A case of Lenz microphthalmia syndrome

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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.

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Lenz microphthalmia syndrome, described by Lenz *et al*¹ 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 gesta-

tion 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 anteverted, 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 hydrocele 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.

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Figure 1 Front view of the patient. Note the high forehead, bilateral microphthalmia, prominent nose, long neck, and sloping shoulders.

Figure 2 Lateral view of the patient showing sparse hair, prominent nasal bridge, thin and poorly developed antihelix, and preauricular tag.

In cerebro-oculo-facio-skeletal syndrome (COFS), inherited as an autosomal recessive trait, survival is rare after the age of 5 years.⁴ Patients with COFS usually show generalised hypotonia, areflexia, camptodactyly, flexion contractures of the elbows and knees, and osteoporosis, in addition to microphthalmia.⁵⁻⁷ Our case does not show the cardinal features of

Figure 3 Sacral dimple and scar.

Table 1 Clinical features of the patient

General	
	Developmental retardation
	Growth retardation
Cranium and brain	
	Microcephaly
	Long head
	Sparse hair
	Dysgenesis of corpus callosum
	Dilated lateral ventricles
Eyes	
	Microphthalmia
	Microcornea
	Sclerocornea
	Small pupil
	Diminished vision
Ears	
	Prominent and poorly developed
Mouth	
	Long philtrum
	High arched palate
	Abnormal teeth
Skeletal abnormalities	
	Short clavicles
	Sloping shoulders
	Long and proximally placed thumbs
Genital	
	Hydrocele
	Hypospadias

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.⁸ 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

Figure 4 MRI scan of the patient showing dysgenetic corpus callosum.

Shapiro syndrome, and Fryns syndrome, include dysgenesis of the corpus callosum as one of their cardinal features, while in some others (Meckel syndrome, fetal alcohol syndrome, Dandy-Walker malformation) dysgenesis of the corpus callosum is an occasional or rare abnormality.⁹ Whether the corpus callosum abnormalities can cause severe CNS dysfunction is still not clear. It has been reported that corpus callosum abnormalities are commonly found within the healthy population.¹⁰ In another report the authors found that dysgenesis of the corpus callosum is common in people with learning disabilities.¹¹

The cases of Lenz microphthalmia syndrome reported so far were not examined by CT or MRI scan. Dysgenesis of the corpus callosum and ventricular dilatation seen on the MRI of this patient may be a part of this syndrome and further studies by MRI or CT scanning are needed to support this suggestion.

Dysgenesis of the corpus callosum and microphthalmia are among the main features of Aicardi syndrome of which other findings are seizures, specific chorioretinal lacunar changes, and motor and mental retardation. Its inheritance is X linked dominant. All cases with Aicardi syndrome are female apart from a male with 47,XXY, which is, of course, consistent with X linked inheritance.¹²

Microphthalmia is also seen in Goltz syndrome in which the characteristic features are dental abnormalities, syndactyly of the fingers/toes, and skin abnormalities such as angiofibromatous changes around the lips and anus and atrophy and altered pigmentation in localised areas.¹³

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 (table 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

Table 2 Major abnormalities seen in Lenz microphthalmia syndrome² and the findings in our patient

	%	Our patient
Microphthalmia	100	+
Retardation	92	+
Ear abnormalities	83	+
Microcephaly	83	+
Blepharoptosis	75	-
Skeletal abnormalities	67	+
Dental anomalies	67	+
Digital anomalies	58	+
Urogenital anomalies	50	+
Cleft lip/palate	33	+

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 al*¹⁴ 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 al*¹⁵ studied the Xp22 region in Aicardi patients by using polymorphic DNA markers. They found no evidence for a microdeletion. Graham *et al*¹⁶ 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.

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