Uterine hemangioma in pregnancy: a case report and systematic review

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Abstract

Objectives: This systematic review summarizes all published uterine hemangioma cases in pregnant women. Search strategy: The databases PubMed and Scopus were searched systematically. The reference lists of all retrieved articles were also screened. Selection criteria: The online tool Rayyan QCRI was used for registration of the selection process. Articles reporting on cases of uterine hemangioma in pregnancy were included, non-English articles were excluded. Data collection and analysis: Data extraction was done by one reviewer and thereafter verified by the second reviewer. All data were described in a narrative format. Results: Fifteen case reports were included. In most cases, the diagnosis was established by antenatal ultrasound and pregnancy course was uneventful. More than half of the patients developed a postpartum hemorrhage, necessitating a hysterectomy for bleeding control in four cases, although the risk for both seemed lower in those patients in whom the hemangioma was diagnosed before delivery. One case of maternal mortality and two cases of fetal death were reported. There was one case of neonatal respiratory morbidity, although the neonatal data were not routinely reported upon. Conclusion: Current knowledge on uterine hemangioma in pregnancy is limited, but it seems to hold substantial risks for both mother and child. We recommend routine screening for this condition at the standard mid-trimester anomaly scan. Pregnant women with uterine hemangioma should ideally be cared for in centers of expertise. An international registry will help to build a better understanding of this rare pathology. Funding: None.

Uterine hemangioma in pregnancy: a case report and systematic review

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Key words: hemangioma; uterine; pregnancy; case report; review

Tweetable abstract

Uterine hemangioma holds substantial risks for both mother and child during pregnancy.

Introduction

Hemangiomas are benign vascular tumors that originate from either endothelial cells lining the vessels or pericytes that are found outside the vascular wall.[1] They consist of multiple anastomosing vessels lined by a single layer of endothelium. Hemangiomas are named 'capillary' when they are composed of small size capillary vessels, and 'cavernous' if they consist of large anastomosing vascular spaces ('caverns').[1–5] They rarely occur in the uterus and the exact incidence of uterine hemangioma is unknown. Hemangioma can be found at all levels of the uterine wall, although most cases involve the myometrium.[6] The lesion has been described in various age groups and is known to have many heterogenous clinical presentations, commonly reported in the context of obstetric complications.[1–3]

Current literature on uterine hemangioma in pregnancy mainly consists of case reports. The hormonal and physical changes of pregnancy have been proposed to affect these pre-existing lesions. The most reported complication is peripartum hemorrhage which can be life-threatening.[2,7] Diagnosis is often made on hysterectomy specimens or more recently through antepartum imaging, by ultrasound (US) and/or magnetic resonance imaging (MRI).[8]

Herein we present a recent case in our tertiary care center followed by a systematic review of all published uterine hemangioma cases in pregnant women.

Case report

A 30-year-old nulliparous patient was referred to our center, University Hospitals Leuven, for a suspicion of a molar pregnancy. The patient had an unremarkable medical and familial history. On initial ultrasound examination, an intrauterine pregnancy with crown-rump length (CRL) corresponding to a gestational age of 8 weeks 4 days was seen. The trophoblast appeared normal, but the myometrium was overall diffusely thickened due to venous plexuses that contained low flow rates**(figure 1)** . The presumptive diagnosis of a uterine hemangioma was confirmed on MRI at 10 weeks of gestation that demonstrated marked T2-hyperintens, T1-hypointens and non-diffusion restrictive enlargement of the entire myometrium enclosing multiple vessels **(figure 2)** .

The course of the pregnancy was rather uneventful, except for a minor bleeding episode at 13 weeks of pregnancy and a short admission at 28 weeks due to a single episode of nonspecific lower abdominal pain. The sonographic appearance of the myometrium remained unchanged during pregnancy **(figure 3)** . The patient was hospitalised from the 36^{th} week of pregnancy onwards for observation to address the increased intra- and postpartum bleeding risk.

