Clinics in Surgery

Research Article
Published: 11 Nov, 2021

Pubertal Evolutionary Profile of Children Monitored for Fetal Ovarian Cyst (FOC Study)

*Sarah Tolleron[1], Audrey Cartault[1], Sofia Mouttalib[2], Julie Vial[3], Lea Gauthier[3], Agnes Sartor[4], Marion Groussolles[4], Caroline Munzer[5], Olivier Abbo[2] and Catherine Pienkowski[1]**

[1]Endocrinology and Medical Gynecology Unit, Rare Gynecological Pathologies Reference Center, Children's Hospital, University of Toulouse Hospital Center, France

[2]Visceral Surgery Unit, Children's Hospital, University of Toulouse Hospital Center, France

[3]Children's Hospital Medical Imaging Center, University of Toulouse Hospital Center, France

[4]Prenatal Screening Center, Hospital Paule De Viguier, France

[5]The Pediatric Clinical Research Unit, Children's Hospital, University of Toulouse Hospital Center, France

Abstract

Objective: To evaluate the outcomes of puberty in girls followed for Fetal Ovarian Cysts (FOC).

Design: We included 83 girls of eight and more, followed at Toulouse Hospital for FOC. Historical data were collected through computerized medical record. Recent clinical, US and hormonal data were collected through a questionnaire filled up by the patients and their parents.

Results: Of 83 eligible patients, 51 agreed to participate. Their median age was 11.6 years [8.6-17.6], 37 patients (72.5%) had pubertal signs, 18 patients had menarche (36%). The median age of puberty onset was 11 years 95% CI (10.5-11.5) and that of first menstruation was 13 years 95% CI (12.2-13.6). Fifty-two patients (96%) had no recurrence of ovarian cysts.

No significant difference in the age of menarche, AMH levels, ovarian volume was noted.

Regarding the 54 FOC including 3 bilateral cysts, 32 were simple (59.3%) and 22 (41%) were complex. The rate of cyst regression is 90% of cases in 2.1 months [0-8.9] for simple cysts and 54% of cases in 3.7 months [1.1-10.2] of complex cysts (rate p<0.0001 and time p=0.06). 23 small Cysts (diameter <40 mm) regressed in 90% of cases against 56% for the largest cysts (n=31) (p=0.01). The duration of regression of small cysts was 1.9 months, significantly less than that of largest cysts (median 3.4 months) punctured or not (p=0.05).

Conclusion: The occurrence of FOC, whether liquid or complex, does not modify the pubertal profile, and no recurrence was observed.

Keywords: Fetal ovarian cyst; Menarche; Recurrence; Long term follow-up; Ultrasound

Abbreviations

FOC: Fetal Ovarian Cyst; AMH: Antimullerian Hormone

Introduction

Ovarian cysts are the most common abdominal mass diagnosed in female fetuses, with an estimated incidence of about 1 in 2,600 pregnancies [1,2]. They are common in pregnancies complicated by maternal diabetes, pre-eclampsia, or rhesus isoimmunization [3-5]. These cysts appear during the 3rd trimester. They must be distinguished from the persistence of urogenital sinus or cloaca and from gastrointestinal duplications. Ovarian cysts are categorized according to their sonographic appearance. It can be simple (Thin-walled cyst, anechoic with a diameter greater than 20 mm) or complex [6]. For Nussbaum et al. a twisted or hemorrhagic cyst may contained, deposit, fluid level or retracting clot, can be septate, with or without internal echoes, or even solid [6].

Management of fetal ovarian cyst has been controversial for a long time and the evolution was variable [7-11]. Simple cysts have a good prognosis because most of them disappear within a few weeks after birth [12]. The risk of twisting remains unpredictable and can vary from 15% to 29% according to various studies [12]. It seems that this risk increase when the cyst is over 40 mm or when its size raises quickly [8]. The pathophysiology of the genesis of these cysts is not

OPEN ACCESS

Correspondence:
Catherine Pienkowski, Endocrinology and Medical Gynecology Unit, Rare Gynecological Pathologies Reference Center, Children's Hospital, University of Toulouse Hospital Center, 330 Avenue de Grande Bretagne TSA 70034, 31059 Toulouse cedex, France, Tel: +33534558556; Fax: +33534558558; E-mail: pienkowski.c@chu-toulouse.fr

Received Date: *29 Sep 2021*
Accepted Date: *08 Nov 2021*
Published Date: *11 Nov 2021*

Citation:
Tolleron S, Cartault A, Mouttalib S, Vial J, Gauthier L, Sartor A, et al. Pubertal Evolutionary Profile of Children Monitored for Fetal Ovarian Cyst (FOC Study). Clin Surg. 2021; 6: 3356.

fully understood. This is a benign functional abnormality of the fetal ovary resulting either from ovarian hypersensitivity or fragility to the hormonal stimuli or from excessive ovarian stimulation. No study data on the long-term outcome of these patients has been reported and moreover at the onset of puberty when the ovary undergoes hormonal hypothalamic-pituitary stimulation again.

