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Autosomal dominant cataracts of the fetus: early detection by transvaginal ultrasound

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ABSTRACT

Cataracts are lens opacities that account for approximately 10% of blindness in children. We report on four consecutive pregnancies in a woman at risk for recurrent autosomal dominant cataracts in which extensive ultrasound studies were helpful in establishing the correct diagnosis. The normal appearance of the fetal lens is that of a ring with a central sonolucency, but in cases of cataracts the lens appears hyperechogenic to various degrees. In the first pregnancy, normal lenses were seen at 15 postmenstrual weeks and, at birth, the baby girl had normal lenses. In the second pregnancy, the male fetus was affected by a left-sided cataract and a right-sided anophthalmia which were diagnosed at 16 postmenstrual weeks. The histological examination of the specimen from the aborted fetus correlated with the sonographic diagnosis. The third pregnancy, also a male fetus, had bilateral cataracts suspected at 14 weeks, but the final diagnosis was made at 19 weeks and confirmed at 21 weeks. The couple opted to terminate the pregnancy and the histology confirmed the presence of congenital cataracts. In the fourth pregnancy, we diagnosed asymmetry of the orbital sizes and bilateral cataracts at 15 weeks. In conclusion, the diagnosis of fetal cataract from the second trimester of pregnancy is possible and imaging of the fetal lenses should be part of the routine anatomical survey. Since the exact onset of fetal cataracts is uncertain at present, in cases at risk, serial sonograms may be indicated.

INTRODUCTION

The introduction of high-frequency transvaginal transducers and the improved resolution of transabdominal transducer technology has resulted in clear ultrasound images. Delicate and relatively small anatomical structures, such as the developing and maturing fetal eye, can now be studied.

Cataracts are lens opacities interfering with the transfer of light to the retina. Congenital cataracts account for about 10% of blindness at ages 5–7 years[1,2]. Autosomal dominant and recessive inheritance are known to exist[3,4].

Early prenatal diagnosis of congenital malformations of the eye by ultrasound has been published[5–8]. We report on the ultrasound evaluation of four consecutive pregnancies at high risk for recurrent autosomal dominant cataracts.

CASE REPORT

A 29-year-old woman, gravida 1, para 0, was referred to our institution in 1991 for evaluation of the fetus. The family history was significant for the husband being affected with congenital cataracts. He has no siblings. His father and paternal aunt are affected. The aunt has no children.

First pregnancy

In 1991, the fetal orbits and eyes were examined during the 15th and 21st postmenstrual weeks by transvaginal ultrasound (Elscint-1000, 6.5-MHz probe, Hackensack, New Jersey). At 15 postmenstrual weeks, both orbits and the lenses appeared clear and equal in size in the coronal as well as the sagittal plane (Figure 1). A follow-up scan at 22 postmenstrual weeks and 3 days showed orbits of normal appearance, measuring 1.03×1.07 cm; the lenses appeared normal (Figure 1c and d). At term, a healthy girl was delivered vaginally. The eyes were examined and found to be normal. To date, the infant is 4.5 years old and has no eye disease.

Second pregnancy

The fetus was examined in 1994 during the 16th postmenstrual week. The ultrasound equipment used was an ATL-HD1-ESP Ultramark-9 with a IC5-9 transducer

