Clinical value of ultrasonography in screening trisomy 13 during the second and third trimesters of gestation

PAN Yu-ping¹,²
1.Medical College, Eastern Liaoning University, Dandong, Liaoning 118003 China;
2.Department of Ultrasound, Shengjing Hospital of China Medical University, Shenyang, Liaoning 110004 China
E-mail: Panxy900@sina.com

Abstract: Objective To investigate the clinical value of ultrasonography in screening trisomy 13 during the second and third trimesters. Methods Amniocentesis and cordocentesis were performed on 3297 pregnant women with indications for prenatal diagnosis to detect the karyotype of the fetus during second trimester and late pregnancy. The detection rates of trisomy 13 were compared among different indications of pregnant women. The relationship between the ultrasonography abnormalities and trisomy 13 was analyzed. Results In chromosomal karyotypes analysis of 3297 pregnant women by amniocentesis and cordocentesis, 3 trisomy 13 were detected with a detection rate of 0.09%. There were 226 in 3297 pregnant women with simple ultrasonography abnormalities, and 2 of them was found with trisomy 13 with a detection rate of 0.88%. The detection rate of trisomy 13 detected with ultrasound (0.88%) was higher than that with the Down’s syndrome high risk (P=0.001). Conclusion During the second and third trimester, ultrasonography contributes to detect the trisomy 13 and has a great clinical value.

Key words: Amniocentesis; Cordocentesis; Karyotyping; Ultrasonography, prenatal; Trisomy; etc.

0. Introduction

Ultrasonography as a kind of prenatal screening method, which can observe fetal anatomical structure malformation, with painless non-invasive, convenient and quick, real-time dynamic, economic and effective, can repeat and so on many kinds of advantage, has been widely used in prenatal screening [1]. Trisomy 13 neonatal mortality is high, the prognosis is poor, the mean survival time was 2.5 days, about 45% trisomy 13 after the birth death in 1 months, about 90% death in 6 months [2], a few can live to be a few years old even teens, has serious brain delays and epilepsy, bring to the family mental pain and economic burden. Prenatal ultrasonography has the important meaning in screening trisomy 13. In this paper, to investigate the clinical value of ultrasonography in screening trisomy 13 during the second and third trimesters through chromosomal karyotypes analysis of 3297 pregnant women by amniocentesis and cordocentesis.

1. Clinical data and Methods

1.1 Clinical data

All subjects are pregnant women sought medical examination or consultation in Shengjing Hospital of China Medical University. Three thousand one hundred thirty nine patients with amniocentesis indications were included from January 5, 2008 - May 4, 2010, and amniotic fluid cell culture was succeeded in 3110 patients, aged 19~48 years, with a mean age of (31.6 ± 5.9) years old and 17 ~ 24 weeks of gestational age. Additional 188 patients with indications of fetal cord blood puncture were included from January 5, 2009 - May 10, 2010, and umbilical cord blood cell culture was succeeded in 187 patients, aged 18~46 years, with a mean age of (28.9 ± 4.6) years old and 24~37 weeks of gestation age. All indications of amniotic fluid puncture and umbilical cord blood sampling were detected during prenatal diagnosis, including: advanced maternal age (35 years old and above), high risk of Down syndrome (rate≥1/270), abnormal ultrasound findings, high risk of neural tube defects (NTD) and 18-trisomy syndrome, abnormal pregnancy history, history of chromosomal abnormalities of the parents, family history of genetic diseases, maternal mental retardation, drug history, viral infection and other history of obvious exposure to teratogenic factors.

All pregnant women signed informed consent for post-puncture karyotyping analysis.
1.2 Methods

1) Sample collection and cell culture: ultrasound-guided amniocentesis was performed and 20~30 ml amniotic fluid was drawn for laboratory culture. Umbilical cord puncture was also performed under guidance of ultrasound, and 2 ml blood sample was placed in anticoagulant sodium heparin-treated disposable collection tube for laboratory culture.

2) Chromosome karyotype analysis: after G-band staining, cultured cells were observed and 15~30 metaphase images were counted. Three to five karyotypes were analyzed and abnormal karyotype was carefully observed and analyzed.

3) I have obtained permission from my institution’s ethics committee to perform this study and approval from my institution’s review board or ethics committee.

1.3 Instruments and ultrasound methods

Voluson E8 ultrasound diagnostic apparatus by GE company was used, with probe frequency of 4~6 MHz. Through abdominal multiplanar scanning, fetal head, face, neck, chest and abdomen, internal organs, limbs and spine etc. were scanned and suspicious sites were carefully observed. During follow-up, routine measurement of relevant data was performed including fetal biparietal diameter, limb length, amniotic fluid volume and placental thickness etc. Results were recorded.

