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Research Letter

Maternal transmission of interstitial microdeletion in 5q13.2 detected during prenatal diagnosis of coarctation of the aorta

Chih-Ping Chen [a,b,c,d,e,f,g,*], Chen-Ju Lin [a], Chen-Yu Chen [a], Schu-Rern Chern [b], Peih-Shan Wu [h], Jun-Wei Su [a,i], Wayseen Wang [b,j]

[a] *Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei, Taiwan*
[b] *Department of Medical Research, Mackay Memorial Hospital, Taipei, Taiwan*
[c] *Department of Medicine, Mackay Medical College, New Taipei City, Taiwan*
[d] *Department of Biotechnology, Asia University, Taichung, Taiwan*
[e] *School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan*
[f] *Institute of Clinical and Community Health Nursing, National Yang-Ming University, Taipei, Taiwan*
[g] *Department of Obstetrics and Gynecology, School of Medicine, National Yang-Ming University, Taipei, Taiwan*
[h] *Gene Biodesign Co. Ltd, Taipei, Taiwan*
[i] *Department of Obstetrics and Gynecology, China Medical University Hospital, Taichung, Taiwan*
[j] *Department of Bioengineering, Tatung University, Taipei, Taiwan*

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A 31-year-old primigravid woman underwent amniocentesis at 23 weeks of gestation because of fetal coarctation of the aorta detected by level II ultrasound. Prenatal ultrasound at 23 weeks of gestation showed a fetus with biometry equivalent to 20 weeks, a left single umbilical artery, coarctation of the aorta, a left-to-right shunt across the foramen ovale, and asymmetry of atrial and ventricular size (right side larger than the left side). The husband was 34 years of age. She and her husband were healthy and nonconsanguineous and there was no family history of congenital malformations. Approximately 30 mL of amniotic fluid was obtained, of which 10 mL was used for array comparative genomic hybridization (aCGH) analysis using uncultured amniocytes, and 18 mL was used for conventional cytogenetic analysis using cultured amniocytes. Whole-genome aCGH analysis using a NimbleGen ISCA Plus Cytogenetic Array (Roche NimbleGen, Madison, WI, USA) for uncultured amniocytes detected a 1.83-Mb deletion in the chromosome band of 5q13.2, or arr 5q13.2 [(68,829,117–70,660,524) ×1; NCBI build 37] (Fig. 1). The deleted region of 5q13.2 contains part of the *OCLN*, *SERF1A*, *SMN2*, *SMN1*, *NAIP*, and *GTF2H2* genes. *OCLN* was disrupted beginning in the region between exons 6 and 7. Conventional cytogenetic analysis of cultured amniocytes revealed a karyotype of 46,XX. Whole-genome aCGH analysis of the mother's peripheral blood revealed a 1.81-Mb deletion in the chromosome band of 5q13.2, or arr 5q13.2 [(68,851,138–70,660,524)×1; NCBI build 37] (Fig. 1). The deleted region of 5q13.2 in the mother contains part of the *OCLN*, *SERF1A*, *SMN2*, *SMN1*, *NAIP*, and *GTF2H2* genes. *OCLN* was disrupted beginning in the region of exon 12. The father did not have such a microdeletion. The mother decided to terminate the pregnancy, and a 540-g female fetus was delivered with no gross phenotypic abnormalities.

This is the first report of a prenatal case of 5q13.2 interstitial microdeletion due to maternal transmission. The mother presented no phenotypic abnormalities and had a 1.81-Mb 5q13.2 microdeletion encompassing part of the *OCLN*, *SMN2*, *SERF1A*, *SMN1*, *NAIP*, and *GTF2H2* genes. The fetus presented coarctation of the aorta and had a 1.83-Mb 5q13.2 microdeletion encompassing part of the *OCLN*, *SERF1A*, *SMN2*, *SMN1*, *NAIP*, and *GTF2H2* genes.

The present case had a deletion encompassing the region responsible for spinal muscular atrophy (SMA; OMIM 253300). Homozygous deletion of *SMN1* (OMIM 600354) and expression changes for *SMN2* (OMIM 601627) cause the SMA phenotype. *SERF1A* (OMIM 603011) encodes SMA modifier 1 and is a candidate modifying gene for SMA. *GTF2H2* (OMIM 601748) encodes transcription factor IIH, which is associated with SMA. *NAIP* (OMIM 600355) encodes baculoviral IAP repeat-containing protein 1 (BIRC1), which inhibits apoptosis. *OCLN* (OMIM 602876) encodes occludin, which is an integral membrane protein that is located at tight junctions and regulates the directional migration of epithelial cells [1]. Compound heterozygous mutations or homozygous mutations of *OCLN* have been associated with autosomal

* Corresponding author. Department of Obstetrics and Gynecology, Mackay Memorial Hospital, 92, Section 2, Chung-Shan North Road, Taipei, Taiwan.
E-mail address: cpc_mmh@yahoo.com (C.-P. Chen).