At our center, we decided a decade ago to perform a regular, multidisciplinary supervision for neonates with simple or complex cyst during the first year of life. Thus, punctures were discussed, and surgical indications were restricted to cases recent complications to preserve the ovary.

The main objective was to describe the pubertal profile of these girls, and to assess the risk of recurrence from early infancy to the menarche. We also tried to describe the ovarian ultrasound aspect and its evolution along with the hormonal data available.

Materials and Methods

This is an observational, prospective, monocentric, and non-comparative study conducted at Toulouse University Hospital about pubertal outcome of girls with FOC during their pubertal development.

The study population concerns 83 patients aged over 8 years, followed during the 1st year of life in our unit for FOC detected during the 3rd trimester of pregnancy.

Patients and their families were contacted by post and phone to inform them of the objective of this study. After obtaining their written consent, a questionnaire was completed during a medical appointment or at home. To preserve anonymity, a code as well as the connection link has been sent by email to the families. This questionnaire was about clinical data, patient history, their lifestyle (physical activities, school level), and pubertal data (age at breast growth, age at menarche, course of menstrual cycles, precocious puberty or hyperandrogenism). A prescription for a pelvic ultrasound and for a blood test for hormonal assay was sent to them.

Ante and neonatal data were collected through medical record systems (ORBIS software, Agfa, Deutschland). The data collected included clinical features (parity, gestational age, weight and height at birth, diagnosis of gestational diabetes), US and hormonal data of the cyst(s), the management of the cyst and their evolution during the first year of life. All data collected have been anonymized.

The statistical analysis was performed using SAS software, version 9.4. Frequencies were presented as percentages. The mean with Standard Deviation (SD) or median with minimal and maximal ranges were used to describe parametric or nonparametric continuous variables, respectively. The χ^2 tests or Fisher's exact tests if necessary were used for comparison of proportions. Student's t-tests or non-parametric Wilcoxon tests were used to compare continuous variables depending on preconditions.

To consider the censored data, the ages of puberty and menarche were estimated using the Kaplan-Meier method and compared with log rank test. In all tests, a p value <0.05 was considered statistically significant.

This study was approved by the ethic committee in February 2020 (Etude KOF/N° RC31/19/0497/N° 2019-A03285-52) and by the national commission for data processing and freedoms (CNIL) (Number: 2139277).

Results

General features

Of the 83 patients followed between 2002 and 2011 for fetal ovarian cysts contacted, 51 patients responded positively including 3 patients with bilateral cysts. The participation rate was 61.4%. The

