

CASE REPORT

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Advanced tubal pregnancy at 34 weeks with eclampsia and HELLP syndrome: a case report and literature re

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Abstract

Background Tubal ectopic pregnancies in the late stages of pregnancy are uncommon, and reports on their complications are scarce. We present the case of a woman who had a tubal ectopic pregnancy at around 34 weeks and developed severe pre-eclampsia complications.

Case A 27-year-old woman presented to our hospital several times with vomiting and convulsions. A physical exam revealed hypertension, scattered ecchymosis, and a large abdominal mass. A computed tomography (CT) scan performed in an emergency revealed an empty uterus, a stillbirth baby in the abdominal cavity, and a crescent-shaped placenta. Blood tests revealed that the patient had a low platelet count and clotting dysfunction. Laparotomy confirmed advanced right fallopian tube pregnancy without rupture, and salpingectomy was performed. Pathological examination revealed a significantly thickened tubal wall, adhesion of the placenta, and poor placental perfusion.

Conclusion The unusually thickened muscular layer of the tube may be one of the reasons for tubal pregnancy progressing to an advanced stage. Placenta adhesion and the special site to which it is attached reduce the risk of rupture. The detection of a crescent-shaped placenta on imaging may aid in the accurate diagnosis, distinguishing between abdominal and tubal pregnancy. Women with advanced ectopic pregnancy are more likely to develop pre-eclampsia and have poorer maternal-fetal outcomes. These negative outcomes may be influenced by abnormal artery remodeling, villous dysplasia, and placental infarction.

Keywords Tubal pregnancy, Pre-eclampsia, Eclampsia, HELLP syndrome

Background

Tubal pregnancy, which accounts for 94% of all ectopic pregnancies [1], is always treated early for the typical clinical manifestations of amenorrhea, bleeding, and abdominal pain, as well as massive intraperitoneal hemorrhage. Almost 80% of them have ruptured fallopian tubes during early pregnancy due to a thin wall [2, 3]. Therefore, there are few reports of late-stage cases, particularly with complications that always occur in normal pregnancy. We present the case of a woman with tubal pregnancy at 34 weeks who was admitted to our hospital for pre-eclampsia with a series of severe complications rather than abdominal pain or massive hemorrhage.

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Case report

On August 18, 2022, a 27-year-old woman, gravida 3, para 1, was referred to our hospital with complaints of vomiting and convulsions. She was unconscious and under the influence of intravenous diazepam when she arrived. Her last menstrual period was unknown; however, her relatives reported an irregular menstrual pattern for 8 months. Her first child died at 27 weeks for unknown reasons, and she gave birth to a live male baby in our hospital a year later. Albuminuria was confirmed in both pregnancies without hypertension. Her family history was unremarkable.

Her blood pressure, respiratory rate, pulse rate, and temperature were all 190/139 mmHg, 25/min, 150/min, and 36.8°C, respectively, on physical examination. Her skin was covered in ecchymosis, and she had significant edema in the lower part of her shank. A soft mass with a fetus of more than 8 months and no heart tones was discovered during an abdominal examination using Doppler ultrasound. Without dilation, a vaginal examination revealed a long, thick cervix.

Her laboratory parameters were abnormal; alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, amylase, and creatinine levels were elevated up to 195 U/L (normal reference value: 7–40 U/L), 755 U/L (13–35 U/L), 2355 U/L (120–250 U/L), 227 U/L (0–100 U/L), and 341.6 μmol/L (41–73 μmol/L), respectively. Blood clotting test revealed coagulation dysfunction, with an activated partial thromboplastin time of 24.00 s, fibrin degradation product level of 94.10 mg/L, and D-dimer level of 22.74 mg/L. Her hemoglobin levels were normal, but her platelet count had dropped to $46 \times 10^9/L$, and her proteinuria was +2.

An abdominal ultrasound revealed an empty uterus and an extra-uterine fetus with no heartbeat or movement; the fetus' estimated gestational age was 34 weeks. Following contrast-enhanced CT, these findings were confirmed (Fig. 1). An abdominal pregnancy was thus suspected. A CT scan also revealed mild cerebral edema (Fig. 2), hydrocholecystitis, and an enlarged pancreas.

