

# Double trouble in an ectopic pregnancy

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## Abstract:

Gestational trophoblastic diseases are histologically different types of tumors originating from the placenta with an incidence of 0.2–5.8/1000 pregnancies. Ectopic pregnancy is the implantation of the fertilized ovum outside the uterine cavity, and a 0.64% incidence is reported. Ectopic cornual pregnancy and molar pregnancy are rare cases, and a combination of these two rare entities occurring simultaneously is even rare and very few cases have been reported in the literature. A cornual pregnancy refers to the implantation and development of a gestational sac in one of the upper and lateral portions of the uterus, whereas an interstitial pregnancy is a gestational sac that implants within the proximal, intramural portion of the fallopian tube that is enveloped by the myometrium. We present one of the rare combinations of molar pregnancy and cornual/interstitial ectopic pregnancy in a 30-year-old G<sub>3</sub>P<sub>1</sub> who presented with a triad of amenorrhea, vaginal bleeding, and abdominal pain. Laparotomy was done in view of an ultrasound which was suggestive of a well-defined complex thick-walled lesion of size 3.2 × 3.3 with a gestational sac and no cardiac activity in the right fallopian tube/adnexa suggesting tubal ectopic pregnancy. Beta-human chorionic gonadotropin (β-hCG) levels were done and noted to be as high as 9998 mIU/mL. Intraoperatively, a cornual ectopic pregnancy was found with no hemoperitoneum which was excised. Histopathology showed chorionic villi with variable size and hydropic change, myxoid stromal changes, and cistern formation with polar trophoblastic proliferation, based on which a diagnosis of molar pregnancy was made. Although ultrasonography and higher than usual serum β-hCG levels are diagnostic of uterine molar pregnancy, they do not yield a proper diagnosis in ectopic molar pregnancy, hence, making it difficult to distinguish between an early ectopic molar pregnancy from a nontrophoblastic tubal pregnancy. The final diagnosis is usually made only after histopathology. A high degree of clinical suspicion of cornual pregnancy followed by histopathological examination of the products of conception is the standard for arriving at an appropriate diagnosis. Serial serum β-hCG level follow-up is recommended to rule out its malignant potential.

## Keywords:

Beta-human chorionic gonadotropin, cornual pregnancy, ectopic pregnancy, molar pregnancy

## Introduction

The incidence of ectopic pregnancy is 1%–2%, and out of these, cornual pregnancy accounts for only 2%–3%.<sup>[1,2]</sup> Molar pregnancy is a form of gestational trophoblastic disease (GTD) characterized by an abnormal proliferation of trophoblasts.<sup>[3,4]</sup> This could be either partial or complete, and the incidence of complete and partial hydatidiform moles is 1:1945 and 1:695 pregnancies, respectively.<sup>[2]</sup> Although ultrasonography is useful in the diagnosis of

uterine molar pregnancies, there is a chance of missing this diagnosis in cases of an ectopic molar pregnancy.<sup>[5,6]</sup> The treatment of molar pregnancy is suction and evacuation. However, its ectopic entity requires surgical removal (laparoscopy or laparotomy) which may or may not be combined with chemotherapy using methotrexate and folinic acid.<sup>[2,7]</sup> Its malignant potential is similar to that of an intrauterine molar pregnancy. Follow-up is usually done by serial serum beta-human chorionic gonadotropin (β-hCG) levels similar to the one done in its intrauterine entity which is done with weekly β-hCG levels until normalized. After three consecutive normal

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$\beta$ -hCG levels are observed, its assay is repeated twice in 3-month intervals.<sup>[8]</sup> The monitoring is continued every month for 6 months and then at 2 monthly intervals for the next 6 months.<sup>[9]</sup> During follow-up, elevated  $\beta$ -hCG ( $>20,000$  mIU/mL) more than 4 weeks post evacuation/surgery, plateauing (decline of  $<10\%$  or rise), and clinical or histologic evidence of metastasis at any site counts for immediate evaluation and suspicion of malignant transition should be raised.<sup>[9]</sup>

