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Original Article

Pathology Section

Retained Trophoblastic Tissue: A Clinicopathological Study

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ABSTRACT

Introduction: Remnants of Conception (ROC) are routinely submitted for Histopathological Examination (HPE) to confirm the presence of trophoblastic tissue, to rule out gestational trophoblastic diseases, for ascertaining the aetiology of recurrent abortions as well as diagnosing foetal pathologies apart from medicolegal purposes. However, there is a lot of debate about the usefulness of routine HPE of all ROC.

Aim: To assess the usefulness of routine histopathological examination for remnants of conception.

Materials and Methods: This retrospective study was conducted between January 2021 to May 2021at Department of Pathology, Guntur Medical College (Government General Hospital) Guntur, Andhra Pradesh, India. The data of cases were collected between June 2017 to July 2019. There were a total of 104 cases during the study period. The cases were retrieved by retrospective search of pathology records and patient details and other relevant clinical information was obtained from patient requisition form and clinical case sheet. The Haematoxylin and Eosin (H&E) slides were reviewed. Statistical analysis was performed using percentages and frequencies.

Results: Gestational age was known in 54 cases out of which cases presenting in first trimester were 41 (75.93%) cases, second trimester were 11 (20.37%) cases, and third trimester or postdelivery were 2 (3.70%) cases. Out of 41 first trimester cases, 22 (40.7%) cases were below eight weeks of gestation. The indication of surgical uterine evacuation was incomplete miscarriage in 50 cases, missed miscarriage in 19 cases, suspected molar pregnancy in 17 cases and anembryonic miscarriage in two cases, and suspected ectopic in five cases. On HPE, ROC was confirmed in 77 (74.04%) cases, 12 (11.5%) cases showed only decidual tissue with arias stella reaction and no villi. There was choriocarcinoma in 1 (0.9%) case and molar pregnancy in 13 (12.5%) cases. On HPE, there was no evidence of trophoblastic tissue in 1 (0.9%) case.

Conclusion: Remnants of conception was most common in first pregnancy, and during the first trimester in the study. Histopathological examination is required for confirmation of trophoblastic tissue and in diagnosis of molar pregnancy and other trophoblastic diseases.

Keywords: Arias stella reaction, Chorionic villi, Miscarriage, Molar pregnancy

INTRODUCTION

The Remnants Of Conception (ROC) following abortion, either spontaneous or induced and following delivery complicate up to 6% of pregnancies and are routinely submitted for Histopathological Examination (HPE) [1]. The routine HPE not only helps in confirming the presence of trophoblastic tissue inside the uterus, but also aids in ruling out gestational trophoblastic diseases, the prevalence of which can be as high as 12 per 1000 pregnancies in Asian countries like India [2-5]. In addition, HPE is also useful in ascertaining the aetiology of recurrent abortions as well as diagnosing foetal pathologies apart from medicolegal purposes [3]. However, there is a lot of debate about the usefulness of routine HPE of all ROC; some studies recommend routine HPE of all ROC, as HPE can more effectively identify different pathologies as compared to other laboratory investigations and radiology [6], while some authors believe that HPE of ROC should be restricted to specific indications like when there is a suspicion of an ectopic pregnancy or a molar pregnancy which require further follow-up [6].

So, the authors have taken up the study with an aim to assess the usefulness of routine HPE in ROC. The objective of this study was to review all cases which were sent for HPE for the presence of trophoblastic tissue and to analyse the histopathological findings of all these cases and assess the usefulness of HPE.

MATERIALS AND METHODS

This retrospective study was conducted between January 2021 to May 2021 at Department of Pathology, Guntur Medical College (Government General Hospital) Guntur, Andhra Pradesh, India. The data of cases were collected between June 2017 to July 2019. The approval from the Institutional Ethics Committee (IEC application no GMC/IEC/02/2021) was obtained.

Inclusion criteria: All cases of dilatation and curettage sent for retained products of conception submitted to the Department of Pathology of present medical college hospital were included in the study.

Exclusion criteria: Cases of ectopic gestation were excluded from the study.

