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Original Article

Specific Ultrasound Pattern of Perinatal Torsioned Ovarian Cysts: Sonographic-pathologic Correlation

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ABSTRACT

Background: The accurate differentiation of perinatal torsioned ovarian cysts (PTOCs) in neonates is of utmost importance. This importance is due to the fact that if PTOCs are diagnosed properly, minimally invasive or conservative management approaches can be offered. The present study aimed to describe the ultrasound findings of PTOCs and compare the results with pathological findings.

Methods: This prospective cross-sectional study was conducted in Mashhad University of Medical Sciences, Mashhad, Iran, within 2014-2019. All infants with an intra-peritoneal cyst underwent meticulous ultrasound examination. Patients were followed up until reaching the final diagnosis. In surgically approved PTOCs, the correlation between sonographic and pathologic findings was examined.

Results: Twenty two cases (aged 2 days to 6 months, mean age = 6 weeks) with PTOC were diagnosed during this time. Cysts were mainly on the right side (86%) with mean diameter of 51 mm (27-73mm). The ultrasonogrphic signs of fluid debris level, triple-layer wall and wrinkled inner layer were observed in almost all of patients.

The pathologic triple-layer of perinatal torsioned ovarian cysts included necrotic content with granulation, stroma, and epithelium layers was observed by ultrasound as a uni-locular cyst containing fluid debris level with an echogenic wrinkled inner layer, a hypoechoic uneven non-uniform middle layer and echogenic outer epithelial surface.

Conclusion: Sonographically detected triple-layered pattern for PTOCs was completely in agreement with pathologic results. Then, this specific ultrasound pattern is pathognomonic for PTOC.

Keywords: Pathology, Perinatal ovarian cyst, Ultrasound, Sensitivity, Specificity, Torsion

Introduction

Ovarian cysts (OCs) are the most common abdominal masses found in female newborns (1). The incidence of OC is 1 out of every 2500 female newborns (2). Most ovarian cysts have follicular origin. Uncomplicated small OCs may remain clinically unrecognized and may be regressed spontaneously. Functional cysts larger than 5 cm are associated with such complications as hemorrhage, rupture, or ovarian torsion, which may result in adnexal infarction (4). Regarding ultrasonographic pattern, ovarian cysts can be classified into “simple” and “complex” cysts (3). The term “complex cyst” is used to describe a thick-walled septated cyst which contains heterogeneous solid components, blood clot, and debris. On the other hand, complex cysts are usually complications of large follicular cysts (5, 6) which should be differentially diagnosed from dysgeneses and neoplasms. Surgery is usually the first choice for the treatment of complex cysts (3). Perinatal torsioned ovarian cysts (PTOCs) are complicated cysts which result from adnexal torsion in utero. PTOCs usually lead to auto-amputation of the affected ovary; nonetheless, they have been historically removed by laparotomy due to complex features of these cysts. However, if preoperative definite

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diagnoses had been available, they would have undergone minimally invasive approaches with more safety, effectiveness, and fewer cosmetic changes. Therefore, the differentiation between PTOCs and other cystic masses is of paramount importance in neonates (7-9). PTOCs are hardly diagnosed by clinical findings. Accordingly, paraclinical modalities, especially ultrasound (US) examination, play a critical role in the diagnosis and following-up (10).

Very little data is available on ultrasound features of PTOCs in literature (7, 11-14). This prospective cross-sectional study aimed to describe the ultrasound features of PTOCs, in comparison to pathologic findings.

Methods

This prospective descriptive cross-sectional study was conducted on patients who were referred to two tertiary referral centers (Dr. Sheikh and Akbar Children Hospitals) in Mashhad University of Medical Sciences, Mashhad, Iran, within 2014-2019.

Fifty two neonates (aged 2 days to 6 months) with an intra-peritoneal cyst which was suspected to be neonatal ovarian cyst (NOC) underwent meticulous ultrasound examination using a Voluson E6, Samsung Model H60, or Esoate class C with a 10-12 MHz linear superficial probe. All ultrasound examinations were performed by an experienced pediatrics radiologist. Exclusion criteria included genitourinary tract cysts, hepatobiliary cysts, and other extra-peritoneal cystic diseases. Intra-peritoneal cysts were previously diagnosed with routine prenatal or antenatal ultrasound examination.