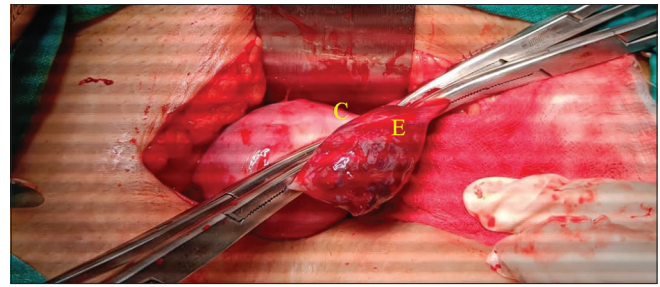
## Case Report

This is a case of 32-year-old  $G_3P_1$  who presented to our outpatient department at 9 weeks and 2 days of period of gestation with complaints of hypogastric pain for 2 days and vaginal bleeding for 1 day. She  $G_3P_1$  with a history 6 years back of previous lower segment cesarean section presented with the triad of 2-month amenorrhea, with hypogastric pain and vaginal bleeding, and a suspicion of ectopic pregnancy was raised. On internal examination, the uterus was enlarged to 8 weeks with cervical motion and forniceal tenderness; however, no forniceal mass was felt. An emergency ultrasound was done which revealed an empty uterus with a right-sided well-circumscribed mass measuring of size  $3.1 \text{ cm} \times 3.2 \text{ cm}$ . On color flow, a ring of fire was noted around the mass. A baseline  $\beta$ -hCG was requested, and a decision of conservative management was made due to a small size of  $3.1 \text{ cm} \times 3.2 \text{ cm}$  and a hemodynamically stable patient. The  $\beta$ -hCG, however, came to be 9998.00 mIU/mL. Due to this high  $\beta$ -hCG, a decision of emergency laparotomy was taken. Intraoperatively, no hemoperitoneum was observed, and on evaluating the pelvic organs, a  $4 \text{ cm} \times 3.2 \text{ cm} \times 3.6 \text{ cm}$  mass was found on the right cornua of the uterus, thus implying a cornual pregnancy. The associated right-side tube was intact and in continuity and had no morphologically abnormality. The implantation of ectopic pregnancy also showed thinning of the overlying serosa, with the internal mass being partially visible suggestive of an impending rupture [Figure 1]. Both ovaries and uterus with left fallopian tube were grossly normal. The specimen was found to be vesicular in nature with no evidence of a fetus.

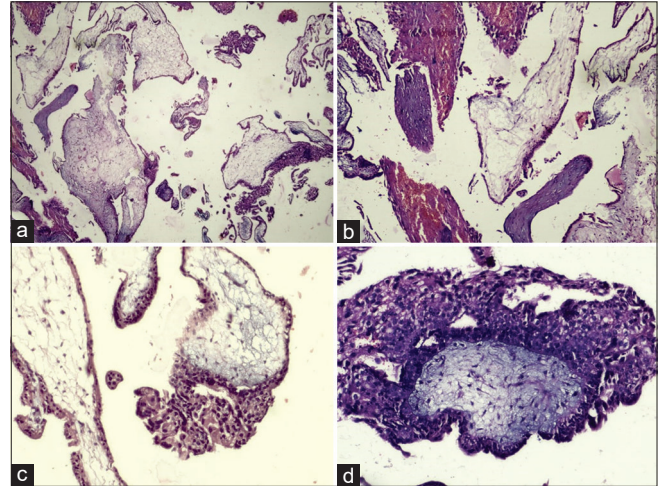
A resection was done for the ectopic pregnancy. Histopathological examination revealed the presence of molar ectopic pregnancy [Figure 2].<sup>[10]</sup> Postoperatively, the  $\beta$ -hCG levels declined on weekly monitoring and were normalized by the end of the 3<sup>rd</sup> month [Figure 3].

## Discussion

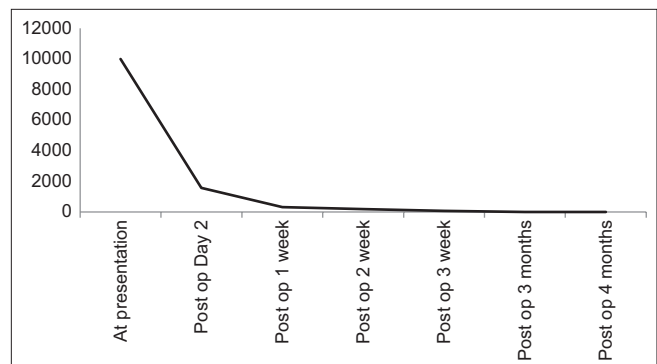
Cornual pregnancy refers to the implantation and development of a gestational sac within the uterine angles medial to the ostia.<sup>[2]</sup> On the other hand, an