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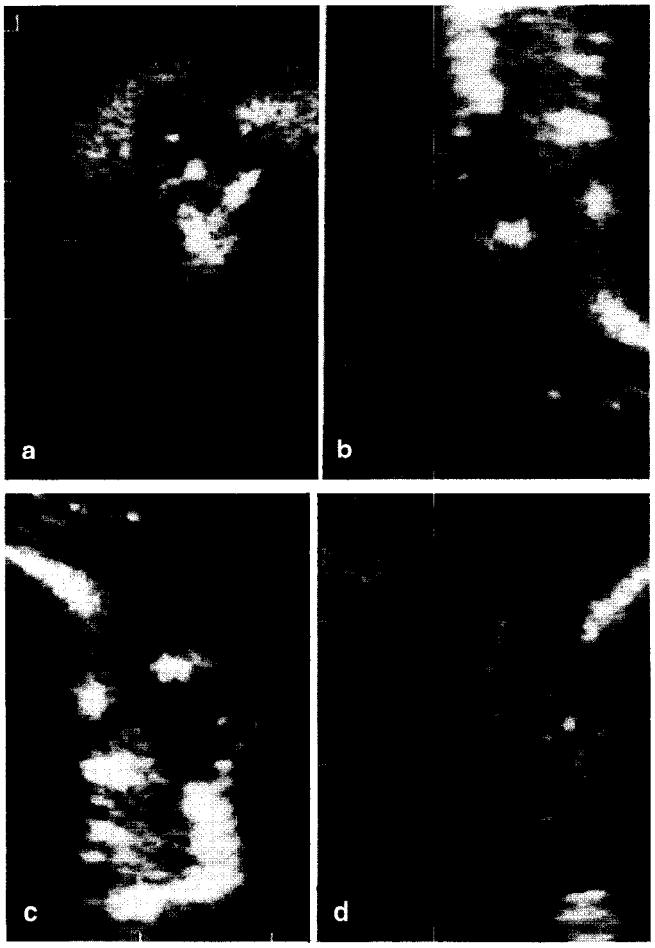

Figure 1 Transvaginal ultrasound image of the normal fetal orbits and lenses at 15 and 22 postmenstrual weeks in the normally developing first fetus. (a) Coronal view (15 weeks); (b) sagittal view (15 weeks); (c) sagittal view (22 weeks); (d) coronal view (22 weeks). Note that, regardless of the age and the view, the central part of the lens is completely sonolucent

(Bothell, Washington). The orbits were present and measured 0.82 × 0.80 cm. The right lens appeared of normal size, showing a ring-like echogenicity with a central opacity. We could not demonstrate a lens within the left orbit (Figure 2). The prenatal sonographic diagnosis was right congenital cataract and possible right anophthalmia. No other malformations were detected.

At 18 postmenstrual weeks, after detailed counselling, the patient requested an elective termination of the pregnancy. This was achieved by dilatation and evacuation. The only visible malformation of the fetus involved the eyes. The pathology report confirmed the right-sided cataract, along with the tunica vascularis lentis and microcornea (Figure 3). On the left side, the orbit contained a mass with striated muscle, fibrovascular connective, mesenchymal tissue as well as primitive neuroepithelial tissue.

Third pregnancy

In 1995 the fetus was examined for the first time at 14 postmenstrual weeks, with the use of ATL 3000 and HDI-ESP Ultramark-9 machines with the IC5-9 probe (Bothell, Washington). The orbits measured 0.73 × 0.73 cm. The

Figure 2 Transvaginal ultrasound image of the fetal orbits and the right lens in the first affected fetus at 16 postmenstrual weeks. Note that the lens of the right eye (arrow) contains an outer and an inner hyperechoic ring. The outer one is the border of the lens; the inner represents the cataract. The left orbit appears to be empty. Right cataract and left anophthalmia was the sonographic interpretation of this image

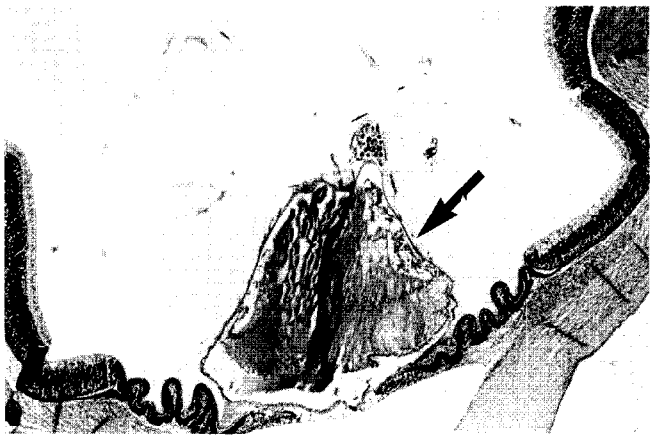

Figure 3 Photograph of the lens from the first affected pregnancy. This shows vacuolization and fragmentation of lens cortical fibers (arrow), especially posteriorly. Hematoxylin and eosin, × 3.5)