An emergency laparotomy was performed based on the findings of abdominal pregnancy and eclampsia. The abdomen was entered without incident while under general anesthesia. A female stillbirth weighing 2.1 kg was delivered from the intact amniotic sac, which was completely enveloped in the right unruptured salpinx. The uterus, left fallopian tube, and ovaries appeared normal (Fig. 3). The placenta measured 15 × 10 × 2 cm in size and covered the majority of the ampulla cavity. Due to the dense adhesion, the surgeons were unable to separate it from the tissue. A right salpingectomy was carried out. The total amount of blood lost was 800 mL. Six units of cryoprecipitate and four units of packed fresh frozen



Fig. 1 Abdominal CT revealing an empty uterus and a longitudinal fetus outside

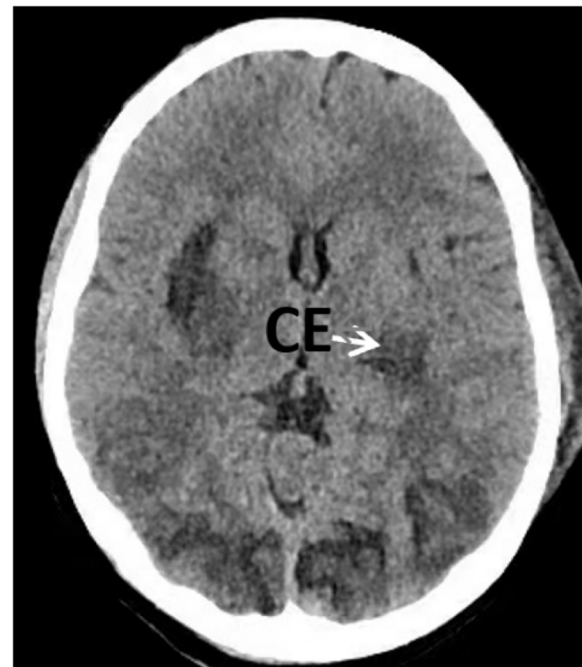


Fig. 2 Head CT revealing extensive narrowing of the cerebral sulcus and a decrease in the density of the bilateral basal ganglia and centrum semiovale, indicating cerebral edema

