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Review of fetal choroid plexus cysts: A cross-sectional study on 9244 pregnant women

Koroid pleksus kistlerinin değerlendirilmesi: 9244 gebe kadın üzerine kesitsel bir çalışma

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Abstract

Aim: It was revealed in many studies conducted on unselected populations that the size, bilaterality and number of choroid plexus cysts (CPCs) are correlated with various degrees of aneuploidy risk. This article deals with the natural history and significance of numbers, sizes and bilaterality of CPCs in a selected population.

Methods: This cross-sectional study was conducted on 9244 pregnant women attending to our department between March 2014 and March 2018. After exclusion criteria was applied, 87 patients with isolated CPCs remained. All records of the patients were screened and needed data were recorded.

Results: A total of 9244 prenatal sonographies had been performed during this period. Isolated CPC was detected in 87 fetuses. CPCs were visualized unilaterally in 83 cases (95.4%) and bilaterally in 4 cases (4.6%). Among 83 unilateral cases, 45 had left sided (51.7%) and 38 had right sided CPCs (43.7%). The size of the cysts ranged between 3 mm to 5.1 mm with an average of 3.51 (0.06) mm. Double tests (n=24) and quadruple tests (n=63) had 2 and 5 abnormal results, respectively. All had normal karyotypes. Four samples were dropped out due to premature rupture of membranes (n=2) and intrauterine fetal death (n=2). It was found that the outcomes of all remaining fetuses (n=83) were normal and no anomalies were seen until birth.

Conclusion: Multiple CPCs in a single choroid plexus or bilaterality were not associated with abnormal fetal karyotype and therefore we think that isolated CPCs has a good prognosis.

Keywords: Choroid plexus cyst, Ultrasonography, Fetus

Öz

Amaç: Rastgele popülasyonlar üzerinde yapılmış bir çok çalışmada koroid pleksus kistlerinin (KPK) boyut, bilateralite ve sayısının çeşitli derecelerde anöploidi riski ile ilişkili olduğu ortaya konulmuştur. Bu makale seçilmiş bir popülasyonda, KPK'ların sayı, boyut ve bilateralitesinin doğal seyri ve önemini ele almaktadır.

Yöntemler: Bu kesitsel çalışma Mart 2014 ve Mart 2018 arasında departmanımıza başvuran 9244 gebe kadın üzerinde yürütüldü. Dışlama kriterleri uyguladıktan sonra geriye izole KPK'li 87 hasta kaldı. Hastaların tüm kayıtları tarandı ve ihtiyaç duyulan veriler alındı.

Bulgular: Bu dönemde 9244 prenatal sonografi uygulanmıştı. 87 fetüste izole KPK tespit edildi. KPK'lar 83 (%95,4) vakada tek taraflı ve diğer 4 (%4,6) vakada çift taraflı olarak izlendi. Tek taraflı olan 83 vakanın 45'inin (%51,7) sol taraflı ve 38'inin (%43,7) sağ taraflı KPK'sı vardı. Kistlerin boyutu, 3,51 (0,06) mm lik bir ortalamayla, 3mm den 5,1mm ye uzanıyordu. İkili test (n=24) ve dörtlü testlerin (n=63) sırasıyla 2 ve 5 anormal sonucu vardı. Hepsi normal karyotipe sahipti. Dört vaka membranların prematür rüptürü (n=2) ve intrauterin fetal ölüm (n=2) nedeni ile çalışmadan çıkarıldı. Kalan tüm fetüslerin (n=83) akıbetinin normal olduğu bulundu ve doğuma kadar hiçbir anomali izlenmedi.

Sonuç: Tek bir koroid pleksusta çoğul KPK ve bilateralite anormal fetal karyotiple ilişkili değildi, bu yüzden izole KPK' lerinin iyi bir prognoza sahip olduğunu düşünüyoruz.

Anahtar kelimeler: Koroid pleksus kisti, Ultrasonografi, Fetüs

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Introduction

Fetal choroid plexus cysts (CPC) are often detected during the second trimester ultrasound screening as fluid-filled structures within the lateral ventricles of the fetal brain and requires a need to formulate a protocol for management and counseling [1-3]. These cysts may be single/multiple, unilateral/bilateral [4]. They are detected in 1-3,6% of all fetuses, and 90% are resolved by 26-28th week of gestation [5]. Although it is mostly a benign condition occurring after accumulation of CSF within rapid growing ventricles, it may be as a result of a chromosomal abnormality, mainly, Trisomy 18 (T18) [3,4].

