Follow-up of neonatal ovarian cysts. A retrospective cross-sectional study

Didem Baskın Embleton1, Betül Zengin2, Ahmet Ali Tuncer1, Ahmet Afşin Kundak3, Evrim Özkaraca Boyacı1, Salih Çetinkurşun1

1Department of Pediatric Surgery, Faculty of Medicine, Afyonkarahisar University of Health Sciences, Afyonkarahisar, Turkey
2Department of Radiology, Faculty of Medicine, Afyonkarahisar University of Health Sciences, Afyonkarahisar, Turkey
3Department of Neonatology, Faculty of Medicine, Afyonkarahisar University of Health Sciences, Afyonkarahisar, Turkey

Abstract

Objective: This study was planned to see the results of follow-up of ovarian cysts in newborn patients at a university hospital.

Methods: Newborns with ovarian cysts that were diagnosed by US between 2010 and 2018 were retrospectively evaluated. US follow-up was performed in 2 to 3 month periods. Initial largest diameter of the ovarian cyst, number of cysts, bilateral or unilateral localization, if the cyst is complex or simple, alpha fetoprotein and β-HCG levels, if operated the type of the operation and pathology results were retrieved.

Results: Nineteen patients were included. Seven patients had ovarian cysts ≥20 mm and 5 were complex cysts. Two of 5 complex cysts were performed for abdominal mass and ovarian torsion was diagnosed. Other 3 complex cysts are having a conservative treatment due to lack of any clinical symptoms. All regressed in size. All simple cysts had non-operative management and regressed in size during follow-up. AFP levels were high in all. Control AFP levels decreased in all patients.

Conclusion: Conservative management seems appropriate for patients both with complex or simple cysts, because nearly all cysts were regressed and both ovaries persisted during follow-up. Surgical decision was the clinical presence of a mass in complex cysts. This is a small series and follow-up is short to make a final decision for management. A consensus is needed among the surgeons about the treatment options after discussing the complications related to conservative and surgical approaches of complex ovarian cysts.

Keywords: infant, newborn, ovary, ovarian cysts

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Нәрестелердегі аналық безінің жылауығын бақылау. Ретроспективті көлденең зерттеу

Д.Б. Эмблтон1, Б. Зенгин2, А.А. Түнжер1, А.А. Кундак3, Э.О. Бояджи1, С. Четинкуршун1

1Педиатриялық хирургия бөлімі, Медицина Факультеті, Афьон-Карахисар қ. Медицина ғылымдарының университеті, Афьон-Карахисар қаласы, Түркия
2Радиология бөлімі, Медицина Факультеті, Афьон-Карахисар қ. Медицина ғылымдарының университеті, Афьон-Карахисар қаласы, Түркия
3Неонатология бөлімі, Медицина Факультеті, Афьон-Карахисар қ. Медицина ғылымдарының университеті, Афьон-Карахисар қаласы, Түркия
NEWBORN OVARIAN CYSTS: A RETROSPECTIVE TRANSVERSAL STUDY

Introduction

Management of ovarian cysts in the newborn is problematic. The incidence of diagnosing ovarian cysts in the neonate has been increased with the widespread use of ultrasonography [1-3]. Earlier studies detected only larger cysts and surgery was the first line of treatment [4]. With the evolution of the ultrasonography devices, more detailed information of the human body, including smaller ovarian cyst became possible. Again, in earlier studies, complex cysts were considered as surgical, but as the time passed, it was seen that some were having spontaneous resolution so conservative management became an option to save the newborn from unnecessary surgery regarding the side effects of anesthesia [2].

Hipothalamic-pituitary-gonadal axis is effective on ovarian development. This axis regulates the production of sex hormones. While luteinizing hormone (LH) is responsible from the production of gonadal steroid production in ovarian follicles, follicle stimulating hormone (FSH) is responsible from the follicle development. Their secretions were regulated by gonadotrophin releasing hormone (GnRH). Hipothalamic-pituitary-gonadal axis has five different activity stages: fetal, early infancy, childhood, late prepubertal and pubertal [5]. Ovarian activity starts at early stages of fetal life. Gonadotrophins cause follicle enlargement even before birth. The stages of follicular development are primordial follicle, primary follicle, secondary follicle, preantral follicle, early antral follicle, and small antral follicle. Between postnatal 2nd week and 12 months, GnRH activity increases the levels of FSH and LH in girls. Although high levels of FSH sometimes seen as late as 4 years, normal behavior is the decrease in the LH and FSH levels beginning from the 6th month of life. Central nervous system inhibition is the highest at the age of 4 years. After the age of 6, the number and size of the antral follicles increase. This is in accordance with the progressive increase in FSH levels. The level and frequency of GnRH increase in late prepubertal stage. Diurnal rhythm of LH, FSH and sex steroid levels start years before the phenotypic puberty. Puberty is the stage when children start to become adults. The autopsy study of Peters that was performed on 52 girls aged 2 months-11 years showed that ovaries actively grow and have follicles in all age groups [6]. All this information shows us that the ovaries are being stimulated even in intrauterine life and can have follicles at all times. So, it is not surprising to see ovarian follicles or cysts in girls during US evaluation. What is important is to understand which ovarian cysts need treatment. Our study was planned to see the results of follow-up of ovarian cysts in newborn patients in a university department.