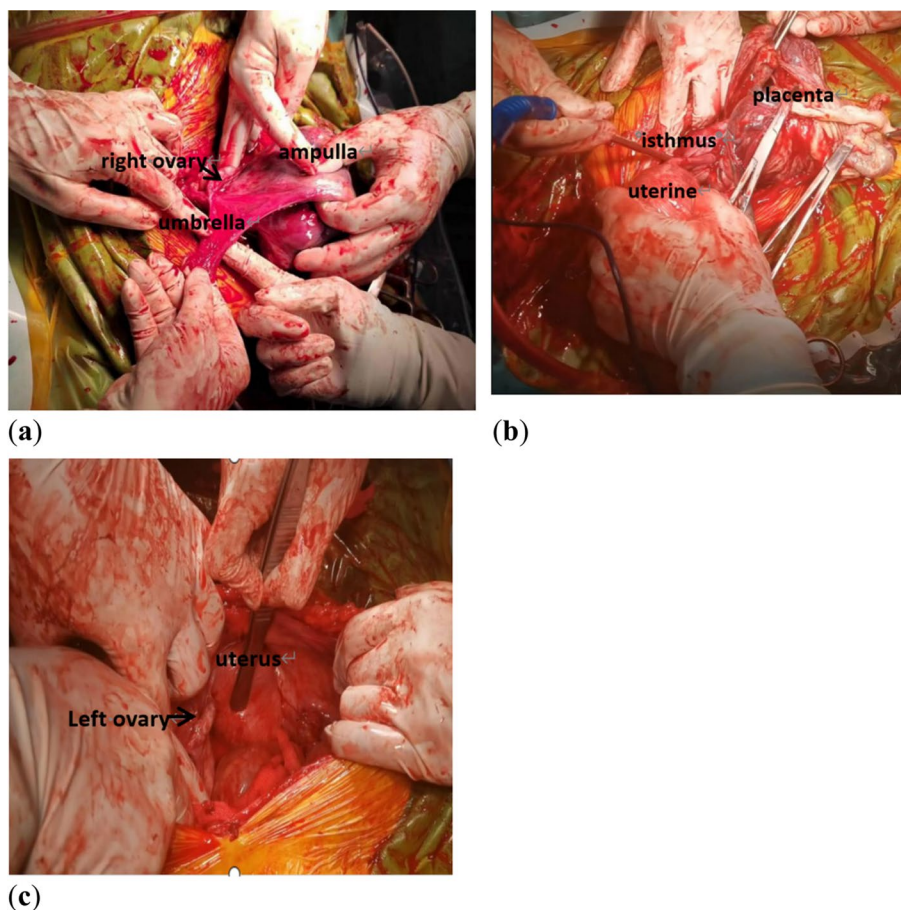


Fig. 3 The placenta was located in the enlarged ampulla of the right fallopian tube, which was connected to the ipsilateral horn via the thickened and prolonged isthmus. The left fallopian tube, bilateral ovaries, and uterus were normal in appearance

plasma were transfused during the procedure. Following the operation, she was transferred to the intensive care unit. To control blood pressure, nitroglycerin and urapidil were administered intravenously via a micro-pump. Additionally, concentrated platelets were infused to boost counts, and ceftriaxone was given to prevent infection. Fortunately, the patient regained consciousness 2 days later and was released 18 days later. A one-month follow-up visit revealed normal blood pressure and no albuminuria.

The myometrium of the tube was significantly thickened, and the myocytes were hypertrophic, according to histopathological examination. Furthermore, the placenta had adhered directly to the musculature due to the absence of the decidual plate. There were no trophoblasts invading the inner wall of the poorly remodelled artery, and a large number of villus cells had lost their nuclei, with syncytiotrophoblast nuclei aggregating along the villi, known as syncytial knots; some terminal villi were elongated, less branched, and sparse, and some did not have vessels (Fig. 4).

Discussion and conclusion

Why some tube pregnancies can reach the second or third trimester?

The tube wall struggles to accommodate the gradually increasing sac and trophoblast erosion, frequently resulting in rupture at 7.2 ± 2.2 weeks [4]. However, a few cases of advanced gestation have been reported: 14 [5], 15 [6], 17 [7], 29 [8], 42 [9], 45, and 50 [10] weeks. In our case, an 8-month-old fetus and appendage were discovered in the intact tube cavity and were evaluated by CT and ultrasound at 34 weeks. According to Lichtenstein and Schumann, placental development occurs at a point along the mesosalpinx attachment line, and adequate blood supply and greater elasticity of the tube wall are important factors. Christopher proposed that adhesion could have also been a source of blood supply for the sac [11]. In our case, the patient did not have synechia surrounding the oviduct; however, her placenta almost completely covered the inner side of the tube, including the location mentioned by Lichtenstein and Schumann. We also noticed that the thickness of the tube wall was approximately

