



# A Case with Microphthalmia and Multiple Congenital Anomalies

## Mikroftalmi ve Çoklu Konjenital Anomalili Bir Olgu

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### Summary

We present a 7-month-old girl with bilateral microphthalmia, sclerocornea, iris and chorioretinal coloboma, blepharophimosis and dacryostenosis. Microphthalmia is one of the most common features in many syndromes as Micro syndrome, oculodentodigital dysplasia, oculofaciocardiodental syndrome, and Lenz microphthalmia syndrome. Our patient's clinical features also involved microcephaly, cleft palate, developmental delay, digital and urogenital anomalies, cardiac septal defects and hearing loss, which diagnosis is mostly consistent with the Lenz microphthalmia syndrome. Lenz microphthalmia syndrome is a very rare conditions and their expressions are more often in countries with high rates of consanguineous marriages. Hence, recognizing such rare syndromes in patients with multiple congenital anomalies is essential. (*Turk J Ophthalmol 2013; 43: 468-70*)

**Key Words:** Microphthalmia, congenital anomalies, Lenz Microphthalmia syndrome

### Özet

Bu olgu sunumunda iki taraflı mikroftalmi, sklerokornea, iris ve koryoretinal kolobom, blefarofimozis ve dakriyostenozu olan 7 aylık bir kız çocuğu değerlendirilmektedir. Mikroftalmi başta Micro sendromu, okülodontodigital displazi, okülöfasiyokardiyodental sendrom ve Lenz mikroftalmi sendromları olmak üzere pek çok sendroma eşlik edebilmektedir. Bizim olgumuzda ayrıca mikrosefali, yarık damak, gelişme geriliği, parmak ve urogenital anomaliler, kardiyak septal defekt ve işitme kaybı da mevcuttu ve bu bulgular olgumuzda tanı açısından Lenz mikroftalmi sendromunu düşündürmekteydi. Lenz mikroftalmi sendromu oldukça nadir görülmekle birlikte özellikle akraba evliliklerinin sık olduğu ülkelerde daha fazla karşımıza çıkabilmektedir. Bu nedenle çoklu konjenital anomalisi olan olgularda bu nadir sendromun mutlaka akla getirilmesi gerekmektedir. (*Turk J Ophthalmol 2013; 43: 468-70*)

**Anahtar Kelimeler:** Mikroftalmi, konjenital anomaliler, Lenz Mikroftalmi sendromu

### Introduction

Lenz microphthalmia syndrome was first described by Lenz in 1955<sup>1</sup> and is accompanied by multiple congenital anomalies. It is a rare disorder inherited as an X-linked recessive trait and consists of microphthalmia, development retardation, skeletal, digital, cardiac, orofacial and urogenital anomalies.<sup>2,3</sup> Here, we report a case of Lenz microphthalmia syndrome in order to draw attention to the clinical features of this rare syndrome.

### Case Report

In this report, we present a 7-month-old girl with dysmorphic face, ocular and other systemic abnormalities. She was born at term by a spontaneous vaginal delivery as a first child of non-consanguineous parents. There was no complication or drug exposure history during pregnancy.

Ophthalmologic examination revealed bilateral microphthalmia, sclerocornea, iris and chorioretinal coloboma, blepharophimosis and dacryostenosis (Figure 1a,b). In fundus

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examination, bilateral chorioretinal colobomatous areas in the lower half of the retina, including the inferior margin of the optic discs were observed. The maculas were normal in both eyes. Intraocular pressures were 14 in both eyes by Tonopen®, and both lenses were clear.

The patient was born with intrauterine growth retardation (birth height and weight under 10 percentile), microcephalia (under 10 percentile), broad nasal root, hypoplastic ala nasi, long philtrum, cleft palate, micrognathia, and low set ears (Figure 1c). Dental structure could not be evaluated due to her age.

Multiple system abnormalities became apparent with the consultations: 1) incomplete cutaneous syndactyly in both hands and feet (Figure 1d,e: syndactyly of 3<sup>rd</sup> and 4<sup>th</sup> fingers and of 4<sup>th</sup> and 5<sup>th</sup> toes); 2) severe bilateral sensorineural hearing defect; 3) atrial and pulmonary septum defects in cardiac echocardiography; 4) hydrometrocolpos uteri due to high type vaginal atresia; and 5) mild dilatation of lateral ventricles at supratentorial level detected with cerebral magnetic resonance imaging (MRI). The brain parenchyma, corpus callosum and other structures on cerebral MRI, renal and renal calyces' sizes in abdominal ultrasonography and long bone X-rays of the extremities were normal. Chromosome analysis performed on a peripheral blood sample showed a normal karyotype (46, XX). Unfortunately, the patient died due to respiratory failure after a surgical procedure for cleft palate and molecular genetic studies could not be applied to her.