At 38 weeks and 5 days, labour was induced by means of prostaglandin E2 administration and subsequent artificial rupture of the membranes. This was followed by oxytocin labour augmentation and a spontaneous vaginal delivery of a healthy son weighing 2835 grams. Apgar scores were 9/10/10 and umbilical artery pH was 7.29. Intravenous carbetocin 100 µg and tranexamic acid 1 g were administered immediately, but within minutes a primary postpartum hemorrhage occurred with the placenta still in-utero. Sulprostone 500 µg perfusion was initiated, and a manual removal of the placenta was done. Additionally, a gentle curettage was performed to remove some retained membranes after which the uterus atony resolved, and the bleeding ceased. The total blood loss was estimated to be 1200 mL. Both the mother and newborn had an unremarkable postpartum course. Prophylactic postpartum low-molecular-weight heparin was continued for 6 weeks. After 3 months the myometrial hemangioma was markedly regressed on ultrasound. A whole-body MRI performed 8 months after delivery additionally noted a small 11 mm hemangioma in the liver segment 7.

Written consent was obtained from the patient whose case is presented above.

Methods

The protocol for this systematic review was prospectively registered on The International Prospective Register of Systematic Reviews (PROSPERO, registration number CRD42021237519). We reported it according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[9]

Types of studies

We included case reports, case series, randomized studies, and case control studies. All articles of other types (systematic reviews, narrative review articles and studies published only as abstracts) were excluded. Non-English articles were also excluded, except for those with an English abstract that already provided the primary outcomes.

Types of participants

Study participants were pregnant women with a hemangioma of the uterine corpus, diagnosed either before, during or directly after pregnancy. Articles reporting on non-pregnant women with uterine hemangioma that provided information on their obstetrical antecedents were also included.

Outcomes

The primary outcomes were maternal and neonatal (until discharge) mortality and morbidity. Secondary outcomes were the occurrence of pregnancy complications, preterm delivery rate, perinatal blood loss, perinatal hysterectomy incidence and neonatal ICU-admission.

Search strategy

We searched the electronic databases PubMed and Scopus from their inception until 21 February 2021 using the following search terms: "((hemangioma) OR (cavernous) OR (vascular malformation)) AND (pregnancy) AND (uterus)". We also screened the reference list of all retrieved articles to identify additional eligible articles not captured by our electronic search, thereby identifying 2 additional case reports.

Process of study selection, data extraction and risk of bias assessment

The online tool Rayyan QCRI was used for registration of the selection process.[10] Duplicate articles were automatically excluded. Two assessors independently screened all titles and abstracts. Eligible articles were retained for full-text reading. Uncertainties at each stage were discussed and resolved by consensus with a low threshold for inclusion.

One reviewer extracted all data on pregnancy course and complications occurring during delivery and the postpartum period, which was thereafter verified by the second reviewer. Uncertainties at each stage were again discussed and resolved by consensus. All data were described in a narrative format.

Results

Of the initial 476 identified articles, 23 full text articles were assessed for eligibility. Eventually, 15 case reports were included in this review **(figure S1)** . Baseline patient characteristics, clinical presentation, mode of diagnosis, pregnancy course and the maternal and neonatal outcomes in the 15 pregnancies described in these articles are given in **table S1 and S2.**

Of the 15 pregnancies, two (2/15, 13.3%) resulted in a stillbirth possibly due to the uterine hemangioma. The first one occurred at 28 weeks after massive thrombosis of the uterine and placental vessels, the latter following acute rupture of the uterine hemangioma at 36 weeks. Another two pregnancies were delivered preterm (2/15, 13.3%). One patient delivered at 35 weeks after preterm prelabour rupture of the membranes (PPROM) at 26 weeks, and a second patient had a cesarean section at 30 weeks due to progressive abdominal discomfort and the assumed bleeding risk of the hemangioma. Forty percent of women (6/15, 40.0%) went into labour spontaneously, which resulted into a vaginal delivery in four cases. Most patients were delivered by cesarean section (10/15, 66.7%), of which seven (7/10, 70%) were unplanned/in an emergency setting. The postpartum period was complicated by a hemorrhage in eight women (8/15, 53.3%), which necessitated a hysterectomy in four cases (4/8, 50%). Two women developed progressive hypovolemic shock (2/8, 25%). Of those for whom data was provided (5/8, 62.5%), all had an estimated blood loss of [?] 1000 mL. Furthermore, another two patients developed a pulmonary embolism in the postpartum period, ultimately fatal in one of them. Perinatal outcomes were mentioned in only six reports (6/15, 40%). Only half of these cases (3/6, 50%) had an uneventful outcome. One case of respiratory problems due to preterm birth at 30 weeks was described beyond the two stillbirths mentioned above.

