Gynecology and Obstetrics Clinical Medicine 1 (2021) 83–86

Contents lists available at ScienceDirect

Gynecology and Obstetrics Clinical Medicine

journal homepage: www.keaipublishing.com/en/journals/gynecology-and-obstetrics-clinical-medicine

Analysis of the clinical characteristics and neonatal outcomes of seven cases of pregnancy luteoma discovered incidentally at cesarean section

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ARTICLE INFO

Keywords:
Pregnancy luteoma
Tumor-like ovarian lesion
Ovarian tumor
Masculinization

ABSTRACT

Objective: In this study, we summarize the clinical characteristics and neonatal outcomes of patients with pregnancy luteomas that were identified incidentally at cesarean section in our hospital. We also provide a review of the existing literature relating to this condition.

Methods: A total of seven cases of pregnancy luteoma were enrolled from our hospital into this retrospective study between March 2013 and February 2018. We then evaluated the clinical characteristics and neonatal outcomes of these patients.

Results: All seven patients with pregnancy luteomas found incidentally during Cesarean sections at term as a result of obstetric indications. These masses were unilateral and ranged from 2 to 10 cm in size. All patients underwent partial ovariectomies or oophorocystectomy due to presumptive benign ovarian tumors. Two patients had gestational diabetes and one patient had gestational hypertension. One patient developed hirsutism and a deepened voice. Of the seven newborns, three were girls and four were boys. Physical examinations of the newborns were normal and no virilization was detected among the infant girls.

Conclusion: Pregnancy luteoma may be more common than expected. Better strategies are now needed to educate obstetricians about the clinical features of pregnancy luteoma so that they can avoid unnecessary surgery.

1. Introduction

Pregnancy luteomas, as non-neoplastic tumor-like masses of the ovary, were first described by Sternberg in 1963. Kaitlin provided a summary of cases reported between 1990 until the end of 2010; there were only 20 cases reported in the English literature during this period.[1] Literature searches, carried with Medline, revealed only a few sporadic cases over the last few years. However, the true incidence of pregnancy luteoma has yet to be fully elucidated.

Generally, this disease is discovered incidentally during Cesarean delivery or tubal ligation. These lesions are benign, and can vanish without any specific treatment[1,2]; however, most reports describe the use of partial ovariectomies or oophorocystectomy for presumptive ovarian tumors.[1,3–7]

In occasional cases, the mass can cause abdominal pain due to symptoms associated with compression or torsions.[7–9] In particular, hyperandrogenism may occur in up to 60% of cases involving pregnancy luteomas.[10] Rapisarda et al. reported that the peak maternal serum testosterone level can increase by as much as 76-fold.[11] Furthermore, pregnancy luteoma may have serious short-term and long-term effects on fetal growth and development. For example, Roth reported an infant with signs that were consistent with Antley-Bixler syndrome, disturbed adrenocortical hormone metabolism, and maternal pregnancy luteoma.[12]

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Publishing services by Elsevier on behalf of KeAi

https://doi.org/10.1016/j.gocm.2021.03.006
Received 10 January 2021; Received in revised form 14 March 2021; Accepted 29 March 2021
Available online 24 April 2021

Another factor that inspired us to investigate this disease is that we fully expect a greater number of masses (pregnancy luteomas) to be discovered in future due to the increased use of imaging examinations (ultrasonography and Magnetic Resonance Imaging [MRI]) during pregnancy. However, reports indicate that ultrasonography and MRI cannot distinguish pregnancy luteomas from other ovarian tumors, especially malignancy.[1,13,14] Improved imaging techniques may help to differentiate pregnancy luteoma from malignancy and need to be developed urgently to avoid unnecessary exploratory laparotomy.

Patients with pregnancy may easily undergo unnecessary surgical treatment, although this does not have any significant effect on maternal or fetal health. Further research into the diagnosis and treatment of pregnancy luteoma is important if we manage this condition in an appropriate manner. Such research should involve a greater number of patients.

