ORIGINAL RESEARCH

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Should All Abortion Materials Be Sent for Histopathological Evaluation?

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ABSTRACT Objective: Partial hydatidiform mole is the type of mole in which a foetus and/or cardiac activity is seen. Clinical diagnosis of missed abortion and anembryonic gestation may cause the partial mole to be missed or misdiagnosed if a histopathologic examination is not carried out. Our objective in this study was to clarify whether it is really necessary to send all abortion materials for histopathological examination considering the rate of mole (complete/partial) among all abortion materials in a university hospital. **Material and Methods:** In this retrospective cohort study, we evaluated the clinical and histopathological results of 1,004 women with a clinical diagnosis of abortion that were diagnosed at the University of Kütahya Health Sciences Evliya Çelebi Hospital between January 2015 and December 2020. **Results:** Missed abortion was the most common diagnosis with 638 women (63.5%) among the abortion materials that were sent for histopathology. Complete mole was diagnosed in only one (1/1,004) woman, which was sent to pathology with a diagnosis of anembryonic gestation. The partial mole rate was 9/1,004 and most were diagnosed after a clinical diagnosis of anembryonic gestation (n=5, 55%). Placental villi were seen in 93% (934/1,004) but not in 6% (60/1,004) of the subjects (Arias-Stella reaction) on histopathology, which was possibly an ectopic pregnancy or a very early aborted early gestation in which placenta villi could not be identified. Partial and complete mole hydatidiform constituted 1% (9/1,004) and 0.1% (1,004) of the total cohort respectively. **Conclusion:** When taking into account the rate of mole hydatidiform (10/1,004) in a clinic where all abortion materials are being sent for histopathological examination routinely, we think that routine histopathological examination of abortion material seems reasonable and safe.

Keywords: Abortion; anembryonic gestation; partial mole hydatidiform; complete hydatidiform; histopathology

Pregnancy loss is called abortion before the 20th week of pregnancy or when the foetus is less than 500 g.[1] Approximately 15% of clinically diagnosed pregnancies are lost in the first trimester.[2] Spontaneous abortion can be seen as inevitable, incomplete, complete or missed abortion.[3] Although there is no agreement as to whether clinically diagnosed or suspected post-abortion pregnancy material should be routinely sent for histopathological examination, most physicians send the material for histopathological examination.[4] Routine histopathological examination protects physicians from medicolegal problems that may occur as a result of possible molar pregnancy or ectopic pregnancy. However, the cost and the increased burden of workload for histopathology remains an important problem.

Mole hydatidiform incidence varies between countries. In the United Kingdom, complete mole hydatidiform incidence was reported as 1/1,000 and partial mole hydatidiform incidence was reported as 3/1,000.[5] On the other hand, mole hydatidiform in Turkey is observed in 0.3-16/1,000 of pregnancies.[6] The probability of detecting molar pregnancy in abortion materials is 2.2/1,000.[7]

Partial mole hydatidiform is a mole hydatidiform type that can develop with the presence of a foetus or foetal cardiac activity. In cases diagnosed with missed abortion or incomplete abortion, the diagnosis of partial mole hydatidiform can be overlooked in clinical evaluation because the definitive diagnosis can only be made by histopathological examination.[8] Therefore, there are controversial approaches suggesting

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either that the material should be routinely sent for histopathological examination or only in case of clinical suspicion of molar pregnancy.

The objective of this study was to help to clarify whether it is really necessary to send all abortion materials for histopathological examination considering the rate of mole (complete/partial) among all abortion materials in a university hospital.

MATERIAL AND METHODS

In this retrospective cohort study, the demographic data and histopathology results of 1,004 women whose pregnancy resulted in abortion and whose products of conception were sent for histopathological examination between January 2015 and December 2020 at the Kütahya Health Sciences University Evliya Çelebi Training and Research Hospital following approval of the local ethics committee (2021-75) were analysed. All reported research involving "human beings" were conducted in accordance with the principles set forth in the Helsinki Declaration 2008. If the foetus is less than 20 weeks of gestation or foetal weight is less than 500 g, this is considered an abortion. In our hospital, products of conception after abortion are routinely sent for histopathological examination. Pregnancy of all cases were confirmed by either transvaginal or transabdominal ultrasound and/or serum β-human chorionic gonadotropin (hCG) level monitoring.