The minimum sample size required, assuming rate of positivity for ROC in HPE to be 97% [6], with 95% confidence interval and precision of 5% was calculated as 45 cases. The cases were retrieved by retrospective search of pathology records and patient details and other relevant clinical information was obtained from patient requisition form and clinical case sheet. All the specimens were received in formalin and Haematoxylin and Eosin (H&E) stained paraffin sections were prepared after routine processing. The H&E slides were reviewed.

STATISTICAL ANALYSIS

Data entry was made in Microsoft excel sheet. Frequencies and percentages were calculated. Mean was calculated for continuous variables.

RESULTS

There were a total of 104 cases during the study period; the age range was between 17-39 years, with mean age of 24.5 years.

Parity was known in 63 cases, of which, cases presenting in first pregnancy were 28 cases, second pregnancy were 20 cases, third were 10 cases, fourth were three cases, and fifth were two cases.

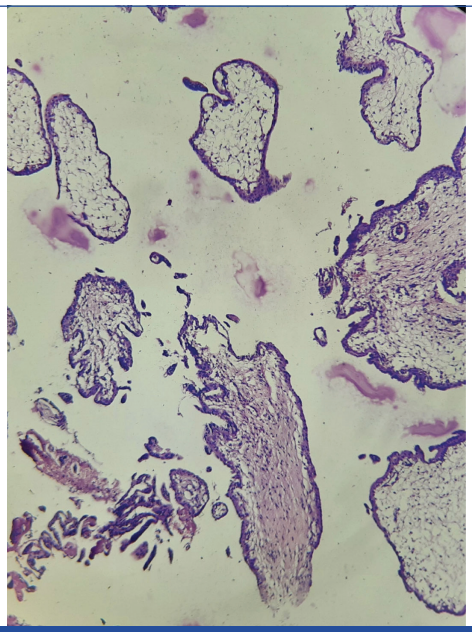
Gestational age was known in 54 cases [Table/Fig-1], of which cases presenting in first trimester were 41 (75.93%) cases, second trimester were 11 (20.37%) cases, and third trimester or postdelivery were cases 2 (3.70%). Out of 41 first trimester cases, 22 (53.65%) cases were below eight weeks of gestation.

The indication of surgical uterine evacuation was known in 93 cases [Table/Fig-1], of these, incomplete miscarriage was in 50 (53.76%) cases, missed miscarriage in 19 (20.43%) cases, suspected molar pregnancy in 17 (18.27%) cases anembryonic miscarriage in 2 (2.15%) cases, and suspected ectopic pregnancy in 5 (5.37%) cases.

Variables	N (%)
Gestational age (n=54)	
First trimester	41 (75.93%)
Second trimester	11 (20.37%)
Third trimester or postdelivery	2 (3.70%)
Indication of surgical uterine evacuation (n=93)	
Incomplete miscarriage	50 (53.76%)
Missed miscarriage	19 (20.43%)
Suspected molar pregnancy	17 (18.27%)
Anembryonic miscarriage	2 (2.15%)
Suspected ectopic	5 (5.37%)

[Table/Fig-1]: Frequency distribution of gestational age and indication of surgical uterine evacuation.

On Histopathological Examination (HPE), which was studied in 104 cases, ROC was confirmed in 77 (74.04%) cases which showed chorionic villi with trophoblastic rimming along with decidua and arias stella reaction [Table/Fig-2]. Out of theses 77 cases, villi showed hydropic change in 45 (58.45%) cases, stromal fibrosis in 26 (33.77%) cases, peri villous fibrin in 4 (5.19%) cases and hyalinised in 2 (2.59%) cases. A 12 (11.54%) cases out of 104 cases, showed only decidual tissue with arias stella reaction and no villi; of these 12 cases, three cases were missed abortion, six cases were incomplete abortion, two cases were suspected molar pregnancy, and two cases were suspected ectopic pregnancy. There was choriocarcinoma in 1 (0.96%) case and molar pregnancy in 13 (12.50%) cases, of which four were complete moles, three were invasive moles on radiology. On HPE, there was no evidence of trophoblastic tissue in 1 (0.96%) case.



[Table/Fig-2]: Haematoxylin and eosin (H&E, 100X) showing product of conception comprising chorionic villi with trophoblastic rimming.

Ectopic pregnancy was suspected clinically in five cases, of which HPE showed evidence of products in three cases and only decidual tissue in two cases.