During the study, all cysts were followed up until reaching the final diagnosis. Occasionally, follow up ultrasound examinations were performed to detect any structural changes in size, appearance, and complications. The patients with complex or complicated ovarian cysts underwent surgery and the others who mainly had functional follicular cysts with less than 50mm size were managed under the supervision of clinician. The surgical indication would be established if no regression was observed. Correlation between sonographic and pathologic findings was performed in surgically approved PTOCs. Histopathologic and ultrasound findings results were analyzed in SPSS software (version 11.5) and MedCalc.

Results

Twenty two cases (aged 2 days to 6 months, mean age = 6 weeks) with PTOC were diagnosed during this time. Cysts were unilateral, including 19 cases on the right (86%) and 3 cases (14%) on the left side. Mean diameter of cysts was 51 mm (27-73mm). Ultrasonographic characteristics of cases with PTOC are presented in Table 1. Mobile solid clot components were observed in three newborn. Debris level was not formed in two third of these cases and the other 20 patients had a fluid debris level.

Structure of triple-layer wall was observed in all patients. This structure was composed of a bright internal layer (focal or diffuse), an uneven non-uniform middle hypo-echoic layer and echogenic outer epithelial surface. Inner layer was wrinkled in 11 patients. Detachment of layers was noticed in 12 (54.5%) patients.

The diagnostic value of ultrasound findings were analyzed in the detection of PTOC, which the results due to the triple-layer wall and internal wrinkled wall are presented here; Sensitivity, specificity, positive predictive value, and negative predictive value for the triple-layer wall index were measured at 100%, 65%, 70.83%, and 100%, respectively. These values were reported as 70.59%, 100%, 100%, and 76% for wrinkled inner layer index, respectively. Based on the results of Receiver Operating Characteristic (ROC) curves analysis, the area under the curve (AUC) was 0.825 (95% confidence interval [CI], 0.648–0.92) for triple-layer wall and 0.853 (95% CI, 0.681–0.948) for the wrinkled inner layer (Figure 1).

The same triple layered pattern which was detected in the ultrasound examination of cases with PTOC was also observed in pathologic examinations. Pathologic findings were in agreement with ultrasound results in all patients. Contents of cysts included hemorrhagic and necrotic tissues. In ultrasound, they were observed as a fluid containing debris and debris-fluid level (Figure 2 A, B, C). Occasionally, an internal floating solid clot was inspected inside very young cysts (Figure 3).

Histopathology of heterogeneous tissue of the

Table 1. Ultrasonographic characteristics of 16 infants with perinatal torsioned ovarian cysts

Mean size (Min-Max)	Right Location	Internal Wrinkled Wall	Septa	Triple-layer wall	Debris level	Cyst within cyst	Solid component	Bright inner wall	Uneven hypoechoic middle layer	Detached of wall
51(27-73)	14	11	0	16	15	0	2	16	16	10