lenses were not completely sonolucent, as in a normal lens. We strongly suspected bilateral cataracts (Figure 4a and b). Rescans were scheduled to confirm the diagnosis. No other malformations were seen. The follow-up scans at 19 and 21 postmenstrual weeks revealed bilateral lens opacities (Figure 4c–f). A serial and parallel study of the lens in the coronal plane depicted the hyperechoic and concentric cataract (Figure 5). A second opinion was requested from Drs M. Bronshtein and E. Zimmer (Haifa, Israel), who confirmed the findings. After counselling, the patient elected to have a termination of the pregnancy by dilatation and evacuation at another institution. Only one eye was available for pathological examination. This revealed extensive vacuolization as well as fragmentation of the cortical lens fibers. This process was more accentuated on the posterior surface of the lens, where fibrovascular growth was evident into a clearly seen dehiscence (Figure 6).

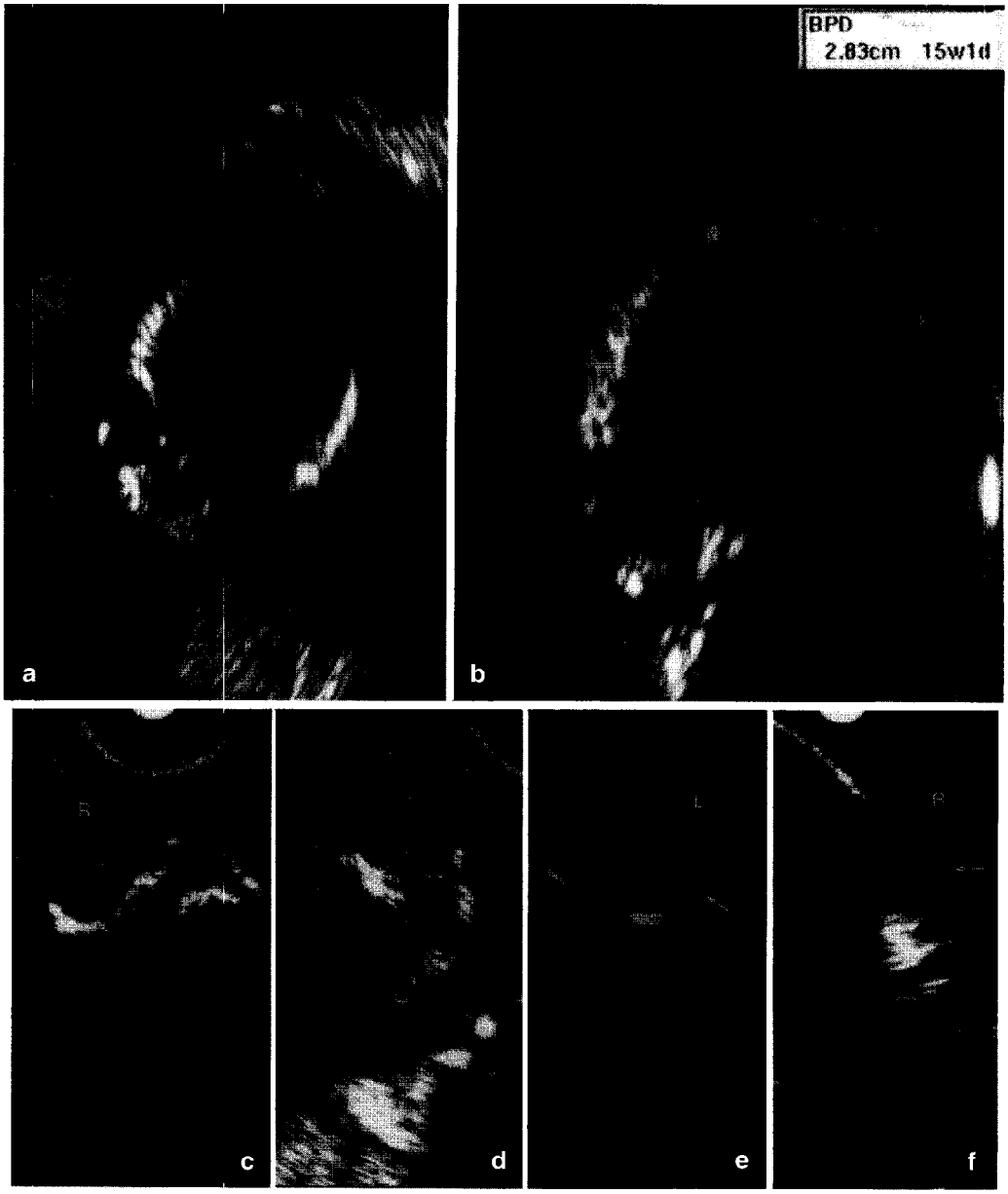

Figure 4 Sonographic images of the affected fetal eyes in the third pregnancy. (a) Coronal and (b) sagittal transvaginal image at 15 postmenstrual weeks. A certain degree of hyperechogenicity was seen. (c), (d), (e) and (f): Transabdominal views at 19 weeks obtained with the vaginal probe through the maternal umbilicus. (c) and (d) Coronal views of the right (R) and left (L) lenses. (e) and (f) Sagittal sections of the left (L) and right (R) lenses, respectively