1.4 Statistical analysis

SPSS13.0 software was used for statistical analysis. Count data of each group were compared using $\chi^2$ test and $P < 0.05$ was considered statistically significant.

2. Results

2.1 Chromosome karyotyping of pregnant women

In chromosomal karyotypes analysis of 3297 pregnant women by amniocentesis and cordocentesis, 3 trisomy 13 were detected with a detection rate of 0.09% (Table 1). There were 226 in 3297 pregnant women with simple ultrasonography abnormalities, and 2 of them was found with trisomy 13 with a detection rate of 0.88%; Combined with two or more puncture indications 708, 1 trisomy 13 were detected, with ultrasonography abnormalities and advanced maternal age two kind of puncture indications. The detection rate of trisomy 13 in 3297 patients with amniotic fluid and umbilical cord blood puncture indications was shown in Table 1.

<table>
<thead>
<tr>
<th>Puncture indications</th>
<th>Patients number</th>
<th>trisomy 13 (n)</th>
<th>Trisomy 13 detection rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>simple ultrasonography abnormalities</td>
<td>226</td>
<td>2</td>
<td>0.88</td>
</tr>
<tr>
<td>the Down’s syndrome high risk</td>
<td>1230</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>advanced maternal age</td>
<td>694</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>abnormal pregnancy history</td>
<td>231</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>other puncture indications</td>
<td>208</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Combined with two or more puncture indications</td>
<td>708</td>
<td>1</td>
<td>0.14</td>
</tr>
<tr>
<td>total</td>
<td>3297</td>
<td>3</td>
<td>0.09</td>
</tr>
</tbody>
</table>

$\chi^2$ test found that the detection rates of trisomy 13 among groups were significantly different ($\chi^2=20.928$ and $P < 0.001$). Inter-group comparison by $\chi^2$ test found that trisomy 13 detection rate of simple ultrasonography abnormalities group (0.88%) was significantly higher than that of the Down syndrome high risk group ($P=0.001$); However, no significant difference was detected in trisomy 13 detection rate between simple ultrasonography abnormalities group (0.88%) and advanced maternal age group ($P=0.06$), abnormal pregnancy history group ($P=0.244$).

2.2 Correlation of trisomy 13 with ultrasonography abnormalities

Correlation of 3 trisomy 13 with ultrasonography abnormalities and other puncture indications was shown in Table 2.

<p>| Table 2 Correlation of 3 trisomy 13 with ultrasonography abnormalities and other puncture indications |</p>
<table>
<thead>
<tr>
<th>Serial number</th>
<th>Maternal age and gestational age</th>
<th>abnormal karyotype</th>
<th>ultrasonography abnormalities and other puncture indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34-year-old, 32 weeks</td>
<td>47,XN,+13</td>
<td>Fetal three tricuspid valve moderate regurgitation; double renal pelvis mild expansion</td>
</tr>
<tr>
<td>2</td>
<td>36-year-old, 21 weeks</td>
<td>47,XN,+13</td>
<td>Holoprosencepha; limbs bone short; advanced maternal age</td>
</tr>
<tr>
<td>3</td>
<td>27-year-old, 21 weeks + 4</td>
<td>47,XN,+13</td>
<td>Holoprosencepha; bilateral upper limbs deformity; ventricular septal defect; single umbilical artery</td>
</tr>
</tbody>
</table>

3. Discussion

Trisomy 13 is known as Pateau syndrome\(^5\), is an autosomal aneuploidy disease, because 13 chromosome did not separate in one of the parents germ cells meiosis, most come from the mother, advanced maternal age and roche translocation carriers increase incidence. Trisomy 13 usually associated with multiple deformity, its incidence is about 1/25000 ~ 1/12 000 of living newborn, woman is obviously more than men. Trisomy 13 main structure malformation and tiny lesions have: ① brain malformation: Holoprosencepha, microcephaly, neural tube defects, ventricle expansion, corpus callosum loss, posterior fossa pool expand, Dandy-Walker malformation; ② facial deformity: Holoprosencepha is associated with eye malformation such as the one eye malformation, small eyes, close distance between the eyes; nasal deformity may display single nostrils, no nostrils and long nasal deformity, nasal dysplasia: in the middle of the cleft lip, ear low, etc; ③ neck malformation: water sac tumour of neck; ④ limbs deformity: the most common limbs deformity is extra finger(toe) deformity after the shaft, can have the radius dysplasia, foot turn inward, flat bottom feet, finger overlapping and buckling is relatively uncommon; ⑤ cardiac anomalies: ventricular septal defect, common atrioventricular canal defects, patent ductus arteriosus, atrial septal defect, hypoplastic left heart syndrome, ventricle echo in focus; ⑥ abdominal malformation: acromphalus, colon spin bad, umbilical and groin hernia, single umbilical artery, pancreas or spleen organization ectopic, a few have umbilical cord cyst etc; ⑦ genitourinary and reproductive system malformation: polycystic kidney disease, multiple cystic renal dysplasia, hydronephrosis, double horns uterine etc; ⑧ obviously intrauterine growth restriction (IUGR): before 30 weeks of gestational age, most are uniformity IUGR, after 30 weeks of gestational age, most are heterogeneity IUGR, is usually associated with polyhydramnios; ⑨ can have fetal entire edema.

