First-trimester Diagnosis of Micrognathia as a Presentation of Stickler Syndrome

Gui-Lan Chen, Dong-Zhi Li*

Department of Prenatal Diagnosis, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou, Guangdong, China

Dear Editor,

Micrognathia is a facial malformation characterized by a small mandibular size, giving the impression of a receding chin. As one of the common craniofacial deformities, fetal micrognathia can be an isolated feature, or be associated with a wide variety of chromosomal abnormalities, varied syndromes, and skeletal dysplasias.[1] We report a fetal case of micrognathia who was identified by the first-trimester ultrasound and was confirmed to have a genetic anomaly using prenatal exome sequencing.

A 32-year-old Chinese woman (para 0, gravida 1) undergoing first-trimester routine sonography screening at 12 weeks of gestation. The patient was in a nonconsanguineous marriage. There was no relevant past medical or family history in both partners. The 9-week ultrasound revealed a live singleton intrauterine pregnancy with fetal dimensions consistent with the last period. The 12-week survey revealed a crown-rump length of 64 mm and nuchal translucency measurement of 3.8 mm, with an abnormal profile with a small mandible and receding chin, the features suggestive of micrognathia [Figure 1]. The fetal hard palate appeared intact, and no other malformations were noted in the heart, abdomen, and limbs. Based on the sonographic findings, the couple consented to chorionic villus sampling. The chromosomal microarray analysis reported a normal result. Rapid trio exome sequencing detected a *de novo* variant c. 1286G>A (p.Gly429Asp) in the *COL2A1* gene (NM_001844.5) [Figure 1]. This variant was classified as likely pathogenic according to ACMG guidelines. After genetic counseling, the patient opted for termination of the pregnancy at 14 weeks. The aborted male fetus showed dysmorphic features with severe micrognathia and cervical cutaneous edema [Figure 1].

Received: 23-05-2024 **Revised:** 08-06-2024 **Accepted:** 17-06-2024 **Available Online:** 05-09-2024

Access this article online

Quick Response Code:

Website: https://journals.lww.com/jmut

DOI: 10.4103/jmu.jmu_58_24

Stickler syndrome (SS) is a connective tissue disorder characterized by distinctive facial features, eye abnormalities, hearing loss, and joint problems. It is caused by pathogenic variants in one of the six genes: *COL2A1*, *COL11A1*, *COL11A2*, *COL9A1*, *COL9A2*, or *COL9A3*.[2,3] *COL2A1*-associated SS with the autosomal dominant inheritance is the most common form, accounting for approximately 80%–90% of cases. Micrognathia is a common feature of SS and may be associated with cleft palate as part of the Pierre Robin sequence. The degree of micrognathia may compromise the upper airway, necessitating tracheostomy in the neonatal period. Most patients with SS have mild spondyloepiphyseal dysplasia resulting in short stature, possibly associated with short femora. However, this nonspecific sonographic feature usually occurs in the third trimester. Micrognathia is the only marker that can be detected in early pregnancy.

One retrospective study including 41 fetuses with a prenatal diagnosis of micrognathia reported a genetic cause in 21 cases (67%), with monogenic disorders in 9 cases (22%).[4] The prognosis was good for the fetuses, with no associated findings and normal chromosomal analysis. Another study included 13 cases of first-trimester micrognathia with a normal array.[5] Monogenic syndromes were identified in 8 cases (8/13), including six with *de novo* dominant alleles and two with recessive conditions. Our case is the first one in which a first-trimester sonographic detection of micrognathia combined with advanced molecular testing resulted in an early prenatal diagnosis of SS. This is critical to predict the developmental prognosis of fetuses with micrognathia.

Address for correspondence: Dr. Dong-Zhi Li, Department of Prenatal Diagnosis, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou, Guangdong, China.
E-mail: drlidongzhi2014@sina.com

How to cite this article: Chen GL, Li DZ. First-trimester diagnosis of micrognathia as a presentation of Stickler syndrome. J Med Ultrasound 2025;33:179-80.

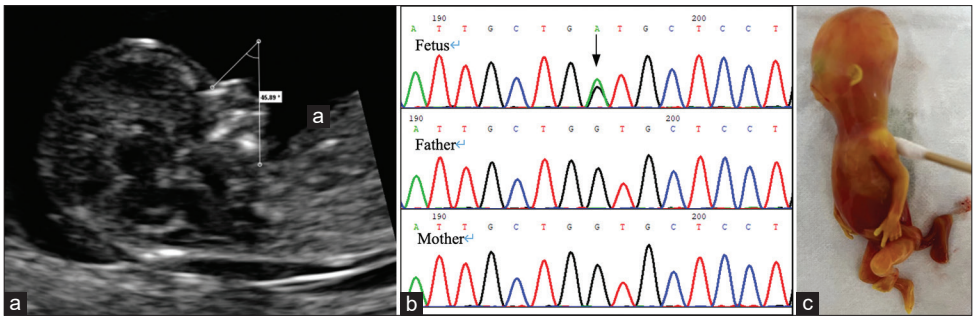

Figure 1: A fetus of stickler syndrome with micrognathia and a variant of *COL2A1*. (a) Sagittal plane of increased nuchal translucency and micrognathia at 12 weeks with an inferior facial angle of 45.9° (normal reference, ≥65°), (b) Chromatograms of the *COL2A1* c. 1286G>A variant (arrow) in the family, showing the de novo heterozygous state in the fetus, (c) Micrognathia and cervical cutaneous edema of the aborted fetus

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

This study was supported by the National Key Research and Development Program (2022YFC2702600).

Conflicts of interest

There are no conflicts of interest.

References

1. Society for Maternal-Fetal Medicine, Benacerraf BR, Bromley B, Jelin AC. Micrognathia. Am J Obstet Gynecol 2019;221:B13-5.
2. Boothe M, Morris R, Robin N. Stickler syndrome: A review of clinical manifestations and the genetics evaluation. J Pers Med 2020;10:105.
3. Huang F, Wang TJ, Cho WH, Chen YH, Wu PC, Kuo HK. Mutation survey in Taiwanese patients with Stickler syndrome. Taiwan J Ophthalmol 2022;12:423-9.
4. Mouthon L, Busa T, Bretelle F, Karmous-Benailly H, Missirian C, Philip N, *et al.* Prenatal diagnosis of micrognathia in 41 fetuses: Retrospective analysis of outcome and genetic etiologies. Am J Med Genet A 2019;179:2365-73.
5. Zhen L, Yang YD, Xu LL, Cao Q, Li DZ. Fetal micrognathia in the first trimester: An ominous finding even after a normal array. Eur J Obstet Gynecol Reprod Biol 2021;263:176-80.