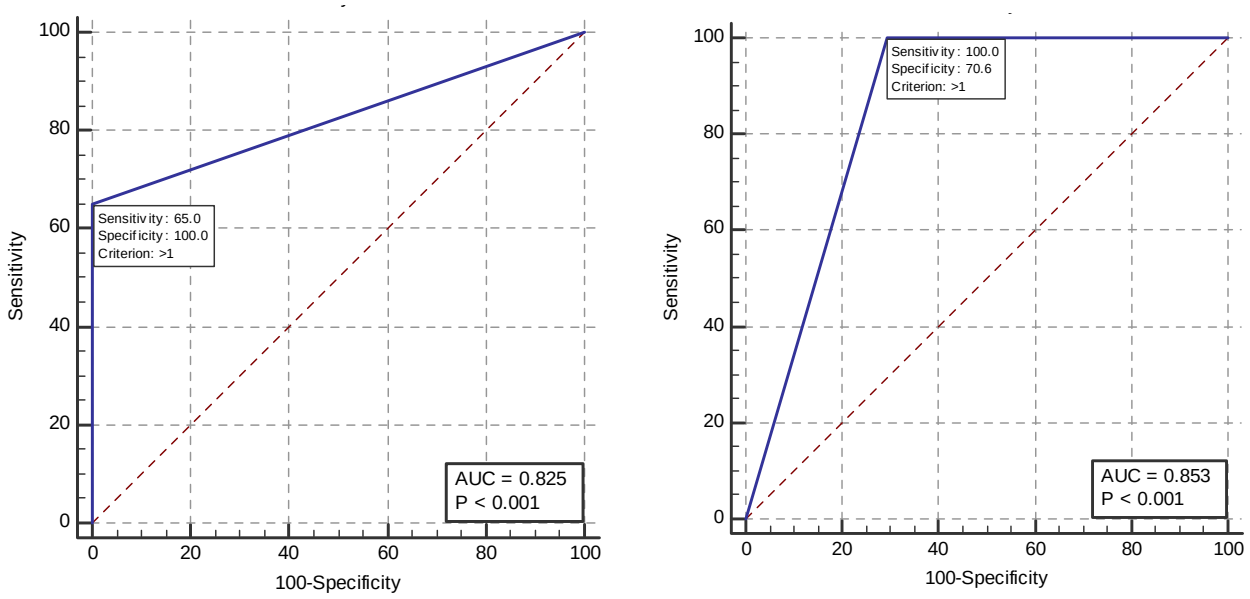

Figure 1. Receiver operating characteristic curve for demonstration of test accuracy for Triple Layer Wall (Right) and Internal Wrinkled Wall (Left) of perinatal torsioned ovarian cysts

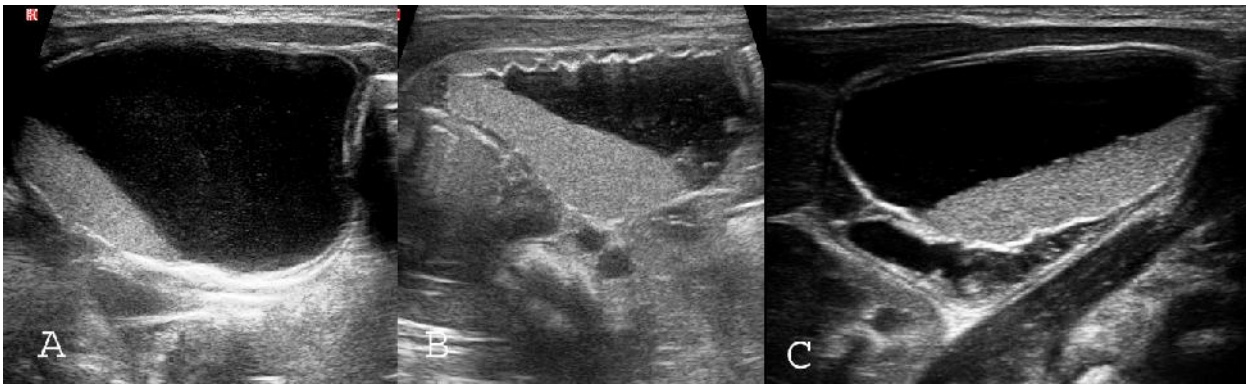

Figure 2. Ultrasound images of perinatal torsioned ovarian cysts. A and B): Usual view of cysts as triple layered pattern with smooth or wrinkled echogenic inner layer and a hypoechoic middle layer with uneven variable thickness. The cysts contain debris and debris-fluid level. C) This image illustrates detached layers of an old cyst (3 months age).

