R. Monzavi Sani MD[1]
F. Savadkuhi MD[2]
Z. Rohani MD[2]

Chorionic Villus Sampling Complications in Prenatal Diagnosis of Thalassemia Major

Background/Objective: Early diagnosis of thalassemia with chorionic villus sampling has an important role in fetal evaluation. Because of the increasing risk of fetal loss and other probable risks, it seems there are some considerations about the safety of this method. Since different studies have mentioned variable complications of this method for the mother and her fetus and also the fact that this information is limited in most areas of our country, this study was performed to compare the complications of this procedure with other reports.

Patients and Methods: This prospective case series study was performed in the chorionic villus sampling (CVS) center of Zahedan University of Medical Sciences from October 2003 till July 2006. One-hundred thirty seven patients who were referred to this center were sampled and examined by sonography regarding early complications of CVS in mothers and fetuses and deformities in their neonates.

Results: The most common early complication of CVS was subchorionic hematoma (6.5%), of which one case finally resulted in placenta abruption and abortion. The fetal loss rate after CVS was the same as the abortion rate following subchorionic hematoma. In this study, we did not find any chorioamnionitis, oligohydramnios and fetal loss during the sampling. Furthermore, in the follow up control of their neonates, there were neither limb deficiency and oromandibular defects nor cutaneous hemangioma.

Conclusion: Results show that minor complications of CVS such as subchorionic hematoma can be dangerous and may increase the risk of fetal loss. In addition, this study agrees that sampling after 10 weeks of pregnancy on the hands of an expert is a safe procedure.

Keywords: Chorionic Villus Sampling, Thalassemia Major, Abortion, Complication

Introduction

Nowadays, early diagnosis of certain hereditary diseases such as thalassemia is accepted all around the world because therapeutic abortion can prevent birth of affected neonates, leading to improvement of community health. This diagnosis could be done with different methods like chorionic villus sampling (CVS).

On the other hand, a normal result reduces the parents' anxiety. As this invasive diagnostic method still has an important role in fetal evaluation, its risk is one of the most important questions during the parents' genetic consultation.

Because of the increasing risk of fetal loss and other probable risks, it seems there are some considerations about the safety of this early diagnostic method in pregnancy.[1] As in one study, the most common early complication of CVS was massive bleeding which may lead to abortion; and the fetal loss rate was 4.5%.[2] Although in recent studies, the fetal loss rate has been 2%, which was less in the transabdominal method compared to the transcervical method.[3] In another case report, fetal death was reported due to infection following CVS in the first trimester of pregnancy and the fetus had a defect in his arm too.[4]

According to the above-mentioned complications, and as such a study has

1. Assistant Professor, Department of Radiology, Rohani Hospital, Babol University of Medical Sciences, Babol, Iran.
2. Assistant Professor, Department of Radiology, Imam Ali Hospital, Zahedan University of Medical Sciences, Zahedan,Iran.

Corresponding Author:
Rahele Monzavi Sani
Address: Department of Radiology, Imam Ali Hospital, Zahedan, Iran.
Tel: +98541 3411260
Fax: +98541 3411251
E-mail: sany_monzavi@Yahoo.com

Received September 7, 2009;
Accepted after revision May 10, 2010.

Iran J Radiol 2010;7(2):101-104

not been carried out in the Southeast of Iran, in which thalassemia is an endemic disease, and on the other hand, because the risks of this invasive method should be evaluated in each person during genetic consultation the conduction of this study seemed essential.

Patients and Methods

This descriptive study was performed as a prospective case series at the CVS center of Zahedan University of Medical Sciences from October 2003 till July 2006. One-hundred thirty-seven patients, including pregnant women who had a child with thalassemia major and the parents carrying the thalassemia gene were referred to this center during genetic consultation or by relevant specialists.

Subsequently, pregnant women were controlled again to prove whether they were thalassemia gene carriers, were referred to our center at 10-13 weeks of gestation for chorionic villus sampling, and were enrolled into the study.

Then, ultrasonography was performed to estimate the gestational age and to determine the anatomy of the uterus and location of the placenta. If there were no vaginal bleeding or spotting, transabdominal chorionic villus sampling was performed via US guide after antisepticizing the abdominal skin with Deconex antibiotic solution.

Ultrasound examination was performed using a Siemens unit (Adara) with a 2.5-5 MHz convex-array transducer. The needle used for sampling was an echogenic tip Chiba with 20-21 gauge, and the vacuum used for aspiration was a PAC/PAC-UF model.

Under ultrasound guidance, the needle was entered into the chorionic trophoblasts. Then negative pressure was used and the needle was pushed up and down through the trophoblasts and 5-10 cc of the sample was aspirated. Samples were gathered in special dishes containing physiologic serum. Consequently, fetoplacental samples were separated from mother samples and their DNA were evaluated by the ARMS/PCR (amplification refractory mutation system polymerase chain reaction) method.

