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Research Letter

# 22q13 deletion syndrome in a fetus associated with microtia, hemivertebrae, and congenital heart defects on prenatal ultrasound

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*Dear Editor,*

We present the prenatal diagnosis and molecular cytogenetic characterization of a fetus associated with 22q13 deletion syndrome and congenital malformations.

A 32-year-old, gravida 2, para 1, woman was referred for amniocentesis at 28 weeks of gestation because of abnormal prenatal ultrasound findings of right microtia, hemivertebrae of the lumbar spine, ventricular septal defect, and total anomalous pulmonary venous return. Amniocentesis revealed a karyotype of 46,XX,del(22)(q13.31q13.33). The parental karyotypes were normal. Array comparative genomic hybridization analysis on uncultured amniocytes using Roche ISCA Plus Cytogenetic Array Chips (Roche, Basel, Switzerland) revealed a 6.48-Mb deletion of 22q13.31-q13.33 or arr 22q13.31q13.33 (44,731,454–51,209,196) ×1 (Figure 1). The deleted region encompasses 113 genes including 46 Online Mendelian Inheritance in Man (OMIM) genes of *PRR5*, *ARHGAP8*, *NUP50*, *UPK3A*, *SMC1B*, *FBLN1*, *ATXN10*, *WNT7B*, *MIRLET7A3*, *MIRLET7B*, *PPARA*, *PKDREJ*, *GTSE1*, *TRMU*, *CELSR1*, *GRAMD4*, *CERK*, *BRD1*, *ZBED4*, *ALG12*, *CRELD2*, *PIM3*, *IL17REL*, *MLC1*, *MOV10L1*, *PANX2*, *SELO*, *TUBGCP6*, *HDAC10*, *MAPK12*, *MAPK11*, *PLXNB2*, *PPP6R2*, *SBF1*, *ADM2*, *MIOX*, *NCAPH2*, *SCO2*, *TYMP*, *CPT1B*, *CHKB*, *MAPK8IP2*, *ARSA*, *SHANK3*, *ACR* and *RABL2B*. A 1170-g malformed female fetus was subsequently delivered with right microtia and facial dysmorphism of left large ear, full brow, dolichocephaly, full cheeks, a bulbous nose, and a pointed chin.

Phelan–McDermid syndrome (OMIM 606232) or 22q13 deletion syndrome is characterized by normal to advanced growth (91%), global developmental delay (96%), absent or severely delayed speech (96%), hypotonia (89%), seizures (27%), sensorineural hearing loss (8%), dolichocephaly (50%), ptosis (43%), epicanthic folds (39%), prominent/dysplastic ears (58%), pointed chin (52%), tendency to overheat/lack of perspiration (51%), relatively large fleshy hands (60%), fifth-finger clinodactyly (13%), abnormal toenail growth (79%), 2–3 syndactyly of toes (34%), cardiac anomalies (6%), genitourinary anomalies (9%), increased tolerance to pain (86%), frequent mouthing/chewing of objects (70%), and other manifestations (<5%) of puffy swollen feet, arachnoid cysts, and increased incidence of respiratory infections [1]. Haploinsufficiency of the *SHANK3* gene (OMIM 606230) has been known to be an important factor responsible for the neurological symptoms of the 22q13 deletion syndrome such as hypotonia, developmental delay, absent to delayed speech, and autistic behavior [2].