The hemangioma was diagnosed before delivery in the majority of cases (10/15, 66.7%), generally during the second trimester of pregnancy. Most often, symptoms such as abdominal discomfort, dyspnea, or vaginal bleeding and/or the finding of an enlarged uterus led to a work-up. Four patients were referred for abnormal ultrasound findings, which in all but one case were suspicious for a partial mole. The antenatal diagnosis was generally based on ultrasound findings, MRI was used to confirm the hemangioma in only one patient.

Half of the patients (5/10, 50%) with an established diagnosis of hemangioma before delivery had a non-planned cesarean section. In two of these patients (2/5, 40%), this was for reasons related to the hemangioma: one patient had a cesarean section for fetal death at 28 weeks and another patient was delivered at 30 weeks due to progressive abdominal discomfort as mentioned earlier. Five of the 10 antenatal diagnosed patients (5/10, 50%) developed a postpartum hemorrhage, which necessitated a hysterectomy in only one of them. Among the patients with an antenatal diagnosis of a uterine hemangioma, one more patient underwent a hysterectomy at 17 weeks because of recurrent syncopes and the presumed risk of uterine rupture.

These numbers contrast with the undiagnosed group in which three out of the five patients (3/5, 60%) had a postpartum hemorrhage and a hysterectomy was necessary in all of them (3/3, 100%). There were no cases of maternal mortality in the group of antenatal diagnosed patients.

Discussion

Main findings

Our literature search identified 15 cases of uterine hemangioma during pregnancy. High rates of complications were encountered in these women, particularly peripartum hemorrhage that in some cases even necessitated a hysterectomy. Above and beyond the clear maternal risks, there is also significant fetal-neonatal morbidity.

Strengths and limitations

As far as we know, this is the first systematic review reporting on uterine hemangioma and pregnancy outcomes. We have adopted the international PRISMA guidelines in our study methodology. Since it is clear from this review that uterine hemangioma can go unnoticed during pregnancy, it begs the questions whether there is an underreporting of uncomplicated outcomes.

Interpretation (in light of other evidence)

As this is the first systematic review on uterine hemangioma in pregnancy, a comparison of our findings with literature is difficult. Establishing the diagnosis of a uterine hemangioma before delivery seems beneficial for maternal outcome, as we found a lower number of postpartum hemorrhages and peripartum hysterectomies in this patient group. This highlights the importance of delivery planning to anticipate the peripartum bleeding risk. On the one hand, antenatal diagnosis is relatively straightforward and can be made by standard 2D ultrasound. Once identified the patient can be referred to a tertiairy care center for more comprehensive care. On the other hand however, this could lead to overtreatment, as in the case where a hysterectomy was performed at 17 weeks of gestation because of the assumed risk of uterine rupture. Furthermore, subsequent pregnancies may lead to more morbidity since four of the included patients were multiparous and half of them developed a severe postpartum hemorrhage with the need for hysterectomy. Data on obstetrical antecedents were provided for only one patient, who had an uneventful pregnancy followed by a spontaneous post-term delivery complicated by placental retention and a postpartum hemorrhage.[17]

Future perspective

Data are currently too limited to provide clear guidelines for diagnosis and management of uterine hemangioma in pregnant women. It is also unclear whether additional imaging beyond standard 2D ultrasound adds any value. Therefore, we strongly recommend the establishment of an international registry for uterine hemangioma in pregnancy to obtain better knowledge on this subject.

Conclusion

Although our current knowledge on uterine hemangioma during pregnancy is limited to 15 case reports, the condition seems to hold substantial risks for both mother and child. Therefore, these pregnancies should ideally be followed-up and cared for in centers of expertise. Routine screening for this clearly visible condition is feasible and possibly sufficient at the standard mid trimester anomaly scan. We feel all obstetricians and sonographers should at least eyeball the uterus during this evaluation. An international registry for uterine hemangioma in pregnancy would be of great value to obtain better knowledge on this subject and could serve as a basis for the development of clinical management guidelines.