All pregnant women clinically diagnosed as missed abortion, complete abortion, incomplete abortion, anembryonic gestation, medically indicated abortion, electively-induced abortion (non-medically indicated, on patient demand) and those suspected of having ectopic pregnancy (with the consent of the woman) were included in the study. Abortion materials of complete abortion were sent to pathology after collecting the material during speculum examination.

Complete abortion was diagnosed in case of increased endometrial thickness during transvaginal examination in a patient previously known to be pregnant, at the discretion of the clinical evaluation of the physician. In the absence of no cardiac activity on ultrasonography, subjects were included as missed abortion. Anembryonic pregnancy was diagnosed in our hospital if there was no visible embryo in a gestational sac 20 mm or more or no visible yolk sac despite a gestational sac of more than 15 mm. In case of heterogeneous tissues that distorted the form of the endometrial cavity, regardless of the presence of gestational sac, incomplete abortion was diagnosed in a woman known to be pregnant previously with ultrasonography or serum β-hCG.

Exclusion criteria included any material obtained from the intrauterine cavity without a diagnosis of concomitant pregnancy either by sonographic evidence or serum β-hCG (i.e. the pathology resulted from gynaecologic reasons).

In our hospital, abortion materials were sent for histopathological examination and the samples were classically fixed with 4% formaldehyde and embedded in paraffin. They were prepared with haematoxylin and eosin staining technique and 4 mm sections were cut. Both the diagnosis and differentiation of mole (complete or partial mole) was based on the histopathological examination of abortion material.

STATISTICAL ANALYSIS

Descriptive values are given as mean±standard deviation and number and % frequencies. Kolmogorov-Smirnov test was used in the normal distribution test of numerical features. Relationships between categorical features and groups were examined using chi-square test. $p \leq 0.05$ was taken as the statistical significance level and all statistical calculations were made in the Statistical Package for the Social Sciences (SPSS ver. 21) program.

RESULTS

The mean age of 1,004 subjects included in the study was 30.16±6.44 years. The mean gestational week during diagnosis was calculated as 9.54±3.35 weeks. Missed abortion was the most common diagnosis among those whose intrauterine materials were sent for histopathological examination with 638 subjects (63.5%). The incidence of complete mole hydatidiform was 1/1,004 (0.1%), and this was reported as the result of a case who underwent curettage due to anembryonic pregnancy. The incidence of partial hy-

datidiform mole was 9/1,004 (1%), mostly diagnosed in subjects terminated due to anembryonic pregnancy, with 5 cases (55%). Histopathological diagnoses of the cases regarding the type of pregnancy termination are given in Table 1.

Placental villi were seen in 93% (934/1,004) but not in 6% (60/1,004) of the subjects (Arias-Stella reaction) on histopathology, which was possibly an ectopic pregnancy or a very early aborted early pregnancy in which placenta villi could not be identified. Partial and complete mole hydatidiform constituted 1% (9/1,004) and 0.1% (1,004) of the total cohort respectively. Arias-Stella reaction was most commonly seen in the complete abortion group 17.3% (9/52) followed by incomplete abortion 11.2% (22/195).

DISCUSSION

In the present study, missed abortion was found to be the most frequent diagnosis with 638 (63.5%) of the pregnancies whose abortion materials were sent for histopathological examination. The incidence of complete mole hydatidiform was 1/1,004 (0.1%), and this was reported as the result of a case that underwent curettage due to anembryonic pregnancy. The incidence of partial hydatidiform mole was 9/1,004 (1%), with 5 (55%) diagnoses reported as products of conception terminated due to anembryonic pregnancy. In the histopathological diagnosis of the cases, 934 (93%) placental villi were the most frequently reported. In 60 (6%) of the cases, no chorionic villi were observed.

Placental villi were seen in 93% (934/1,004) but not in 6% (60/1,004) of the subjects (Arias-Stella reaction) in histopathology. Arias-Stella reaction was most commonly seen in the complete abortion group (17.3%, 9/52) followed by incomplete abortion, 11.2% (22/195). Arias-Stella is a histological pattern of decidua where villi are not observed, such as ectopic pregnancy. But not limited to that, it can also be seen in some intrauterine early pregnancies, especially if they are pathologic with lower serum β-hCG levels. Thus, when confronted by a pathology report of Arias-Stella reaction without any other diagnosis, one should keep the diagnosis of ectopic pregnancy in mind but also it should be remembered that this is also possible in some early intrauterine abortion material. Various studies reported Arias-Stella reactions as high as 3.33%, which is comparable to our rate (6%).[9] This increased rate of Arias-Stella reaction in our study (as high as 17.3%) in complete abortion cases probably resulted from at least some of these clinically diagnosed complete abortions being actually ectopic pregnancies missed by the clinician. Therefore, one may conclude that routine histopathological examination of a clinically diagnosed abortion may alert the physician to a possible ectopic pregnancy.