Immediately after CVS, control ultrasound was performed to detect intraplacental hemorrhage in the sampling location, subchorionic hematoma and fetal heart rate. After 2 hours rest, the mother was dismissed and was asked to return 10 days later for control sonography. Patients had to return in case of vaginal bleeding, spotting, abdominal pain or fever during this 10-day period. Thereafter, the patients were followed up and divided into two groups:

1. The group in which ARMS/PCR results showed thalassemia major in the fetus. These fetuses were excluded from the final evaluation of neonates, and legal abortion was performed subsequently.

2. The group in which the results of ARMS/PCR were negative for thalassemia. In this group, the pregnancy continued and the final evaluation of neonates was performed. In this final assessment, the neonates were examined for known anomalies following CVS such as limb defects, especially minor defects of fingers and cutaneous hemangiomas.

Results

In this study, 137 women with the mean age of 25.3±4.3 years and average gestational age of 11.7±1.7 weeks were sampled, of which fetuses of 37 patients (27%) were aborted therapeutically as a result of thalassemia major of the fetuses (Table 1).

The complications of CVS in mothers were evaluated in all 137 patients, but the final assessment on neonates was only carried out on 100 patients who had normal genetic laboratory results and the therapeutic abortion was not performed for them.

Subchorionic hematoma was the most common early complication of CVS, which was detected in 9 out of 137 patients (6.5%) (Fig. 1).

Spontaneous abortion following CVS occurred in only one case (0.73%), which was due to massive subchorionic hematoma and placental abruption on the third day after sampling. This was the only placental abruption case. However, it must be noted that the sampling result in this case was thalassemia major. No chorioamnionitis occurred after 2 weeks sampling and no decreased fetal heart rate happened during sampling.

It should also be noted that in five patients, we had to enter into the placenta through the amniotic sac because of the inappropriate location of the placenta. It was interesting that PROM (premature rupture of membranes) did not occur after CVS neither in the

Table 1. Patient Distribution by Gestational Age

Gestational Age	No.	Percent	Fetal Loss	Percent
10 w	10	7.2	0	0.00
11 w	31	22.6	0	0.00
12 w	73	53.2	0	0.00
13 w	23	16.7	1	0.73
Total	137	100	1	0.73

five cases mentioned above nor in the other patients.

At the final evaluation of 100 neonates, no limb defect, cutaneous hemangioma, or oromandibular defect was seen in the physical examination and all were healthy.

Discussion

As noted previously, according to the increasing need for prenatal diagnosis and the important role of CVS, it is necessary to provide information about the risks of this invasive method during genetic consultation.

The results of different studies show that there are variations in CVS complications in the mother and fetus in different CVS centers.

In Hsieh et al.'s study in 1989 in Taiwan,[2] hemorrhage was the most common early complication of CVS and only one abortion was reported following massive bleeding.

Also, in another study in 1996 in USA,[5] it was shown that subchorionic hematoma after CVS may increase the risk of abortion, IUFD (intra uterine fetal death), placental abruption and preterm labor in the future. But in another study in Sweden in 2003,[6] CVS did not have any major complication such as placental abruption or abortion.

In our study, the most common complication was subchorionic hematoma (6.5%) leading to placental abruption in one case, which ended in fetal abortion (11%). This finding shows that minor complications following CVS such as subchorionic hemorrhage may be dangerous and can increase the risk of fetal loss.

Furthermore, fetal abortion was found in 0.7% of the cases, almost equal to the results of a study performed in Canada in 1992 (0.6%),[7] but much lower than the results of the same study in Taiwan in 1989 (4.5%).[2]

Although in the Myoclinic Journal in 2010 and recent papers the miscarriage rate was one percent in general, it appears to be slightly higher when is performed transcervically.[8]

In another study carried out by Akhlaghpoor from June 1999 till June 2005 in Iran, a fetal loss rate of 1.45% was reported in 1381 cases.[9]

These findings show that CVS is very dependent on the performer's expertise; therefore, having specialized education and perseverance in gaining skills are essential before CVS. However, in larger studies the results will be more realistic.

In our study, CVS did not cause PROM and oligohydramnios, even in cases that were sampled through the amniotic sac. Trans-sac sampling does not cause an increasing risk of PROM compared to direct sampling of the placenta.

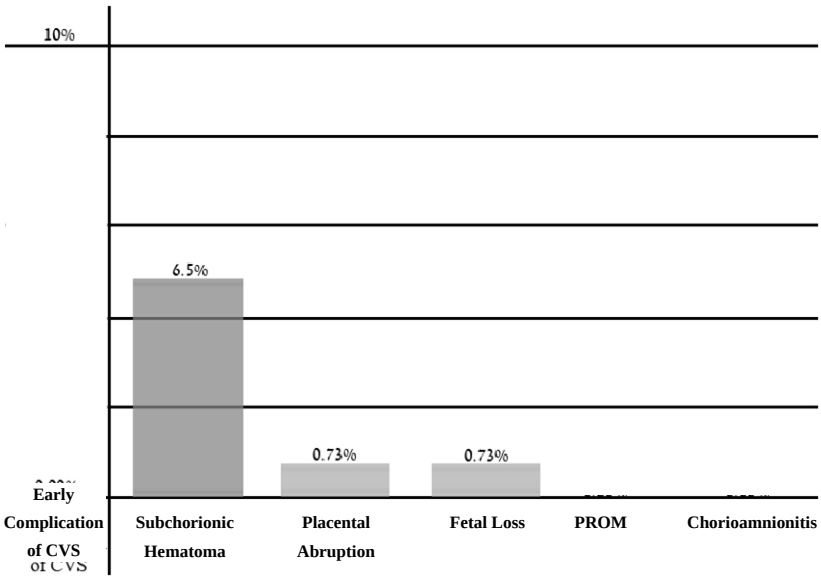

Fig. 1. The complications in the order of frequencyare shown in percent in this histogram. The most common complication was subchorionic hematoma (6.5 %).