DISCUSSION

Miscarriage is defined as pregnancy termination before 20 weeks of gestation or a foetus being born with weight of less than 500 gm [7]. As high as 20% of pregnancies can be lost spontaneously and few of these cases undergo surgical evacuation to look for retained products based on the radiological diagnosis, clinical scenario and therapeutic interventions being applied [8,9]. Histopathology confirmed products of trophoblastic tissue in 99% of cases in present study.

The retained products of conception can be defined as intrauterine tissue that develops after conception and persists after cessation of pregnancy or after delivery. Remnants of conception is the most common cause of Postpartum Haemorrhage (PPH) both primary and secondary PPH. The patients present with complaints of irregular vaginal bleeding, abdominal cramps and signs of infection or may be asymptomatic and detected incidentally during routine follow-up sonography or scan done for various other indications [10,11]. Patients can also present with infertility, hypomenorrhea and amenorrhea because of intrauterine adhesions secondary to ROC [12].

The pathognomic features of ROC are a demonstration of chorionic villi which indicates retention of placental tissue. However, sometimes only decidual tissue showing an arias stella reaction is seen, which is also considered as evidence of pregnancy. Van den Bosch T et al., in their study, diagnosed ROC in 27% of 3rd trimester, 40% of 2nd trimester and 1st trimester pregnancies [1]. However, in the present study ROC was common in first trimester pregnancies (75.9%), of which 40.7% were below eight weeks of gestational age.

In this study, HPE confirmed ROC in 74% cases and 11.5% showed only decidual tissue with aria stella reaction and no villi; molar pregnancy was diagnosed in 12.5% of cases, the present study results are comparable to other studies shown in [Table/Fig-3] [13-15].

Histological diagnosis	Fram KM study (2002) [13]	Tohma YA et al., study (2016) [14]	Ohayi SR and Onyishi NT (2020) [15] Total n=107	Present study Total n=104 (%)
Confirm POC	100%	69.7%	73 (68.2%)	77 (74.04%)
Only decidua, no villi	-	16.9%,	8 (7.5%)	12 (11.54%)
Choriocarcinoma	-	-		1 (0.96%)
Molar pregnancy	17%	2.1% (partial mole) 0.43% (complete mole)	8 (7.5%) (partial) 1 (0.9%) (complete)	13 (12.50%)
No evidence of POC	-	-	15 (14.0%)	1 (0.96%)
Undiagnosed abnormality	2.7%	-		-

[Table/Fig-3]: Comparison of histological diagnosis with various studies [13-15].
POC/ROC: Products of conception/Remnants of conception

The ROC is usually diagnosed based on clinical, radiological findings and urine/serum beta human chorionic gonadotropin levels. Sellmyer MA et al., suggest that ROC can be diagnosed accurately by ultrasonography based on presence of certain findings like: 1) thickened endometrial echo complex and 2) a vascularised endometrial mass visualised by colour and power doppler ultrasound, and when appropriate clinical history is present. However, differentiating blood clots from ROC is not always easy on radiology [16]. Arteriovenous malformation, endometrial polyp and submucosal fibroid are the other entities which are difficult to differentiate from ROC on radiology [15]. In all these situations histopathology is essential in arriving at the diagnosis. Invasive mole can also present with PPH and is a complication of molar pregnancy and have overlapping features on radiology; in two of presented cases also invasive mole was suspected.

Whether HPE should be done routinely for all cases of miscarriage is still a point of debate and several authors differ in their opinion about this. Alsibiani SA in their study of first trimester abortions have recommended HPE only in selected cases where the diagnosis is uncertain or when there is risk of trophoblastic disease or when radiology suggests molar pregnancy [6]. On contrary Ohayi SR and Onyish NT were of the opinion that HPE should be done for all of ROC since HPE, in addition to diagnosing molar pregnancy and other trophoblastic disease, also aids in overall wellbeing of patient by confirming ROC, since it is associated with major anxiety in women especially those who want to conceive a child [15]. Routine HPE is useful especially in infertile women as it helps confirm the pregnancy though it may not be viable [15].

Histopathology aids in confirming the trophoblastic tissue and in the diagnosis of molar pregnancy and other trophoblastic diseases. Though, we have not diagnosed any cases which were unsuspected clinically and radiologically, mere confirmation of ROC helps the clinician in planning the further management of patients especially for those undergoing evaluation for infertility. In addition, histological confirmation of molar pregnancy aids clinician in identifying those needing special follow-up as it can be potentially premalignant [3]. Furthermore, submitting cases with dysmorphic features for genetic analysis will be useful in management of cases with recurrent abortions and in planning for future pregnancies [4].