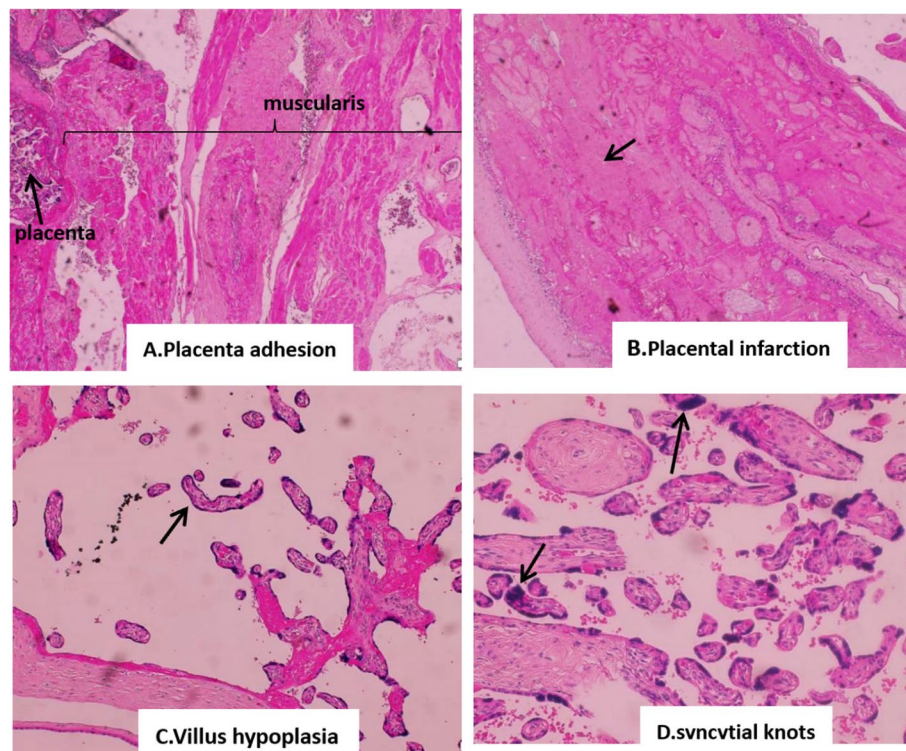


Fig. 4 Pathological findings under a microscope revealing several remarkable manifestations and no artery remodeling. **A** The muscular layer of the oviduct wall was obviously thickened, the decidua was absent, and the placenta was adhering directly to the muscularis; **B** Most trophocytes had lost their nuclei, with inadequate blood supply; **C** Several terminal villi had become elongated, less branched, and sparse and some did not have vessels; **D** Aggregation of syncytiotrophoblast nuclei was along villi to form syncytial knots

0.5 cm, which was significantly thicker than normal; we suspected that these two factors were the primary causes of the no rupture. Pathological examination revealed only a few hypertrophic myocytes, which resembled the myometrium in a normal pregnancy.

How to distinguish tubal pregnancy from abdominal pregnancy in the advanced trimester?

A paraovarian mass, thickened fallopian tube, uterine endometrium with a ≤ 10 mm thickness, and a high echo are all indicators of an early tubal pregnancy [12]. Based on these considerations, early diagnosis becomes simple. On the other hand, sonographic findings based on diagnosis are less useful in the advanced stage and always mimic abdominal pregnancy until laparotomy is performed for similar clinic manifestations and imaging characteristics [13, 14]. In our case, the woman did not have abdominal pain and mistook her irregular bleeding for a menstrual disorder, causing her to miss her early ultrasonic examination. When she was admitted to the hospital in late pregnancy, her condition was misdiagnosed as abdominal pregnancy until the surgeon entered his abdominal cavity.

According to Joseph et al., a well-defined gestational sac with a crescent placenta most likely represented a tubal pregnancy in the second trimester. In contrast, a missshapen sac with a flattened placenta most likely represented an abdominal pregnancy [14]. We also discovered the same crescent-shaped placenta in the MRI figure reported by Baruah [13]. After that, we reviewed our CT images and discovered the same crescent-shaped placenta (Fig. 5). While the placenta is obviously attached to the inner side of the fallopian tube, it is slightly curled inward to accommodate the round tube cavity, giving the placenta the appearance of a curved moon when viewed longitudinally. In an abdominal pregnancy, however, the placenta does not have to be curved because it usually lies flat on the surface of the omentums, bowel, or mesentery. By using different CT or MRI imaging, we can distinguish tubal pregnancy from an abdominal pregnancy. These findings support our recommendation of CT as an alternative technique for distinguishing between these two advanced extra-uterine pregnancies without considering the fetus. In emergency rooms, CT scans are more easily obtained than MRIs.