2. Materials and methods

2.1. Patients

The pregnant women recruited into our study were admitted to the Women's Hospital, Zhejiang University School of Medicine between March 2013 and February 2018; this is one of the largest maternity centers in China. These pregnant women underwent routine examinations in our hospital. Pregnancy luteomas were detected incidentally during Cesarean sections performed due to obstetric indications. The diagnosis was confirmed by pathological examination in all cases. A total of seven patients with pregnancy luteomas were enrolled into our study. The study was approved by the Institutional Review Board in our hospital. Informed consent was obtained from all participants. The clinical characteristics and outcomes of these patients are shown in Table 1.

2.2. Follow-up

The gravidas and fetuses had follow-up interviews at the clinic on postpartum day 42 and telephone follow-up 18 months postpartum irrespective of whether menstruation had returned to normal. The clinical characteristics were recorded by experienced physicians.

2.3. Statistical analysis

Statistical differences were evaluated by SPSS (version 22.0; SPSS, Chicago, IL, USA) and results presented as mean ± SD.

3. Results

Seven patients with pregnancy luteomas were enrolled into this study between March 2013 and February 2018. All of the cases were detected incidentally during Cesarean sections at term. During this period, a total of 88,421 gravidas gave birth in our hospital.

As shown in Table 1, among the seven patients, six were primiparas and one was a multipara. The age of the patients ranged from 29 to 39 years (33.57 ± 4.28 years); three patients were of advanced maternal age. The termination of pregnancies ranged from 37 + 5 to 40 + 4 weeks (38.43 ± 0.98 weeks). The standardized mean Body Mass Index (BMI) in the patients increased from 23.90 ± 4.36 kg/m^2 (confidence interval, 20.4–32.3 kg/m^2) to 29.74 ± 4.87kg/m^2 (confidence interval, 24.6–39.1 kg/m^2); the mean weight gain was 14.71 ± 3.31 kg. Two patients had gestational diabetes mellitus and subsequently sustained good glycemic control without pharmacological intervention. One patient developed pre-eclampsia; interestingly, she was the only patient to complain of masculine changes. Specifically, her voice deepened, and facial hair growth increased during the third trimester; these symptoms were mild and hormonal testing was not performed. The other patients had no symptoms or signs of masculinization. All seven patients underwent ultrasound screening in the first and second trimesters; this testing included the ovaries. No abnormal ovarian findings were detected. The pregnancy luteomas were all detected incidentally at the time of Caesarean section at term. The indications for Cesarean section were as follows: fetal distress in four cases; breech presentation in one case; complete placenta previa in one case; and cephalopelvic disproportion in one case.

The pregnancy luteomas were all unilateral. The contralateral ovaries were normal in terms of their gross appearance and were therefore not evaluated pathologically. The external surface of the masses was bosselated and ranged from 2 to 10 cm in size. In case number 2, multiple nodules were apparent with abundant peripheral blood vessels, as shown in Fig. 1A and B. All of the masses were solid; the cut surfaces were yellow-white or red-tan, fleshy, and soft with hemorrhagic foci. All of the patients underwent oophorocystectomy or partial ovariectomy. Microscopic examinations revealed the diffuse growth of cells with conspicuous eosinophilic cytoplasm, and the follicle-like spaces contained eosinophilic, colloid-like secretions (Fig. 1C.)

Among the seven newborns, there were three girls and four boys. The Apgar scores were all 10-10 after 1–5 minutes. The newborns weighed between 2.77Kg and 5.10Kg (mean: 3.35±0.81Kg). Physical examinations of the newborns were normal and no virilization was detected among the infant girls. The mothers had recovered a normal postpartum

Table 1
The cases with pregnancy luteoma.