Trisomy 13 main ultrasonography abnormalities in this study have: ① Holoprosencepha: forebrain is not completely separated into left and right two lobes of the brain, and cause a series of brain malformation and facial deformity, is Trisomy 13 the most important brain abnormalities, is also the most typical deformity characteristics\(^2,5\), including three kinds of types: no lobe of the brain Holoprosencepha, half lobe of the brain Holoprosencepha, and lobes of the brain Holoprosencepha. no lobe of the brain Holoprosencepha is the most serious among them, brain hemisphere completely fusion not separate, cerebral falx and hemisphere fracture is lack (Figure 1 A), only single original ventricle (Figure 1 B), thalamus merge into one. In this group Holoprosencepha of 2 Trisomy 13 is all no lobe of the brain Holoprosencepha, accounted for 66.67% (2/3). ② cardiac anomalies: Most Trisomy 13 have different types of cardiac anomalies, In this group, 2 Trisomy 13 have cardiac anomalies (2/3), one of them has ventricular septal defect, another has three tricuspid valve moderate regurgitation. A research report\(^6\) 16% fetuses of single heart structural abnormalities have chromosomal abnormalities, 66% fetuses of combined with other structural abnormalities have chromosomal abnormalities, in this study, 2 fetuses of cardiac anomalies are all heart structural abnormalities combined with other structural abnormalities (Figure 1 C). ③ umbilical cord abnormalities: In this study, 1 Trisomy 13 has umbilical cord abnormalities (1/3, 33.33%), single umbilical artery combined with other ultrasonography abnormalities (Figure 1 D). ④ deformity of limbs skeletal system: In this group, skeletal abnormalities have totally 2 types, accounted 66.67% (2/3), one of them has limbs bone short, another has bilateral upper limbs deformity, radius lack (Figure 1 E, Figure 1 F).

Most of the trisomy fetuses have 2 or more abnormal ultrasound findings, so detection of more than 2 ultrasonic signs suggests possible aneuploidy\(^7,10\). In this study, 3 trisomy 13 have all more than 2 ultrasonography abnormalities.

In this study, pregnant women with ultrasonography abnormalities by amniocentesis and cordocentesis, trisomy 13 detection rate of ultrasonography abnormalities group was significantly higher than that of the Down
syndrome high risk group; namely among various trisomy 13 high risk, the value of ultrasonography abnormalities obviously better than that of the Down serological abnormal results. Therefore, some typical deformity is closely correlated with trisomy 13, trisomy 13 can be effectively detected by ultrasonography screening. A study of Lehman et al found that 91% of trisomy 13 can appear obvious multiple structural malformations[9], suggests that the remaining 9% of trisomy 13 ultrasonography can be found no abnormalities, namely there is false-negative phenomenon of ultrasound screening, Joint screening methods can effectively improve the detection rate of trisomy 13. 3 trisomy 13 of this group, simple ultrasonography abnormalities detected 2 cases of 3 trisomy 13, ultrasonography abnormalities combined with advanced maternal age detected 1 cases of 3 trisomy 13, namely 3 trisomy 13 have all ultrasonography abnormalities, there is no false-negative phenomenon, it might be related to less trisomy 13 number of cases in this study.

4. Conclusion

In summary, ultrasonography in screening trisomy 13 has a great clinical value during the second and third trimesters.

References
A. It did not see the obvious midline and pseudocele, two side of thalamus merge into one;
B. single lateral ventricle about the size of 4.3 cm x 4.1 cm;
C. Around the bladder to display only single umbilical artery;
D. ventricular septal echo interrupt about 0.56 cm;
E~F. Bilateral forearms both only see a long bone; Both hands is hooked; The nasal bones show not clear, seem to be single nostrils.

Ultrasound tip: 1. Holoprosencepha; 2. Bilateral upper limbs deformity (such as radial lack not except); 3. Congenital heart disease (ventricular septal defect, pulmonary artery stenosis not except); 4. Single umbilical artery. Karyotype is 47, XN, + 13 (umbilical cord blood).