Epidemiological and morphological pattern of complete hydatidiform mole in Aminu Kano Teaching Hospital, Kano Northwestern Nigeria

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Abstract

Background: Complete hydatidiform mole (CHM) is the most common form of non-neoplastic gestational trophoblastic diseases (GTD) that is associated with progression to choriocarcinoma without prompt intervention. The objectives of this study is to morphologically analyze all cases of complete hydatidiform mole in Aminu Kano Teaching Hospital using set down criteria, look at the epidemiological pattern and compare with similar studies in order to stimulate proper identification from other forms of moles, hence reduce morbidity and mortality associated with the known complication of progressing to deadly Choriocarcinoma.

Material and Methods: This was a retrospective study of all molar specimens submitted to Histopathology Pathology Department of Aminu Kano Teaching Hospital, Kano between 1st January 2015 and 31st December 2016. Formalin fixed paraffin embedded tissue blocks and corresponding Haematoxylin and Eosin (H&E) stained slides were retrieved. Cases with final diagnosis of complete mole were selected for further detailed microscopic evaluations. The collected data were presented using simple frequency tables and figures including photomicrographs of representative lesions.

Results: There were sixty-seven cases of complete hydatidiform mole during the study period out of the 61,780 deliveries, giving an approximate incidence of 1:1000 deliveries in Kano metropolis and its environs. The peak incidence was observed in women between 20-24 years of age with majority presenting between 11-14 weeks of pregnancy. The ratio of complete to partial mole was approximately 3:1. Constant morphologic features associated with CHM includes; villous enlargement, trophoblastic hyperplasia, round shape chorionic villi and fibromyxoid stroma. Least prominent features of CHM is myxoid stromal type.

Conclusion: Complete hydatidiform occurs commonly in the gestational ages of between eleven to fourteen weeks; need histopathologic evaluations and prompt intervention to avoid consequences of both immediate complication such as invasive mole and long-term complication of choriocarcinoma.

Keywords: Hydatidiform Mole, Complete Mole, Choriocarcinoma

Introduction

Hydatidiform mole is a non-neoplastic form of gestational trophoblastic diseases (GTD) characterized by proliferation of either the villous or the trophoblastic component of placental tissue. It includes, complete mole, partial mole, invasive mole and metastatic mole. Hydatidiform mole is the most common disorder among GTD’s occurring commonly among reproductive women (1). Complete hydatidiform mole (CHM) is the most common form of non-neoplastic GTD that is associated with progression to choriocarcinoma without prompt intervention (1, 2). Though, hydatidiform moles are being diagnosed at earlier gestational ages (≤ 9 weeks) due to routine ultrasound scan and close monitoring of early pregnancy (2), however, histopathologic evaluation remains an invaluable tool in differentiating the various forms of the disorder. The incidence of molar gestation varies across regions worldwide, In Africa, incidences of 0.02 and 3.4 per 1,000 deliveries were respectively reported in South Africa and Uganda (2, 3). Studies conducted in Nigeria, reported incidences of 1.7 to 5.8 per 1,000 deliveries in the Southwest (4, 5), 1.6-4.7 per 1,000 deliveries in the Southeast (6, 7, 8) and 1.3 to 4.5 per 1000 deliveries in the northern parts of the country (3, 9, 10, 11, 12). Complete hydatidiform mole (CHM) results from fertilization of an empty ovum by a haploid (23X or 23Y) sperm which then undergoes duplication giving rise to 46XX or 46XY karyotypes. Development of hydatidiform mole has been associated with an excess in the ratio of...
paternal to maternal haploid set of chromosomes, thus higher ratio of 2:0 is associated with CHM (13, 14). Morphologically, complete mole has been typically described as a ‘bunch of grapes’, with most villi showing hydropic degeneration. The individual vesicles usually measures between 1-30 mm in diameter, and the total weight is in most cases over 200g (15). In a hysterectomy specimen, these swollen villi are seen to fill and distend the uterus, characteristically, there is no identifiable embryo, cord, or amniotic membranes (15). The two constant histologic features of complete mole are trophoblastic hyperplasia and vesicular swelling. Severity of the changes vary considerably from case to case and from villus to villus, and may be difficult to appreciate in very early cases, as evidenced by the high degree of inter- and intra-observer variability (16). Some of the villi are surrounded by an attenuated layer of degenerating trophoblasts. In others, the trophoblast is composed of large hyperplastic sheets of cells. The distended core of the villus is traversed by widely separated, broken strands of fibrillary material (‘cistern’ formation). Vessels seem absent or very scanty in hematoxylin–eosin-stained sections, even though they do not seem much diminished in number in CD34-stained preparations (16).