Methods

Newborns with ovarian cysts that were diagnosed by ultrasonography and followed up by pediatric surgeons between January 2010 and August 2018 were retrospectively evaluated in the study. Ethical approval was obtained (2018/144, 04.05.2018). Of the 108 patients with ovarian cysts, patients that were initially diagnosed in the newborn period were evaluated (n = 21). Two of them were excluded because of missing information, and 19 patients were included in the study (Table 1).

Doppler ultrasonography was performed by the same radiologist after the initial diagnosis (HI VISION Preirus, Hitachi, 2013, Japan). US follow-up was performed in 2 to 3 month periods. Initial largest diameter of the ovarian cyst, number of cysts, bilateral or unilateral localization, if the cyst is complex or simple was noted. Anechoic cysts with thin walls were accepted as simple cysts. The cyst was considered as a complex cyst if any of the following features were present: 1) partially anechoic with a fluid-debris level; 2) partially anechoic with a retracting clot; 3) septated with or without internal echoes; 4) solid mass [2]. Any ultrasonographic change during follow-up was also noted. Cysts ≥ 20 mm were considered as ovarian cysts, cysts < 20 mm were considered as follicle cysts. Alpha fetoprotein (AFP) and β-human chorionic gonadotrophin (β-HCG) levels were retrieved from hospital patient information system. Initial high levels of AFP were always checked for a decrease at least a week later. If the patient was operated, the type of the operation and pathology result were also retrieved. Current status of the patients was noted.

Results

Of the 19 patients that were included in the study, 2 patients had prenatal diagnosis. The rest were diagnosed during a routine abdominal ultrasonography that is being performed in all neonates in this center. Patients were followed up for 2-23 months.
Cyst sizes varied between 4 mm and 50 mm. Seven patients had ovarian cysts ≥ 20 mm (Table 1). Five patients had bilateral ovarian cysts initially.

Fourteen patients had simple ovarian cysts and 5 had complex cysts and all complex cysts were ≥ 20 mm. Initial diagnosis was abdominal mass in 2 patients, US appearance of the masses were consistent with complex ovarian cyst, ovarian torsion was suspected and at operation ovarian torsion was discovered. One had salpingo-oophorectomy and the other had oophorectomy. Pathology revealed complete necrosis of the ovary with calcification in both. Other 3 complex cysts are having a conservative treatment due to lack of any clinical symptoms. All complex cysts regressed in size during follow-up. Two were septated cysts and one had a fluid and a debris level. One of the 2 septated cysts became a simple cyst at 16 months of age (Table 1). One cyst with fluid and debris level is still a cyst with a fluid and debris level at the age of 5 months. These patients are still in follow-up.

Patients with simple cysts had US evaluation only: 3 patients had single US, the rest had serial US evaluations. There was no change in ultrasonography findings in 3 patients, the rest of the simple cysts were regressed in size between 2-23 months. Follow-up was stopped in simple cyst patients if the cyst size became ≤ 10 mm.

β-HCG levels were normal in all patients and AFP levels were high in all. Control AFP levels decreased in all patients.

**Discussion**

Ovarian cysts are a concern both for the family and the doctor. They can be just follicular cysts, but they may also cause ovarian torsion or a tumor might be missed. Both are a threat for the future fertility of the child. Follow-up with US with detection of AFP and β-HCG levels is the current practice of neonatal ovarian cysts larger than 20 mm in our department. If the cyst is simple and getting smaller, US evaluation may be done in 3-6 months. AFP levels are always high in newborns, so one more detection one week later was performed to make sure that the level is decreasing. Neither the levels of tumor markers nor the size of the cysts increased in the series.

Although we did not see any increase in size or any complication due to the cyst size in simple cysts which are < 20 mm, we preferred to be on the safer side and followed these patients with US until we make sure that they start to regress.

