

Choroid Plexus Cysts

Jose A. Lopez, MD, and Douglas Reich, MD

Background: Research shows that there is an association between choroid plexus cysts and aneuploidy. Family physicians treating prenatal patients should understand the management of this sonographic finding.

Objective: To determine the epidemiology, pathophysiology, and management of prenatal choroid plexus cysts.

Case report: A 23-year-old patient, gravida 1, para 0, was seen at an inner city Family Medicine health center for prenatal care. A screening ultrasonogram performed at 16 weeks of gestation showed bilateral choroid plexus cysts approximately 5 mm in diameter. The patient declined amniocentesis. Maternal serum triple screen markers (maternal serum α -fetoprotein, human chorionic gonadotropin, and estriol) were all normal, as was the level II sonogram at 20 weeks and the fetal echocardiogram at 28 weeks. At birth the baby was found to be normal after a clinical assessment was performed.

Methods: A review of the literature using MEDLINE with the search strategy of choroid plexus, choroid plexus fetus/fetal, choroid plexus management, choroid plexus treatment, and choroid plexus epidemiology. (J Am Board Fam Med 2006;19:422–5.)

The first description of choroid plexus cyst (CPC) on antenatal sonogram appeared in the literature in 1984,¹ and soon after its association with trisomy 18 was described.² Despite the publication of numerous articles, controversy still remains concerning appropriate management. Prenatal karyotyping is recommended when maternal serum screening markers are abnormal and abnormalities are found on sonogram.^{3–12} However, the presence of CPC on sonogram without other abnormalities is a cause of controversy and should be recognized in early pregnancy as an important issue which must be addressed with proper management and care.

Case History

A 23-year-old female patient, gravida 1, para 0, was seen at an urban community-based Family Medicine health center for prenatal care. A screening sonogram performed at 16 weeks of gestation showed bilateral CPC approximately 5 mm in diameter. The patient, a Jewish immigrant from Russia, declined amniocentesis. Maternal serum triple screen markers (maternal serum α -fetoprotein, hu-

man chorionic gonadotropin, estriol) were all normal, as well as the sonogram at 20 weeks of gestation and the fetal echocardiogram at 28 weeks of gestation. At birth, the baby was found to have normal Apgar scores and to be in healthy condition.

Discussion

Epidemiology

In the second trimester, the incidence of CPC has been estimated by several population studies to be 1%,^{3,4,13–19} and other studies have found the incidence to vary from 0.18% to 3.6%.^{20,21} Despite the low incidence, CPC has clinical implications for aneuploidy because of an association of choroid plexus with trisomy 18^{2,5–12,22} and trisomy 21.^{4,10,13,19,22–24} Researchers have been more concerned with trisomy 18 because the prevalence of CPC for fetuses with trisomy 21 and for the general population are the same.^{13,23,24} Prenatal sonography in 44% to 50% of pregnancies with trisomy 18 show CPC,^{15,16} whereas only 1.4% of pregnancies with trisomy 21 show CPC.¹³ Approximately three fourths of abnormal fetal karyotypes associated with choroid plexus cysts are trisomy 18 and one fourth are trisomy 21.²³ Thus, trisomy 18 has greater clinical relevance than trisomy 21.

Pathophysiology

Choroid plexus develops at approximately 6 weeks gestation. At the onset, a bulge from the medial wall of the lateral ventricle becomes covered with

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From Wyckoff Heights Medical Center, Brooklyn, NY.

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Corresponding author: Jose A. Lopez, MD, Wyckoff Heights Medical Center, 374 Stockholm Street, Brooklyn, NY 11237 (E-mail: JOL9033@nyp.org).

pseudo-stratified epithelium and then lobulated with villi. The cells at this time change from cuboid to columnar epithelium. As the villi grow and become entangled, a cystic space is formed, which traps cerebral spinal fluid. Choroid plexus produces cerebrospinal fluid and is seen prominently in the posterior horn of the lateral ventricle in second-trimester ultrasounds. In the 9th week of gestational age, the choroid plexus begins producing cerebrospinal fluid leading to expansion of the ventricular system. Most villi form at 13 to 18 weeks of gestation, and the cysts regress by 28 weeks of gestation. Frequently, fluid accumulates and results in the formation of cysts, which can be detected on sonogram.^{25–28}

Management

The American College of Obstetrics and Gynecology (ACOG) advises careful anatomic survey of the fetus in cases of isolated CPC. If no anomalies are observed on ultrasound then amniocentesis should be offered but not encouraged. If a mother presents with risk factors for trisomy 18, such as advanced age, abnormal triple marker screen, and abnormal fetal abnormalities on sonogram, amniocentesis may be recommended.²⁹

In an effort to guide clinical practice, research has focused on 3 factors that modify the risk for trisomy 18. These factors are physical characteristics on sonography, the role of maternal age, and serum markers. Consensus has not been established due to the variability in study design, selection of study population, and lack of consistency in ultrasound technique.