## Discussion

There are many syndromes where ocular anomalies are associated with other congenital anomalies. When microphthalmia and congenital cataract are associated with



**Figure 1.** Ocular, orofacial and digital anomalies of the patient:

a) Right eye, b) Left eye showing microrcornea, sclerocornea, iris coloboma, blepharophimosis and epiphora, c) Dysmorphic face appearance of the patient, d) Left hand with incomplete syndactyly of the 3<sup>rd</sup> and 4<sup>th</sup> fingers, e) Left foot with incomplete syndactyly of the 4<sup>th</sup> and 5<sup>th</sup> toes

congenital heart defects, an idea of congenital rubella infection arises in minds frequently. But it should be kept in mind that microphthalmia, which is one of the most common feature in many syndromes can also be observed in Micro syndrome<sup>4</sup>, oculodentodigital dysplasia<sup>5,6</sup> (ODDD), oculofaciocardiodental syndrome<sup>7</sup> (OFCDS), and Lenz microphthalmia syndrome<sup>1-3</sup>.

Micro syndrome is associated with mental retardation, microcephaly, congenital cataract, microcornea, microphthalmia, agenesis/hypoplasia of the corpus callosum, and hypogenitalism.<sup>4</sup> Our patient had clear lenses, and cerebral MRI showed normal corpus callosum.

Oculodentodigital dysplasia (ODDD) is a rare autosomal dominant inherited disorder affecting the development of the face, eyes, teeth, and limbs.<sup>5,6</sup> Although some autosomal recessive transmitted cases are reported, cardiac and genital anomalies have never been declared as in this patient.

Concerning all the ocular and systemic features, the diagnosis of this patient is mostly applicable for either oculofaciocardiodental syndrome or Lenz microphthalmia syndrome. OFCD syndrome is an X-linked dominant condition involving eye anomalies (congenital cataract, microphthalmia, or secondary glaucoma), facial anomalies (long narrow face, high nasal bridge, pointed nose with cartilages separated at the tip, cleft palate), cardiac anomalies (atrial septal defect, ventricular septal defect, or floppy mitral valve), and dental abnormalities.<sup>7</sup> This syndrome is first described by Wilkie<sup>8</sup> and Aalfs<sup>9</sup> in 1993 and 1996, respectively, and different types of mutations in the BCOR gene has shown to be responsible.<sup>10,11</sup>

Lenz microphthalmia syndrome was first described by Lenz in 1955.<sup>1</sup> The phenotype features of OFCD and Lenz microphthalmia syndrome overlap in many points, and these 2 syndromes are likely to result from defects in alternative functions of BCOR. Lenz microphthalmia syndrome is inherited in an X-linked recessive pattern, by a mutation in the BCL<sup>6</sup> interacting corepressor gene, BCOR.<sup>10,11</sup> The clinical features associated with Lenz microphthalmia syndrome are as follows: microphthalmos in all patients, developmental retardation (92%), external ear abnormalities (83%), microcephaly (83%), blepharoptosis (75%), skeletal anomalies (excluding digital anomalies, 67%), dental abnormalities of number and position (67%), digital anomalies (58%), urogenital anomalies (50%), and cleft lip and palate abnormalities (33%).<sup>2,3</sup> Cardiac anomalies and hearing loss are rarely seen. The patients are always female and the chromosome analysis usually comes out as 46 XX. But, Temtamy et al.<sup>12</sup> reported the association of 5-alpha reductase deficiency with this syndrome, with a karyotype of 46XY in a female patient.

We consider that our patient's clinical features (microphthalmos, microcephaly, cleft palate, development delay, digital and urogenital anomalies, cardiac septal defects and hearing loss) are mostly compatible with the Lenz microphthalmia syndrome. This syndrome is consisted of multiple congenital anomalies with variable expressions. Therefore, it may not always be possible to make the

exact diagnosis, especially without molecular genetic studies. Although both Lenz microphthalmia syndrome and OFCDs are very rare conditions, their expressions are much higher in countries having high rates of consanguineous marriages. Hence, we think recognizing such rare syndromes in patients with multiple congenital anomalies is imperative.

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