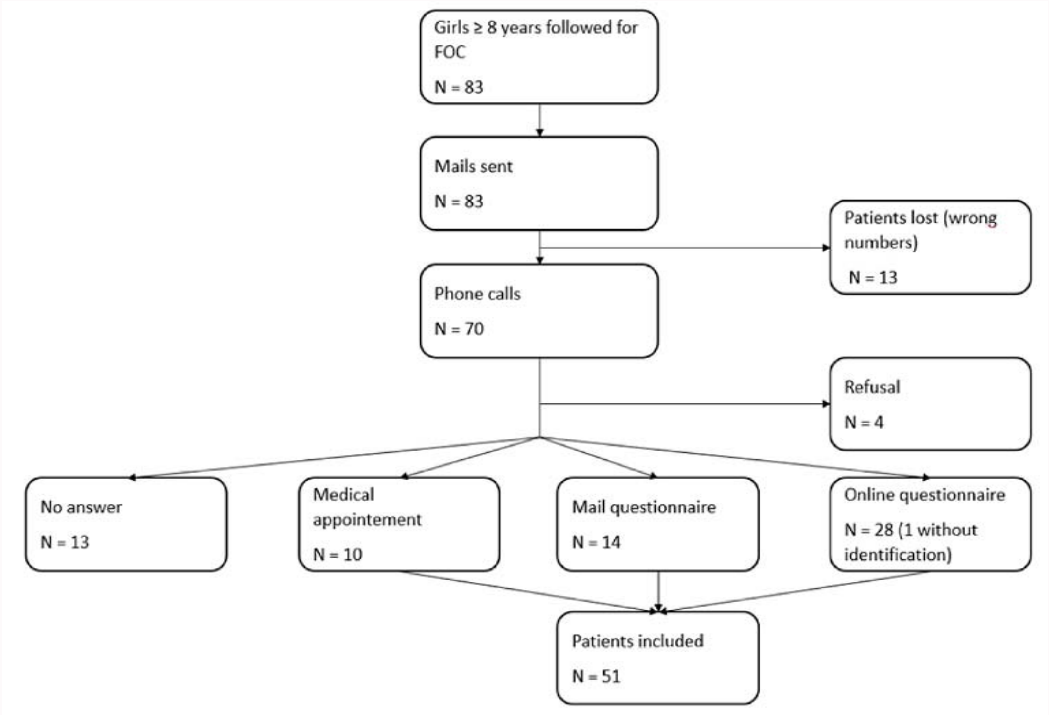

Figure 1: Flow chart.

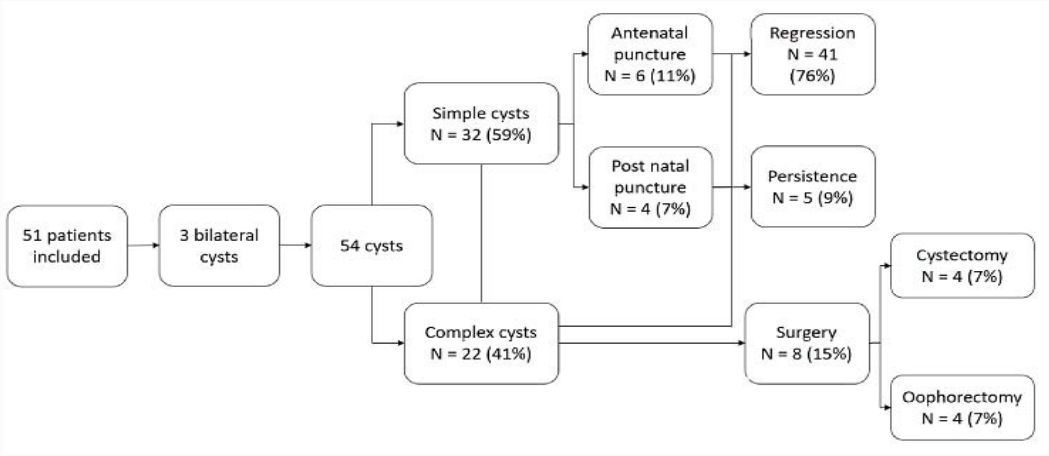

Figure 2: Characteristics of the cysts and neonatal evolution.