Theoretically, transcervical CVS has a higher risk of infection than transabdominal CVS.[10] Although this theory is not proved in large studies, our study has confirmed it because transabdominal sampling did not induce any chorioamnionitis in our study.

On the other hand, there are some considerations about CVS and fetal limb defect in articles. This discussion was brought up by Firth and colleagues in 1991, reporting five cases of fetal defect following CVS in 539 cases. All samplings in that study were done during 55 to 66 days of pregnancy and by the transabdominal method.[11]

Several other small studies reported an increased incidence of fetal limb defect following CVS, and it seems that it mostly occurs in samplings before day 70 (10 weeks) of pregnancy.[12] Although this was not confirmed in all studies, in the follow-up of our 100 neonates, there was no limb defect, oromandibular defect, cutaneous hemangioma, or any other anomalies. Therefore, this confirms that sampling of chorionic villus after 10 weeks of pregnancy by a well-educated expert does not increase the risk of fetal defects,[13] with a 6 per 10000 incidence in the community.[14]

Anyway, this information must be explained to all patients who refer for CVS as there still is diversity of opinions about the complications.

References

1. Cunningham FG, Gant NF, Leveno KJ, Gilstrap LC, Hauth JC, Wenstrom KD. Williams Obstetrics. 23rd edition. NY: McGraw-Hill; 2010: 300-1.
2. Hsieh TT, Lee JD, Kuo DM, Lo LM, Hsieh CC, Chiu TH et al. Perinatal outcome of chorionic villus sampling versus amniocentesis. Taiwan Yi Xue Hu ZaZhi. 1989 Sep;88(9):894-9.
3. Mujezinovic F, Alfirevic Z. Procedure-related complications of amniocentesis and chorionic villus sampling: a systematic review. Obstet Gynecol 2007 sep;110(3):687-94.
4. Wilson RD, Gibson W, Bebbington M, Walker M, Shaw D.First trimester fetal heart rate: response to chorionic villus sampling in the chromosomally normal fetus. Fetal Diagn Ther. 1997 Jul-Aug;12(4):236-40.
5. Ball RH, Ade CM, SchoenbornJA, Crane JP. The clinical significance of ultrasonographically detected subchorionic hemorrhages. Am J Obstet Gynecol 1996 Mar;174(3):996-1002.
6. Cederholm M, Haglund B, Axelsson O. Maternal complications following amniocentesis and chorionic villus sampling for prenatal karyotyping. BJOG 2003 Apr;110(4):392-9.
7. Lippman A, Tomkins DJ, Shime J, Hamerton JL. Canadian multicentre randomized clinical trial of chorion villus sampling and amniocentesis. Final report. Prenat Diagn 1992 May;12(5):385-408.
8. Ghidini A. Chorionic villus sampling: risks, complications and techniques. Available from: www.uptodate.com/home/index.html. Accessed January 18, 2010.
9. Akhlaghpoor S .Chorionic villus sampling for beta-thalassemia: the first report of experience in Iran. Prenat Diagn 2006 Dec;26(12):1131-6.
10. Kenneth W. Genetic and prenatal diagnosis. In: James RS, Ronald S, Gibb MD, Beth R, editors. Danforth obstetrics and gynecology. 9th ed. Philadelphia: Lippincott Williams and Wilkins; 2003. p. 31-3.
11. Firth HV, Boyd PA, Chamberlain P, MacKenzie IZ, Lindenbaum RH, Huson SM. Severe limb abnormalities after chorion villus sampling at 56-66 days' gestation. Lancet 1991 Mar 30;337(8744):762-3.
12. Brambati B, Simoni G, Travi M, Danesino C, Tului L, Privitera O et al. Genetic diagnosis by chorionic villus sampling before 8 gestational weeks: efficiency, reliability, and risks on 317 completed pregnancies. Prenat Diagn 1992 Oct;12(10):789-99.
13. Goldberg JD, Norton ME. Genetics and prenatal diagnosis. In: Callen PW, editor. Ultrasonography in obstetrics and gynecology. 4th ed. Philadelphia: W.B. Saunders; 2000. p. 31-3.
14. Bianchi DW, Williams JM, Sullivan LM, Hanson FW, Klinger KW, Shuber AP. RCR quantitation of fetal cells in maternal blood in normal and aneuploid pregnancies. AM J Hum Genet 1997 Oct;61(4):822-9.