The relationship between CPC and Trisomy 18 was first discussed in 1984 by Chudleigh et al. [1], and CPC was observed in 30-50% of Trisomy 18 cases [5,6]. The probability of aneuploidy rises if other structural anomalies are detected in ultrasonographic examination, or if maternal serum screening indicates higher risk of abnormality [7,8]. Most of the studies have assessed the correlation of T18 and CPC in these situations. These published trials have failed to address the potential bias in the patient population being studied. In many ultrasound referral centers, advanced maternal age, abnormal alpha-fetoprotein (AFP), and previous anomaly comprise the majority of patients undergoing second-trimester sonography. In such a high-risk population, it would not be surprising to see an occasional Trisomy 18 or 21 fetus that coincidentally has a choroid plexus cyst. Concordantly, few have discussed isolated CPCs (with no other abnormal sonographic findings). Therefore, this relatively common finding seems to cause some degree of anxiety and worry among parents getting confused and uncertain regarding the health condition of their fetuses. Thus, this study was designed to evaluate the outcome of isolated CPCs detected in screening sonography and to specify its clinical significance.

Materials and methods

This descriptive study was conducted on 9244 pregnant women undergoing prenatal screening in our department at Special Koru Hospital, between March 2014 and March 2018. All sonography reports had been documented by a computerized database, along with medical records of laboratory and genetic tests.

The ultrasound reports of all 9244 pregnancies were evaluated to find out fetuses with CPC. We carefully noted whether there was any document of major anomalies in the cerebellum, lateral cerebral ventricles, spine, facial profile, four-chamber view of the heart, extremities, abdomen, umbilical cord, kidneys, bladder and/or any sonographic soft markers. If there was any abnormality, the patient was excluded from the study. Then, results of double test, quadruple test, fetal echocardiography, and amniocentesis (which were performed as ordered by a perinatologist) were reviewed. Demographic parameters (to detect possible risk factors), ultrasound examinations and results of para-clinical tests were obtained from the database. Then we checked delivery records and first postnatal visit records of babies for any anomalies. Consequently, we had 87 patients that had isolated CPCs.

This study was approved by a research ethics committee and institutional review board at Special Koru Hospital ethics committee (9/29/2018-10).

Statistical analysis

All information obtained was entered into statistical package for the social sciences, version 15.0, SPSS Inc, Chicago, Illinois, USA (SPSS). Descriptive statistics were used to calculate the frequency (n), percentage (%), central tendency (mean, median & mode) and dispersion (range, variance, SD, maximum & minimum) for each variable when appropriate.

Results

In a period between March 2012 and March 2018, we found that prenatal screening sonography had been performed on 9244 pregnant women in our department. Totally, 87 fetuses with isolated CPCs were found during this period.

The mean age of the mothers was 28.21 (0.6) years. There were 87 fetuses with CPCs. CPCs were visualized unilaterally in 83 cases (95.4%) and bilaterally in other 4 cases (4.6%). Among 83 unilateral cases, 45 had left sided (51.7%) and 38 had right sided CPCs (43.7%). Among the left sided group, 6 patients (7%) had multiple (two) CPCs whereas in right sided group there were 8 (9%) patients having multiple (two) CPCs. As a result, there were a total of 98 CPCs in 87 patients (Table 1). The size of the cysts ranged between 3 mm to 5,1 mm with a mean of 3.51 (0.06) mm. Mean gestational weeks at detection and resolution of the cysts were 16.20 (0.05) and 30.71 (0.39), respectively (Table 2). Locations of the cysts within the ventricle were anterior (15 cysts-15.3%), posterior (13 cysts-13.3%) and middle (48 cysts-48.9%) portions for single cysts. For multiple cysts, locations were anterior-posterior (8 cysts-8.2%), anterior-middle (10 cysts-10.2%) and posterior-middle (4 cysts-4.1%) (Table 3). Of the 87 patients, 9 cases (10%) were above 36 years old. Age distribution of the cases is presented in Table 4.