Case No.	Age	Gravidity and Parity	Cesarean Indications	Newborns Gender/Weight (Kg)	Complication of Pregnancy	Intraoperative Finding
1	30	G1P0	Fetal distress	Female/3.06	GDM	Right ovary mass about 3.0cm × 3.0cm × 3.0cm
2	29	G2P0	Fetal distress	Female/2.77	pre-eclampsia, virilization	Right ovary mass about 10.0cm × 7.0cm × 6cm
3	37	G2P1	Fetal distress	Male/2.87	GDM, oligohydramnios	Right ovary mass about 2.0cm × 1.5.0cm × 1.5cm
4	30	G1P0	Breech presentation	Male/3.60	/	Right ovary mass about 5.0cm × 4.0cm × 4.0cm
5	32	G1P0	Fetal distress	Female/2.98	oligohydramnios	Right ovary mass about 4.0cm × 3.0cm × 2.0cm
6	39	G2P0	Complete placenta previa	Male/3.10	/	Left ovary mass about 5.0cm × 5.0cm × 4.0cm
7	38	G2P0	Cephalopelvic disproportion	Male/5.10	/	Right ovary mass about 4.0cm × 2.5cm × 2.5cm

GDM, gestational diabetes mellitus.

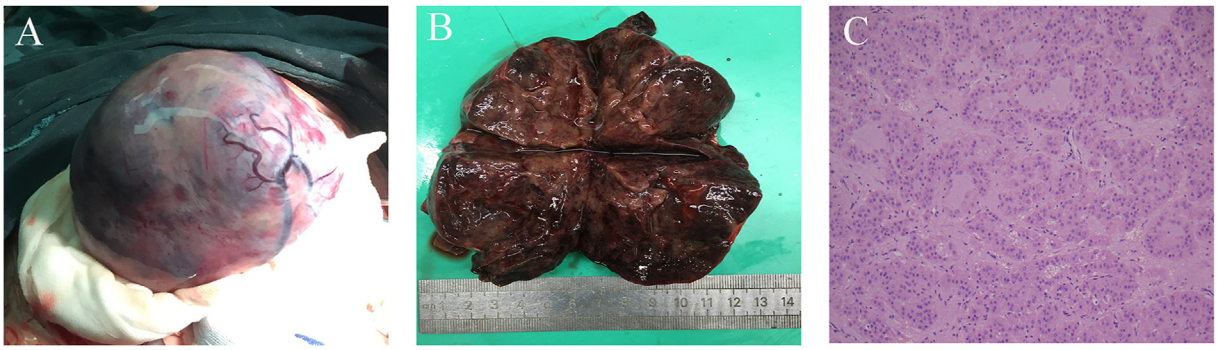

Fig. 1. Luteoma of pregnancy [Case 2]. (A) Gross pathology of the luteoma showed multiple nodules and an abundance of peripheral blood vessels. (B) The cut surface was red-tan, fleshy, and soft with hemorrhagic foci. (C) Microscopic H and E staining of the luteoma showed a patchy and homogenous population of bland cells with an abundant and delicate cytoplasm. There were typical follicle-like spaces, some of which contained colloid-like secretions. Magnificati ×400.

menstruation when assessed during our telephone follow-up, although there were no specific assessments of whether ovarian function was impaired as a result of ovarian surgery.

4. Discussion

We calculated the occurrence of pregnancy luteoma in our hospital to be approximately 7.9 per 100,000 pregnancies. Since all of the cases described herein were discovered incidentally at cesarean section and there was no information relating to the possible number of cases in mothers who underwent vaginal deliveries (and accounting for the majority of the total number of women experiencing labor), the estimated morbidity must be much higher than that reported in the existing literature (200 cases).[1]

As confirmed by other researchers, these lesions are typically discovered at or near term and are rarely symptomatic.[2] All of the patients described herein underwent ultrasonographic scans of their ovaries during early and mid-gestation; there were no abnormal findings, thus suggesting that the pregnancy luteomas grew quickly during the third trimester of pregnancy. Hyperandrogenism may be a valuable clinical symptom to help with diagnosis; however, reports indicate that only a minority of cases showed maternal signs of virilization.[1] Unfortunately, we did not perform androgen testing in these patients; we found that masculinization only affected the patient out of the seven with the largest ovarian mass; it is possible that the symptoms of this patient were related to tumor size.

