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Identification of a Ring Chromosome as a Ring 8 Using Fluorescent In Situ Hybridization (FISH) in a Child With Multiple Congenital Anomalies

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To the Editor:

We read with interest the report by Melnyk and Dewald [1994] of a small supernumerary ring chromosome 8 identified by fluorescence in situ hybridization (FISH) in a child with developmental delay and minor anomalies. Although ring chromosomes resulting in loss of parts of chromosome 8 have been reported [Minuquarelli et al., 1991; Verma et al., 1992], Melnyk and Dewald [1994] reported the first small ring chromosome 8 diagnosed by FISH. Previously nonsatellited markers derived from chromosomes 1, 3, 6, 9, 11, 13–16, 18, 20, 21, and X have been identified using FISH [Callen et al., 1991; Rauch et al., 1992]. Their study illustrated the value of FISH techniques in identifying the chromosomal source of markers or rings.

CLINICAL REPORT

We report a second patient with a ring chromosome identified as a ring 8, using an alpha satellite chromosome 8-specific DNA probe following the manufacturer's protocol (Oncor, Inc., Gaithersburg, MD). Our patient was first seen for genetic evaluation at age 3 days because of a poor suck and minor anomalies. She was born to a 27-year-old G1 mother and 28-year-old father after a pregnancy complicated by preterm labor at 32 weeks of gestation, treated with terbutaline. A prenatal ultrasound study showed possible polyhydramnios. She was delivered vaginally at 41 weeks of gestation and weighed 3,799 g (90th centile); length was 54 cm (95th centile), and head circumference was 34.5 cm (60th centile). Other anthropometric measurements included: hand length of 7.4 cm (90th centile), middle finger

length of 2.8 cm (50th centile), ear length of 3.5 cm (40th centile), inner canthal distance of 2.4 cm (90th centile), chest circumference of 34 cm (60th centile), and internipple distance of 9.5 cm (90th centile). She had a weak cry at birth, and multiple congenital anomalies included a small anterior fontanelle, a high sloping forehead, epicanthal folds, small palpebral fissures (palpebral fissure length was 1.4 cm (<5th centile), low posterior hairline with excess nuchal skin, absence of the clitoris, and bilateral fifth finger clinodactyly. The family history was unremarkable for similarly affected children, birth defects, mental retardation, miscarriages, or consanguinity.

A peripheral blood specimen was obtained for chromosome studies. The routine chromosomal analysis of 22 GTG-banded metaphases showed an extra ring chromosome resembling the size of a C-group chromosome ring in 9 of the 22 cells, and a normal 46,XX female complement in 13 cells. Parental chromosome studies were normal. A skin fibroblast culture was established for the patient, and 9 of 20 cells analyzed showed the extra ring chromosome (a double ring was seen in 2 of the cells), and the remaining 11 cells were 46,XX. G-, C-, AgNOR and Q-banding were performed but were not helpful in identifying the origin of the extra ring chromosome. A specific ring chromosome syndrome was not readily apparent based on the physical findings of the patient. In order to identify the origin of the ring chromosome, alpha satellite DNA probes for 13, 18, 21, X, and Y from Oncor, Inc. (Gaithersburg, MD) were initially hybridized to the metaphase chromosomes using FISH techniques. No hybridization of the ring chromosome was observed using these probes. Additional alpha satellite probes were then used, and hybridization of the ring chromosome was successfully accomplished using the chromosome 8 probe, establishing that the ring chromosome was derived from a chromosome 8 (Fig. 1).

At age 4 months, several manifestations consistent with trisomy 8 mosaicism were observed, including simple abnormal cupped ears, small upturned nose, high-arched palate, low posterior hairline, absent clitoris, and developmental delay. At this time she was able to hold her head, roll from side to side, and reach for objects. She also smiled appropriately. There were no feeding difficulties and her growth was normal (weight of 7.0 kg (90th centile)). She also had a prominent forehead, long slender trunk, and decreased range of motion at both elbows and the right shoulder. A roentgenogram of the shoulder showed a high rotated scapula suggestive of Sprengel anomaly, and contraction of the shoulder muscles. At this time she was diagnosed with a grade IV vesicoureteral reflux on the left and grade II on the right, as well as low insertion of both ureters and right hydronephrosis. At age 6 months she required surgical reinsertion of both ureters. The parents refused to have clinical photographs taken. Genetic counseling and medical information about mosaic trisomy 8 were supplied to the family and the primary care physician after identification of the ring as derived from chromosome 8.

REFERENCES

- Callen DF, Eyre HJ, Ringenbergs ML, Freemantle CJ, Woodroffe P, Haan EA (1991): Chromosomal origin of small ring marker chromosomes in man: characterization by molecular genetics. *Am J Hum Genet* 49:503.

- Melnyk AR, Dewald G (1994): Identification of a small supernumerary ring chromosome 8 by fluorescent in situ hybridization on a child with developmental delay and minor anomalies. *Am J Med Genet* 50:12–14. [PubMed: 7512788]
- Minuqarelli R, Valorani G, Zelante L, Dallapicola B (1991): Ring chromosome 8 associated with microcephaly. *Ann Genet* 34:90–92. [PubMed: 1746890]
- Rauch A, Pfeiffer RA, Trautmann U, Liehr T, Rott HD, Ulmer R (1992): A study of ten small supernumerary (marker) chromosomes identified by fluorescence in situ hybridization (FISH). *Clin Genet* 42:84–90. [PubMed: 1424236]
- Verma RS, Conte RA, Pitter JH, Luke S (1992): Pericentric inversion of chromosome 7 (inv(7)(p22qll. 2) and ring chromosome 8 (r(8) (p23q24.3) in a girl with minor anomalies. *J Med Genet* 29: 66–67. [PubMed: 1552550]

Fig. 1. A GTG-banded chromosome number 8 pair and ring from the same metaphase (**left**), an RBG-banded ring chromosome (**middle**), and the ring chromosome using FISH and the alpha satellite chromosome 8 probe (**right**), with the hybridization signal (arrowhead) establishing that the ring chromosome was derived from chromosome 8.