Table 1: Laterality of cysts

	Patient n (%)	Cyst n (%)
Left sided	45 (51.7)	48 (48.9)
Right sided	38 (43.7)	42 (43)
Bilateral	4 (4.6)	8 (8.1)
Total	87 (100)	98 (100)

Table 2: Maternal age, gestational age when detected and resolved, and cyst diameter

Maternal age (y) mean (SD)	Gestational age when detected (w) mean (SD)	Gestational age when resolved(w) mean (SD)	Cyst diameter (mm) mean (SD)
28.21 (0.6)	16.20 (0.5)	30.71 (0.39)	3.51 (0.06)

y: year, w: week; mm: millimeter

Table 3: Locations of the cysts within the ventricle and maternal age

Location	Number of cases n (%)	Maternal age (y) Mean (SD)
Anterior	15 (15.3)	29.4 (2.14)
Posterior	13 (13.3)	28.30 (1.53)
Middle	48 (48.9)	27.43 (0.72)
Anterior + posterior	8 (8.2)	30.25 (1.93)
Anterior + middle	10 (10.2)	29.4 (1.6)
Posterior + middle	4 (4.1)	30.5 (1.5)

y: year

Table 4: Maternal ages in pregnancies complicated by choroid plexus cysts

Maternal age (y)	Number of cases n (%)
15-19	9 (10.3)
20-24	13 (15.1)
25-29	30 (34.4)
30-35	26 (29.9)
≥36	9 (10.3)
Total	87 (100)

y: Year

Twenty-four women had been assessed by double test, of which 22 were normal. In addition, quadruple tests were performed for 63 fetuses, which demonstrated normal results in 58 cases. Among fetuses with abnormal quadruple test results,

the risk factors of Down syndrome were 1/33, 1/58, 1/76, 1/82, 1/88, 1/88, 1/90 and 1/92. However, amniocentesis did not reveal any abnormality (Figure 1). Fetal echocardiography was performed for 58 cases (66.6%), which were all normal.

During the study, four patients were excluded due to premature rupture of membranes (PROM) (n=2) and intrauterine fetal death (IUFD) (n=2). CPCs gradually disappeared by 30th week in all other 83 fetuses and no anomaly was seen in follow-up sonographic examinations (Figure 2).

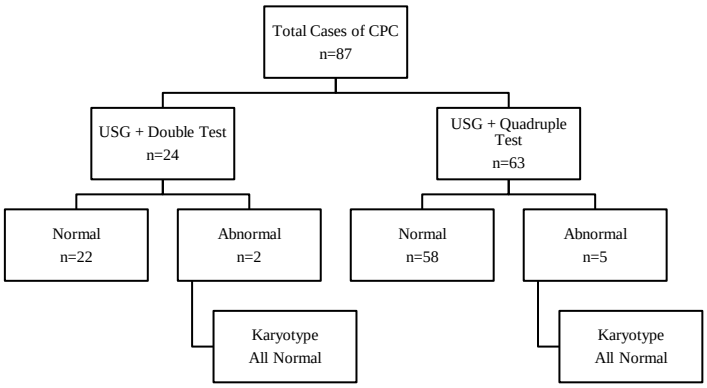

Figure 1: Mother Serum Screening correlated with ultrasound evaluation of isolated choroid plexus cyst cases