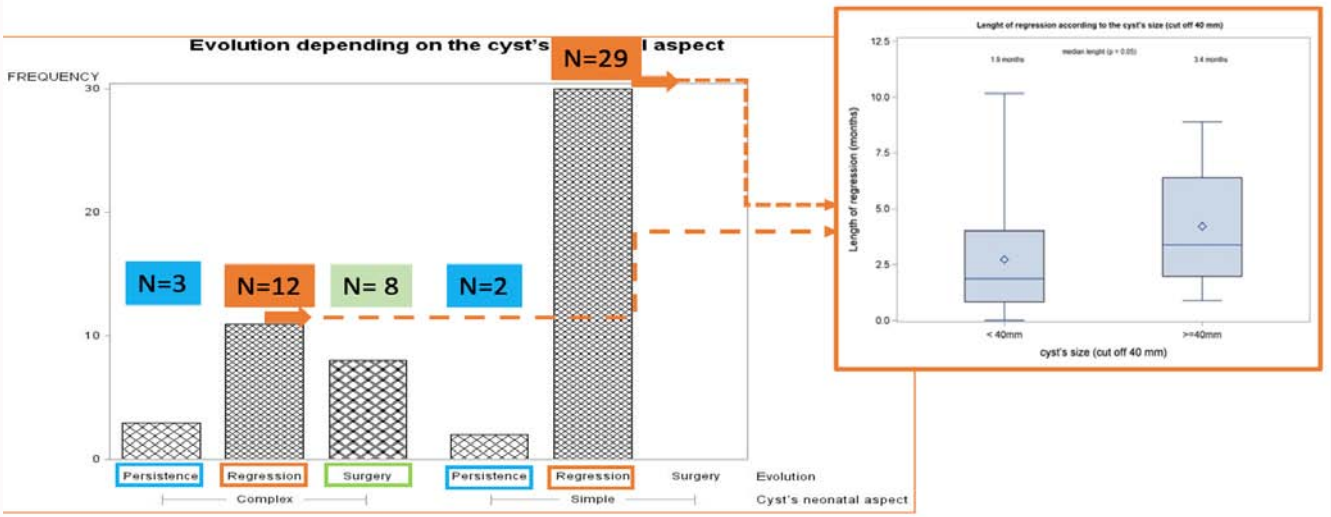

Figure 3: Evolution depending on the cyst's neonatal aspect and duration of regression according to the cyst's size.

analyzes therefore focused on 54 cysts, the flow chart is described on Figure 1. The characteristics and neonatal evolution on Figure 2.

Answer to the questionnaire: The median age of patients at the time of the questionnaire was 11.6 years [8.6-17.6]; the average body mass index was 0.8 ± 1.6 Z-score. 37 patients have already entered puberty (72.5%) and 18 patients had menarche (36%). The median age of breast development (tanner stage 2) was 11 years IC95 [10.5-11.5] and the median age of first menstruation was 13 years IC95 [12.2-13.6]. Daughter's age at menarche was significantly correlated with mother's period age (r: 0.57, p=0.0131). Two patients were followed for an isolated premature the larche, and 2 patients declared having a puberty onset at the age of 8 years but none of them had been treated by GnRH analogues. After menarche, four patients (7.8%) declared to present a hirsutism (abdominal, back, or root of the thighs). None of them received specific treatment. Regarding the course of menstruation, the median of cycles was 28 days [21-42]; the duration of menstruation was 5 days [2-7]. Eight patients (44.4%) presented with a menstrual cycle disorder, 3 patients reported irregular cycles (17%), 7 patients reported heavy periods (39%) including 5 patients (28%) with menorrhagia requiring appropriate treatment in 3 cases (17%). Six patients reported having dysmenorrhea (33%) requiring analgesic treatment. Two 15 and 17-years old patients had declared taking contraception. No significant difference in the age of menarche, AMH levels, ovarian volume is noted in patients with or without menstrual cycle disorder. The distribution of cycle disorders according to gynecological age (< or > 2 years of menarche) is no different.

Neonatal period: Regarding neonatal period, the median term of birth was 39.5 weeks [35-42]; two patients (4%) were born before 37 weeks. Pregnancy parity was P1 in 46.4%, P2 in 42.9% and P3 or more in 10.7%. Five cases of gestational diabetes were reported (9.8%); there was no significant difference in comparison with the French general population. Only 1 patient (1.9%) was born low for gestational age (<10^{th} percentile).

Regarding the 54 cysts of the neonatal period, 32 were simple (59.3%) and 22 were complex (40.7%). Neonatal evolution according to the aspect of cyst was described on Figure 3. The rate of cyst regression was 90% for simple cysts and 54% of complex cysts (p<0.0001). Time to regression was 2.1 months [0-8.9] for simple cysts and 3.7 months [1.1-10.2] for complex cysts (p=0.06). The data concerning all cysts are summarized in Table 1.

Table 1: Statistical comparison on the aspect of the cyst.