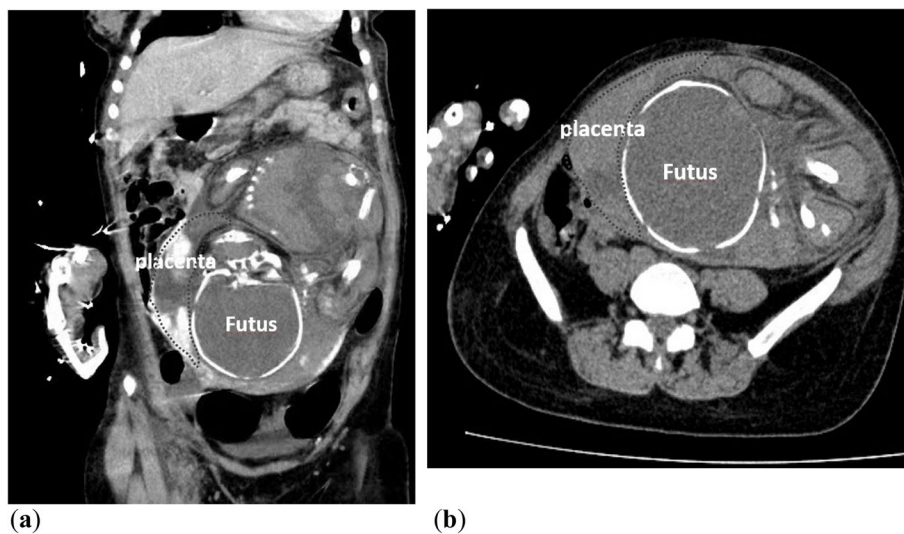


Fig. 5 Sagittal- or coronal-view CT revealing crescent placenta

What is the status of pre-eclampsia in ectopic pregnancies?

Worldwide, 3-5% of intrauterine pregnancies have pre-eclampsia [15]. Except for a few case reports, there are no statistics on ectopic pregnancy due to its low incidence. Using the keywords “ectopic/extra-uterine/tubal/abdominal/residual horn pregnancy” and “hypertensive disorder of pregnancy/pre-eclampsia/eclampsia/HELLP syndrome/thrombocytopenia/coagulation dysfunction” in PubMed, we collected 17 English reports, including 26 cases with hypertensive disorder of pregnancy or pre-eclampsia and relative complications” (Table 1) [16–32]. In summary, almost all patients had pre-eclampsia (25, 96.15%), with 24 having severe pre-eclampsia (92.31%) and 9 having eclampsia (34.62%), both of which were significantly higher than those observed in normal pregnancies as reported by Baig et al. (34.5 and 8.5%, respectively) [33]. However, until ours, no case of HELLP syndrome has been reported. In addition, there were 15 fetal or neonatal deaths, 7 had intrauterine growth restriction, and 12 were low-birth-weight infants, except for 9 live births and 2 unknown births. Ectopic pregnancy with pre-eclampsia appears to have negative consequences for both the mother and the fetus.

Although the pathogenesis is complex, most researchers believe that impaired extravillous trophoblast infiltration, which results in abnormal spiral artery remodeling, causes maternal vascular malperfusion and resistance elevation [34, 35]. What about in the case of a tubal pregnancy? For the first time, the pathological characteristics of the placenta in an

ectopic pregnancy with pre-eclampsia were revealed in our report. Because the decidua was missing, the placenta attached directly to the musculature, as Radaelli reported [36]. The placenta was severely infarcted, and the terminal villi were underdeveloped. Because of endometrial agenesis of the salpinx tissue and insufficient blood supply, artery remodeling may have been abnormal, resulting in poor placental perfusion and possibly causing pre-eclampsia in women with advanced tubal pregnancy.

Hypoperfusion of the placenta leads to placental ischemia and placental factors release into the maternal circulation. These events trigger a series of immune responses and lead to various complex and serious manifestations [36–39]. It is not known if there will be a more intense response in women with tubal pregnancy with less placental perfusion. Except for eclampsia and HELLP syndrome, this women’s brain, gallbladder, pancreas, and kidneys were all involved. As mentioned above, women with ectopic pregnancy with the hypertensive disorder may have a higher risk of developing severe conditions. However, Hailu et al. and Han et al. reported that there is no clue to manifest this relationship [32, 40], and more clinical case studies and explorations are needed.