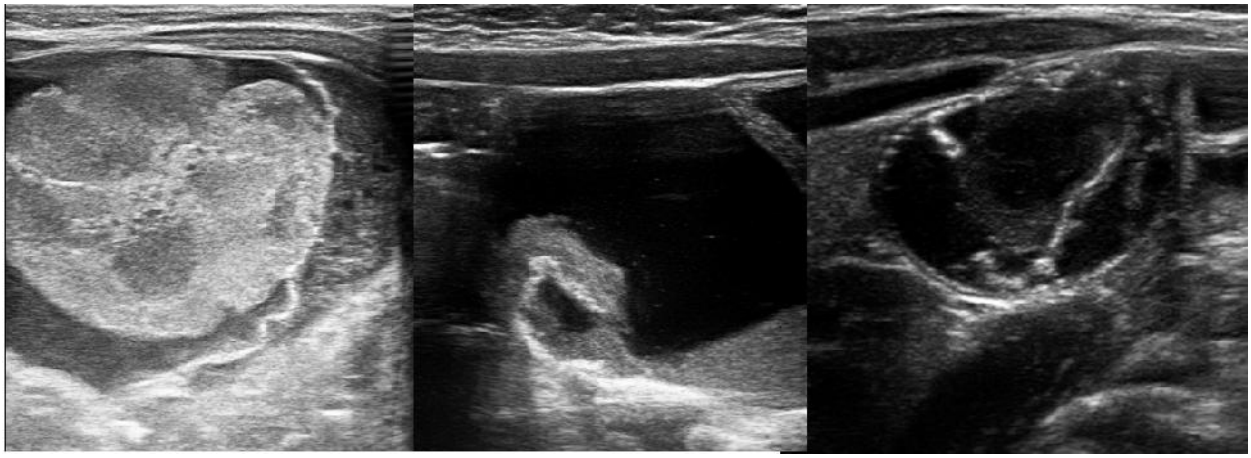

Figure 3. Unusual forms of ultrasound images of perinatal torsioned ovarian cysts. A) The typical pattern of layered cyst wall with mass like internal hematoma (10-day-old). B) The ruptured and detached internal layer of the old cyst (6-month-old). C) The ruptured and detached internal layer of the old cyst with internal echo and scatter fleck of calcification (4-month-old).

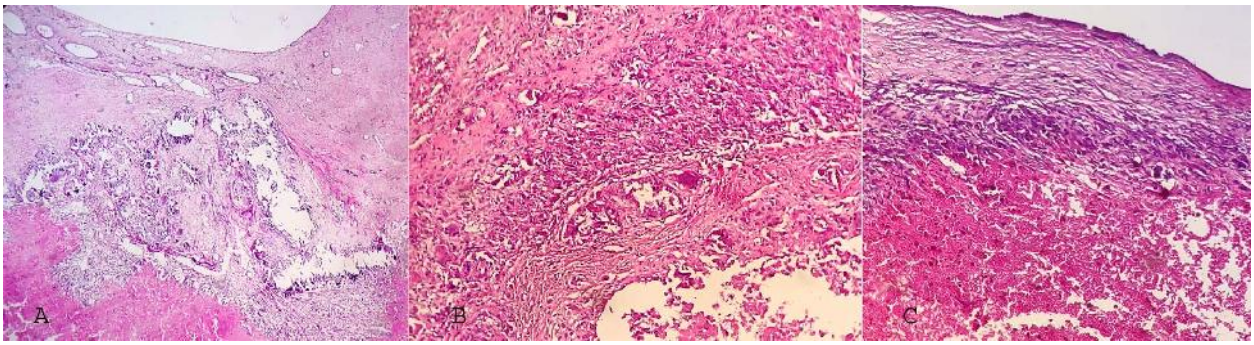

Figure 4. Haemotoxylin and Eosin (H&E) staining of perinatal torsioned ovarian cysts specimens (40x magnification) demonstrates hemorrhagic necrosis surrounded by granulation tissue with infiltration of inflammatory cells, hemosiderin-containing macrophages, foci of dystrophic calcification, and foreign body containing giant cells as an innermost layer (figures 2A and 1B). The outermost layer is covered with edematous or fibrotic ovarian stroma and superficial epithelium (figures 3A, and 2C).

inner layer revealed granulation and inflammation reactions, foci of dystrophic calcification, hemosiderin-containing macrophages, and foreign body giant cells (Figure 3A). In ultrasound examinations, the inner layer was observed as a bright echogenic layer which was smooth or wrinkled (Figure2). This layer was occasionally ruptured and detached as an internal floating layer in old cysts (Figure2D).

The homogeneous stroma of the middle layer was edematous or fibrotic (Figure 3A-B). In ultrasound examinations, this homogenous tissue was observed as a hypo-echoic layer with variable thickness (Figure 2A-C). The outermost layer of cyst wall was composed of outer epithelial cells (Figure 3A-B). Although this layer is negligible in pathologic specimens with no significant discrete third layer, in ultrasound, it was observed as a thin echogenic outer layer in the outer surface of cyst in all patients. This can be attributed to the considerable difference between the interface of the external surface of the cyst wall and surrounding tissues or peritoneum (Figure2 B).

