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Research Letter

Prenatal diagnosis of low-level mosaicism for trisomy 21 with rare karyotype detected by noninvasive prenatal testing

Hong Wu, Zong-Yu Miao, Xiao-Fei Hou, Xiao-Yan Liu, Hui-Yuan Shao*

Medical Laboratory Center, The Affiliated Yantai Yu Huang Ding Hospital of Qingdao University Medical College, Shandong, China

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Dear Editor,

Trisomy 21 (Tri21), which causes the Down syndrome (DS), is the most common chromosome abnormality [1]. Patients with DS are always accompanied by intellectual disability, congenital heart disease and so on. Therefore, only 20% of Tri21 may progress to term delivery, but it is necessary to prevent the birth of neonatus with Tri21 [1,2]. Noninvasive prenatal testing (NIPT), which is the newest detection method, provides a more precise and fast screening method for the early detection of Tri21, and the detection rate is more than 99% [3]. Nevertheless, the effect of the application of NIPT in the detection of aneuploidy chromosome mosaicism is still uncertain, and it poses a challenge for clinicians to deal with the genetic consultancy of low-level mosaicism after being detected by hypersensitized NIPT. In this article, we present a prenatal diagnosis of low-level mosaicism for trisomy 21 with rare karyotype detected by NIPT.

This case involves a 32-year-old woman, presented with a positive result of NIPT for Tri21 and the Z-scores were 4.267. At 20 weeks of gestation, the woman underwent amniocentesis, which followed by fluorescence in situ hybridization (FISH) and chromosome karyotype analysis of amniotic fluid cells. Amniocentesis revealed a karyotype of 47,XX,+21[20]/47,XX,+der(21) (q21;q21)[30]/46,XX[120] (Fig. 1) and FISH revealed a mosaic level of 5.00% (5/100 cells) for Tri21 (Fig. 2). Ultrasound examination showed the development of fetus was normal. Following genetic counseling, the parents refused the cord blood lymphocytes chromosome karyotype analysis, and decided to continue the pregnancy, which was carried to term. A healthy female baby was delivered, and peripheral blood lymphocytes chromosome karyotype analysis revealed a karyotype of 47,XX,+21[11]/47,XX,+der(21) (q21;q21)[15]/46,XX[74] (Fig. 3), which was similar to the result of amniocentesis. The neonate was phenotypically normal at the age of 10 months during follow-ups. The chromosome karyotype of the couples and their older daughter were normal.

As is known, the range of Tri21 from 90% to 96% is generally classified as standard Tri21, 2%–5% is Robertsonian Tri21, and less than 4% is other Tri21 forms [4]. In this report, amniocentesis revealed a karyotype of 47,XX,+21 [20]/47,XX,+der(21) (q21;q21)[30]/46,XX[120], which is rarely seen, and that the phenotype of the neonate was normal during follow-ups. So this report is especially helpful in genetic counseling of parents who wish to continue the pregnancy following a diagnosis of mosaic trisomy 21 at amniocentesis.

In addition, FISH plays an important role in the rapid detection of Tri21 [5]. As is known, the probe of chromosome 21 tags in 21q22, which is inefficient to detect the cells with 47,XX,+der(21)(q21;q21). So the chimeric rate of Tri21 was only 5% detected by FISH in this case, which was significantly lower than the result of amniocentesis. The result alerts us that it is necessary to treat the low-level mosaicism detected by FISH carefully.

In summary, we demonstrate that NIPT may be useful for screening of low-level mosaicism for trisomy 21 during early pregnancy. Fetus with low-level mosaic Tri 21 could be associated with a favorable fetal outcome.

* Corresponding author. Medical Laboratory Center, The Affiliated Yantai Yu Huang Ding Hospital of Qingdao University Medical College, 20#, The East Road of Yu Huang Ding, Zhifu District, Yantai, 264000, Shandong, China.
E-mail address: shaohuiyuan313@163.com (H.-Y. Shao).

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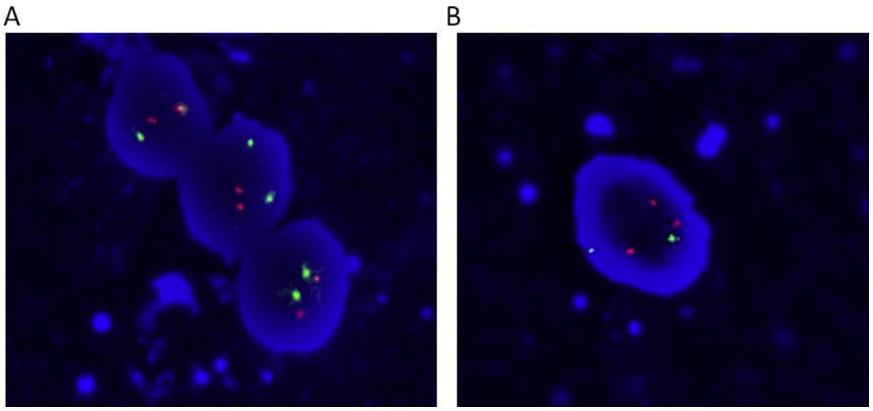

Fig. 1. The number of Tri21 was detected by FISH using a 21q22.1-specific probe (Tetramethyl rhodamine, spectrum red). (A) The normal amniotic fluid cells with two red signals. (B) A trisomy 21 cell with three red signals. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

