Pathomorphology of Molar Gestation in Zaria

*A. A. Mayun, **A. H. Rafindadi, **M. S. Shehu

SUMMARY

Background: Molar gestations are a source of significant morbidity with increased risk of mortality from their complications if not identified and treated early enough.

Objective: This study aims at histologically reviewing and analyzing all cases of molar gestations seen in the Histopathology Department of Ahmadu Bello University Zaria between January 1995 and December 2004, and comparing the findings with other studies done elsewhere.

Methods: Cases for this study were identified from the departmental bench book. The relevant request forms, slides and in some cases, tissue paraffin blocks for the study period were retrieved. All cases were stained with Haematoxylin and Eosin. The slides were reviewed based on the histological criteria published by Gehrig and Van-Lee.

Main findings: Seventy three cases of molar gestations were seen out of which 17 were excluded and 56 were analyzed as follows: Complete hydatidiform mole, 34; Partial hydatidiform mole, 20; Invasive mole, 2. There were 43 cases of choriocarcinoma making 37% of gestational trophoblastic diseases (GTDs) and were exempted from this study. The frequency of Hydatidiform mole was 1: 612 deliveries. The mean age of the patients was 25.7 years and their leading mode of presentation was vaginal bleeding between 11-18 weeks of gestation.

Conclusions: Hydatidiform mole was found to be a common problem and the complete type occurred more frequently than the partial type.

Niger Med J. Vol. 51, No. 1, Jan. – Mar, 2010: 1 – 4.

Key words: **Complete Hydatidiform Mole; Partial Hydatidiform Mole; Zaria.**

INTRODUCTION

Molar gestations are a source of significant morbidity with increased risk of mortality from their complications if not identified and treated early enough. The most important reason for the correct recognition of true moles is that they may precede choriocarcinoma,[1] which is a highly malignant trophoblastic tumour. The correct recognition of true moles however depends largely on accurate histopathological diagnosis. Frequent histopathological reviews with appropriate criteria for the diagnosis of moles is therefore necessary to minimize incorrect diagnosis. Hydatidiform mole is characterized by vesicular or cystic swelling of the chorionic villi, accompanied by variable trophoblastic proliferation.[2] Most patients present in the fourth or fifth month of pregnancy with vaginal bleeding and with a uterus that is usually but not always, larger than expected for the duration of pregnancy.

Moles have been found to occur at any age during active reproductive life, but the risk is higher in the teens or between the ages of 40 and 50 years.[3,4] The incidence of hydatidiform mole varies considerably in different regions of the world. It is said to be 1 in 1000 pregnancies in the United States, [4] 1 in 100 pregnancies in Indonesia,[4] 1 in 314 pregnancies in Iran[5] and 1 in 205 pregnancies in Ibadan, Nigeria.[6] Most women present with abnormal uterine bleeding [7] that may begin early in the course of the pregnancy and this is accompanied by passage of thin watery fluid and bits of vesicles. The uterine size is larger than expected and ultrasound examination can be diagnostic in most cases. Human chorionic gonadotrophin (hCG) levels are greatly increased and exceeds that of normal pregnancy of same age. Molar pregnancies can be classified into three namely: Complete hydatidiform mole (CHM), Partial hydatidiform mole (PHM), and Invasive mole (IM). In CHM, there is absence of any identifiable embryonic or foetal tissues, contrary to what is obtained in PHM. In IM there is evidence of invasion of the myometrium by the molar villi and trophoblast.

Until recently, the diagnosis of hydatidiform mole was based on microscopic appearances and histopathology. It was recognized that this was not a uniform entity and that the histological features varied.[8] Histological reviews in Charing Cross Hospital London by Paradinas have shown that first trimester non-molar hydropic abortions and complete hydatidiform moles are often erroneously called partial hydatidiform moles by the pathologist.[9] CHMs were not often detected before the second trimester of pregnancy until the last decade.[10,11] with earlier recognition of CHMs, now often during the first trimester, the histologic picture shows less significant proliferation of villous trophoblasts; prominent polar trophoblastic proliferation, as in normal anchoring villi; non-hydropic, cellular, and basophilic villous stroma; numerous

From: *Department of Pathology, College of Medical Sciences, University of Maiduguri, Nigeria. **Pathology Department A.B.U. Teaching Hospital Zaria, Kaduna State, Nigeria. Pathology Department, Ahmadu Bello University, Zaria, Nigeria

Correspondence: **Dr Ahmed A Mayun**, Histopathology Department University of Maiduguri Teaching Hospital PMB 1414, Maiduguri

immature vascular network; sulbous outline; and frequent stromal karyorrhexis and apoptosis.[12,13,14,15,16]

CHM and PHM have widely different prognosis and therefore require very accurate diagnostic criteria for their recognition. The purpose of this study is therefore to review and analyze all cases of molar gestations seen in the histopathology department of Ahmadu Bello University Teaching Hospital Zaria and compare the findings with other studies done in Nigeria, other parts of Africa and other parts of the world.