Advanced tubal pregnancy is uncommon. The unusually thickened muscular layer, placenta adhesion, and the unique location of placenta implantation could be the cause. The identification of crescent-shaped placenta on imaging is valuable in the accurate diagnosis, distinguishing from abdominal pregnancy. Physicians

Table 1 Cases of ectopic pregnancy with the hypertensive disorder

Author	Mother						Fetus	
	Gestation	Sac site	Eclampsia	Severe PE features	Postoperative complications	Outcomes	Weight(kg)	outcomes
1. EDWARD Ar, LEN, 1928	32 ⁺⁶ weeks	Abdominal cavity	yes	no	Placental retention phlogosis	recovery	1.93	died (8 h later)
2. DR.A.FLASH, 1938	33 ⁺⁴ weeks	Abdominal cavity	no	SP ≥ 160 or DP ≥ 110	no	recovery	2.55	alive
3. C.B. PRIDE, 1942	18 weeks	ovary	yes	no	hemorrhage	died	unknown	stillbirth
	term	tube	yes	no	no	died	3	stillbirth
	unknown	unknown	yes	no	no	died	unknown	stillbirth
	6 + m	Abdominal cavity	yes	no	no	recovery	unknown	stillbirth
	8 m	Abdominal cavity	yes	no	no	recovery	unknown	stillbirth
	term	Abdominal cavity	yes	no	psychosis	recovery	1.93	died (8 h later)
4. Fred Benjamin, 1961	8 m	Abdominal cavity	yes	no	hemorrhage	died	unknown	unknown
	34 ⁺³ weeks	Abdominal cavity	no	SP ≥ 160 or DP ≥ 110	no	recovery	2.27	alive
5. M Felbo, 1966	36 weeks	Abdominal cavity	no	SP ≥ 160 or DP ≥ 110	no	recovery	2.41	alive
	37 weeks	abdominal cavity	no	SP ≥ 160 or DP ≥ 110	hemorrhage	recovery	3	alive
6. JOHN F. J. CLARK, 1967	38–39 weeks	abdominal cavity	no	SP ≥ 160 or DP ≥ 110 headache	no	recovery	unknown	stillbirth
	36–38 weeks	abdominal cavity	no	SP ≥ 160 or DP ≥ 110	no	recovery	unknown	unknown
7. W.G. Paterson, 1975	37 ⁺⁴ weeks	broad ligament	no	SP ≥ 160 or DP ≥ 110	hemorrhage	recovery	2.03	alive
8. R.W. Baehler, 1975	term	abdominal cavity	no	no	no	recovery	1.96	alive
9. K.J. ANDERTO, 1976	35 ⁺⁴ weeks	abdominal cavity	no	SP ≥ 160 or DP ≥ 110	no	recovery	2.1	stillbirth
10. C.C. Ekwempu, 1979	36 + weeks	abdominal cavity	no	no(2+ proteinuria)	no	recovery	3.15	Died (4 days later)
11. J. MOODLEY, 1987	39 weeks	abdominal cavity	no	SP ≥ 160 or DP ≥ 110 Headache nausea	no	recovery	3.1	alive
	26 weeks	abdominal cavity	no	SP ≥ 160 or DP ≥ 110	no	recovery	0.6	Died (several hours later)
12. J.O. Emembolu, 1989	26 weeks	abdominal cavity	no	SP ≥ 160 or DP ≥ 110 headache blurred vision	no	recovery	unknown	unknown
13. Walter F. Piering, 1993	37 weeks	abdominal cavity	no	SP ≥ 160 or DP ≥ 110	no	recovery	2.8	stillbirth
14. Hiroyuki Seki, 1997	30 weeks	ovary	no	SP ≥ 160 or DP ≥ 110 renal dysfunction	no	recovery	1.40	stillbirth
15. Helga M. de Muelenaere, 2003	33 weeks	abdominal cavity	no	SP ≥ 160 or DP ≥ 110 thrombocytopenia	no	recovery	1.6	stillbirth
16. B.A. Ekele, 2007	8 m	abdominal cavity	yes	SP ≥ 160 or DP ≥ 110	hemorrhage	recovery	1.1	stillbirth
17. Hailu, 2017	37 + 2 weeks	abdominal cavity	no	headache blurred vision	no	recovery	1.8	alive

should also keep an eye out for complications; women with advanced-stage ectopic pregnancy are more likely to develop pre-eclampsia and have poorer maternal-fetal outcomes. These negative outcomes may be influenced by abnormal artery remodeling, villous dysplasia, and placental infarction.