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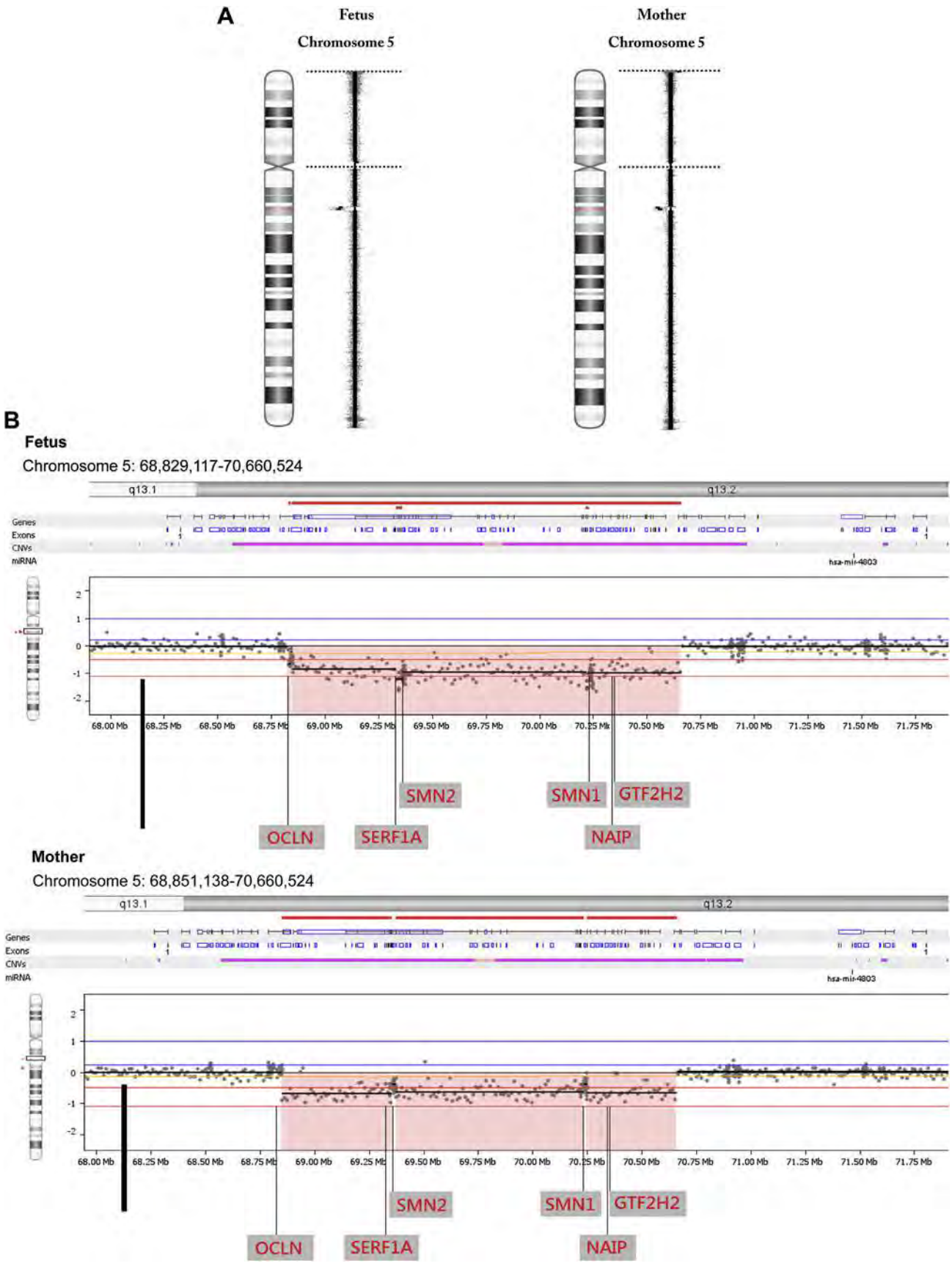

Fig. 1. Array comparative genomic hybridization of uncultured amniocytes shows a 1.83-Mb deletion in chromosome band 5q13.2, or arr 5q13.2 [(68,829,117–70,660,524)×1, NCBI build 37], in the fetus and a 1.81-Mb deletion in chromosome band 5q13.2, or arr 5q13.2 [(68,851,138–70,660,524)×1, NCBI build 37], in the mother. (A) Chromosomal view, (B) magnified view and (C) view of the *OCLN* region.