	All cysts N=54		Simple cysts N=32		Complex cysts N=22		p-value
Diameter (mm)	35 [10-70]		33 [10-70]		40 [19-66]		NS
Antenatal puncture	N=6	11%	N=6		N=0		p=0.07
Postnatal intervention	N =12	22.2%	N=4	12.5%	N=8	36.4%	p=0.05
Postnatal puncture	N=4	7.4%	N=4		N=0		p=0.1
Cystectomy	N=4	7.4%	N=0		N=4		p=0.02*
Oophorectomy	N=4	7.4%	N=0		N=4		p=0.02 *
Evolution							
- Regression	N=41	75.9%	N=29	90.6%	N=12	54.5%	p<0.0001 *
- Persistence	N=5	9.3%	N=2	6.3%	N=3	13.6%	p<0.0001 *
- Surgery	N=8	14.8%	N=0		N=8		p<0.0001 *
Visible Homolateral ovary in the 1st year of life	N=31 (MD =8)	67.4%	N=25	78%	N=8	36%	
Follicles on homolateral ovary	N=28 (MD =24)	93.3%	N=24	75%	N=6	27%	
Duration of regression (months)	2.4 [0-10.2]		1.9 [0-8.9]		4.24 [1.1-10.2]		p=0.06
AMH M1 (ng/ml)	N=31	1.7 [0.1 - 9.2]	N=19	3.1 [0.1-9.2]	N=12	1.5 [0.4-3.2]	p=0.07
AMH M6 (ng/ml)	N=41	1.3 [0.1 - 6.8]	N=23	2 [0.1-6.8]	N=18	0.8 [0.1-3.1]	p=0.004
AMH ≥ 8 years (ng/ml)	N=16	2.1 [0.2 -6.7]	N=9	3.6 [0.5-6.4]	N=7	0.9 [0.2-6.7]	p=0.04

Table 2: Statistical comparison on the managing of the cyst.

	All patients N=51		Monitoring N=37		Puncture or surgery N=14		p-value
AMH M1 (ng/ml)	N=31	1.7 [0.1 -9.2]	N=25	1.7 [0.1 -9.2]	N= 6	2 [0.5 -8.4]	p=0.8
AMH M6 (ng/ml)	N=41	1.3 [0.1 -6.8]	N=31	1.5 [0.1 -6.8]	N= 10	1.2 [0.1 -5.1]	p=0.9
AMH ≥ 8 years (ng/ml)	N=16	2.1 [0.2 -6.7]	N= 12	2.2 [0.2-6.7]	N=4	1.75 [1.1 - 3.9]	p=0.9
Age at onset of puberty (years)	N=37	11 [8-13]	N=21 (DM=3)	10.5 [8 - 13]	N=13	11.5 [8 -12]	p=0.1
Age at menarche (years)	N=18	12.3 [9.5-14.3]	N=10	11.8 [9.5-14.4]	N=8	12.7 [11.7 -13.6]	p=0.2
Pelvic Ultrasound							
Homolateral ovarian volume (ml)	N=9	3 [0.5-15]	N=6	3.7 [0.6 - 15]	N=3	1.7 [0.5 - 14.1]	p=0.6
Vizualized follicles on homolateral ovary	N=10/11 (DM=40)	91%	N=7/7		N=3/4		p=0.3
Menstrual cycle disorder	N=8	44%	N=5	62.50%	N= 3	37.50%	p=0.6

Regarding the diameter of the cyst, thirty-one large cysts (57.4%) had a diameter >40 mm. Small cysts (<40 mm) regressed in 90% of cases against 56% for the largest cysts (p=0.01). The time to regression of small cysts was 1.9 months, it was not significantly less than large cysts (median 3.4 months) (Figure 3). Among the large and simple cysts (N=12), 7 were punctured. Their median regression was 4 months [1.5-6.6], no statistical difference was found for the 5 non-punctured cysts (4.2 months [0.9-8.9]). There was no significant difference in the age of puberty, menarche or the existence of cycle disorders between patients according to the aspect, size, puncture and bilaterality of the cyst (Table 2).

Ultrasound Follow up: The 52 patients (96%) had no recurrence of ovarian cysts. One patient underwent a cystectomy for mature teratoma of the left ovary at the age of 8.8 years and the second patient presented with a spontaneously regressive functional cyst at the age of 11.6 years.

Only 24 patients (47%) were able to control the ultrasound due to the difficulty of accessing a radiology center during the COVID period. The right ovary was visible in 13 patients, follicular in 93% of cases; it measured 3.6 ml [0.5-15]. For the 3 patients with menarche, the volume was 4.3 ml [1.7-9]. The left ovary was visible in 17 patients, follicular in 94.7% of cases; it measured 2.6 ml [0.6-14]. For 6 patients with menarche, it was 7.4 ml [0.6-14]. The ipsilateral ovary was visible in 11 out of 14 cases (78%) when the initial cyst was fluid, and it was visible in 3 out of 10 (30%) cases (adnexectomy in 2 cases) when the initial cyst was complex.

Hormonal follow up: The level of AMH at 6 months age and pubertal AMH was significantly higher for simple cyst compared to complex cyst (p=0.004 and p=0.04 respectively).