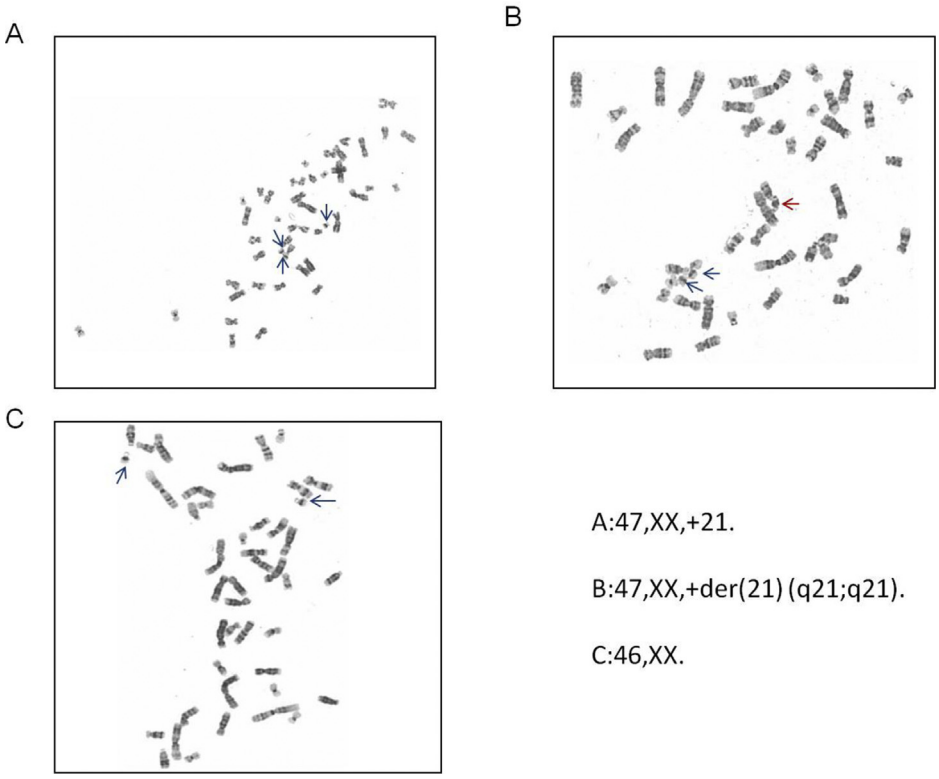

Fig. 2. The chromosome karyotype of amniotic fluid cells. The normal Chromosome 21 was marked by blue arrow, and the der(21)(q21;q21) was marked by red arrow. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

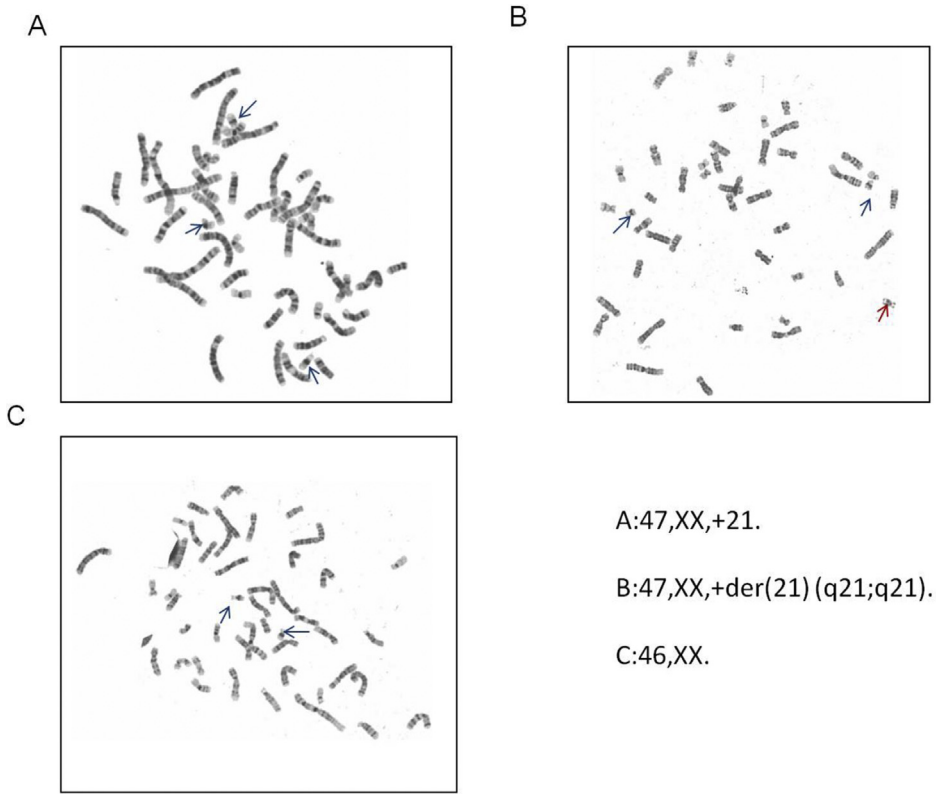

Fig. 3. The chromosome karyotype of lymphocytes in peripheral blood. The normal Chromosome 21 was marked by blue arrow, and the der(21)(q21;q21) was marked by red arrow. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Authors' contributions

Hong Wu and Zong-Yu Miao wrote the manuscript and coordinated the clinical analysis of the patients, so they contributed equally to this work.

Disclosure of interests

The authors declare that they have no competing interests.

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