Fourth pregnancy

In 1996, at 15 postmenstrual weeks, the fetus was examined with the same ultrasound equipment. The left orbit measured 0.70 × 0.64 cm, the right orbit measured 0.59 × 0.50 cm (Figure 7a). Both lenses were hyperechoic (Figure 7b) and showed the 'double hyperechoic rings' (Figure 7c). The decision of the parents was again to terminate the pregnancy. At this time, the pathological examination of the eyes is pending.

DISCUSSION

To place the prevalence of congenital cataracts into proper perspective, it is important to review the incidence of congenital eye malformations detectable from birth to 1 year. Stoll and colleagues[4] studied 131 760 consecutive births and found 78 such cases, giving an incidence of approximately 5.9/10 000 births. The breakdown for the different congenital eye lesions in this study was: cataracts, 30% (2.3/10 000 live births); microphthalmia, 24% (1.8/10 000 live births); coloboma 9% (0.7/10 000 live births); microphthalmia and glaucoma, 4% each (0.3/10 000 live births); and others 29% (ectopia lentis, megalocornea, aniridia, chorioretinitis, etc.). The factors associated with eye malformations in the same study were: consanguinity, inheritance (Mendelian), non-chromosomal and chromosomal factors, occurrence in twins and family history.

In the EUROCAT study, the prevalence of cataracts was 1.2/10 000 live births[9] and in the American Collaborative