Gonadotropin levels were within the norm for age (n=17), but interpretation was difficult for those after menarche (n=6) without knowing the exact timing of the cycle. The AMH level was 2.1 ng/ml [0.23-6.7] for 13 patients and 1.5 ng/ml [0.23-6.7] for 6 post menarche patients.

Discussion

To our knowledge, our work is the first longitudinal prospective study to evaluate the pubertal profile of girls diagnosed with a FOC. For the past two decades, our attitude has been as conservative as possible, where as being aware of the need of puncture or surgery in case of torsion [7,8]. Moreover, its importance is based on the duration of the follow up which is unique along with an acceptable participation rate.

Indeed, other long-term reports were difficult to evaluate due to the small size of their cohort. It focused principally on ultrasound evaluation without information on clinical and biological evolutions [13-15].

The main goal of our study was to determine if a history of FOC was related to modifications of puberty onset. At the time of questionnaire, we found that only one third of the population had their menarche whereas 75% had begun puberty. For us, this is linked to the young age of the studied population (11 years old). These data are similar to the described ages of puberty and menarche onset in the general population in France and in Europe [16-18].

It suggests that the discovery of a neonatal FOC, whether it is simple or complex, do not modify the age of the onset of the puberty. The occurrence of FOC does not influence the ovarian activation age in response to the hypothalamic gonadostat pulsatility. Finally, the occurrence of a FOC is not linked to an increased recurrence risk of cyst during the puberty as only one patient presented a functional cyst during the follow up.

AMH evaluation is poorly documented before the age of 25 years in the literature. However, it is well established that AMH is a predictive factor for the follicular stock. Several studies have established norms in neonates [19,20]. In the same way, Hagen et al. have described standards for children during the prepubertal and pubertal periods [21,22]. For them, the AMH rate was correlated with the number of small to median size follicles as in adult women. Other studies link the AMH rate with the ovarian volume [23,24], which we were not able to demonstrate in our study.

It is well established that the age of menarche in girls is close to their mothers [18,25,26]. Our results confirm this data, without a higher rate of precocious puberty requiring a medication, which incidence has been described around 2.68/10,000 among girls younger than 9 years old by Moal et al. [27].

From 20% to 80% of adolescent experiment cycle disorder during the two years following the menarche in the literature [28,29] which has been confirmed in our cohort. In the report of Friberg et al. a questionnaire was sent to 1,014 Swedish girls, among them, one third declared to have menorrhagia requiring an adapted medication [30]. During the post-menarche period, most of the cycles will only get a steady rate with an efficient ovulation after five years [31].

Concerning the prenatal and the neonatal data, we did not find any proved predisposing factor (parity, prematurity) but only a slight over presentation of gestational diabetes, which has been previously described [32,33].

The ultrasound definition of complex FOC according to Nussbaum et al. includes two entities with different prognosis [6]. Indeed, it can be quite challenging to distinguish an adnexal torsion, and its potential consequences on the ovarian vitality, from an intracystic bleeding, with a deposit, which can spontaneously disappear. Several authors have demonstrated that the risk of torsion is linked to the size of the cyst [7,12,34]. In 2016, a meta-analysis including 954 fetuses from 34 studies has highlighted a rate of spontaneous disappearance (pre- and post-natal included) of 53.8%. To be more precise, this rate was 69.4% for all simple cysts but reached 84.8% for small cyst. At the opposite, this rate was quite lower for complex cysts with a 33.1% rate reported and 31.8% when the main diameter was >40 mm. Our data confirmed these findings. For us, the size and the ultrasound characteristics of the FOC are the main determinants of the perinatal outcome of the ipsilateral ovary. In the past, some teams have also justified the need for an early intervention to prevent a potential risk of intestinal obstruction [35]. Few reports of intestinal obstruction have been made to date [7]. In our study no case of such complication has been reported and for us this potential event should not be considered to justify a surgical indication.

Our study also bears some limits despite its strengths. Among them the size of our cohort remains small, and more specifically concerning the number of girls who reached the menarche. Finally, the actual COVID-19 pandemic does not allow us to get more ultrasound data due to the organization struggles. No validated questionnaire has been developed concerning the puberty and its onset, but it is a part of our pediatric practice experience.

To Sum up, we tried to simplify our follow up calendar according to our results, especially in the case of simple cysts. The current attitude is to carry out an ultrasound control at the time of puberty. In the case of a single ovary, information must be given to the patient to discuss and suggest preservation of fertility in the post menarche years.

