anomalies with other systemic deformities and cognitive, psychological and behavioral changes, allowing a correct diagnosis and proper treatment.

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