MATERIALS AND METHODS

This retrospective analysis was done in Ahmadu Bello University Teaching Hospital Zaria between January 1995 and December 2004 (10 years). This hospital is a referral centre for hospitals in Kaduna, Kano, Zamfara, Katsina, Jigawa and Niger states. The bench books were the main source of the subjects from which histology numbers were identified and the relevant request forms, slides and tissue blocks for the study period were retrieved. All sections were stained with standard Haematoxylin and Eosin. Cases were diagnosed and categorized using the histologic features published by Gehrig and Van Lee.[17] Age of patient, gestational age, clinical features and type of tissue submitted were amongst the information extracted from the request forms.

Cases that did not fulfill the diagnostic criteria or lack any of the information required above, and cases whose slides and tissue blocks could not be retrieved were eliminated from the study. Ten histopathological features were graded as grades I., II and III depending on their degree of presence. Grade I here means the absence or presence in mild form, grade II in moderate form and grade III in marked or severe form.

RESULTS

Eight hundred and sixty six (866) products of conceptions and 116 cases gestational trophoblastic diseases (GTDs) were recorded between January 1995 and Decembder 2004. Out of this number, 73 cases were molar pregnancies and 43 were choriocarcinomas. Molar gestations constituted 63% of GTDs and 8.4% of all products of conception recorded within this period. Seventeen of the molar gestations were excluded due to lack of complete information and only 56 cases were analyzed. Choriocarcinomas were exempted from this study.

The molar pregnancies were distributed as follows: Complete hydatidiform mole (CHM) – 34, Partial hydadiform mole (PHM) – 20, and Invasive mole (IM) – 2. One of the CHMs was a tubal mole (TM). Table 1 shows the histologic classification of the 56 cases of molar gestations.

Request cards were used to obtain demographic data and clinical information. The following information was obtained: age, gestational age, and various clinical presentations. The age range for all the cases of molar pregnancies was 15 – 49 years, with a mean of 25.7 years. The peak incidence was in the third decades of life with 26 cases (46%) – Table 2. The tissues submitted to the laboratory were labeled molar tissues (grape-like vesicles) in 55% of cases; products of conception in 30%; and endometrial curetting in 8.9% of cases. Two cases (3.6%) were submitted as uterus while one case (1.8%) came as fallopian tube (FT) – Table 2.

Table 3 shows the various clinical presentations. Over 78% of cases presented with vaginal bleeding with PHM having the highest number. Passage of vesicles was seen in 28.6% of all cases out of which two thirds were CHM. Pre-eclampsia and hyperemesis gravidarum were more frequent in CHM than PHM. Abdominal pain occurred in over 14% of all cases. Table 4 shows the gestational age distribution. None of the cases presented before seven weeks. Thirty eight (67%) cases presented between 11 – 18 weeks. Table 5 shows the grades of histopathological features for CHM cases. Variation in shapes and sizes of chorionic villi was evenly distributed from grades I to III. Trophoblastic hyperplasia and hydropic degeneration occurred in moderate to severe form in over 80% of cases. Low grade changes were mainly dystrophic calcification, necrosis, and stromal fibrosis (70 – 90%). Grades I and II changes together mainly involved inflammation and trophoblastic atypia.

Table 6 shows the grades of histopathological features for PHM cases. High grade changes involved mainly variation in shapes and sizes of chorionic villi and stromal fibrosis. Low grade changes were mainly dystrophic calcification, necrosis and trophoblastic atypia. Intermediate grade changes (i.e grades I and II) involved mainly hydropic degeneration, haemorrhage

Table 1: Histological Classification of 56 Cases of Molar

Type of Mole	Gestations Number	Percentage
Complete hydatidiform mole	34	60.7
Partial hydatidiform mole	20	35.7
Invasive mole	2	3.6
Total	**56**	**100**