Conclusion

Our results suggest that the occurrence of FOC, whether liquid or complex, does not modify the pubertal profiled and the age of menarche. Moreover, only one cyst recurrence was found in our study and no case of intestinal occlusion was reported. Future parents should be reassured concerning the outcome of FOC in the long term and discuss follicles preservation of unique ovary.

Acknowledgment

We would like to first thank the patients and their families who agree to participate in the study. Thank you to the obstetricians, midwives and neonatal pediatricians who referred patients to the Prenatal Screening Center or the Children's Hospital Imaging Center to standardize follow-up. Thanks to Céline Mercier, project manager of the Rare Gynecological Pathology Reference Center for all administrative procedures and her contact with families.

References

1. Trinh TW, Kennedy AM. Fetal ovarian cysts: Review of imaging spectrum, differential diagnosis, management, and outcome. Radiographics. 2015;35(2):621-35.
2. Bryant AE, Laufer MR. Fetal ovarian cysts: Incidence, diagnosis and management. J Reprod Med. 2004;49(5):329-37.
3. Perrotin F, Potin J, Haddad G, Sembely-Taveau C, Lansac J, Body G. Fetal ovarian cysts: A report of three cases managed by intrauterine aspiration. Ultrasound Obstet Gynecol. 2000;16(7):655-9.
4. Sedin G, Bergquist C, Lindgren PG. Ovarian hyperstimulation syndrome in preterm infants. Pediatr Res. 1985;19(6):548-52.
5. Peters H, Byskov AG, Grinsted J. Follicular growth in fetal and prepubertal ovaries of humans and other primates. Clin Endocrinol Metab. 1978;7(3):469-85.
6. Nussbaum AR, Sanders RC, Hartman DS, Dudgeon DL, Parmley TH. Neonatal ovarian cysts: Sonographic-pathologic correlation. Radiology. 1988;168(3):817-21.
7. 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.
8. Galinier P, Carfagna L, Juricic M, Lemasson F, Moscovici J, Guitard J, et al. Fetal ovarian cysts management and ovarian prognosis: A report of 82

cases. J Pediatr Surg. 2008;43(11):2004-9.

9. Monnery-Noché M-E, Auber F, Jouannic J-M, Benifla JL, Carbonne B, Lenoir M, et al. Fetal and neonatal ovarian cysts: is surgery indicated? Prenat Diagn. 2008;28(1):15-20.

10. Brandt ML, Luks FI, Filiatrault D, Garel L, Desjardins JG, Youssef S. Surgical indications in antenatally diagnosed ovarian cysts. J Pediatr Surg. 1991;26(3):276-81.

11. Bagolan P, Rivosecchi M, Giorlandino C, Bilancioni E, Nahom A, Zaccara A, et al. Prenatal diagnosis and clinical outcome of ovarian cysts. J Pediatr Surg. 1992;27(7):879-81.

12. Bascietto F, Liberati M, Marrone L, Khalil A, Pagani G, Gustapane S, et al. Outcome of fetal ovarian cysts diagnosed on prenatal ultrasound examination: Systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2017;50(1):20-31.

13. Luzzatto C, Midrio P, Toffolutti T, Suma V. Neonatal ovarian cysts: Management and follow-up. Pediatr Surg Int. 2000;16(1-2):56-9.

14. Ben-Ami I, Kogan A, Fuchs N, Smorgick N, Mendelovic S, Lotan G, et al. Long-term follow-up of children with ovarian cysts diagnosed prenatally. Prenat Diagn. 2010;30(4):342-7.

15. Cesca E, Midrio P, Boscolo-Berto R, Snijders D, Salvador L, Antona D, et al. Conservative treatment for complex neonatal ovarian cysts: A long-term follow-up analysis. J Pediatr Surg. 2013;48(3):510-5.

16. Gaudineau A, Ehlinger V, Vayssière C, Jouret B, Arnaud C, Godeau E. Age at onset of menarche: Results from the French health behaviour in school-aged children study. Obstet Fertility Gynecol. 2010;38(6):385-7.

17. Parent A-S, Teilmann G, Juul A, Skakkebaek NE, Toppari J, Bourguignon J-P. The timing of normal puberty and the age limits of sexual precocity: Variations around the world, secular trends, and changes after migration. Endocr Rev. 2003;24(5):668-93.