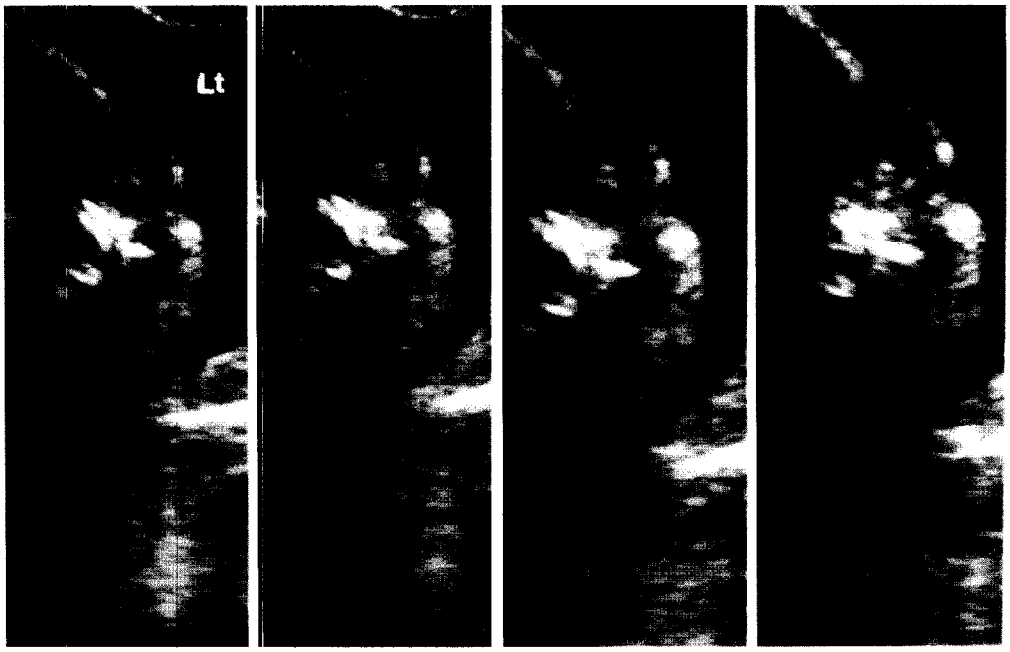

Figure 5 Serial and parallel coronal sections of the left (Lt) lens. The sections start on the left, barely 'touching' the lens tangentially, and ending with a 'mid-coronal' section of the lens through its longest diameters. Note the progressively increasing size and the hyperechogenicity of the lens

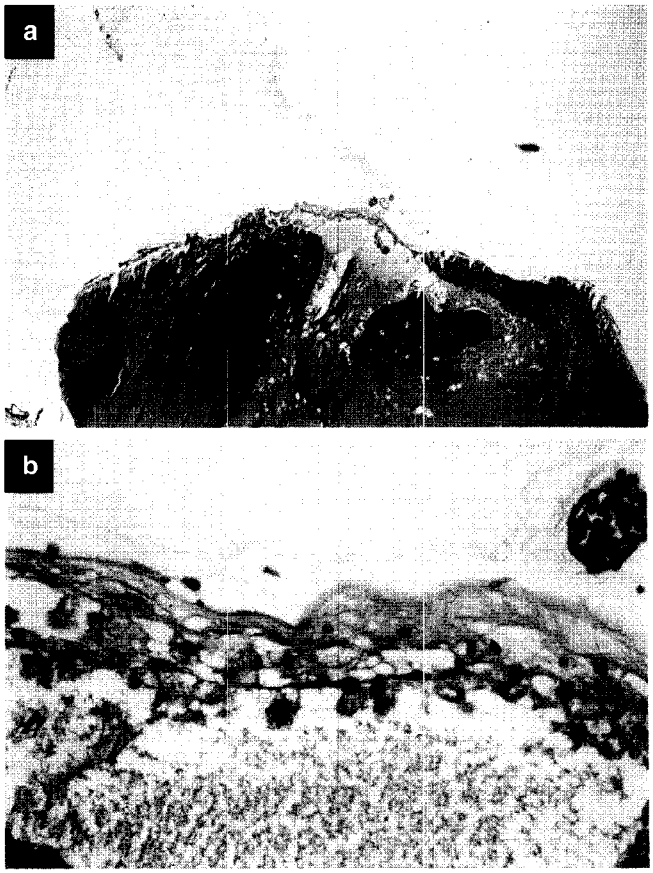

Figure 6 (a) Photomicrograph of the lens from the third pregnancy, showing fragmentation and vacuolization of the posterior cortical lens fibers. In addition, there is a dehiscence of the posterior lens capsule (arrows) with fibrovascular ingrowth (hematoxylin and eosin, × 17); (b) higher power view, showing the posterior lens capsule dehiscence with fibrovascular ingrowth (hematoxylin and eosin, × 54)

Study, the prevalence of congenital cataracts was 9.4/10 000 live births[10]. In another study, performed in Louisiana, a review of birth certificates revealed a prevalence rate of congenital cataract of 0.64/10 000 live births[11].

In our case, the history of cataracts spans over three generations. It is clear that the three affected siblings of this family demonstrated an autosomal dominant inheritance pattern. As far as we are concerned, this is the first time that such an autosomal dominant inheritance was discovered *in utero* by using transvaginal sonography. Although the patient in this case elected to terminate the pregnancies, it should be pointed out that most cases are treatable in the neonatal period.