Molar hydatidiform incidence varies depending on the region where the study is conducted.[10-12] While the incidence of hydatidiform mole was 66-121/100,000 in North America and Europe, it was reported as 23-1,299/100,000 pregnancies in Latin America, Asia and the Middle East. In Turkey, de-

TABLE 1: Histopathological diagnoses depending on the clinical type of abortion.

		Anembryonic pregnancy	Incomplete abortion	Elective curettage	Complete abortion	Missed abortion	Therapeutic abortion		
Histopathology report	Complete mole hydatidiform	1 (1.1%)	0	0	0	0	0	1 (0.1%)	<0.001[a]
	Chorionic villus was not shown	9 (10.1%)	22 (11.2%)	0	9 (17.3%)	20 (3.1%)	0	60 (6%)	
	Partial mole hydatidiform	5 (5.6%)	1 (0.5%)	0	0	1 (0.1%)	2 (9.1%)	9 (0.9%)	
	Placental villi	74 (83.2%)	172 (88.3%)	8 (100%)	43 (82.7%)	617 (96.8%)	20 (90.9%)	934 (93.0%)	
	Total	89 (100%)	195 (100%)	8 (100%)	52 (100%)	638 (63.5%)	22 (2.2%)	1,004 (100%)	

[a]Chi-square test; Data are given as n (%).

pending on the region where the study was conducted, mole hydatidiform is observed with a ratio of 0.3-16/1,000 pregnancies.[6] In one study, which covered 1,606 subjects in Turkey, they found that the partial molar pregnancy rate was 2.05% and the complete molar pregnancy rate was 0.43% in abortion materials.[13] Alsibiani, in their study examining 558 first trimester abortion materials, found 1 (0.2%) complete molar pregnancy and 1 (0.2%) partial molar pregnancy on histopathological examination. Also, in their histopathological examination, placental villi were observed in 96.2% of the patients.[14] In the present study, similar to the study of Alsibiani, 934 (93%) placental villi were observed in histopathological examination of the abortion material.

Spontaneous abortion and infertility are risk factors for both complete and partial hydatidiform mole. When compared with women without a history of abortion, the risk of complete hydatidiform mole increases 3.1 times and the risk of partial hydatidiform mole increases 1.9 times in those with a history of abortion.[15,16] In a study conducted by Tasci et al., it was reported that partial hydatidiform mole was diagnosed in 33 patients (2.1%). Complete hydatidiform mole was detected in seven cases (0.43%) in abortion materials.[14] Of women in this study, 7.97% showed an Arias-Stella reaction.

The clinical diagnosis of partial mole hydatidiform may be difficult due to its frequent appearance and appearance with foetus compared to complete mole hydatidiform. In the study where a single-nucleotide polymorphism microarray of 26,000 abortion materials was evaluated as paternal triploids, 638 (2.8%) partial mole hydatidiform and 72 (0.3%) complete mole hydatidiform were reported.[17] They concluded that these rates are higher than the rates reported based on ultrasonographic or histological diagnosis of molar pregnancy. This study showed that when the genetic analysis of the products of conception was performed in addition to the histopathological examination, the rate of the hydatidiform mole was actually higher. In the current study, the diagnoses of partial hydatidiform mole were reported in products of conception terminated due to anembryonic pregnancy, missed abortion and incomplete abortion as 1%. When taking into account the rate of hydatidiform mole (10/1,004) in a clinic where all abortion material is normally sent for histopathological examination, routine histopathological examination of abortion material seems reasonable and safe.

CONCLUSION

In the present study, the incidence of complete hydatidiform mole in pregnancies whose abortion materials were sent for histopathological examination was 1/1,004 in the abortion material, while the rate of the partial hydatidiform mole was 9/1,004. When taking into account the rate of mole hydatidiform (10/1,004) in a clinic where all abortus materials are sent for histopathological examination routinely, routine histopathological examination of abortus material seems reasonable and safe. Additionally, confronting Arias-Stella reaction on pathology may help the clinician to question the diagnosis for a bleeding patient presumed to have a complete abortion.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

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