One case was presented with an intra-abdominal cyst in the prenatal ultrasound examination. All cysts were treated surgically except three cases (14%) that underwent follow-up management. First-week ultrasound images were in differential diagnosis with duplication cyst in only one new born, nonetheless, wall layout was completely typical of PTOC after one month such as other patients.

Discussion

Abdominal cystic masses are common in neonates. When a cystic abdominal mass is detected in a female neonate, the most common diagnosis is an ovarian cyst. Differential diagnosis should be established with an intestinal duplication cyst, lymphangioma (mesenteric cyst), omental cyst, hydronephrosis, urachal cysts, cystic teratoma, and intestinal obstruction. Ovarian cysts are categorized into several types according to ultrasound criteria (15, 16). Firstly, the prenatal or postnatal diagnosis of an ovarian cyst should be made. Thereafter, it is mandatory to perform serial ultrasound examinations to detect any structural changes in the cyst. These changes include the size and appearance of the cyst which may be indicative of serious complications or any other alarming changes (17, 18). Simple cysts could easily lead to complicated cysts through the intracystic hemorrhage, cyst wall rupture, or ovarian torsion. Among the mentioned complications, torsion is the most common and dramatic change (19).

Large neonatal ovarian cysts (larger than 4 cm) or cystic ovaries have been reported to run a considerable risk of torsion. Monnery-Noch et al. demonstrated that NOCs larger than 20 mm involve a high risk of torsion and ovarian loss before or shortly after birth. They claimed a high incidence of ovarian loss in cases with a prenatal ovarian cyst. Most of complex neonatal ovarian cysts had torsion. They explained that the ultrasound scan was not able to distinguish torsioned from hemorrhagic cysts in their study (20). Early diagnosis and appropriate management is critical to decrease the side effects (5, 6). In addition, differentiation between subtypes is important since different subtypes are managed differently, ranging from surgery to minimally invasive therapies or supervision without any intervention. Therefore, ultrasound is often the “all in one” approach which is needed not only for diagnosis but also for the suggestion

of therapeutic plan due to its reliable pathognomonic imaging features. For instance, the daughter cyst sign is a specific ultrasound finding for uncomplicated ovarian cyst and ultrasound is useful to differentiate them from other cystic masses (12, 20, 21).

In the study conducted by Kim et al., a number of pathologically proven torsioned NOCs were examined. Considering initial postnatal ultrasound, they reported a complex cyst (4.7 cm diameter) with a triple-layer wall, intra-cystic hemorrhage and debris, a fluid-fluid level, and multiple septations (12).

In addition, Chinchure et al. indicated that NOCs with 'fish-net appearance' or fluid-debris level and cysts with echogenic nodules favor torsion (21). They did not provide further information regarding cyst wall features, such as triple-layer wall sign and wrinkled inner layer.

In the last two studies, the mentioned ultrasound findings would be specific for ovarian torsion if fluid-fluid level and retracted blood clots were also present or if the cyst wall had calcification (12, 21). On the other hand, some other researchers believe that observation of fluid-debris level in a complex heterogeneous ovarian cyst is a significant ultrasound hallmark for the diagnosis of ovarian torsion. The key concept is that the mentioned ultrasound findings are non-specific signs which could also be observed in other conditions, such as hemorrhagic cysts. In other words, although the sensitivity of these characteristics is acceptable, the specificity is not sufficient (13, 14, 22-24).

Traditionally, triple-layer wall sign is mentioned as a highly specific sign for intestinal duplication cyst. It is characterized by the presence of an internal echogenic line showing the mucosa and an external hypo-echoic line representing the muscle layer (11). Although the triple-layer wall has been described as a specific sign for intestinal duplication cyst, it can be observed in ovarian cysts which are complicated by torsion. PTOCs are unilocular cysts with the ovarian origin which undergo degenerative changes or hemorrhagic necrosis secondary to perinatal torsion.