Limitation(s)

The limitations of the study were small sample size and that it was a single centre study. Genetic analysis was not performed as the facility was not available at present centre and results of those cases which were sent to other centres for genetic analysis were not available.

CONCLUSION(S)

Remnants of conception was most common in first pregnancy, and during the first trimester in the present study. Histopathological Examination (HPE) is required for confirmation of trophoblastic tissue and in diagnosis of molar pregnancy and other trophoblastic diseases.

REFERENCES

[1] Van den Bosch T, Daemen A, Van Schoubroeck D, Pochet N, De Moor B, Timmerman D. Occurrence and outcome of residual trophoblastic tissue: A prospective study. J Ultrasound Med. 2008;27(3):357-61.
[2] Novais Nogueira Cardoso RMA, Nogueira Cardoso PLN, Azevedo AP, Cadillá JS, Oliveira Rodrigues Amorim MGR, Rocha Gomes ME, et al. First-trimester miscarriage: A histopathological classification proposal. Heliyon. 2021;7(3):e06359.
[3] Lama P, Pariyar J. Histological analysis of the products of conception in first trimester spontaneous abortions. Nep J Obstet Gynecol. 2021;16(32):31-33.
[4] Shilpa, Supreetha, Varshashree. Histomorphological study of chorionic villi in products of conception following first trimester abortions. Trop J Path Micro. 2018;4(7):499-504.
[5] Jaiswal P, Shrestha S, Dwa Y, Manandhar S. Correlation of ultrasound imaging with histopathological findings in gestational trophoblastic disease. Journal of Patan Academy of Health Sciences. 2020;7(3):41-46.
[6] Alsibiani SA. Value of histopathologic examination of uterine products after first-trimester miscarriage. Biomed Res Int. 2014;2014:863482.
[7] Schorge JO, Schaffer J, Halvorson LM, Hoffman BL, Bradshaw KD, Cunningham FG. "First trimester abortion," in Williams Gynecology, McGraw-Hill, New York, NY, USA, 1st edition, 2008.
[8] World Health Organisation. Safe Abortion: Technical and Policy Guidance for Health Systems. 2nd ed. Geneva: WHO; 2012.
[9] Hinshaw K, Fayyad A, Munjuluri P. The Management of Early Pregnancy Loss. Revised Guideline no. 25. Green.top Guideline no. 25. London: Guidelines and Audit Committee of the Royal College of Obstetricians and Gynaecologists; 2006.
[10] Russo JA, DePiñeres T, Gil L. Controversies in family planning: Retained products of conception. Contraception. 2012;86(5):438-42.
[11] Maslovitz S, Almog B, Mimouni GS, Jaffa A, Lessing JB, Many A. Accuracy of diagnosis of retained products of conception after dilation and evacuation. J Ultrasound Med. 2004;23(6):749-56; quiz 758-9.
[12] Ben-Ami I, Ofir T, Melcer Y, Smorgick N, Schneider D, Pansky M, et al. Infertility following retained products of conception: Is it the surgical procedure or the presence of trophoblastic tissue? Eur J Obstet Gynecol Reprod Biol. 2014;182:132-35.
[13] Fram KM. Histological analysis of the products of conception following first trimester abortion at Jordan University Hospital. Eur J Obstet Gynecol Reprod Biol. 2002;105(2):147-49.
[14] Tohma YA, Dilbaz B, Evliyaoğlu Ö, Çoşkun B, Çolak E, Dilbaz S. Is ultrasonographic evaluation essential for diagnosis of retained products of conception after surgical abortion? J Obstet Gynaecol Res. 2016;42(5):489-95.
[15] Ohayi SR, Onyishi NT. Routine Histopathological Analysis of the Products of Conception: Is there a Value? Niger Med J. 2020;61(3):136-39.
[16] Sellmyer MA, Desser TS, Maturen KE, Jeffrey RB, Kamaya A. Physiologic, histologic, and imaging features of retained products of conception. Radiographics. 2013;33(3):781-96.

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