Does pregnancy luteoma have adverse effects on pregnancy outcome? Previous reports suggest that pregnancy luteoma may coexistence with such conditions as polycystic ovarian syndrome and diabetes.[1,15,16] In our cohort of patients, 2 of the 7 were diagnosed with gestational diabetes mellitus; however, none of these patients had a history of diabetes or polycystic ovarian syndrome. We calculated BMI and weight gain during pregnancy for all 7 women; these data were in line with other pregnant women.[17] In addition, we diagnosed oligohydramnios in two cases. Coincidentally, the only patient showing masculinization in our study developed pre-eclampsia; there are case reports in the literature involving patients who developed pre-eclampsia and had masculinization.[1,18–20] It may be possible that there is an unknown relationship between pregnancy luteoma, gestational hypertension, and masculinization. Another interesting point is that in contrast to most other reports, which reported that patients with pregnancy luteoma were usually multiparous, 6 out of the 7 reported in the current paper were primigravidae; our findings are therefore in line with the review published by Kaitlin Masarie.[1] The clinical significance of parity, if there is any, remains unknown.

Successive pregnancy luteomas that are associated with maternal hyperandrogenism may cause phenotypic variation and masculinization of the external genitalia in female infants.[10,21] These effects can be serious. We will continue to follow up these newborns to investigate the possibility of long-term effects.

The gross characteristics of our patients were generally similar to those recorded in the literature. The size of pregnancy luteomas can range from microscopic to 20 cm in diameter. The gross characteristics of these luteomas have been described as soft, yellow-white to red-tan, fleshy, and circumscribed areas with frequent hemorrhagic foci.[2] However, all of the pregnancy luteomas were unilateral in our series; the literature mostly refers to bilateral cases.[2] Of note, in case 2, we were able to see large vessels around the mass, meaning that this particular pregnancy luteoma had an abundant blood supply.

The clinical setting and gross characteristics of patients may provide major clues to the diagnosis of pregnancy luteoma, although this is not always straightforward.[2] It is puzzling that although earlier reports stated that this tumor-like lesion can vanish without treatment, in most cases, the authors of these reports performed partial ovariectomy or oophorectomy.[1] We were unable to ascertain any further surgical detail from these reports. In 6 of our patients, the surgeons performed oophorocystectomy directly because the patients were being treated for a benign tumor. Case 2 was different; we performed an intraoperative freezing test. The results of this test indicated a “benign lesion, considering pregnancy luteoma”. However, we still performed the partial ovariectomy because the surgeon could not determine whether the lesion would return to normal spontaneously. However, an existing case report described a patient with an intestinal metastatic ovarian tumor that mimicked a pregnancy luteoma; this highlights the fact that conservative management should be recommended very carefully.[22] Therefore, we believe that frozen biopsy is a better strategy during cesarean section for patients with suspected pregnancy luteoma.

Our study had several limitations that need to be considered. This was a retrospective study with a small number of patients; these cases were discovered incidentally. Consequently, there is a lack of systematic examinations, including imaging and androgen tests before and after surgery. Moreover, the specific details of surgery are incomplete.

5. Conclusion

Pregnancy luteoma may be more common than we ever expected. Unnecessary surgery also appears to be common. We hope that our results contribute to a better understanding of the natural history and management of patients with pregnancy luteomas. However, we need more specific tools to help us to recognize this disease in future.

Author contributions

Junhua Shen: Conceptualization, Methodology, Software, Writing - Original Draft, Lanlan Tang: Data curation, Visualization, Genping

Huang: Investigation, Xiaoxia Bai: Supervision. Baohua Li: Writing-Reviewing and Editing, Supervision, Zhengping Wang：Supervision.

Declaration of competing interest

The authors declare no conflict of interest.

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