A case of fetal inherited congenital cataract

TO THE EDITOR: We report a fetus aged 23+5 weeks of gestation diagnosed with congenital cataracts (Figure, A) by prenatal ultrasound and whole exon sequencing (WES). The fetus had a number of additional abnormalities, including bilateral cleft lip and palate (Figure, B), a double-outlet right ventricle (Figure, C), and thymic hypoplasia, which were consistent with the ultrasonic characteristics of 22q11.2 deletion syndrome. Therefore, syndromic congenital cataracts was suspected. The mother was 25 years old and had no pregnancy complications. However, she and her mother had the same history of congenital cataracts and visual impairment.

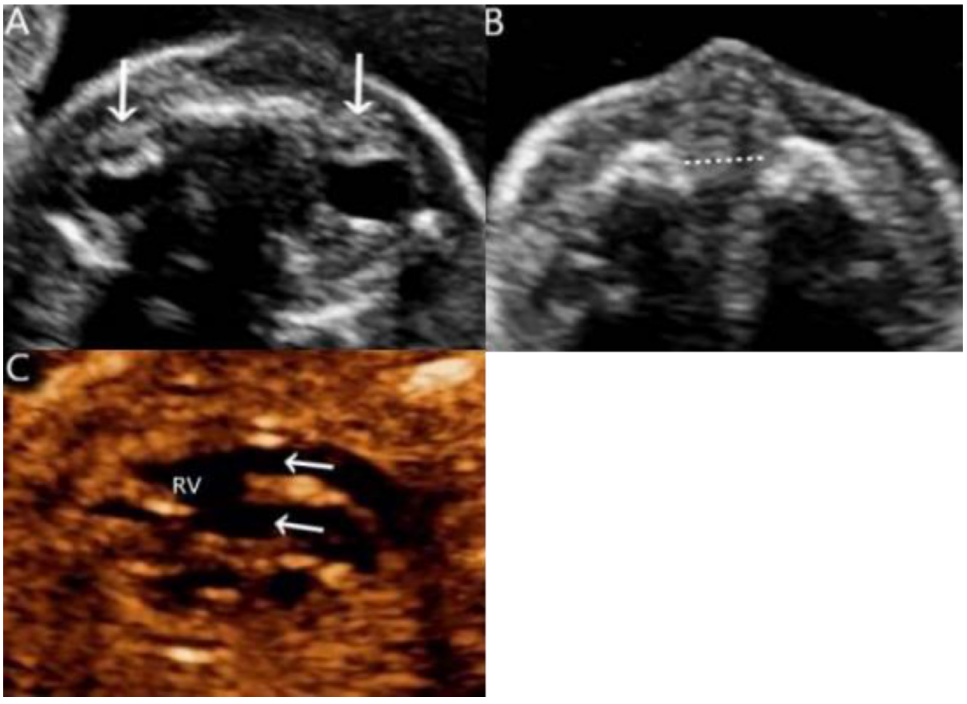
To better assess these conditions, WES from peripheral blood samples and fetal amniotic fluid was carried out to investigate pathogenic mutations. This identified a heterozygous variant —c.432C>A (p.Y144X)—in exon 3 of the gamma-D-crystallin gene (*CRYGD*), which belongs to the crystallin gene family. This variant is known to cause isolated congenital cataracts, so a diagnosis of inherited congenital cataracts overlapping with syndromic cataracts was made. The mother chose to terminate the pregnancy.

Congenital cataract is the partial or total opacity of the lens that occurs or gradually forms within the first year of life. It is the most common cause of childhood blindness, with a global prevalence ranging from 2.2 of 10,000 to 13.6 of 10,000.[1] It can occur as an isolated condition or as part of genetic syndromes, such as trisomy 21, trisomy 18, and 22q11.2 deletion syndrome; isolated and syndromic cataracts can overlap.[2] Approximately 8% to 25% of cataracts are inherited, with the remainder secondary to intrauterine insults, metabolic disorders, and chromosome disorders.[2]

Genetic mutations, including the 308 crystallin gene variants that have thus far been identified, are the leading cause of inherited cataracts, accounting for 23% of all disease-causing variants.[3] Crystallin gene variants affect the stability, solubility, and oligomerization feature of crystallin proteins and disturb their ordered arrangement, eventually resulting in lens opacity. Our case is an example of autosomal dominant inheritance of the variant of *CRYGD*, which is a member of the γ-crystallin gene cluster and 1 of 2 highly expressed genes in embryonic stage lens cells.[3] Approximately 25 *CRYGD* mutations have been reported to date.[4]

Recent work investigating prenatal cataract diagnosis by ultrasound showed that continuous scanning of fetal eyes reveals the morphology and echo of the lens and can

FIGURE
prenatal ultrasound image



A, A circular high echo in the bilateral lens (*arrow*). **B,** The anterior alveolar eruption (*broken line*). **C,** The aorta and pulmonary artery travel in parallel from the right ventricle (*arrow*).

RV, right ventricle.

Zhao. A case of fetal inherited congenital cataract. Am J Obstet Gynecol Glob Rep 2022.

accurately diagnose abnormal echo changes. On the basis of the characteristics of prenatal ultrasound images, the lens manifestations of congenital cataracts include complete high echo, dot or cluster strong echo in the center, and irregular thickening of the lens edge echo.[5] In the present case, lens ultrasound imaging showed enhanced irregular thickening of the bilateral edges of the lens.

Early diagnosis of congenital cataracts is extremely important, because the time of surgery is still 1 of the main factors affecting visual outcome. Previous reports have mainly focused on the postpartum period, whereas our study shows that congenital cataracts can be accurately diagnosed by both ultrasound examination and WES as early as the antenatal period. ■

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The authors report no conflict of interest.
No funding was obtained for this study.
Patient consent is not required because no personal information or details are included.

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 https://doi.org/10.1016/j.xagr.2022.100068