18. Sørensen S, Brix N, Ernst A, Lauridsen LLB, Ramlau-Hansen CH. Maternal age at menarche and pubertal development in sons and daughters: A nationwide cohort Study. Hum Reprod. 2018;33(11):2043-50.

19. Guibourdenche J, Lucidarme N, Chevenne D, Rigal O, Nicolas M, Luton D, et al. Anti-Müllerian hormone levels in serum from human foetuses and children: Pattern and clinical interest. Mol Cell Endocrinol. 2003;211(1-2):55-63.

20. Kollmann M, Obermayer-Pietsch B, Lerchbaum E, Lang U, Herzog SA, Trummer C, et al. Androgen and anti-mullerian hormone concentrations at term in newborns and their mothers with and without polycystic ovary syndrome. J Clin Med. 2019;8(11).

21. Hagen CP, Aksglaede L, Sørensen K, Main KM, Boas M, Cleemann L, et al. Serum levels of anti-müllerian hormone as a marker of ovarian function in 926 healthy females from birth to adulthood and in 172 turner syndrome patients. J Clin Endocrinol Metab. 2010;95(11):5003-10.

22. Hagen CP, Mouritsen A, Mieritz MG, Tinggaard J, Wohlfart-Veje C, Fallentin E, et al. Circulating AMH reflects ovarian morphology by magnetic resonance imaging and 3D ultrasound in 121 healthy girls. J Clin Endocrinol Metab. 2015;100(3):880-90.

23. Van Rooij IAJ, Broekmans FJM, te Velde ER, Fauser BCJM, Bancsi LFJMM, De Jong FH, et al. Serum anti-Müllerian hormone levels: A novel measure of ovarian reserve. Hum Reprod. 2002;17(12):3065-71.

24. Pigny P, Merlen E, Robert Y, Cortet-Rudelli C, Decanter C, Jonard S, et al. Elevated serum level of anti-mullerian hormone in patients with polycystic ovary syndrome: Relationship to the ovarian follicle excess and to the follicular arrest. J Clin Endocrinol Metab. 2003;88(12):5957-62.

25. Ersoy B, Balkan C, Gunay T, Egemen A. The factors affecting the relation between the menarcheal age of mother and daughter. Child Care Health Dev. 2005;31(3):303-8.

26. Wohlfahrt-Veje C, Mouritsen A, Hagen CP, Tinggaard J, Mieritz MG, Boas M, et al. Pubertal onset in boys and girls is influenced by pubertal timing of both parents. J Clin Endocrinol Metab. 2016;101(7):2667-74.

27. Moal JL, Rigou A, Tertre AL, Crouy-Channel PD, Léger J, Carel J-C. Marked geographic patterns in the incidence of idiopathic central precocious puberty: A nationwide study in France. Eur J Endocrinol. 2018;178(1):33-41.

28. Slap GB. Menstrual disorders in adolescence. Best Pract Res Clin Obstet Gynaecol. 2003;17(1):75-92.

29. Duflos-Cohade C, Thibaud E. Les troubles du cycle menstruel de l'adolescente. Arch Pédiatrie. juill 2000;7(7):767-72.

30. Friberg B, Kristin Örnö A, Lindgren A, Lethagen S. Bleeding disorders among young women: A population-based prevalence study. Acta ObstetGynecol Scand. 2006;85(2):200-6.

31. van Hooff MH, Voorhorst FJ, Kaptein MB, Hirasing RA, Koppenaal C, Schoemaker J. Relationship of the menstrual cycle pattern in 14-17 year old adolescents with gynaecological age, body mass index and historical parameters. Hum Reprod. 1998;13(8):2252-60.

32. Bower R, Dehner LP, Ternberg JL. Bilateral ovarian cysts in the newborn: A triad of neonatal abdominal masses, polyhydramnios, and material diabetes mellitus. Am J Dis Child. 1974;128(5):731-3.

33. DeSa DJ. Follicular ovarian cysts in stillbirths and neonates. Arch Dis Child. 1975;50(1):45-50.

34. Tyraskis A, Bakalis S, Scala C, Syngelaki A, Giuliani S, Davenport M, et al. A retrospective multicenter study of the natural history of fetal ovarian cysts. J Pediatr Surg. 2018;53(10):2019-22.

35. Dolgin SE. Ovarian masses in the newborn. Semin Pediatr Surg. 2000;9(3):121-7.