Table 2: Age distribution and types of tissue submitted for 56 cases of moles

Age range (yrs)	No of cases	Types of tissue submitted: Molar tissues	POC	EC	Uterus	FT
15 – 19	12	7	3	2	0	0
20 – 24	12	7	3	2	0	0
25 – 29	14	8	4	1	0	1
30 – 34	6	3	2	0	1	0
35 – 39	7	2	4	0	1	0
40 – 44	2	2	0	0	0	0
45 – 49	3	2	1	0	0	0
Total	**56(100%)**	**31(55.4%)**	**17(30.1%)**	**5(8.9%)**	**2(3.6%)**	**1(1.8%)**

Table 3: Clinical presentation of 56 cases of moles

Clinical feature	Frequency: CHM	PHM	IM	Total %
Vaginal bleeding	20	22	2	44(78.6)
Hyperemesis gravidatum	4	2	1	7(12.5)
Pre-eclampsia	3	1	1	5(8.9)
Passage of vesicles	11	5	0	16(28.6)
Abdominal pain	3	3	2	8(14.3)
Post-abortal bleeding	1	1	0	2(3.6)
Post-Pregnancy bleeding	0	1	0	1(1.8)

and trophoblastic hyperplasia. Two cases of invasive mole (IM) and one case of tubal mole (TM) were seen within the study period. Both cases of IM had the histopathological features of CHM invading the myometrium. The TM also showed histopathological features of CHM within the fallopian tube.

Table 4: Gestational age distribution for 56 cases of moles.

Frequency Gestational age(wks)	CHM	PHM	IM	TM	Total(%)
7 – 10	4	6	0	1	11(19.6)
11 – 14	12	10	1	0	23(41.0)
15 – 18	8	6	1	0	15(26.8)
19 – 22	3	0	0	0	3(5.4)
23 – 26	2	2	0	0	4(7.2)
Total	**28**	**24**	**2**	**1**	**56(100)**

Table 5: Histopathological features of 34 cases of CHM

Grades Histopathological feature	1(%)	11(%)	III(%)	Total
Variation in shapes and sizes of CV	13(38.2)	11(32.4)	10(29.4)	34(100)
Trophoblastic hyperplasia	4(11.8)	13(38.2)	17(50.0)	34(100)
Trophoblastic atypia	22(64.7)	7(20.6)	5(14.7)	34(100)
Inflammation	22(64.7)	6(17.6)	6(17.6)	34(100)
Hydropic degeneration	6(17.6)	8(23.5)	20(58.8)	34(100)
Haemorrhage	20(58.8)	10(29.4)	4(11.8)	34(100)
Fibrin deposition	23(67.6)	8(23.5)	3(8.8)	34(100)
Dystrophic calcification	31(91.2)	3(8.8)	0(0.0)	34(100)
Necrosis	28(82.4)	5(14.7)	1(2.9)	34(100)
Stromal fibrosis of CV	26(76.5)	6(17.6)	2(5.9)	34(100)

CV= Chorionic villi.

Table 6: Histopathological features of 22 cases of PHM

Grades Histopathological feature	1(%)	II(%)	III(%)	Total
Variation in shapes and Sizes of CV	6(27.3)	5(22.7)	11(50.0)	22(100)
Trophoblastic hyperplasia	2(9.1)	14(63.6)	6(27.3)	22(100)
Trophoblastic atypia	17(77.3)	4(18.2)	1(4.5)	22(100)
Inflammation	10(45.5)	7(31.8)	5(22.7)	22(100)
Hydropic degeneration	12(54.5)	5(22.7)	5(22.7)	22(100)
Haemorrhage	11(50.0)	10(45.5)	1(4.5)	22(100)
Fibrin deposition	12(54.5)	6(27.3)	4(18.2)	22(100)
Dystrophic calcification	20(91.0)	2(9.1)	0(0.0)	22(100)
Necrosis	12(54.5)	10(45.5)	0(0.0)	22(100)
Stromal fibrosis of CV	2(9.1)	12(54.5)	8(36.4)	22(100)

CV = Chorionic villi.

DISCUSSION

In trying to determine the frequency of molar pregnancies, the total number of moles was compared with the total number of deliveries conducted in Ahmadu Bello University Teaching Hospitals (ABUTH) complex. During the review period, 44.679 women were delivered in ABUTH complex. This gives an occurrence of 1 in 797 deliveries. This is lower than 1 in 623 deliveries seen in Calabar [18] and 1 in 625 deliveries in an earlier study in Zaria[7] Nigeria. This is probably due to the strict elimination criteria used in this study that excluded almost one third of the total number of cases. The age range for all the cases of molar pregnancies was 15 – 49 years. This compares favourably with 15 to over 40 years and 15 – 45 years reported in other parts of Nigeria.[19,20] The mean age of 25.7 is close to 27 years reported by Ogunbode in Ibadan Nigeria.

