Journal of Pediatric Surgery xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

A retrospective multicenter study of the natural history of fetal ovarian cysts

Athanasios Tyraskis [a], Spyros Bakalis [b], Carolina Scala [c], Argyro Syngelaki [d], Stefano Giuliani [e], Mark Davenport [a], Anna L. David [b], Kypros Nicolaides [d], Simon Eaton [f], Paolo De Coppi [f,*]

[a] Paediatric Surgery Unit, King's College Hospital, London, UK
[b] Institute for Women's Health, University College London, UK
[c] Fetal Medicine Unit, St. George's Hospital, London, UK
[d] Harris Birthright Centre, King's College Hospital, London, UK
[e] Department of Paediatric and Neonatal Surgery, St. George's University Hospitals NHS Foundation Trust, Blackshaw Rd, SW17 0QT, London, UK
[f] Stem Cells and Regenerative Medicine, DBC, UCL Institute of Child Health and Great Ormond Street Hospital London, UK

ARTICLE INFO

Article history:
Received 21 September 2017
Received in revised form 31 January 2018
Accepted 4 February 2018
Available online xxxx

Key words:
Fetal ovarian cyst
Ovarian torsion
Prenatal diagnosis
Ultrasound
Prenatal aspiration
Fetal intervention

ABSTRACT

Aim: We investigated the natural history of fetal ovarian cysts to estimate the risk of torsion according to size.
Methods: Cases were identified from 1/1/2000 until 1/1/2015. Data were collected pre- and postnatally on cyst size and sonographic features until an outcome of surgery, torsion, or resolution. Fisher's exact test for categorical data and logistic regression for continuous data were used to test the significance of size on torsion; P value <0.05 was considered significant.
Results: 37 patients with unilateral ovarian cysts were included. 12 (32%) resolved spontaneously prenatally, 14 (38%) resolved spontaneously postnatally, 5 (14%) underwent surgery postnatally and 6 (16%) cases underwent torsion. Rate of torsion increased with size from 0% ($n = 0$) in cysts ≤20 mm to 33% ($n = 2$) in cysts >50 mm; however, the overall trend failed to reach statistical significance ($P = 0.1$). Cysts of 0–40 mm had a significantly higher rate of spontaneous resolution (90% vs. 44% in >40 mm, $P = 0.003$), but the rate of torsion was not significantly different (10% in 0–40 mm vs. 25% in >40 mm, $P = 0.26$). The median time to postnatal resolution was 10 (5–27) weeks in those treated conservatively.
Conclusion: Cysts >40 mm are significantly less likely to resolve spontaneously; however torsion showed no significant correlation with cyst size. No complications were observed in cysts <20 mm.
Level of Evidence: IV, case series with no comparison group.

Follicular ovarian cysts in fetal life are a response to maternal and placental estrogens and gonadotrophins and occur as commonly as 1 in every 1000 fetuses [1]. These cysts are often treated conservatively prenatally and managed expectantly postnatally until resolution. There are increasing data to suggest that there is a significant risk of ovarian torsion prenatally and that this risk is related to the cyst diameter [2]. This has led some groups to attempt prenatal aspiration of cysts to decrease their size and hopefully their chance of prenatal torsion. Most groups advocate a cutoff cyst diameter of 40 or 50 mm as an indication for prenatal aspiration [3–5]. However, all previous studies have investigated a single cyst size cutoff to determine the risk of torsion rather than describe the prevalence of torsion according to cyst size.

The sonographic appearance of the cyst may also be significant in determining treatment strategy in addition to its size. Simple cysts are assumed to be viable whereas complex cysts (especially if a fluid-debris level is present internally) have a high likelihood of already having torted. Thus the simple cysts would be the target of treatment in order to prevent ovarian loss [6,7].

Owing to the rarity of large ovarian cysts and incomplete follow-up, the natural evolution of these cysts has not been well studied, and the degree of risk of torsion with increasing cyst diameter has yet to be quantified.

The aim of this study was to investigate the natural history of prenatally diagnosed ovarian cysts; to estimate the risk of torsion for cysts according to their size and sonographic appearance, and to assess likelihood of cyst resolution.

1. Method

This is a multicenter retrospective study of pregnant women referred to three tertiary-referral fetal medicine units with follow-up of their infants in three pediatric surgery centers. Three fetal medicine

* Corresponding author at: Developmental Biology& Cancer Programme, UCL Great Ormond Street Institute of Child Health, 30 Guilford Street, London WC1N 1EH.
E-mail address: p.decoppi@ucl.ac.uk (P. De Coppi).

https://doi.org/10.1016/j.jpedsurg.2018.02.049
0022-3468/

centers and their respective pediatric surgical centers were included in this study (King's College Hospital, St. George's Hospital, University College London Hospital) with a further contribution from the department of pediatric surgery at Great Ormond Street Hospital (the referral center for babies born at University College London Hospital). Cases of fetal ovarian cysts were identified using the ViewPoint (GE Healthcare, UK) ultrasound (US) database at each hospital. To ensure complete capture of fetal ovarian cysts, a search for "ovarian or pelvic or abdominal cyst (s)" was performed on scans from January 2000 until January 2015. All identified cases were screened for eligibility where inclusion criteria were unilateral or bilateral cyst(s) that were suspected to be of ovarian origin. Patients were excluded if they were not followed up in one of the three fetal medicine centers, but rather had just been referred for a second opinion and one ultrasound scan to ensure completeness of both prenatal and postnatal information.