PTOCs contain hemorrhagic and necrotic tissues. The inner layer of the cyst wall is composed of a heterogeneous tissue consisting of granulation and inflammatory tissue with foci of dystrophic calcification, hemosiderin-containing macrophages, and foreign body-containing giant cells. The middle layer of the cyst wall is edematous or consists of fibrotic ovarian stroma. The outermost layer of the cyst wall contains superficial epithelial cells. This specific multi-layered structure (granulation tissue, stroma, and epithelium) simulates the triple-layer wall of cyst in ultrasound which is similar to the duplication cyst wall. Therefore, the triple-layer wall alone cannot be regarded as a characteristic sign for a duplication cyst. Triple-layer wall sign in duplication cyst can be differentiated from ovarian torsion by the appearance of the layers. Duplication cysts have a smooth echogenic inner layer and a hypoechoic muscular layer with the same thickness. In PTOCs, the inner echogenic layer is often wrinkled and the middle hypoechoic layer is not uniform and has a variable thickness in different parts (13, 22).

In the current study, the sensitivity of the triple-layer wall sign was more than the wrinkled inner layer. Nonetheless, the specificity of wrinkled inner layer was much more than triple layer wall sign. There was debris in duplication cysts; however, the debris level was unusual. The detection of a triple-layer wall composed of a smooth echogenic inner layer and a hypoechoic outer layer with the same thickness was a specific sign which was suggestive of a duplication cyst. Moreover, the unveiling of a bright wrinkled inner layer and a non-uniform outer layer was a diagnostic clue for ovarian torsion.

However, unusual appearances of the cysts, including cysts with clot, detached layers, and ruptured floating internal layer, have been occasionally observed in some patients that confirmed diagnosis. In contrast to the findings of some prior studies, real septation was not observed in our patients (12-14). The detached and ruptured floating internal layer or incomplete clot lysis may have been reported as internal septation in other researches.

Furthermore, histopathologic examinations revealed the specific ultrasound pattern of PTOCs which was observed as a wrinkled bright inner layer (focal or diffuse) and uneven eccentric middle hypoechoic layer or detachment of layers. Histopathology of the cysts indicated the hemorrhagic necrosis of the cyst content. It was surrounded by granulation tissue containing foci of dystrophic calcification as an innermost layer and edematous or fibrotic ovarian stoma, as well as superficial epithelium, as the outermost layer.

Although in previous calcifications, these cysts were calcified as complex cysts and surgical

intervention were proposed for them. The results of this study show that substantial evidence exists concerning the reliability of ultrasound findings as a benign cystic lesion. Then, surgical or interventional management in these patients, especially in asymptomatic cases has cast considerable doubt and further clinical trial researches are proposed.

Conclusion

A specific sonographic pattern of triple-layer wall was observed in perinatal torsioned ovarian cysts (PTOC) which consist of a uni-locular cyst containing fluid debris level with a bright wrinkled inner layer, a non-uniform middle layer and echogenic outer epithelial surface. Pathologically, this pattern is completely matched with necrotic content and three layers of granulation, stroma, and epithelium. This specific ultrasound pattern is pathognomonic for PTOC.

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Conflicts of interests

The authors declare that they have no conflict of interest regarding the publication of the present article. The authors alone are responsible for the content and writing of the paper.