Complete hydatidiform mole present clinically with weeks history of amenorrhea, vaginal bleeding and in some cases passages of vesicles per vaginum. Other clinical findings can be accompanied theca lutean cyst, elevated level of B human chorionic gonadotrophic hormone (B-hCG), hyperemesis gravidarum and subclinical hyperthyroidism (16). The objectives of the index study is to analyze all cases of complete hydatidiform mole in our centre morphologically using set down criteria, look at the epidemiological pattern and compare with similar studies in order to stimulate proper identification from other forms of moles, hence reduce morbidity and mortality associated with the known complication of progressing to deadly choriocarcinoma.

Materials and Methods
Study Design
This is a retrospective study of all molar specimens submitted to Histopathology Department of Aminu Kano Teaching Hospital, Kano between 1st January 2015 and 31st December 2016.

Sampling Method
Convenience sampling method was used, whereby all consecutive cases of molar pregnancy diagnosed in the Histopathology department of AKTH, within the study period were included.

Methodology
Consecutive surgical specimens with cases having clinical impression of gestational trophoblastic disorders were retrieved from the archive of histopathology department of AKTH between January 2015 and December 2016. Tissue blocks of paraffin embedded tissues and slides made from it, stained with haematoxylin and eosin were reviewed, cases of molar gestation were selected and characterised based on the following morphologic criteria; villous enlargement, trophoblastic hyperplasia, shape of chorionic villi (Round, scalloped, round/scalloped), trophoblastic pseudo-inclusion, cistern formation, foetal nucleated red blood cells, trophoblastic atypia, presence or absence of fetal parts and stromal type (myxoid, fibrotic or mixed myxoid/fibrotic) (17). These were then sub-classified as partial or complete mole. Partial mole were excluded using the four major morphologic criteria for diagnosis of partial mole proposed by Genest (18). These include a mixture of normal and hydropic villi, enlarged villi with cistern, irregular villi with scalloped borders and trophoblastic inclusions and focal mild trophoblastic hyperplasia. Cases with final diagnosis of complete mole were selected for further detailed microscopic evaluations. Information on age, reproductive history, duration of disease, and other clinical history plus ancillary investigations were retrieved from individual case cards. The collected data were presented using simple frequency tables and figures including photomicrographs of representative lesions.

Ethical Consideration
Ethical approval (AKTH/ MAC/ SUB/ 12A/ P-3/ VI/ 2057) was obtained from Health Research Ethical Committee of Aminu Kano Teaching Hospital to conduct the research.

Inclusion criteria
All histologically confirmed cases of Complete Hydatidiform mole within the study period.

Exclusion criteria
1-Cases in which both slides and tissue blocks are missing
2-Cases of not Complete Mole
Results

There were sixty-seven cases of complete hydatidiform mole during the study period out of the 61,780 deliveries giving an approximate incidence of 1:1000 deliveries in Kano metropolis and its environs. The age of the patients ranged from 16 to 56 years with a mean of 29.7 ± 9.1 and a median of 28 years. The highest frequency of cases was seen in patients in their third decade of life; most commonly in the age between 20-24 years (26.1%) and least incidence occurred in the sixth decade of life (3.0%). From the peak in the ages between 20 – 24 years, the overall frequency dropped progressively to stable among patients aged 35 – 39. The frequency then rose slightly higher among those aged 40 – 44 years and then declined sharply to a case each in those aged 50 – 54 years and those 55 – 59 years of age (Figure 1).

Morphologically, villous enlargement and trophoblastic hyperplasia were seen in all the cases (Figure 3), trophoblastic atypia was however observed in 83%. The shapes of the villi vary among cases; while over 60% were round only 12% were solely scalloped, a combination of round to scalloped contour were seen in 42% of cases. Cistern formation is a major feature of CHM and were seen in 93% of all the cases. Composition of the stroma was fibromyxoid in almost all cases, even though fibrotic stroma predominated in 51% while dominant myxoid stromal composition was observed in 49% of cases out of which 10% show purely myxoid stroma (Table 1).

The gestational ages at presentation ranged from 7 - 20 weeks with a mean of 11.3 ± 3.1 weeks. The highest frequency of molar gestation was observed in patients who presented at gestational age of between 11-14 weeks (48%) and lowest in patients who presented at gestational age of between 19-22 weeks (2%). The entire cases after gestational age of 15 weeks formed only nine percent of all the cases (Figure 2).