There is no current standard about the management of complex ovarian cysts (Table 2) [1,2,4,7,8,10]. Doppler ultrasonography is not considered as a reliable technique for the detection of ovarian torsion [8]. Fluid-debris level in a cyst can be bleeding into the cyst or ovarian torsion [9]. Fluid-debris level in a cyst can be a complication of the cyst size which is < 20 mm, we preferred to be on the safer side and followed these patients with US until we make sure that they start to regress.

| Patient | Age (day) | Max. cyst size (mm) | Bilateral cysts | Complex cyst | Operation | Result |
|---------|-----------|---------------------|-----------------|-------------|-----------|--------|
| 1       | 28        | 7                   | Y               | N           | N         | R, 2 mo |
| 2       | 11        | 40                  | N               | Y           | N         | R, 6 mo |
| 3       | 28        | 23                  | N               | N           | N         | R, 3 mo |
| 4       | 2         | 45                  | N               | Y           | Y (ovarian torsion) | Salpingo-oophorectomy, necrosis |
| 5       | 7         | 17                  | N               | N           | N         | R, 10 mo |
| 6       | 4         | 5                   | N               | N           | N         | No change, 6 mo |
| 7       | 4         | 36                  | N               | Y           | N         | R, 16 mo |
| 8       | 29        | 7                   | N               | N           | N         | R, 10 mo |
| 9       | 12        | 16                  | N               | N           | N         | R, 2 mo |
| 10      | 28        | 10                  | N               | N           | N         | R, 12 mo |
| 11      | 28        | 50                  | N               | Y           | Y (ovarian torsion) | Oophorectomy, necrosis, calcification |
| 12      | 20        | 5                   | N               | N           | N         | No change, 16 mo |
| 13      | 7         | 4                   | N               | N           | N         | Single US |
| 14      | 28        | 11                  | N               | N           | N         | No change, 2 mo |
| 15      | 28        | 15                  | N               | N           | N         | R, 23 mo |
| 16      | 13        | 12                  | Y               | N           | N         | Single US |
| 17      | 13        | 20                  | N               | N           | N         | R, 7 mo |
| 18      | 5         | 6                   | Y               | N           | N         | Single US |
| 19      | 26        | 37                  | Y               | N           | N         | R, 5 mo |

N: No, Y: Yes, Mo: Month, US: Ultrasonography, R: regressed

| Year | No. of patients | Prenatal | Complex | Surgery | No surgery | Torsion | O* or SO** |
|------|----------------|----------|---------|---------|------------|---------|------------|
| Papic et al [1]. | 2014 | 39 | 25 | 15 | 27 | 12 | 16 | 12 |
| Gesca et al [2]. | 2013 | 41 | 37 | 41 | 4 | 37 | 4 | 4 |
| Akin et al [4]. | 2010 | 20 | 18 | 6 | 17 | 3 | 6 | 15 |
| Mizuno M et al [7]. | 1998 | 17 | 15 | 4 | 16 | 1 | 9 | 5 |
| Chramont et al [8]. | 2001 | 24 | 24 | 10 | 14 | 10 | 10 | 11 |
| Ozcan et al [10]. | 2014 | 15 | 7 | 15 | 15 | 0 | 15 | 15 |
| Present study | 2019 | 19 | 2 | 5 | 2 | 17 | 2 | 2 |

*ooophorectomy, **salpingo-oophorectomy
level and presence of calcification were found to be related with necrotic torsioned ovary which may also be autoamputated [9]. A bleeding or enlarged ovarian cyst may cause torsion with time. Surgical treatment was preferred in patients with a palpable abdominal mass in the current series. Conservative treatment was chosen for patients with no apparent clinical symptoms.

Two of the newborns that had conservative management had septated cysts and both ovaries are still apparent with US on follow-up in both. Third one had cysts with fluid-debris level and calcification, and according to the findings of Hacettepe, this can be a necrotic ovary due to torsion, but the ovary is still present at 5 months follow-up, still with fluid-debris level. Cesca et al., followed all complex ovarian cysts in the newborn conservatively [2]. Side effects of anesthesia were the main concern for these authors, and after long term follow-up, ovarian loss was 40%. On the other hand, although the difference was not statistically significant, ovarian salvage rate was higher in the immediately operated patients compared to observed patients in the series Papic et al presented [1]. With time, this group also preferred the conservative management. In both of these series, it was not stated if there is a specific US finding in the ovaries that predicts necrosis. In our patients, the number is too small to make a definitive decision.

Another concern is the complications arise after non-operative follow-up of complex cysts such as intestinal obstruction caused by adherence of the torsioned ovary to the intestines, teratoma arousing on the omentum after the implantation of the torsioned autoamputated ovary, and anesthesia risk [11,12]. Anesthesia of the children younger than 3 years, especially in operations taking more than 3 hours and in recurrent surgery, is considered as a risk for neurons of the developing brain, and surgery is recommended only if necessary in such patients in the latest FDA safety announcement [13]. Disappearance of an ovary on follow-up may be a reason for suing a surgeon as well. We did not experience any of the complications regarding the conservative treatment, but again, this is a small series with a not long enough follow-up.

We believe that complex cyst description with US needs revision to rule out the necrotic ovaries for safe follow-up. Also, a consensus is needed among the surgeons following such patients for conservative management after discussing the complications related to conservative treatment of complex ovarian cysts and complications related to newborn anesthesia.

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