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Case Report

Prenatal diagnosis of an 8q22.2-q23.3 deletion associated with bilateral cleft lip and palate and intrauterine growth restriction on fetal ultrasound

Chih-Ping Chen [a, b, c, d, e, f, *], Tung-Yao Chang [g], Fang-Yu Hung [h], Schu-Rern Chern [b], Peih-Shan Wu [i], Shin-Wen Chen [a], Shih-Ting Lai [a], Tzu-Yun Chuang [a], Chen-Chi Lee [a], 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 Biotechnology, Asia University, Taichung, Taiwan
[d] School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan
[e] Institute of Clinical and Community Health Nursing, National Yang-Ming University, Taipei, Taiwan
[f] Department of Obstetrics and Gynecology, School of Medicine, National Yang-Ming University, Taipei, Taiwan
[g] Taiji Fetal Medicine Center, Taipei, Taiwan
[h] Department of Obstetrics and Gynecology, Hsinchu MacKay Memorial Hospital, Hsinchu, Taiwan
[i] Gene Biodesign Co. Ltd., Taipei, Taiwan
[j] Department of Bioengineering, Tatung University, Taipei, Taiwan

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ABSTRACT

Objective: We present prenatal diagnosis of an interstitial 8q22.2-q23.3 deletion associated with bilateral cleft lip and palate and intrauterine growth restriction (IUGR) on fetal ultrasound.
Case report: A 29-year-old, primigravid woman underwent elective amniocentesis at 17 weeks of gestation because of anxiety. Amniocentesis revealed a karyotype of 46, XX. However, level II ultrasound at 21 weeks of gestation revealed a fetus with IUGR and bilateral cleft lip and palate. Repeat amniocentesis was performed at 21 weeks of gestation, and array comparative genomic hybridization using uncultured amniocytes revealed a 13.5-Mb interstitial deletion of 8q22.2-q23.3 encompassing 37 Online Mendelian Inheritance of in Man (OMIM) genes including *SPAG1*, *GRHL2*, *NCALD*, *RRM2B* and *ZFPM2*. Polymorphic DNA marker analysis determined a paternal origin of the deletion. The pregnancy was subsequently terminated, and a malformed fetus was delivered with a depressed nose and bilateral cleft lip and palate.
Conclusion: Prenatal diagnosis of facial cleft with IUGR should raise a suspicion of subtle chromosome deletions.

Introduction

Patients with a chromosome 8q22.2-q22.3 deletion may present a well-described syndrome characterized by similar facial phenotype of blepharophimosis, telecanthus, epicanthus, flat malar region, thin upper lip vermillion, poor facial movement, moderate to severe developmental delay, absent speech, microcephaly, seizures, postnatal short stature, and congenital diaphragmatic hernia if *ZFPM2* gene at 8q23.1 is also deleted [1–3]. Patients with 8q23.3 deletion encompassing *TRPS1* gene at 8q23.3 may present trichorhinophalangeal syndrome (TRPS) type II [4,5]. Patients with del(8)(q22q23) or del(8)(q22q24.1) involving haploinsufficiency of *ZFPM2* gene at 8q23.1 has been reported to be associated with congenital diaphragmatic hernia [1,6].

Prenatal diagnosis of an interstitial deletion of 8q22.2-q23.3 has not previously been reported. Here, we present prenatal diagnosis of an interstitial 8q22.2-q23.3 deletion associated with bilateral cleft lip and palate and intrauterine growth restriction (IUGR) on fetal ultrasound.

* Corresponding author. Department of Obstetrics and Gynecology, MacKay Memorial Hospital, 92, Section 2, Chung-Shan North Road, Taipei 10449, Taiwan. Fax: +886 2 25433642, +886 2 25232448.
E-mail address: cpc_mmh@yahoo.com (C.-P. Chen).

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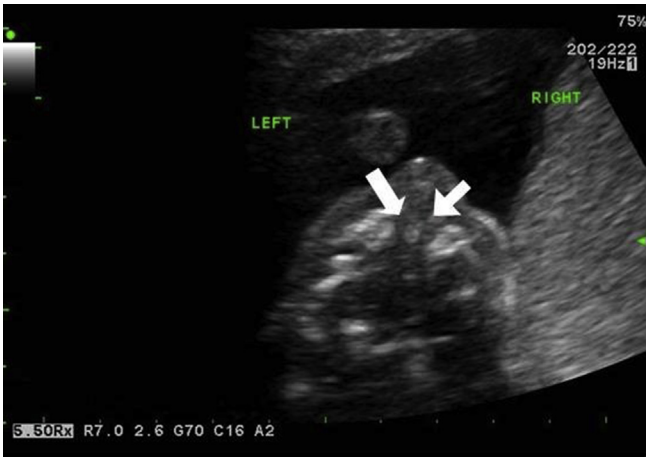

Fig. 1. Prenatal ultrasound at 21 weeks of gestation shows bilateral cleft lip and palate (arrows).