Prenatal diagnosis of pure 22q13 deletion due to abnormal fetal ultrasound is very rare. The peculiar aspect of the present case is the associated prenatal ultrasound findings of microtia, hemivertebrae of the lumbar spine, and congenital heart defects. Riegel et al [3] reported a fetus with mosaic del(22)(q13) at 21 weeks' gestation due to fetal cystic thymus. Phelan et al [4] reported a second-trimester prenatal diagnosis of mosaic 22q13.3 deletion due to a positive maternal serum screening for Down syndrome, and suggested that decreased fetal movement because of hypotonia is an indicator of 22q13 deletion syndrome. Kirkpatrick and El-Khechen [5] reported prenatal diagnosis of a terminal 22q13 deletion (22q13.31→q13.33) in a fetus with unilateral multicystic

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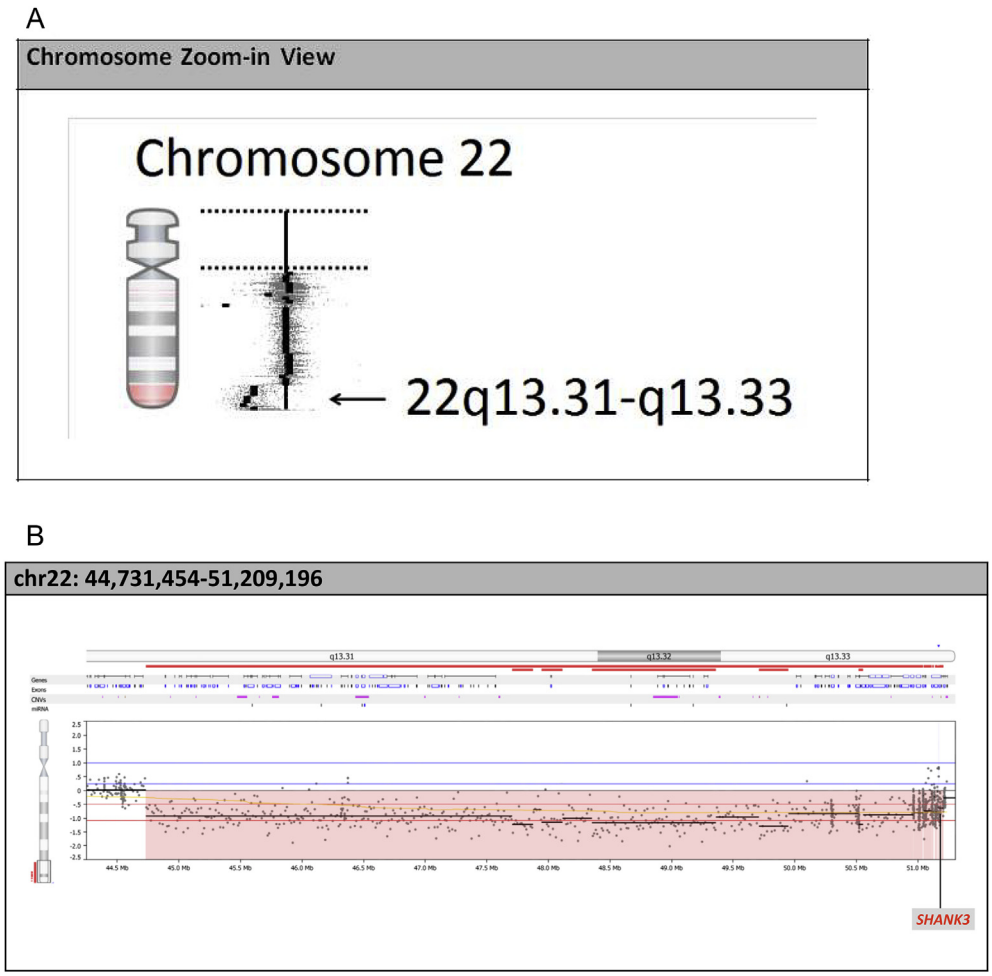


**Figure 1.** Array comparative genomic hybridization analysis shows a 6.48-Mb deletion of 22q13.31-22q13.33 or arr 22q13.31q13.33 (44,731,454–51,209,196)×1 encompassing the *SHANK3* gene. (A) and (B) chromosome zoom-in view.

kidney, unilateral cleft lip, and polyhydramnios. The present case additionally shows that deformities of the ears, spine, and cardiovascular structures can be prenatal ultrasound abnormalities associated with 22q13 deletion syndrome.

## Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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