Abbreviations

HELLP	Hemolysis, elevated liver enzymes, and low platelets
MRI	Magnetic resonance imaging
CT	Computed tomography

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Authors' contributions

Conceptualization, Yang Liu, Xiaoping Xu and Qian Liu were involved in drafting the manuscript. Yang Liu and Xiaoping Xu wrote the paper, and the manuscript was reviewed and edited by Xiaolan Luo, Bin Cai, Jingyuan He and Ruiqian Liu. All authors read and approved the final manuscript.

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Availability of data and materials

The data presented in this study are available on request from the corresponding author.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Deyang People's Hospital. Informed consent was obtained from all subjects involved in the study.

Consent for publication

Written informed consent has been obtained from the patient to publish this paper.

Competing interests

The authors declare no conflict of interest.

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References

- Suresh A, Devasia JM, Adla B, Balachandran A, YVS. A study on ectopic pregnancies in a tertiary care Centre. *J Evid Based Med Healthcare*. 2019;6(24):1654–8.
- Li P-C, Lin W-Y, Ding D-C. Risk factors and clinical characteristics associated with a ruptured ectopic pregnancy: a 19-year retrospective observational study. *Medicine*. 2022;101(24):e29514.
- Kellan Schallert MD, DeAngelis G, et al. Common and uncommon imaging presentations of ectopic pregnancy. *Contemp Diagnostic Radiol*. 2018;41(15):1–8.
- Gari R, Abdulgader R, Abdulqader O. A live 13 weeks ruptured ectopic pregnancy: a case report. *Cureus*. 2020;12(10):e10993.
- Elmoheen A, Salem W, Eltawagny M, et al. The largest tubal pregnancy: 14th week. *Case Rep Obstet Gynecol*. 2020;2020:4728730.
- Stremick JK, Couperus K, Ashworth SW. Ruptured tubal ectopic pregnancy at fifteen weeks gestational age. *Clin Pract Cases Emerg Med*. 2019;3(1):62–4.
- Drakou A, Cosmo E, Ehrstedt C, et al. Tubal pregnancy with fetus in situ in the 17th gestational week, a case report. *Lakartidningen*. 2020;117:FX4F.
- Hong LJ, Chen SS, Oshiro BT. Third trimester tubal pregnancy. A case report. *J Reprod Med*. 2015;60(1–2):83–6.
- Frachtman KG. Unruptured tubal term pregnancy. *Am J Surg*. 1953;86(2):161–8.
- van der Bijl P, Mabesa TP. Tubal pregnancy beyond term. *S Afr Med J*. 2007;97(3):184–6.
- Schokman CM. Advanced tubal pregnancy: a case of survival of mother and baby. *Aust N Z J Obstet Gynaecol*. 1966;6(2):171–4.
- Chu R-R, Liu D-F, Wang M, Liu L. Ultrasonographic diagnosis of early unruptured tubal pregnancy in a community hospital. *J Int Med Res*. 2020;48(5):0300060519894436.
- Baruah S, Latthe P, Downey GP. Presentation of advanced tubal pregnancy. *J Obstet Gynaecol*. 2004;23(4):435–6.
- Liu J, Khan A, Johnson S, Grigorian C, Li T. The usefulness of gestational sac and placental sonographic morphology in differentiating between second-trimester tubal and abdominal pregnancy: case report and a review of literature. *J Clin Ultrasound*. 2014;42(3):162–8.
- Abalos E, Cuesta C, Grosso AL, Chou D, Say L. Global and regional estimates of pre-eclampsia and eclampsia: a systematic review. *Eur J Obstet Gynecol Reprod Biol*. 2013;170(1):1–7.
- Allen E. Abdominal pregnancy complicated by eclampsia. *Am J Obstet Gynecol*. 1933;25(5):753–4.
- Lash AF. Reported a case of preeclampsia in an abdominal pregnancy. *Am J Obstet Gynecol*. 1938;95(5):139–40.
- Pride CB, Morgantown WV, Rucker MP, Richmond V. Eclampsia and ovarian pregnancy. *Am J Obstet Gynecol*. 1942;44(4):575–80.
- Benjamin F, Craig CJT. Uterine distension and preeclamptic toxemia. *BJOG*. 1961;68(5):827–30.
- Felbo M, Fenger HJ. Combined extra- and intrauterine pregnancy carried to term. *Acta Obstet Gynecol Scand*. 1966;45(2):140–54.
- Clark JF, Niles JH. Abdominal pregnancy associated with toxemia of pregnancy. Report of two cases and review of the literature. *J Natl Med Assoc*. 1967;59(1):22–4.
- Paterson WG, Grant KA. Advanced intraligamentous pregnancy. Report of a case, review of the literature and a discussion of the biological implications. *Obstet Gynecol Surv*. 1975;30(11):715–26.
- Baehler RW, Copeland WE, Stein JH, Ferris TF. Plasma renin and aldosterone in an abdominal pregnancy with toxemia. *Am J Obstet Gynecol*. 1975;122(5):545–8.
- Anderton KJ, Duncan SLB, Lunt RL. Advanced abdominal pregnancy with severe pre-eclampsia. *BJOG*. 1976;83(1):90–3.
- Ekwempu CC. Continuation of abdominal pregnancy complicated by pre-eclampsia three weeks after birth of an intrauterine twin. *Int J Gynaecol Obstet*. 1979;16(4):324–7.
- Moodley JSKTS, Pitsoe SB. Advanced extra-uterine pregnancy associated with eclampsia—a report of 2 cases. *S Afr Med J*. 1987;71(7):460–1.
- Emembolu JO. Rudimentary horn pregnancy associated with pre-eclampsia. *Int J Gynaecol Obstet*. 1989;30(4):367–70.
- Piering WF, Garancis JG, Becker CG, Beres JA, Lemann J Jr. Preeclampsia related to a functioning extra-uterine placenta: report of a case and 25-year follow-up. *Am J Kidney Dis*. 1993;21(3):310–3.
- Seki H, Ki K, Takeda S, Kinoshita K. Ovarian pregnancy diagnosed in the third trimester: a case report. *J Obstet Gynaecol Res*. 1997;23(6):543–6.
- De Muelenaere HM. Advanced abdominal pregnancy and pre-eclampsia: a case report and literature review. *Obstet Gynaecol Forum*. 2003;13(3):22–6.
- Ekele BA, Adamu AN, Ladan H, Abitare H. Eclampsia in advanced abdominal pregnancy. *Niger J Clin Pract*. 2007;10(4):343–5.
- Hailu FG, Yihunie GT, Essa AA. Advanced abdominal pregnancy, with live fetus and severe pre-eclampsia, case report. *BMC Pregnancy Childbirth*. 2017;17(1):243.
- Rafiq Baig JA, Jamal MM. Maternal and perinatal outcome in pregnancy induced hypertensive mothers in combined military hospital, Sialkot. *Pak Armed Forces Med J*. 2020;70(4):896–901.