The sonographic appearance of the cataracts so far published as well as that of our three fetuses demonstrated hyperechogenicities of the lens to various degrees. If the lens is imaged in a coronal plane, the sonographic texture of the pathological lens with a cataract may be that of a low-level echogenicity or a hyperechoic circle within the outer borders of the lens (Figures 2 and 4). The 'clean' sonolucent center of the lens within the well-known hyperechoic ring is lost (Figure 1). A central hyperechogenicity may also appear (Figure 4). If the healthy, normal lens is examined using a sagittal section, the oval hyperechoic borders with a completely sonolucent center become evident. In the case of a cataract, a homogeneous low-level echo pattern fills the entire lens (Figure 4).

High-frequency transvaginal ultrasound detects the fetal eye by about 12 postmenstrual weeks. However, the first reports of the use of this diagnostic capability for cataracts were from 15 postmenstrual weeks onward[5,6,8].

To our knowledge, false-positive diagnoses were not published in the literature. However, two previously pub-

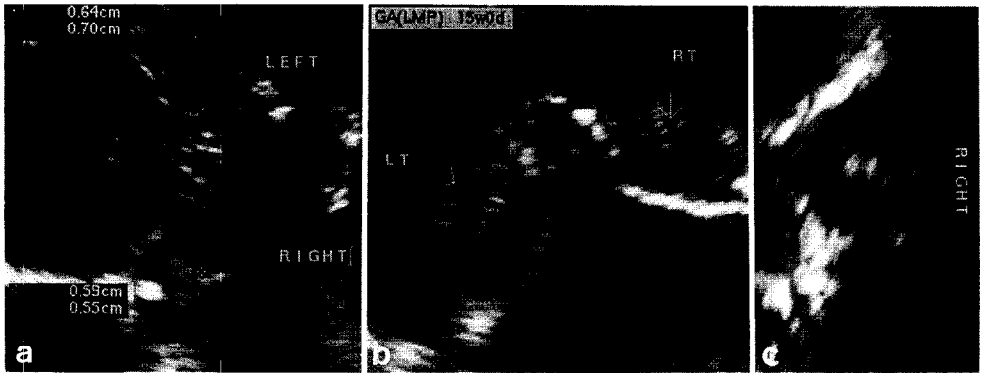

Figure 7 Transvaginal ultrasound image of the orbits and the lenses of the fetus at 15 weeks in the fourth pregnancy. (a) Asymmetry of the orbits; (b) sagittal views of both lenses; (c) coronal view of the right lens

lished false-negative diagnoses are worth mentioning. In one case, the lenses appeared to be normal on three consecutive scans at 12, 16 and 32 postmenstrual weeks. At birth, bilateral mild cataracts and several previously detected malformations were seen[5]. The second case descriptions of a normal lens were given for a structure that at birth was found to be a colobomatous cyst, seen at 12 postmenstrual weeks[5].

As regards the clinical importance of imaging the fetal eye as early as 12–16 weeks, and the ability to detect various anomalies of the eye, including cataracts, we suggest the following:

(1) All targeted structural evaluations of fetuses, regardless of the gestational age, should include a demonstration of the orbits and the lenses.

(2) High-frequency transvaginal scans are more likely to furnish fine details of this small organ. Recently, some abdominal transducers operating in the 4–7-MHz range were found to yield images with good resolution in patients with relatively thin abdominal walls.

(3) If the fetus is found repeatedly in the breech presentation, a high-frequency transvaginal probe can be operated through the 'depression' of the maternal umbilicus. Surprisingly good-quality pictures can be obtained through this thinnest area of the abdominal wall.

(4) Since there is not yet an adequate description of the exact time of onset or natural history of cataracts, a rescan and/or a second opinion from experienced persons in this field should be considered in doubtful or suspicious cases.

The known causes of congenital cataracts include the following: familial syndromes (Lowe's Hallerman–Streiff, Alpert's, Conradi–Hunermann, Smith–Lemli–Opitz syndrome, Walker–Warburg syndrome, Pena–Shokeir syndrome, type II), which account for 9%; prenatal infections (especially rubella), which account for 36%; enzymatic disorders such as galactokinase deficiency, homocystinuria and galactosemia, as well as glucose-6-phosphate dehydrogenase deficiency, which make up 23%; and the remainder of 32% are idiopathic or, as far as we are concerned at this time, their causes have not yet been elucidated[6,7,12]. Our described case may furnish additional information in this last group of unknown causes.

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