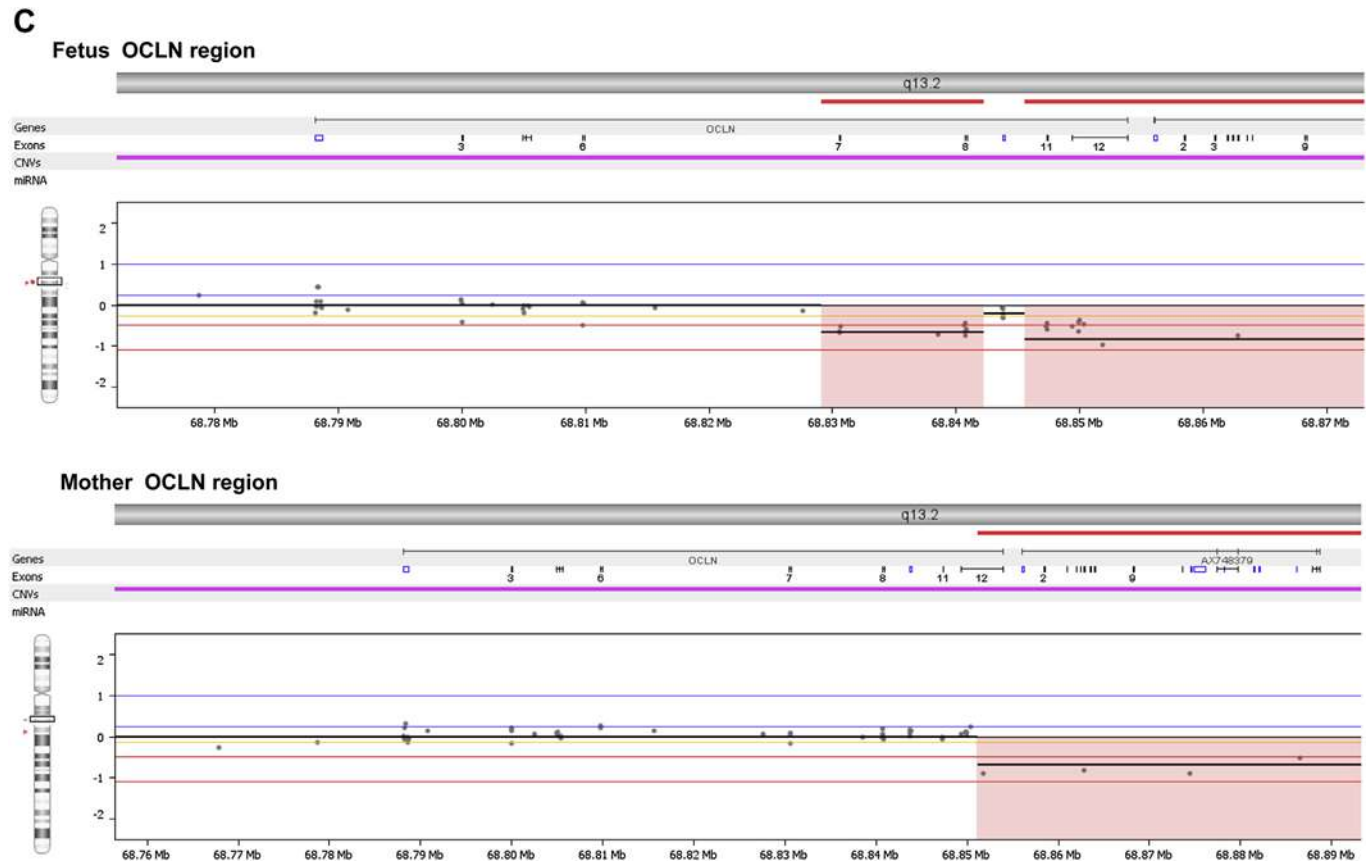

Fig. 1. (*continued*).

recessive band-like calcification with simplified gyration and polymicrogyria (OMIM 251290).

Huang et al found microdeletions in 5q13.2 encompassing *OCLN*, *SMN2*, *SERF1A*, *SMN1*, *NAIP*, and *GTF2H2* in a child with oculo–auriculo–vertebral spectrum (OAVS; or hemifacial microsomia; OMIM 164210) and suggested that *NAIP* and *OCLN* may play a role in craniofacial morphogenesis and susceptibility to OAVS [2]. In that case, an echocardiogram revealed patent ductus arteriosus and foramen ovale on day 2, which closed spontaneously on day 6. Our case did not present an OAVS phenotype but had coarctation of the aorta. This case provides evidence of correlation between 5q13.2 microdeletion involving *OCLN*, *SMN2*, *SERF1A*, *SMN1*, *NAIP*, and *GTF2H2* genes and coarctation of the aorta.

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