Table 1: Morphologic characteristics of Complete Hydatidiform mole

<table>
<thead>
<tr>
<th>Morphologic Feature</th>
<th>No of Cases with level of Distribution per 67</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Villous enlargement</td>
<td>67</td>
<td>100</td>
</tr>
<tr>
<td>Trophoblastic hyperplasia</td>
<td>66</td>
<td>99</td>
</tr>
<tr>
<td>Shape of chorionic villi</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Round</td>
<td>66</td>
<td>99</td>
</tr>
<tr>
<td>Scalloped</td>
<td>38</td>
<td>57</td>
</tr>
<tr>
<td>Round/Scalloped</td>
<td>56</td>
<td>84</td>
</tr>
<tr>
<td>Trophoblastic pseudo-inclusion</td>
<td>59</td>
<td>88</td>
</tr>
<tr>
<td>Cistern formation</td>
<td>43</td>
<td>64</td>
</tr>
<tr>
<td>Trophoblastic atypia</td>
<td>36</td>
<td>54</td>
</tr>
<tr>
<td>Stromal type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myxoid</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Fibrotic</td>
<td>34</td>
<td>51</td>
</tr>
<tr>
<td>Myxoid/Fibrotic</td>
<td>67</td>
<td>100</td>
</tr>
</tbody>
</table>
Discussion

There were approximately 1.1 cases of complete molar gestation in each 1000 deliveries in our environment. This falls within the ranges of several studies conducted in several parts of Northern and Southern Nigeria with incidences ranging between 1.3-4.5 and 1.7-5.8 per 1000 deliveries respectively (4,5, 7-11). Elsewhere in Africa, a lower incidence of 0.02 per 1000 deliveries has been reported in South Africa, however a higher rate of 10 and 8.3 per 1000 deliveries reported in South Asia and Taiwan respectively (2,4, and 19). Though, the index study was based on complete mole only, however in the course of extracting our data, we have found the frequency of complete versus partial mole in this to be 72.8% versus 27.2%, giving a ratio of approximately 3:1. This is higher than the approximate ratio of 2:1 in Zaria, Northwestern Nigeria and lower than the approximate ratio of 4:1 in a previous study in Ile-Ife, Southwestern Nigeria (4, 11).

Maternal age has been identified as an important risk factor, with increased risk in early and late reproductive periods. This is evidenced by findings in this study which shows a peak incidence in patients aged between 20-24 years and a smaller peak in women 40-44 years of age. It also mirrors findings in studies conducted in Zaria and Ilorin in Nigeria and in Baghdad (9, 11, and 20). In a study conducted by Eniola et al (2001) in Ile-Ife, southwestern Nigeria, the peak age frequency was found in patients aged 40 years and older (4). The earlier peak age and the declining pattern with increasing age found in the index study may be a reflection of the socio-cultural practice of early marriage in northern Nigeria. As such, by age 40, most women would have completed their desired family size.

Gestational age of complete hydatidiform mole is an important factor in terms of clinical presentation and degree and severity of complications such as massive vaginal bleeding and progression to choriocarcinoma. Majority of the patients (91%) presented below 15 weeks of gestation. This is comparable with findings by Mayun et al (2010) in Zaria (11), Jimoh et al (2012) in Ilorin (9) and Ekanem et al (2005) in Calabar (8). Findings by Ja’afar et al (2011) in Pakistan (21) and Singh et al (2016) in India (22) also reported that 78% and 84% respectively of their patients also presented at gestational ages below 20 weeks. These may be linked to improved accessibility, availability and to some extent affordability of expertise medical services and recent increase in use of several investigative modalities such as sonographic examinations, chemical pathologic evaluation of serum level for β-

human chorionic gonadotrophin hormone (ß-hCG) and histopathologic services.

The major morphologic features of complete molar gestation seen in this report were villous enlargement, trophoblastic hyperplasia, trophoblastic atypia, cistern formation myxoid stroma and round shaped chorionic villi. Khashaba et al (2016) in a similar study (23) also reported the usefulness of villous shape and outline, trophoblastic hyperplasia, and atypia as three important morphologic features useful in differentiating complete hydatidiform mole from other benign gestational trophoblastic diseases. Similar to our findings, Mayun et al (2008) in a study in Gombe (24), Northeastern Nigeria described the presence of marked villous enlargement and marked trophoblastic hyperplasia in over 50% of complete hydatidiform mole. Similarly, the high frequency of cistern formation, seen in 65% of the described Gombe cases, is reflected in the high frequency (65 (97%) of 67 cases evaluated in the current study. However, unlike the index study and that by Khashaba (23), Mayun et al (24) described a low frequency for trophoblastic atypia. There was relative paucity of villous stromal fibrosis in the index study with marked predominance of myxoid stroma. Similar findings were reported by Singh et al (22) and Jafer et al (21) respectively.

Conclusion

Complete hydatidiform is relatively uncommon in our environment affecting predominantly young lady in their active reproductive years, occurring commonly in the gestational age of between seven to fourteen weeks; need prompt intervention to avoid consequences of both immediate and long-term complication by histopathologic evaluations.

Reference