A case of Lenz microphthalmia syndrome

F Ferda Özkinay, Cihatgir Özkinay, Hasan Yuksel, Ayse Yenigun, Gul Sapmaz, Oguz Aksu

Abstract
Lenz microphthalmia syndrome was first described by Lenz et al in 1955. The cardinal features of the syndrome are microphthalmia or anophthalmos, narrow shoulders, other skeletal anomalies, and dental and urogenital malformations.

Here we present a case of Lenz microphthalmia syndrome who shows the typical characteristics and, additionally, dysgenesis of the corpus callosum associated with dilatation of the lateral ventricles.

The patient, a 13 year old male, was referred to our hospital by a dental hospital for genetic counselling. On physical examination, height, weight, and head circumference were below the 3rd centile and he had brachymicrocephaly, a preauricular tag, microphthalmia, missing teeth, narrow shoulders, long, proximally placed thumbs, hypospadias, cryptorchidism, and a normal IQ. Ophthalmological examination showed microcornea, sclerocornea, absence of the pupil, no vision in the left eye and decreased vision and a small pupil in the right eye in addition to his bilateral microphthalmia. Cranial MRI showed dilatation of the lateral ventricles and dysgenesis of the corpus callosum.

Keywords: Lenz microphthalmia syndrome; microphthalmia; corpus callosum dysgenesis

Lenz microphthalmia syndrome, described by Lenz et al in 1955, is a rare genetic disorder. About 20 cases have been published to date. Cardinal features of the syndrome are unilateral or bilateral microphthalmia, ear deformities, microcephaly, dental, skeletal, and urogenital abnormalities, and mental retardation.1,3 The syndrome is inherited in an X linked recessive fashion. Affected males are always infertile. Differential diagnosis includes autosomal recessive anophthalmia and autosomal recessive or X linked microphthalmia.

Here we present a case of Lenz microphthalmia syndrome who also has dysgenesis of the corpus callosum associated with dilatation of the lateral ventricles in addition to the typical features of the syndrome. This is the first reported case of Lenz microphthalmia with these other anomalies.

Case report
A 15 year old male patient was referred to our hospital by a dental hospital for genetic counselling. He was born at 32 weeks of gestation to non-consanguineous parents after a normal vaginal delivery. There were no other family members with similar features. The mother had had eight pregnancies of which four were aborted by her own choice in the first trimester. The patient was one of the products of a twin pregnancy. His twin sib was a healthy female. The other three sibs were normal males.

Developmental delay was detected in childhood: he gained head control at 3 months, sat at 2 years, walked at 3 years, and gained bladder and bowel control at 5 years. He was attending a special school for people with visual deformities and was in the ninth grade. His mental development seemed to be slightly subnormal.

On physical examination at 15 years old, his weight (31.5 kg), height (150 cm), and head circumference (46 cm) were below the 3rd centile. He had a long head, sparse hair, prominent nasal bridge, bilateral microphthalmia, and abnormal ears that were antverted, prominent, and had poorly developed and thin antihelices with a preauricular tag on the left side (figs 1 and 2). The teeth were hypoplastic, irregular, and widely spaced. He had a highly arched palate and long philtrum. His neck was long with sloping shoulders. The thumbs were long and proximally placed. He had a sacral dimple, a cigarette paper scar on his back (fig 3), a hydropocele on the right side, and incomplete hypospadias. The urethral orifice was dorsally placed.

Ocular examination showed bilateral microphthalmia, microcornea, absence of the pupil and no vision in the right eye, and a small pupil and diminished vision in the left eye. Radiographs showed hypoplastic clavicles.

Laboratory tests (complete blood count, urine analysis, blood electrolytes, liver and renal function tests) and abdominal ultrasonography were normal.

On cranial magnetic resonance imaging (MRI) a dysgenetic corpus callosum and dilatation of the temporal horns of the lateral ventricles were observed (fig 4). Chromosomes were normal. The clinical features of the patient are shown in table 1.

Discussion
Microphthalmia is one of the cardinal features of a number of syndromes.4 Among these, oculo-dento-osseous syndrome, cerebro-oculo-facio-skeletal syndrome, and Goltz syndrome show the most similar findings to Lenz microphthalmia syndrome. Common features of these syndromes are microphthalmia, dental changes, and skeletal deformities.
A case of Lenz microphthalmia syndrome

In cerebro-oculo-facio-skeletal syndrome (COFS), inherited as an autosomal recessive trait, survival is rare after the age of 5 years. Patients with COFS usually show generalised hypotonia, areflexia, camptodactyly, flexion contractures of the elbows and knees, and osteoporosis, in addition to microphthalmia. Our case does not show the cardinal features of the syndrome described above with the exception of the eye findings.

MRI showed dysgenesis of the corpus callosum in our patient. Morphological abnormalities of the corpus callosum can be divided into three categories: agenesis, hypoplasia, and hypogenesis. In agenesis the corpus callosum is totally absent. In hypogenesis the caudal or corpus part of the corpus callosum is shortened. Hypoplasia refers to a thin corpus callosum that is commonly associated with cortical dysgenesis. In a number of syndromes morphological abnormalities of the corpus callosum are associated with other abnormalities. Some of these syndromes, such as acrocallosal syndrome, frontonasal dysplasia, Anderman
inclusions, such as angiofollicular changes around the lips and anus and atrophy and altered pigmentation in localized areas. 15

Our case was diagnosed as having Lenz microphthalmia syndrome because his findings, including craniofacial abnormalities, narrow shoulders, hypoplastic clavicles, cryptorchidism, and skeletal changes in the hands and feet, are the typical characteristics of Lenz microphthalmia syndrome (tab. 2).

Although Goltz syndrome, Aicardi syndrome, and Lenz microphthalmia syndrome have been defined as separate entities, they have a remarkable number of common features, such as microphthalmia, skeletal changes, motor and mental retardation, and X-linked inheritance. However, there have been some linkage studies concerned with the gene locations on the X chromosome (especially the Xp22 region) of these disorders. No gene has definitely been mapped for any of them. Friedman et al14 described a girl with Goltz syndrome who had a terminal deletion of the short arm of the X chromosome with a breakpoint in Xp22.31. Nielsen et al15 studied the Xp22 region in Aicardi patients by using polymorphic DNA markers. They found no evidence for a microdeletion. Graham et al16 excluded a location on Xp for the Lenz microphthalmia gene in a family by linkage analysis. Further molecular studies are needed to understand the genetic relationship between these syndromes.

Table 2 Major abnormalities seen in Lenz microphthalmia syndrome and the findings in our patient

<table>
<thead>
<tr>
<th>%</th>
<th>Our patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microphthalmia</td>
<td>100 +</td>
</tr>
<tr>
<td>Retardation</td>
<td>92 +</td>
</tr>
<tr>
<td>Ear abnormalities</td>
<td>83 +</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>83 +</td>
</tr>
<tr>
<td>Blepharoptosis</td>
<td>75 -</td>
</tr>
<tr>
<td>Skeletal abnormalities</td>
<td>67 +</td>
</tr>
<tr>
<td>Dental anomalies</td>
<td>67 +</td>
</tr>
<tr>
<td>Digital anomalies</td>
<td>58 +</td>
</tr>
<tr>
<td>Urogenital anomalies</td>
<td>50 +</td>
</tr>
<tr>
<td>Cleft lip/palate</td>
<td>33 + (high arched palate)</td>
</tr>
</tbody>
</table>