34. Kaufmann P, Black S, Huppertz B. Endovascular trophoblast invasion: implications for the pathogenesis of intrauterine growth retardation and pre-eclampsia. *Biol Reprod.* 2003;69(1):1–7.
35. Osol G, Mandala M. Maternal uterine vascular remodeling during pregnancy. *Physiology.* 2009;24(1):58–71.
36. Levine RJ, Lam C, Qian C, Yu KF, Maynard SE, Sachs BP, et al. Soluble endoglin and other circulating antiangiogenic factors in pre-eclampsia. *N Engl J Med.* 2006;355(17):1840.
37. Rana S, Lemoine E, Granger JP, Karumanchi SA. Pre-eclampsia: pathophysiology, challenges, and perspectives. *Circ Res.* 2019;124(7):1094–112.
38. Flint EJ, Cerdeira AS, Redman CW, Vatish M. The role of angiogenic factors in the management of pre-eclampsia. *Acta Obstet Gynecol Scand.* 2019;98(6):700–7.
39. Simon-Tillaux N, Lecarpentier E, Tsatsaris V, Hertig A. Sildenafil for the treatment of pre-eclampsia, an update: should we still be enthusiastic? *Nephrol Dial Transplant.* 2019;34(11):1819–26.
40. Han H, Wang S. A case report of rudimentary horn pregnancy complicated with pre-eclampsia. *Chin J Clin Obstet Gynecol.* 2000;1(2):101.

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