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Declaration of interest statement

No potential competing interest was reported by the authors.

Author contribution

All authors have contributed to the writing of this paper. EB and JvdM performed the literature search, extracted the data and merged corrected work.

References

1. Bhavsar T, Wurzel J, Duker N. Myometrial cavernous hemangioma with pulmonary thromboembolism in a post-partum woman: A case report and review of the literature. J Med Case Rep 2012;6:397.

2. Aka KE, Horo GA, Fomba M, Kouyate S, Koffi AK, Konan S et al. A rare case of important and recurrent abnormal uterine bleeding in a post partum woman caused by cavernous hemangioma: A case report and review of literature. Pan Afr Med J 2017;28:130.

3. Chou WY, Chang HW. Uterine hemangioma: A rare pathologic entity. Arch Pathol Lab Med 2012;136(5):567–71.

4. Virk RK, Zhong J, Lu D. Diffuse cavernous hemangioma of the uterus in a pregnant woman: Report of a rare case and review of literature. Arch Gynecol Obstet 2009;279(4):603–5.

5. Comstock CH, Monticello ML, Johnson TW, Wechter D. Cavernous Hemangioma: diffuse enlarged venous spaces within the myometrium in pregnancy. Obstet Gynecol 2005;106(5 Pt 2):1212-4

6. Benjamin MA, Yaakub HR, Telesinghe PU, Kafeel G. A rare case of abnormal uterine bleeding caused by cavernous hemangioma: a case report. J Med Case Rep 2010;4:136.

7. Djunic I, Elezovic I, Ljubic A, Markovic O, Tomin D, Tadik J. Diffuse cavernous hemangioma of the left leg, vulva, uterus, and placenta of a pregnant woman. Int J Gynecol Obstet 2009;107(3):250-1.

9. Thanner F, Suetterlin M, Kenn W, Dinkel HP, Gassel AM, Dietl J et al. Pregnancy-associated diffuse cavernous hemangioma of the uterus. Acta Obstet Gynecol Scand 2001;80(12):1150–1.

10. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. BMJ 2009; 339:b2535

11. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev 2016; 5(1):210..

12. Dawood MY, Teoh ES, Ratnam SS. Ruptured haemangioma of a gravid uterus. J Obstet Gynaecol Br Commonw 1972;79(5):474-5.

13. Gallegos SA, Gaona JMG, Torres BV, Sosa SEI, Pérez MÁS, Huerta MEG. [Diffuse cavernous hemangioma of the uterus diagnosed during pregnancy. Case report] Ginecol Obstet Mex 2011;79(7):447–51.

14. Lotgering FK, Pijpers L, van Eijck J, Wallenburg HCS. Pregnancy in a patient with diffuse cavernous hemangioma of the uterus. Am J Obstet Gynecol 1989;160(3):628–30.

15. Milton PJ, Thonet RG. Myometrial Haemangioma a Rare Cause of Severe Menorrhagia Case Report. Br J Obstet Gynaecol 1981;88(10):1054-5.

16. Reiffenstuhl G. [Diffuse cavernous myometric angiomatosis of the pregnant uterus and its clinical significance]. Geburtshilfe Frauenheilkd 1984;44(9):579–82.

17. Sütterlin MW, Müller T, Rehn M, Rempen A, Dietl J. Successful abdominal delivery in a woman with sonographic diagnosis of diffuse cavernous hemangioma of the uterus. Am J Perinatol 1998;15(7):423–5.

18. Uotila J, Dastidar P, Martikainen P, Kirkinen P. Massive multicystic dilatation of the uterine wall with myometrial venous thrombosis during pregnancy. Ultrasound Obstet Gynecol 2004;24(4):461–3.

19. Weissman A, Talmon R, Jakobi P. Cavernous hemangioma of the uterus in a pregnant woman. Obstet Gynecol 1993;81(5):825–7.