**Figure 1:** Intraoperative picture of the cornual ectopic pregnancy. C: Cornua, E: Ectopic mass



**Figure 2:** Sections examined show diffusely dilated (a) H and E,  $\times 10$  nonvascularized villi with myxoid stroma (bluish tinge of the stroma due to increase in gag proteins in stroma matrix found in benign or malignant condition). (b-d) H and E,  $\times 40$  and central cystern (b) H and E,  $\times 20$  formation with trophoblastic proliferation (c and d) H and E,  $\times 40$



**Figure 3:** Follow-up of beta-human chorionic gonadotropin levels.  $\beta$ -hCG: Beta-human chorionic gonadotropin

interstitial pregnancy is a gestational sac that implants within the proximal, intramural portion of the fallopian tube that is enveloped by the myometrium.<sup>[6,11]</sup> The term cornual ectopic pregnancy is interchangeably used with interstitial pregnancy. Pregnancy with cornual location occurs in only 2%–4% of all ectopic pregnancies and symptomatically present like any other ectopic pregnancies but often present later in gestation.

Therefore, the diagnosis of ectopic pregnancy presenting at a high gestation (more than 8 weeks) should not be restricted to its tubal location, and other sites such as cornual, interstitial, and abdominal should be kept in differential.

Molar pregnancy is an abnormal gestation characterized by the presence of hydropic change affecting some or all of the placental villi, accompanied by circumferential proliferation of trophoblasts. It is also a rare entity seen in 1/1000–2000 pregnancies.<sup>[12]</sup> Ectopic molar pregnancies present in the first trimester with bleeding with or without passage of any vesicles, a uterine size more than the period of gestation, nondetectable fetal cardiac activity, or hyperemesis. Two rare entities with considerable overlap of clinical symptomatology presenting simultaneously posed difficulty in arriving at a definitive preoperative and intraoperative diagnosis.<sup>[13]</sup>

Ultrasonographic criteria for diagnosing interstitial pregnancy condition are an empty uterine cavity, a gestational sac located eccentrically and > 1 cm from the most lateral wall of the uterine cavity, and a thin (<5 mm) myometrial layer surrounding the gestational sac.<sup>[12]</sup> Ultrasound findings of multiple echogenic areas of villi and clots alone with the absence of a fetus are extremely reliable in making the diagnosis of hydatidiform molar pregnancy. In our case, the ultrasonography report was inconclusive, and hence, based on clinical and serum  $\beta$ -hCG levels, a decision for surgical exploration was taken.

$\beta$ -hCG levels in molar pregnancies are elevated more than any normal pregnancy. Its levels are elevated in tubal molar pregnancies but are in the lower range, due to improper implantation and inadequate vascularization, thereby causing its low levels.<sup>[14]</sup> Ultrasound showing multicystic echogenic masses and high serum  $\beta$ -hCG levels are diagnostic of uterine molar pregnancy. The diagnosis is usually obscured in ectopic molar pregnancy as serum  $\beta$ -hCG although elevated is in the lower range. The final diagnosis is thus made only after the histopathological report similar to the presented case.<sup>[15,16]</sup>

A hemodynamically stable patient with an ectopic pregnancy of size <4 cm, with no cardiac activity and no hemoperitoneum, and a  $\beta$ -hCG level of <5000 mIU/mL can be managed conservatively.<sup>[5]</sup>  $\beta$ -hCG level of more than 5000 mIU/mL is a relative contraindication for medical management (methotrexate) of ectopic pregnancy. In our case, although the patient was hemodynamically stable, the  $\beta$ -hCG level was 9998 mIU/mL, and hence, laparotomy was performed.<sup>[12]</sup>

Monitoring of GTD patients is done with serial (weekly) serum  $\beta$ -hCG levels followed by twice in 3 months after three consecutive normal values.<sup>[8]</sup> The monitoring

is continued every month for 6 months and then at 2 monthly intervals for the next 6 months.<sup>[9]</sup> These patients should be advised to avoid conception for at least 6 months, and the simultaneous risk of ectopic pregnancy of about 15% and molar of 1%–6% should be explained.<sup>[2]</sup>

## Conclusion

Molar cornual ectopic pregnancy occurring simultaneously is a rare entity, which can be seen observed anywhere in the female genital tract. The chances of its conversion to invasive mole and choriocarcinoma are similar to the intrauterine pregnancy; therefore, follow-up with weekly  $\beta$ -hCG is advised similar to any other molar pregnancy. To diagnose this rare combination, ultrasonography alone is not sufficient. A high degree of suspicion clinically for diagnosing cornual pregnancy followed by histopathological examination of the products of conception is the current gold standard for the diagnosis. Early diagnosis and timely intervention are the key to appropriate management as delay in diagnosing may cause rupture of the ectopic leading to hypovolemic shock and increased morbidity. This case emphasizes the importance of histological examination of products of conception which helps the pathologist to provide an appropriate diagnosis, thereby guiding the clinician to offer appropriate counseling and follow-up to the patient.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

## Authorship contributions

Shalini Singh - Involved in conceptualization, methodology, data curation, writing of the original draft, review and editing.