The peak incidence occurred in the third decade of life which falls within the same range seen in parts of Nigeria [18] and California [21]. This however is lower than reports from the Far East [22] where patients over 40 years of age were most prone to develop the disease. Certain environmental and genetic parameters could be responsible for this variation, since early marriage is common to both Nigeria and far-east. Vaginal bleeding occurred in 78.6% of cases which is close to 85% reported by Ayangade [20], higher than 60% reported by Ogunbode [6] and lower than 90% reported by Egwuatu and Ozumba.[23] Twenty eight per cent of the patients passed molar vesicles which compares favourably with 27.3% observed by Ayangade.[20] Pre-eclampsia occurred in about 9% of cases which is much lower than 27% reported in south western Nigeria [24] and 24% reported in south eastern Nigeria. [23] This is however closer to 6% reported in a previous study in Zaria.[7] This is most likely due to inadequate clinical information on our request cards with a slight improvement from the previous study.

Sixty seven per cent of cases presented between 11 – 18 weeks of gestation. This is lower than over five months gestational age reported in 1973 in Uganda.[25] This is probably due to the increase in gynaecological, sonographic and histopathological services over the years which has led to early recognition of the disease. Histopathological features were examined and graded from grades I to III. Similar histological grading of moles was done by other workers in Nigeria, [26] Britain[27] and Iran.[5] These workers however limited their grading to trophoblastic hyperplasia and atypia. Over 80% of both CHM and PHM showed moderate to severe trophoblastic hyperplasia. This is much higher than over 50% reported in western Nigeria by Junaid [26] and also higher than over 60% reported in Iran.[5] Trophoblastic atypia was seen in over 30% of CHM cases and over 20% of PHM cases. This is similar to other reports.[26, 27] Hydropic degeneration of chorionic villi occurred in moderate to severe form in over 80% of CHM cases and in over 40% of PHM cases. Stromal fibrosis of chorionic villi was a more prominent feature in PHM (over 90% of cases) than in CHM (over 20% of cases). Another feature that was more prominent in PHM cases was variation in shapes and sizes of chorionic villi.

The least prominent features in all the cases of hydatidiform moles were necrosis, dystrophic calcification, and fibrin

deposition. These variations between CHM and PHM supports the description in various literature.[28,29] In conclusion, this analysis shows that molar pregnancies are common problems in North-western Nigeria and affects only women in their reproductive age mainly during the third decade of life. This is in agreement with other findings in North Central, [19] South-western,[20] South-eastern[18] Nigeria, Eastern Africa[25] and some parts of Asia.[4] It however occurs less frequently in the United states[4] and Britain.[28] Trophoblastic hyperplasia and atypia were more prominent in our cases than in previous reports. [24,27] This could be due to non-uniformity in the grading systems. Collaborative and interdisciplinary research on this disease by pathologists, gynaecologist, radiologists and oncologist will be of immense benefit in reducing morbidity and mortality.