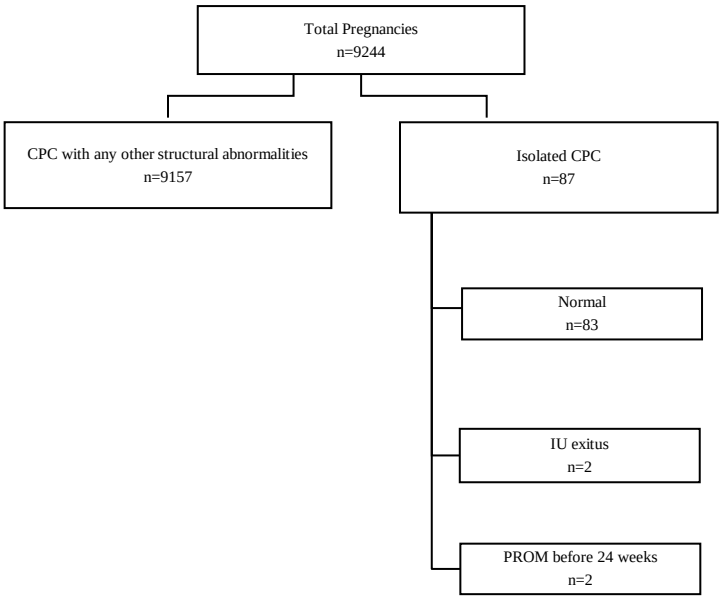

Figure 2: Outcome of isolated fetal choroid plexus cyst cases

Discussion

The mean prevalence of isolated choroid plexus cysts in our population was 2%, which is similar to those reported by Gabrielli et al. [3] and Chan et al. [9] (2.5%, and 2.3%, respectively). Similarly, the prevalence of isolated CPC in the study of Perpignano et al. [10] is 2.5%, while it is 0.18% in the study conducted by Clarke et al. [11] and 0.33% in the study of Camurri et al. [2]. However, the last two studies were conducted on unselected populations. The initial time of sonographic detection of CPC in our study was the 16th week of gestation according to last menstrual period (LMP), whereas it was first diagnosed in 15th week by Bronsteen and colleagues. Mean gestational age of diagnosis in this study was 16th week in comparison with the 19th week in the study of Bronsteen et al. [12]. All CPCs were resolved by the 30th week in our patients while Dipietro and colleagues reported that CPCs regressed by the 28th week in their study [13].

Landy et al. [4] stated that no parameters studied, including maternal demographics (age, race, median gravidity, and median parity), gestational weeks at the time of first and last sonograms, and choroid plexus cyst characteristics (location, number, dimensions, and resolution) are important on predicting aneuploidy. In their 116-patient study there were no aneuploidies. In our trial we also did not encounter any aneuploidy, which is why we could not evaluate the correlation between aneuploidy and choroid plexus cyst characteristics (location, number, dimensions, and resolution).

Bronsteen and colleagues [12] assessed 49435 fetuses aged 16-25 weeks and discovered 1209 CPC cases in 11 years, of which, 1060 CPCs were isolated and without anomalies, similar to our findings. Cheng et al. [14] conducted a follow-up evaluation of CPC, nuchal translucency (NT) and other sonographic markers of aneuploidy (particularly T18) in 7795 pregnancies until birth. CPC was present in 98 fetuses, among which 82 cases were isolated CPCs and 16 cases were NT or other soft markers. All isolated CPCs had good prognosis and no abnormality was seen among them. Their study demonstrated that isolated CPC shows good outcomes, which confirms our current findings.

Lopez et al. [15] believe that "when CPC is detected by sonography, amniocentesis or chorionic villus sampling (CVS) will be required if mother serum screening is abnormal". In this study, there were only 2 abnormal double test results and 5 abnormal quadruple test results, all with normal karyotypes. In a study conducted by Sullivan et al. [16] on 128 fetuses with CPC, mother serum screening (triple test and/or αFP level) was compared to amniocentesis results and physical examination after birth. Their findings demonstrated that among 112 fetuses with isolated CPCs, mother serum screening was positive in 22 cases (19.6%), of which just two fetuses had T18. Although one fetus with T18 was detected among other 90 cases with normal serum screening results, this patient had been evaluated by means of single αFP screening (not triple test). They concluded that triple test adjunct to ultrasound screening is a reliable method to find out high risk fetuses with isolated CPC, whereas amniocentesis needs to be done only in cases with abnormal serum screening.

Contrary to our results Nicolaides et al. [17] stated that Chromosomal abnormalities, specifically trisomy 18, should be ruled out if the CPCs are larger than 1 cm, bilateral, or irregular in shape. In cases of a single CPC, abnormal karyotypes were detected in 3.59%, and in cases of multiple CPCs in both choroid plexuses, they were detected in 3.93%. The risk of trisomy was 2.05% (trisomy 18 in 1.54% and trisomy 21 in 0.26%). Each trisomy 18 occurred in cases where CPCs measured more than 7 mm, and most cases of trisomy 18 (83.3%) were detected when a CPC was larger than 1 cm.

Limitations

This study is limited by its retrospective nature and referred patient population. The referred patient base, which may not be truly representative of the population in general, also may reflect incomplete data. Prospective randomized trials with a larger sample size are needed to solve the controversies over the patients with isolated CPCs.

Conclusion

As a result, with respect to the mentioned findings, it can be concluded that isolated CPC is a benign condition resolving spontaneously, with no clinical significance, especially when mother serum screening is in normal range. Multiple CPCs filling a single choroid plexus and bilaterality were not associated with abnormal fetal karyotype and therefore carry favorable prognosis. These data may be helpful when counseling patients with this unusual appearance of CPCs. Regarding counselling the parents, one should choose the optimistic sentences not to cause unnecessary anxiety.

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