References

1. Luis JD, Ricardo PÃ, PomaresÂ A, BravoÂ C, Francisco GÃ, Aguar Ã, et al. Congenital ovarian cyst: diagnosis and perinatal management. J Gynecol Neonatal Biol. 2015; 1(1):1-5.
2. Spence JE, Domingo M, Pike C, Wenning J. The resolution of fetal and neonatal ovarian cysts. Adolesc Pediatr Gynecol. 1992; 5(1):27-31.
3. Akın MA, Akın L, Özbek S, Tireli G, Kavuncuoğlu S, Sander S, et al. Fetal-neonatal ovarian cysts--their monitoring and management: retrospective evaluation of 20 cases and review of the literature. J Clin Res Pediatr Endocrinol. 2010; 2(1):28-33.
4. Catania VD, Briganti V, Di Giacomo V, Miele V, Signore F, de Waure C, et al. Fetal intra-abdominal cysts: accuracy and predictive value of prenatal ultrasound. J Matern Fetal Neonatal Med. 2016; 29(10):1691-9.
5. Bagolan P, Giorlandino C, Nahom A, Bilancioni E, Trucchi A, Gatti C, et al. The management of fetal ovarian cysts. J Pediatr Surg. 2002; 37(1):25-30.
6. Mostofian E, Ornvold K, Latchaw L, Harris RD. Prenatal sonographic diagnosis of abdominal mesenteric lymphangioma. J Ultrasound Med. 2004; 23(1):129-32.
7. Tseng D, Curran TJ, Silen ML. Minimally invasive management of the prenatally torsed ovarian cyst. J Pediatr Surg. 2002; 37(10):1467-9.
8. Aziz D, Davis V, Allen L, Langer JC. Ovarian torsion in children: is oophorectomy necessary? J Pediatr Surg. 2004; 39(5):750-3.
9. Foley PT, Ford WD, McEwing R, Furness M. Is conservative management of prenatal and neonatal ovarian cysts justifiable? Fetal Diagn Ther. 2005; 20(5):454-8.
10. Nussbaum AR, Sanders RC, Hartman DS, Dudgeon DL, Parmley TH. Neonatal ovarian cysts: sonographic-pathologic correlation. Radiology. 1988; 168(3): 817-21.
11. Godfrey H, Abernethy L, Boothroyd A. Torsion of an ovarian cyst mimicking enteric duplication cyst on transabdominal ultrasound: two cases. Pediatr Radiol. 1998; 28(3):171-3.
12. Kim HS, Yoo SY, Cha MJ, Kim JH, Jeon TY, Kim WK. Diagnosis of neonatal ovarian torsion: emphasis on prenatal and postnatal sonographic findings. J Clin Ultrasound. 2016; 44(5):290-7.
13. Vitezica I, Czernik C, Rothe K, Hinkson L, Ladendorf B, Henrich W. Prenatal diagnosis and management of a massive fetal ovarian hemorrhagic cyst torsion with secondary fetal anemia. J Clin Ultrasound. 2014; 42(4).219-22.
14. Ozcan HN, Balci S, Ekinci S, Gunes A, Oguz B, Ciftci AO, et al. Imaging findings of fetal-neonatal ovarian cysts complicated with ovarian torsion and auto-amputation. Am J Reontgenol. 2015; 205(1):185-9.
15. Brandt ML, Helmrath MA. Ovarian cysts in infants and children. Semin Pediatr Surg. 2005; 14(2):78-85.
16. Cheng G, Soboleski D, Daneman A, Poenaru D, Hurlbut D. Sonographic pitfalls in the diagnosis of enteric duplication cysts. AJR Am J Roentgenol. 2005; 184(2):521-5.
17. Trinh TW, Kennedy AM. Fetal ovarian cysts: review of imaging spectrum, differential diagnosis, management, and outcome. Radiographics. 2015; 35(2):621-35.
18. Llorens Salvador R, Sangüesa Nebot C, Pacheco Usmayo A, Picó Aliaga S, Garcés Iñigo E. Neonatal ovarian cysts: ultrasound assessment and differential diagnosis. Radiologia. 2017; 59(1):31-9.
19. Giorlandino C, Bilancioni E, Bagolan P, Muzii L, Rivosecchi M, Nahom A. Antenatal ultrasonographic diagnosis and management of fetal ovarian cysts. Int J Gynaecol Obstet. 1994; 44(1):27-31.
20. Monnery-Noché ME, Auber F, Jouannic JM, Bénifla JL, Carbonne B, Dommergues M, et al. Fetal and neonatal ovarian cysts: is surgery indicated? Prenat Diagn. 2008; 28(1):15-20.
21. Chinchure D, Ong CL, Loh AH, Rajadurai VS. Neonatal ovarian cysts: role of sonography in diagnosing torsion. Ann Acad Med Singapore. 2011; 40(6):291-5.
22. Ogul H, Havan N, Pirimoglu B, Guvendi B, Kisaoglu A, Kantarci M. Prenatal and postnatal ultrasonographic

findings of the torsioned ovarian cyst: a case report and brief literature review. Int Surg. 2015; 100(3):514-7.
23. McKenzie AS, Dyer RB. The "fishnet" appearance. Abdom Imaging. 2015; 40(6):2058-9.
24. Koike Y, Inoue M, Uchida K, Kawamoto A, Yasuda H, Okugawa Y, et al. Ovarian autoamputation in a neonate: a case report with literature review. Pediatr Surg Int. 2009; 25(7):655-8.