Data on cyst dimensions and sonographic appearance were gathered from all prenatal scans from time of diagnosis until birth. Postnatal follow up data were obtained from all patients until the time of resolution, aspiration or surgical excision. Any cases which during follow-up were determined to have cysts of nonovarian origin were excluded. The size measurements used to subdivide patients for the subsequent analysis were the maximum diameter of the cyst at the time of the first prenatal US scan in one of the three included tertiary fetal medicine centers. Median and interquartile range of cyst size according to gestational age was reported and a subgroup analysis was performed according to the maximum diameter on any prenatal US rather diagnosis. Patients who underwent prenatal aspiration were included in the overall analysis and more information on their individual clinical course was provided.

Ovarian loss in patients with ovarian cysts may occur owing to torsion, and for the purpose of this study was defined as: a necrotic ovary at the time of surgery, or a complex cyst which regressed without any identifiable ovarian tissue on the ipsilateral side on more than one US scans post regression. Simple cysts were defined as a thin-walled cyst with anechoic contents, and complex cysts included those with internal septations, debris, or other echoic content which did not appear solid (solid complex cysts were excluded owing to the risk of being teratomas). Postnatal resolution was defined as resorption of the cyst with two identifiable ovaries on US. Prenatal resolution was defined as resorption of the cyst on subsequent antenatal US (most of these patients did not go on to have postnatal US).

This study was registered as an audit approved by the Clinical Audit and Safety Department of Great Ormond Street Hospital (approval number: 1524) and therefore did not require formal ethical committee approval.

Two-tailed Fisher's exact tests were used to test for significant differences between the different size groups; GraphPad Prism (Version 6)® was used for this statistical analysis. 95% level of confidence was defined as significant. Continuous data were reported as median and interquartile range. Overall trend according to size was tested using a logistic regression on STATA 13®. Finally a 95% confidence interval of proportion was calculated using the GraphPad Quick Calcs online software. A P value of <0.05 was considered significant.

2. Results

A total of 109 patients were identified with a diagnosis of fetal ovarian cyst(s). 58/109 were referred to our centers only for a second opinion, and had no further contact besides a single consultation. As we did not have a complete data for follow-up and outcomes they were excluded from our study. 14 were lost to follow-up either pre or postnatally, and the remaining 37 patients were included in the study (Fig. 1). Spontaneously resolution occurred in 12/37 (32%) cysts prior to birth, and 14 (38%) resolved spontaneously after birth. Postnatal surgery occurred in 7 infants and 4 of those were found to have torted necrotic ovaries and in 1 infant the ovary was twisted along the axis of

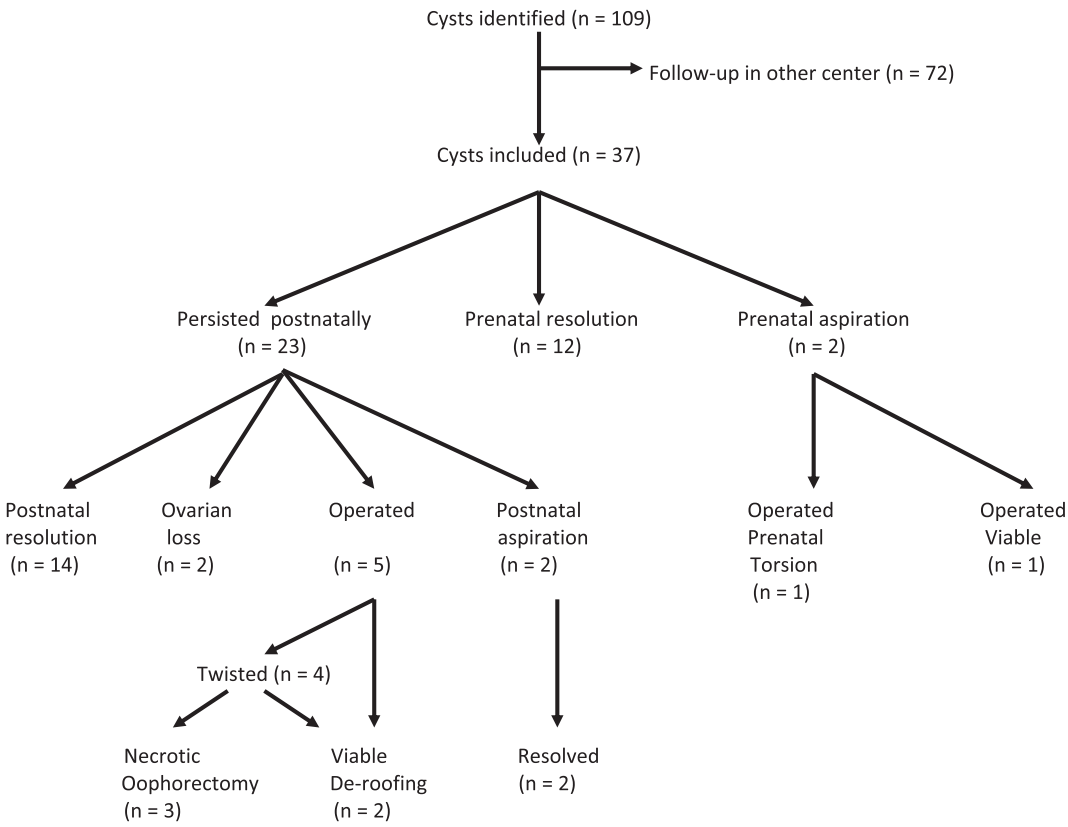

Fig. 1. Flowchart of outcomes for all patients.

Please cite this article as: Tyraskis A, et al, A retrospective multicenter study of the natural history of fetal ovarian cysts, J Pediatr Surg (2018), https://doi.org/10.1016/j.jpedsurg.2018.02.049