Vandana Kamatham - Involved conceptualization, methodology, resources and data curation.

Sharmila Vijayan - Involved in the conceptualization, methodology, review and editing and supervision.

Prashant Joshi - Involved in conceptualization, methodology, data curation and resources.

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## Conflicts of interest

There are no conflicts of interest.



## References

1. Hoover KW, Tao G, Kent CK. Trends in the diagnosis and treatment of ectopic pregnancy in the United States. *Obstet Gynecol* 2010;115:495-502.
2. Jonathan S. Berek and Ncaavak's Gynecology. Philadelphia: Wolters Kulwar Health/ Lippincott Williams and Willkins;2020.
3. Hoffman B. Gestational trophoblastic disease. In: Schorge J, Schaffer J, Halvorson L, editors. *Williams Gynecology*. 23<sup>rd</sup> ed., Ch. 37. Texas: McGraw-Hill Companies; 2010. p. 756-8.
4. Altieri A, Franceschi S, Ferlay J, Smith J, La Vecchia C. Epidemiology and aetiology of gestational trophoblastic diseases. *Lancet Oncol* 2003;4:670-8.
5. Cakmak B, Toprak M, Nacar MC, Koseoglu RD, Demirturk F. Cornual molar ectopic pregnancy. *Int J Reprod Contracept Obstet Gynecol* 2013;2:740-3.
5. Cakmak B, Toprak M, Nacar MC, Koseoglu RD, Demirturk F. Cornual molar ectopic pregnancy, *Int J Reprod Contracept Obstet Gynecol* 2013;2:740-3.
6. Rathod S, Samal SK. A true cornual pregnancy with placenta percreta resulting in a viable fetus. *Int J Appl Basic Med Res* 2015;5:203-5.
7. Hassadia A, Kew FM, Tidy JA, Wells M, Hancock BW. Ectopic gestational trophoblastic disease: A case series review. *J Reprod Med* 2012;57:297-300.
8. Abu-Rustum NR, Yashar CM, Bean S, Bradley K, Campos SM, Chon HS, *et al.* Gestational trophoblastic neoplasia, version 2.2019, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw* 2019;17:1374-91.
9. Philippine Society for the Study of Trophoblastic Diseases, Inc Clinical Practice Guidelines for the Diagnosis and Mana; 2011.
10. Oldt RJ 3<sup>rd</sup>, Kurman RJ, Shih IM. Molecular genetic analysis of placental site trophoblastic tumors and epithelioid trophoblastic tumors confirms their trophoblastic origin. *Am J Pathol* 2002;161:1033-7.
11. Dagar M, Srivastava M, Ganguli I, Bhardwaj P, Sharma N, Chawla D. Interstitial and cornual ectopic pregnancy: Conservative surgical and medical management. *J Obstet Gynaecol India* 2018;68:471-6.
12. Ackerman TE, Levi CS, Dashefsky SM, Holt SC, Lindsay DJ. Interstitial line: Sonographic finding in interstitial (cornual) ectopic pregnancy. *Radiology* 1993;189:83-7.
13. Yamada Y, Ohira S, Yamazaki T, Shiozawa T. Ectopic molar pregnancy: Diagnostic efficacy of magnetic resonance imaging and review of the literature. *Case Rep Obstet Gynecol* 2016;2016: p. 1-7, Article ID-7618631.
14. Han V, Kaye S. A rare case of gestational choriocarcinoma presenting as cornual ectopic pregnancy. *J Obstet Gynaecol Can* 2018;40:351-3.
15. Hwang JH, Lee JK, Lee NW, Lee KW. Molar ectopic pregnancy in the uterine cornus. *J Minim Invasive Gynecol* 2010;17:239-41.
16. Zite NB, Lipscomb GH, Merrill K. Molar cornual ectopic pregnancy. *Obstet Gynecol* 2002;99:891-2.