Agreement has been established that ultrasound characteristics of CPC, such as bilaterality, size, number, complexity, and resolution, are not related to the risk of aneuploidy.^{10,30–33} However, cysts with diameters less than 5 mm may not be linked with trisomy 18,^{14,19} and large cysts in excess of 10 mm may impart a higher risk.^{16,34} Furthermore, the risk for trisomy 18 when compared with normal births has been shown to increase with the presence of CPC without any other sonographic abnormalities, ie, isolated choroid plexus. Studies have estimated the likelihood ratio from 3.5 to 9 and risk from 1/30 to 1/477.^{35–38} A risk estimate for trisomy 18 from 18 studies with over 3000 fetuses in an unselected population was found to be 1 in 189 (95% CI: 1 in 125 to 1 in 385). In the same study population, there were only 2 cases of trisomy 21.³⁹

In a screened high-risk population, 16 studies found the risk for trisomy 18 to be 1 in 128 (95% CI: 1 in 86 to 1 in 250) with 6 cases of trisomy 21 in 2049 cases of CPC.³⁰ These studies guide physicians to be concerned about trisomy 18 but not trisomy 21. In our case, CPC was the only abnormal finding on sonogram.

In an attempt to further refine the risk estimate, many researchers have developed formulas that utilize age as a factor in estimating risk for trisomy 18 coupled with a finding of isolated CPC. Likelihood ratios of 3 to 9 have been found with an age cutoff from 33 to 37.^{6,36,37,40,41} The results from these studies are principally based on reviews with non-specific inclusion criteria, and the risk adjustment is dependent on interpretation of the literature. In our case, the patient's risk would have been low because of young maternal age.

Despite numerous studies on the effects of maternal age and sonographic findings on the risk for trisomy 18, few authors have investigated the use of triple serum markers as an adjunct to sonography.^{33,40,42} One study found that the risk of trisomy 18 for a fetus with isolated CPC (1/270) approaches the amniocentesis risk (1/200) at age 37.⁴⁰ Another author assessed when biochemical testing might be a valuable adjunct to ultrasonography and concluded that triple-screen testing, together with a targeted ultrasonographic examination, followed by selective amniocentesis, is adequate to detect the chromosomal abnormalities in fetuses with choroid plexus cysts.⁴³ More studies need to assess the value of serum markers in determining the risk of trisomy 18 with isolated CPC. The normal results of the triple markers in the current case would not have modified the risk of aneuploidy in a fetus.

Amniocentesis is recommended when CPC is found with other abnormalities on sonogram,^{2–12} but no consensus has been reached on cases of isolated CPC. Recommendations are based on the comparison of the risk of amniocentesis to the calculated risk of trisomy 18 with or without modifying risk factors. Because of a lack of agreement in the medical literature, recommendations have varied. Many research studies have concluded that an isolated CPC is not an indication for genetic testing,^{44–47} whereas many other studies recommend genetic testing.^{4,11,19,22,48} Interestingly, an individualized risk method had been proposed using maternal age, presence of an isolated CPC, and serum markers as modifying risk factor. If

risk is greater than 1/200, amniocentesis is offered. Clearly, more research is needed to accurately estimate the risk of trisomy 18.

In the current case, the risk for aneuploidy was low because of young maternal age, isolated CPC as the only sonogram finding, and normal serum markers. This clinical scenario is similar for many primary care physicians who practice prenatal care. Physicians providing prenatal care to women, who have children later in life after completing their education or starting their careers, need to consider maternal age in any risk assessment.

Studies on isolated CPC lead to inconsistent results because of the variability in research design and analysis. These factors include a retrospective study design, differences in patient population, differences in sonogram expertise, and failure to consider factors that impact aneuploidy, such as maternal age and serum screening results in many studies. A longitudinal study would provide a greater level of evidence, which would respond to many questions regarding modifying risk factors and management of isolated CPC. Unfortunately, the low incidence would make such a study impractical.

Conclusion

Primary care physicians should approach CPC in a practical manner. CPC detected on ultrasound at 18 to 20 weeks warrants an additional sonogram of the fetal hands, heart, and central nervous system by an experienced sonographer to search for other abnormalities.⁴⁹ The nature of the cyst should be fully explained to the patient, as well as the risks associated with trisomy 18 and 21, along with modifying risk factors, such as maternal age, serum markers, and other sonogram findings. The option for genetic testing should be explained along with its risks and benefits. Consultation with a genetic specialist or high-risk obstetrician may be indicated.¹⁹ Despite the low incidence of isolated CPC on prenatal sonogram, physicians must take into consideration the risk of aneuploidy; furthermore, physicians must understand the controversy regarding medical management of CPC. Until further studies are completed, the risks and benefits of genetic testing must be weighed against the risk of aneuploidy in light of modifying risk factors.

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