REFERENCES

1. Redline R. W., Abdul-karim F. N. Pathology of gestational trophoblastic disease. *Semin oncol* 1995; **22:** 96 – 98.
2. Genest D. R., Laborde O., Berkowitze R. S., Goldstein d. P., Bernstein M. R. Laje J. A clinicopathologic study of 153 cases of complete hydadiform mole (1980 – 1990): *Obstet Gynaecol* 1991; **78:** 402 – 405.
3. Attah E. B. 'B. Hydatidiform mole, In: Human Pathology, 1st Ed. Ibadan University Press, Ibadan 2000; 519 – 522.
4. Bracken M. B., Brinton C. A., Hayashi K. Epidemiology of hydatidiform mole and choriocarcinoma. *Epidemiol Rev* 1984; **6:** 52 – 54.
5. Javey H. and Sajadi H. Hydatidiform mole in Southern Iran; a statistical survey of 133 cases. *Int J Gynaecol Obstet* 1978; **15:** 390 – 395.
6. Ogunbode O. Benign Hydatidiform mole in Ibadan, Nigeria. *Int J Gynaecol Obstet* 1978; **15:** 387 – 390.
7. Mayun A. A. Gestational trophoblastic disease in Zaria. A ten year histopathological review. FMCPath dissertation. National Postgraduate Medical College of Nigeria. May 2003.
8. Bagshawe K. D., Lawler S. D. Unmasking moles. *Br J Obstet Gynaecol* 1982; **89:** 255 – 257
9. Paradinas F. J. The diagnosis and prognosis of molar pregnancy; the experience of the National Referral Centre in London. *Int J Gynaecol Obstet* 1998; **60:** 557 – 564.
10. Mosher R., Goldstein D. P., Berkowitz A. Complete hydatidiform mole. Comparison of clinicopathologic features, current and past. *J Reprod Med.* 1998; **43:** 21 – 27
11. Sebire N. J., Fisher R. A., Rees H. C. Histopathological diagnosis of partial and complete hydatidiform mole in the first trimester of pregnancy. *Pediatr Dev Pathol.* 2003; **6:** 69 – 77
12. Keep D., Zaragoza M. V., Hassold T. Very early complete hydatidiform mole. Hum Pathol. 1996; **27:** 708–713.
13. Kim K. R., Lec S. K., Jun S. Y. Complete hydatidiform mole in early gestation: a clinicopathologic study of 51 cases. *Kor J Pathol.* 2002; **36:** 93–99.
14. Kim M. J., Kim K. R., Ro J. Y. Diagnostic and pathogenetic significance of increased stromal apoptous and in complete vasculogenesis in complete hydatidiform moles in very early pregnancy periods. *Am J Surg Pathol.* 2006; 30: 362 – 369.
15. Sebire N. J., Makrydimas G., Agnantis N. J. Updated diagnostic criteria for partial and complete hydatidiform moles in early pregnancy. *Anticancer Res.* 2003; **23:** 1723 – 1728.
16. Yoshida K., Nagasaka T., Nakashima N. Elucidation of vascular structure of molar villi in complete hydatidiform mole by CD – 34 antibody. *Int J Gynecol Pathol.* 2000; **19:** 212 – 218.
17. Gehrig P. A., Van Lee L. Gestational trophoblastic diseases: An update. *Curr Probl Obs Gynaecol Fertil* 2002; **25(5):** 151–165.
18. Ekpo M. D. Pathomorphology and clinical correlation of hydatidiform moles. FMCPath thesis. National Postgraduate Medical College of Nigeria. May 1988.
19. Aboyeji A. P., Ijaiye M. A. Hydatidiform mole in Ilorin, Nigeria: A ten year review. *Nig J Med* 2000; **19(2):** 56–50.
20. Ayangade O. Gestational trophoblastic disease in Nigeria; a ten year review. *East Afr. Med J* 1979; **56:** 278–282.
21. Buckley J. The epidemiology of molar pregnancy and choriocarcinoma. *Clin Obstet Gynaecol* 1984; **27(1):** 153–159.
22. Chun D., Braiga C., Chow C. and Lok L. Clinical observations on some aspects of hydatidiform Moles. *J Obstet Gynaecol Br Comnwlth* 1964; **71:** 180 – 181.
23. Egwuatu V. E., Ozumba B. C. Observations on molar pregnancy in Enugu, Nigeria. *Int J Gynaecol Obstet* 1989; **29:** 219 – 225
24. Agboola A., Abudu O. O. Epidemiology of trophoblastic disease in African-Lagos. Adv Exp Med Biol 1984; 176: 187 – 195.
25. Leighton P. C. Trophoblastic disease in Uganda. *Am J Obstet Gynaecol* 1973; **117(3):** 341 – 344.
26. Junaid T. A., Hendrickse J. P. de V, Aimakhu V. A., Adeleye J. A. Prognostic Value of histological grading of hydatidiform moles. *Afr J Med Sci* 1978; **7:** 99 – 105.
27. Elston C. W., Bagshawe K. D. The value of histological grading in the management of hydatidiform mole. *J Obstet Gynaecol Br Comnwlth* 1972; **79:** 717 – 724.
28. Paradinas F. J., Browne P., Fisher R. A., Foskett H. M., Bagshawe K. D., Newlands E. A clinical, histopathological and flow cytometric study of 149 complete moles, 146 partial moles and 107 non-molar hydropic abortions. *Histopathology* 1996; **28:** 101 – 109.
29. Cotran R. S., Kumar V., Collins T. Gestational trophoblastic disease, In: Pathologic basis of disease. 6th Ed. WB Saunders company, London 1999; 1085 – 1087.