Case report

A 29-year-old, primigravid woman underwent elective amniocentesis at 17 weeks of gestation because of anxiety. Her husband was 36 years old, and there was no family history of congenital malformations. Amniocentesis revealed a karyotype of 46, XX in cultured amniocytes. However, level II ultrasound at 21 weeks of gestation revealed a fetus with IUGR and bilateral cleft lip and palate (Fig. 1). The biparietal diameter (BPD) was 4.68 cm (reference range: 4.87–5.77 cm), the head circumference (HC) was 16.58 cm (reference range: 17.97–20.84 cm), the abdominal circumference (AC) was 13.67 cm (reference range: 13.37–19.47 cm), the femur length (FL) was 2.97 cm (reference range: 3.21–4.01 cm), the HC/AC ratio was 1.21 (reference range: 1.05–1.26), and the HC/FL ratio was 5.58 (reference range: 4.83–5.70). Repeat amniocentesis was performed at 21 weeks of gestation, and array comparative genomic hybridization on uncultured amniocytes using SurePrint G3 Unrestricted CGH ISCA v2, 8 × 60 K Array (Agilent Technologies, Santa

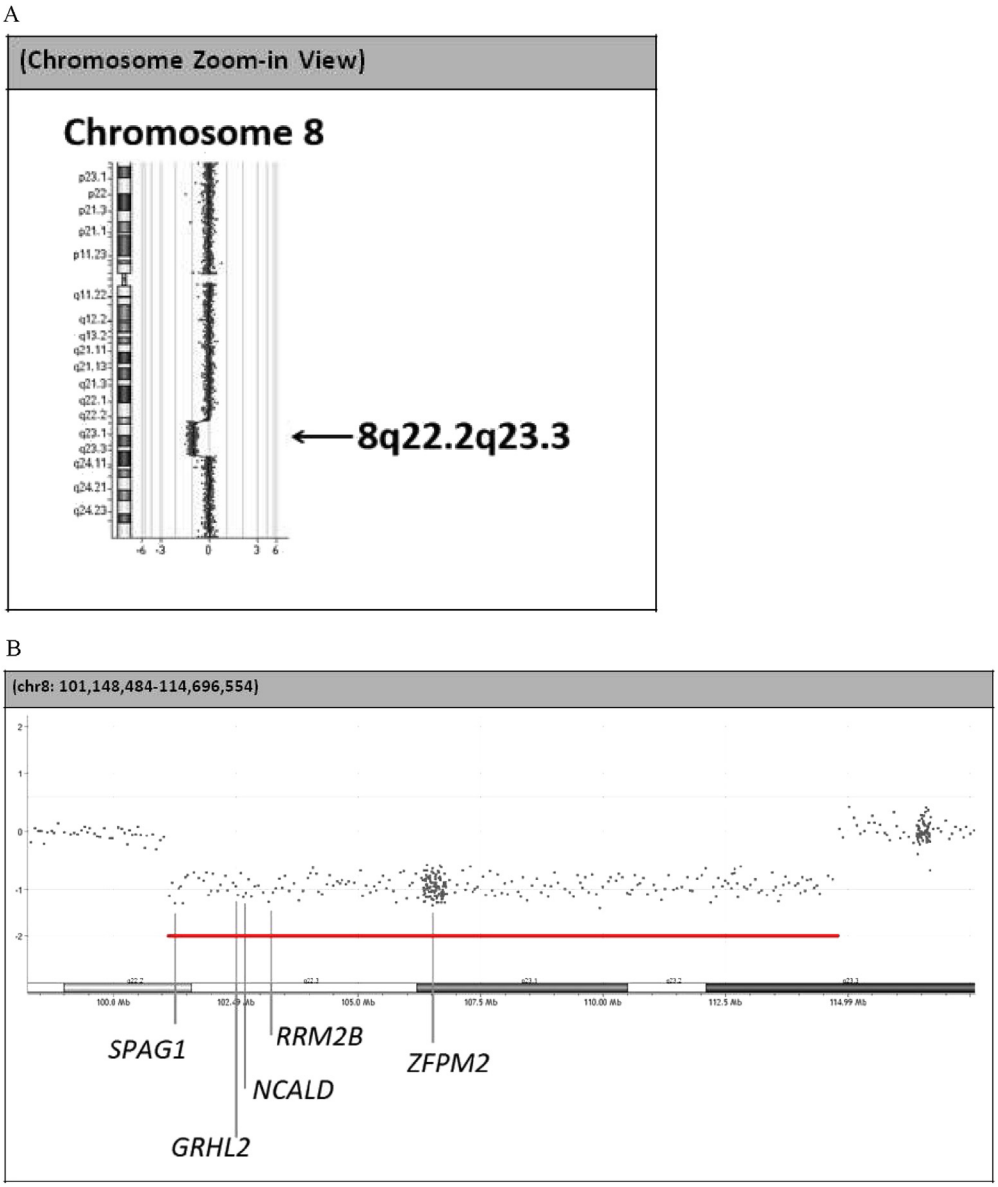

Fig. 2. Array comparative genomic hybridization on uncultured amniocytes shows a 13.5-Mb deletion at chromosome bands 8q22.2-q23.3 encompassing the genes of *SPAG1*, *GRHL2*, *NCALD*, *RRM2B* and *ZFPM2*. (A) and (B) Zoom-in views.